

【4-9 メタアナリシス】

| CQ                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |               |                                     |                                                                                                                                                                                                                                                                                                                                                |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |       |        |      |                   |  |              |       |        |      |                   |  |                  |      |        |      |                   |  |               |       |        |      |                   |  |                |   |   |  |               |  |                 |       |        |       |                   |  |               |       |        |      |                   |  |            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-------------------|--|--|--------------|--------------------------|--|----------------------------------------------------------------------------------------------------------|--|--|--|--|--|---------------------------------------------------|--|--|--|--|--|---------------|---|---|--|---------------|--|------------------|---|---|--|---------------|--|-----------------|---------|--------|-------|-------------------|--|----------------|---|---|--|---------------|--|-----------------|---|---|--|---------------|--|--------------------------|--|--|--------------|--------------------------|--|-------------------------------------------------------------------------------|--|--|--|--|--|----------------------------------------------------------|--|--|--|--|--|------------------|---------|--------|------|-------------------|--|---------------------|---|---|--|---------------|--|-------------------|--------|--------|------|-------------------|--|---------------|---|---|--|---------------|--|------------------|---------|--------|-------|-------------------|--|---------------|---|---|--|---------------|--|-------------------|---|---|--|---------------|--|------------------|--------|--------|------|-------------------|--|--------------------------|--|--|--------------|--------------------------|--|---------------------------------------------------------------------------------------------------------|--|--|--|--|--|-----------------------|--|--|---------------|--------------------------|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|--|
| P                                                                                                                                                                                      | HER2陰性転移・再発乳癌（女性）                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           | I             | アンスラサイクリンを含むレジメン                    |                               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| C                                                                                                                                                                                      | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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| 研究デザイン                                                                                                                                                                                 | RCT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 文献数                                       | 20            | コード                                 | Ackland SP 2001, Falkson G 1991, Erkisi M 1997, Tormey C 1984, Smalley RV 1983, Cummings FJ 1981, Aisner J 1987, Bull JM 1978, Katsumata N 2009, Sledge GW 2003, Prodaens R 2000, Denise A 2009, Zielinski C 2005, Biganzoli L 2002, Jassem J 2001, Nabholtz JM. 2003, Bonnetterre J. 2004, Lyman GH 2004, Langley RE. 2005, Bontenbal M. 2005 |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |       |        |      |                   |  |              |       |        |      |                   |  |                  |      |        |      |                   |  |               |       |        |      |                   |  |                |   |   |  |               |  |                 |       |        |       |                   |  |               |       |        |      |                   |  |         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| モデル                                                                                                                                                                                    | Fixed Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                           | 方法            | Inverse Variance method (RevMan5.3) |                                                                                                                                                                                                                                                                                                                                                |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |       |        |      |                   |  |              |       |        |      |                   |  |                  |      |        |      |                   |  |               |       |        |      |                   |  |                |   |   |  |               |  |                 |       |        |       |                   |  |               |       |        |      |                   |  |            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| 効果指標                                                                                                                                                                                   | Hazard Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                           | 統合値           | 0.93 ( 0.86 – 1.02 ) P= 0.11        |                                                                                                                                                                                                                                                                                                                                                |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |       |        |      |                   |  |              |       |        |      |                   |  |                  |      |        |      |                   |  |               |       |        |      |                   |  |                |   |   |  |               |  |                 |       |        |       |                   |  |               |       |        |      |                   |  |            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| Forest plot                                                                                                                                                                            | <table><thead><tr><th>Study or Subgroup</th><th>log[Hazard Ratio]</th><th>SE</th><th>Weight</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th></tr></thead><tbody><tr><td colspan="6"><b>1.1.1 Anthra containing regimens vs CMF</b></td></tr><tr><td>Ackland SP 2001</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Aisner J 1987</td><td>-0.43</td><td>0.2098</td><td>4.3%</td><td>0.65 [0.43, 0.98]</td><td></td></tr><tr><td>Bull JM 1978</td><td>-0.85</td><td>0.5577</td><td>0.6%</td><td>0.43 [0.14, 1.28]</td><td></td></tr><tr><td>Cummings FJ 1981</td><td>0.06</td><td>0.3647</td><td>1.4%</td><td>1.06 [0.52, 2.17]</td><td></td></tr><tr><td>Erkisi M 1997</td><td>0.131</td><td>0.3275</td><td>1.8%</td><td>1.14 [0.60, 2.17]</td><td></td></tr><tr><td>Falkson G 1991</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Smalley RV 1983</td><td>-0.16</td><td>0.0949</td><td>21.2%</td><td>0.85 [0.71, 1.03]</td><td></td></tr><tr><td>Tormey C 1984</td><td>-0.45</td><td>0.1761</td><td>6.2%</td><td>0.64 [0.45, 0.90]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>35.5%</b></td><td><b>0.79 [0.69, 0.92]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 6.10, df = 5 (P = 0.30); I² = 18%<br/>Test for overall effect: Z = 3.16 (P = 0.002)</td></tr><tr><td colspan="6"><b>1.1.2 Anthra containing regimens vs Taxane</b></td></tr><tr><td>Denise A 2009</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Katsumata N 2009</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Prodaens R 2000</td><td>-0.0834</td><td>0.1251</td><td>12.2%</td><td>0.92 [0.72, 1.18]</td><td></td></tr><tr><td>Sledge GW 2003</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Sparano JA 2009</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>12.2%</b></td><td><b>0.92 [0.72, 1.18]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Not applicable<br/>Test for overall effect: Z = 0.67 (P = 0.50)</td></tr><tr><td colspan="6"><b>1.1.3 Anthra containing regimens vs Anthra+Taxane</b></td></tr><tr><td>Biganzoli L 2002</td><td>-0.1054</td><td>0.1506</td><td>8.4%</td><td>0.90 [0.67, 1.21]</td><td></td></tr><tr><td>Bonnetterre J. 2004</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Bontenbal M. 2005</td><td>0.3577</td><td>0.1528</td><td>8.2%</td><td>1.43 [1.06, 1.93]</td><td></td></tr><tr><td>Jassem J 2001</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Langley RE. 2005</td><td>-0.0202</td><td>0.0786</td><td>30.9%</td><td>0.98 [0.84, 1.14]</td><td></td></tr><tr><td>Lyman GH 2004</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Nabholtz JM. 2003</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Zielinski C 2005</td><td>0.1655</td><td>0.1983</td><td>4.9%</td><td>1.18 [0.80, 1.74]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>52.3%</b></td><td><b>1.04 [0.93, 1.17]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 6.24, df = 3 (P = 0.10); I² = 52%<br/>Test for overall effect: Z = 0.70 (P = 0.48)</td></tr><tr><td><b>Total (95% CI)</b></td><td></td><td></td><td><b>100.0%</b></td><td><b>0.93 [0.86, 1.02]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 20.67, df = 10 (P = 0.02); I² = 52%<br/>Test for overall effect: Z = 1.61 (P = 0.11)<br/>Test for subgroup differences: Chi² = 8.34, df = 2 (P = 0.02), I² = 76.0%</td></tr></tbody></table> |                                           |               |                                     |                                                                                                                                                                                                                                                                                                                                                | Study or Subgroup                 | log[Hazard Ratio] | SE | Weight | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI | <b>1.1.1 Anthra containing regimens vs CMF</b> |  |  |  |  |  | Ackland SP 2001 | 0 | 0 |  | Not estimable |  | Aisner J 1987 | -0.43 | 0.2098 | 4.3% | 0.65 [0.43, 0.98] |  | Bull JM 1978 | -0.85 | 0.5577 | 0.6% | 0.43 [0.14, 1.28] |  | Cummings FJ 1981 | 0.06 | 0.3647 | 1.4% | 1.06 [0.52, 2.17] |  | Erkisi M 1997 | 0.131 | 0.3275 | 1.8% | 1.14 [0.60, 2.17] |  | Falkson G 1991 | 0 | 0 |  | Not estimable |  | Smalley RV 1983 | -0.16 | 0.0949 | 21.2% | 0.85 [0.71, 1.03] |  | Tormey C 1984 | -0.45 | 0.1761 | 6.2% | 0.64 [0.45, 0.90] |  | <b>Subtotal (95% CI)</b> |  |  | <b>35.5%</b> | <b>0.79 [0.69, 0.92]</b> |  | Heterogeneity: Chi² = 6.10, df = 5 (P = 0.30); I² = 18%<br>Test for overall effect: Z = 3.16 (P = 0.002) |  |  |  |  |  | <b>1.1.2 Anthra containing regimens vs Taxane</b> |  |  |  |  |  | Denise A 2009 | 0 | 0 |  | Not estimable |  | Katsumata N 2009 | 0 | 0 |  | Not estimable |  | Prodaens R 2000 | -0.0834 | 0.1251 | 12.2% | 0.92 [0.72, 1.18] |  | Sledge GW 2003 | 0 | 0 |  | Not estimable |  | Sparano JA 2009 | 0 | 0 |  | Not estimable |  | <b>Subtotal (95% CI)</b> |  |  | <b>12.2%</b> | <b>0.92 [0.72, 1.18]</b> |  | Heterogeneity: Not applicable<br>Test for overall effect: Z = 0.67 (P = 0.50) |  |  |  |  |  | <b>1.1.3 Anthra containing regimens vs Anthra+Taxane</b> |  |  |  |  |  | Biganzoli L 2002 | -0.1054 | 0.1506 | 8.4% | 0.90 [0.67, 1.21] |  | Bonnetterre J. 2004 | 0 | 0 |  | Not estimable |  | Bontenbal M. 2005 | 0.3577 | 0.1528 | 8.2% | 1.43 [1.06, 1.93] |  | Jassem J 2001 | 0 | 0 |  | Not estimable |  | Langley RE. 2005 | -0.0202 | 0.0786 | 30.9% | 0.98 [0.84, 1.14] |  | Lyman GH 2004 | 0 | 0 |  | Not estimable |  | Nabholtz JM. 2003 | 0 | 0 |  | Not estimable |  | Zielinski C 2005 | 0.1655 | 0.1983 | 4.9% | 1.18 [0.80, 1.74] |  | <b>Subtotal (95% CI)</b> |  |  | <b>52.3%</b> | <b>1.04 [0.93, 1.17]</b> |  | Heterogeneity: Chi² = 6.24, df = 3 (P = 0.10); I² = 52%<br>Test for overall effect: Z = 0.70 (P = 0.48) |  |  |  |  |  | <b>Total (95% CI)</b> |  |  | <b>100.0%</b> | <b>0.93 [0.86, 1.02]</b> |  | Heterogeneity: Chi² = 20.67, df = 10 (P = 0.02); I² = 52%<br>Test for overall effect: Z = 1.61 (P = 0.11)<br>Test for subgroup differences: Chi² = 8.34, df = 2 (P = 0.02), I² = 76.0% |  |  |  |  |  |
|                                                                                                                                                                                        | Study or Subgroup                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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95% CI                                                                                                                                                                                                                                                                                                              | Hazard Ratio<br>IV, Fixed, 95% CI |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |       |        |      |                   |  |              |       |        |      |                   |  |                  |      |        |      |                   |  |               |       |        |      |                   |  |                |   |   |  |               |  |                 |       |        |       |                   |  |               |       |        |      |                   |  |         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| <b>1.1.1 Anthra containing regimens vs CMF</b>                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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| Ackland SP 2001                                                                                                                                                                        | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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           |         |        |       |                   |  |               |   |   |  |               |  |                   |   |   |  |               |  |                  |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                        |  |  |  |  |  |
| Aisner J 1987                                                                                                                                                                          | -0.43                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 0.2098                                    | 4.3%          | 0.65 [0.43, 0.98]                   |                                                                                                                                                                                                                                                                                                                                                |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |       |        |      |                   |  |              |       |        |      |                   |  |                  |      |        |      |                   |  |               |       |        |      |                   |  |                |   |   |  |               |  |                 |       |        |       |                   |  |               |       |        |      |                   |  |            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| Bull JM 1978                                                                                                                                                                           | -0.85                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 0.5577                                    | 0.6%          | 0.43 [0.14, 1.28]                   |                                                                                                                                                                                                                                                                                                                                                |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |       |        |      |                   |  |              |       |        |      |                   |  |                  |      |        |      |                   |  |               |       |        |      |                   |  |                |   |   |  |               |  |                 |       |        |       |                   |  |               |       |        |      |                   |  |            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           |         |        |       |                   |  |               |   |   |  |               |  |                   |   |   |  |               |  |                  |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                        |  |  |  |  |  |
| Cummings FJ 1981                                                                                                                                                                       | 0.06                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 0.3647                                    | 1.4%          | 1.06 [0.52, 2.17]                   |                                                                                                                                                                                                                                                                                                                                                |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |       |        |      |                   |  |              |       |        |      |                   |  |                  |      |        |      |                   |  |               |       |        |      |                   |  |                |   |   |  |               |  |                 |       |        |       |                   |  |               |       |        |      |                   |  |            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| Erkisi M 1997                                                                                                                                                                          | 0.131                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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                                                                                                                                                                                                                                                                                                                 |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |       |        |      |                   |  |              |       |        |      |                   |  |                  |      |        |      |                   |  |               |       |        |      |                   |  |                |   |   |  |               |  |                 |       |        |       |                   |  |               |       |        |      |                   |  |            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| Falkson G 1991                                                                                                                                                                         | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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| Smalley RV 1983                                                                                                                                                                        | -0.16                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 0.0949                                    | 21.2%         | 0.85 [0.71, 1.03]                   |                                                                                                                                                                                                                                                                                                                                                |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |       |        |      |                   |  |              |       |        |      |                   |  |                  |      |        |      |                   |  |               |       |        |      |                   |  |                |   |   |  |               |  |                 |       |        |       |                   |  |               |       |        |      |                   |  |            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| Tormey C 1984                                                                                                                                                                          | -0.45                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 0.1761                                    | 6.2%          | 0.64 [0.45, 0.90]                   |                                                                                                                                                                                                                                                                                                                                                |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |       |        |      |                   |  |              |       |        |      |                   |  |                  |      |        |      |                   |  |               |       |        |      |                   |  |                |   |   |  |               |  |                 |       |        |       |                   |  |               |       |        |      |                   |  |            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| <b>Subtotal (95% CI)</b>                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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                                                                                                                                                                                                                                                                                                                 |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |       |        |      |                   |  |              |       |        |      |                   |  |                  |      |        |      |                   |  |               |       |        |      |                   |  |                |   |   |  |               |  |                 |       |        |       |                   |  |               |       |        |      |                   |  |            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| Heterogeneity: Chi² = 6.10, df = 5 (P = 0.30); I² = 18%<br>Test for overall effect: Z = 3.16 (P = 0.002)                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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| <b>1.1.2 Anthra containing regimens vs Taxane</b>                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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| Denise A 2009                                                                                                                                                                          | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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| Katsumata N 2009                                                                                                                                                                       | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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| Prodaens R 2000                                                                                                                                                                        | -0.0834                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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| Sledge GW 2003                                                                                                                                                                         | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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| Sparano JA 2009                                                                                                                                                                        | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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| <b>Subtotal (95% CI)</b>                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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| Heterogeneity: Not applicable<br>Test for overall effect: Z = 0.67 (P = 0.50)                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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| <b>1.1.3 Anthra containing regimens vs Anthra+Taxane</b>                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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| Biganzoli L 2002                                                                                                                                                                       | -0.1054                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 0.1506                                    | 8.4%          | 0.90 [0.67, 1.21]                   |                               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| Bonnetterre J. 2004                                                                                                                                                                    | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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| Bontenbal M. 2005                                                                                                                                                                      | 0.3577                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 0.1528                                    | 8.2%          | 1.43 [1.06, 1.93]                   |                                                                                                                                                                                                                                                                                                                                                |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |       |        |      |                   |  |              |       |        |      |                   |  |                  |      |        |      |                   |  |               |       |        |      |                   |  |                |   |   |  |               |  |                 |       |        |       |                   |  |               |       |        |      |                   |  |            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| Jassem J 2001                                                                                                                                                                          | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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| Langley RE. 2005                                                                                                                                                                       | -0.0202                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 0.0786                                    | 30.9%         | 0.98 [0.84, 1.14]                   |                                                                                                                                                                                                                                                                                                                                                |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |       |        |      |                   |  |              |       |        |      |                   |  |                  |      |        |      |                   |  |               |       |        |      |                   |  |                |   |   |  |               |  |                 |       |        |       |                   |  |               |       |        |      |                   |  |            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| Lyman GH 2004                                                                                                                                                                          | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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| Nabholtz JM. 2003                                                                                                                                                                      | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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| Zielinski C 2005                                                                                                                                                                       | 0.1655                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 0.1983                                    | 4.9%          | 1.18 [0.80, 1.74]                   |                                                                                                                                                                                                                                                                                                                                                |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |       |        |      |                   |  |              |       |        |      |                   |  |                  |      |        |      |                   |  |               |       |        |      |                   |  |                |   |   |  |               |  |                 |       |        |       |                   |  |               |       |        |      |                   |  |            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| <b>Subtotal (95% CI)</b>                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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                                                                                                                                                                                                                                                                                                                 |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |       |        |      |                   |  |              |       |        |      |                   |  |                  |      |        |      |                   |  |               |       |        |      |                   |  |                |   |   |  |               |  |                 |       |        |       |                   |  |               |       |        |      |                   |  |            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| Heterogeneity: Chi² = 6.24, df = 3 (P = 0.10); I² = 52%<br>Test for overall effect: Z = 0.70 (P = 0.48)                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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| <b>Total (95% CI)</b>                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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                                                                                                                                                                                                                                                                                                                 |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |       |        |      |                   |  |              |       |        |      |                   |  |                  |      |        |      |                   |  |               |       |        |      |                   |  |                |   |   |  |               |  |                 |       |        |       |                   |  |               |       |        |      |                   |  |            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| Heterogeneity: Chi² = 20.67, df = 10 (P = 0.02); I² = 52%<br>Test for overall effect: Z = 1.61 (P = 0.11)<br>Test for subgroup differences: Chi² = 8.34, df = 2 (P = 0.02), I² = 76.0% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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| コメント： アンスラサイクリンを含むレジメンはCMFに対して有意にOSを延長する。一方でタキサンに対して、またタキサン+アンスラサイクリンに対してはOSに差は認めない。                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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| Funnel plot                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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|                                                                                                                                                                                        | コメント：                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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| その他の解析                                                                                                                                                                                 | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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| メタリグレーション                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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| 感度分析                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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## 【4-9 メタアナリシス】

| CQ                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |                                     |                          |                                                                                                                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |   |   |  |               |  |              |   |   |  |               |  |                  |   |   |  |               |  |               |   |   |  |               |  |                |   |   |  |               |  |                 |   |   |  |               |  |               |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                                                   |  |  |  |  |  |               |   |   |  |               |  |                  |   |   |  |               |  |           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-----------|---------|--------|-------|-------------------|--|----------------|---|---|--|---------------|--|-----------------|---|---|--|---------------|--|--------------------------|--|--|--------------|--------------------------|--|----------------------------------------------------------------------------------|--|--|--|--|--|----------------------------------------------------------|--|--|--|--|--|------------------|--------|--------|-------|-------------------|--|---------------------|---|---|--|---------------|--|-------------------|--------|--------|-------|-------------------|--|---------------|---|---|--|---------------|--|------------------|---------|--------|-------|-------------------|--|---------------|---|---|--|---------------|--|-------------------|---|---|--|---------------|--|------------------|--------|--------|-------|-------------------|--|--------------------------|--|--|--------------|--------------------------|--|---------------------------------------------------------------------------------------------------------|--|--|--|--|--|------------------------------------------------|--|--|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|--|
| P                                                                                                                                                                                           | HER2陰性転移・再発乳癌（女性）                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           | I                                   | アンスラサイクリンを含むレジメン         |                                                                                                                                                                                               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| C                                                                                                                                                                                           | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 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                                                    |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
| 研究デザイン                                                                                                                                                                                      | RCT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 文献数                                       | 20                                  | コード                      | Ackland SP 2001, Falkson G 1991, Erkisi M 1997, Tormey C 1984, Smalley RV 1983, Cummings FJ 1981, Aisner J 1987, Bull JM 1978, Katsumata N 2009, Sledge GW 2003, Prodaens R 2000, Denise A 2009, Zielinski C 2005, Biganzoli L 2002, Jassem J 2001, Nabholtz JM. 2003, Bonnetterre J. 2004, |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |   |   |  |               |  |              |   |   |  |               |  |                  |   |   |  |               |  |               |   |   |  |               |  |                |   |   |  |               |  |                 |   |   |  |               |  |               |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                                                   |  |  |  |  |  |               |   |   |  |               |  |                  |   |   |  |               |  |        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                                                    |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
| モデル                                                                                                                                                                                         | Fixed Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 方法                                        | Inverse Variance method (RevMan5.3) |                          |                                                                                                                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |   |   |  |               |  |              |   |   |  |               |  |                  |   |   |  |               |  |               |   |   |  |               |  |                |   |   |  |               |  |                 |   |   |  |               |  |               |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                                                   |  |  |  |  |  |               |   |   |  |               |  |                  |   |   |  |               |  |           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| 効果指標                                                                                                                                                                                        | Hazard Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 統合値                                       | 0.95 ( 0.86 – 1.04 ) P= 0.26        |                          |                                                                                                                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |   |   |  |               |  |              |   |   |  |               |  |                  |   |   |  |               |  |               |   |   |  |               |  |                |   |   |  |               |  |                 |   |   |  |               |  |               |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                                                   |  |  |  |  |  |               |   |   |  |               |  |                  |   |   |  |               |  |           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                                                    |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
| Forest plot                                                                                                                                                                                 | <table><thead><tr><th>Study or Subgroup</th><th>log[Hazard Ratio]</th><th>SE</th><th>Weight</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th></tr></thead><tbody><tr><td colspan="6"><b>1.2.1 Anthra containing regimens vs CMF</b></td></tr><tr><td>Ackland SP 2001</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Aisner J 1987</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Bull JM 1978</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Cummings FJ 1981</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Erkisi M 1997</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Falkson G 1991</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Smalley RV 1983</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Tormey C 1984</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td></td><td><b>Not estimable</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Not applicable<br/>Test for overall effect: Not applicable</td></tr><tr><td colspan="6"><b>1.2.2 Anthra containing regimens vs Taxane</b></td></tr><tr><td>Denise A 2009</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Katsumata N 2009</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Prodaens R 2000</td><td>-0.5108</td><td>0.1139</td><td>18.7%</td><td>0.60 [0.48, 0.75]</td><td></td></tr><tr><td>Sledge GW 2003</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Sparano JA 2009</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>18.7%</b></td><td><b>0.60 [0.48, 0.75]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Not applicable<br/>Test for overall effect: Z = 4.48 (P &lt; 0.00001)</td></tr><tr><td colspan="6"><b>1.2.3 Anthra containing regimens vs Anthra+Taxane</b></td></tr><tr><td>Biganzoli L 2002</td><td>0.0583</td><td>0.1248</td><td>15.5%</td><td>1.06 [0.83, 1.35]</td><td></td></tr><tr><td>Bonnetterre J. 2004</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Bontenbal M. 2005</td><td>0.4055</td><td>0.1445</td><td>11.6%</td><td>1.50 [1.13, 1.99]</td><td></td></tr><tr><td>Jassem J 2001</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Langley RE. 2005</td><td>-0.0672</td><td>0.0757</td><td>42.2%</td><td>0.94 [0.81, 1.08]</td><td></td></tr><tr><td>Lyman GH 2004</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Nabholtz JM. 2003</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Zielinski C 2005</td><td>0.1044</td><td>0.1422</td><td>12.0%</td><td>1.11 [0.84, 1.47]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>81.3%</b></td><td><b>1.05 [0.94, 1.17]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 8.60, df = 3 (P = 0.04); I² = 65%<br/>Test for overall effect: Z = 0.91 (P = 0.37)</td></tr><tr><td colspan="6"><b>Total (95% CI)</b> 100.0% 0.95 [0.86, 1.04]</td></tr><tr><td colspan="6">Heterogeneity: Chi² = 28.28, df = 4 (P &lt; 0.0001); I² = 86%<br/>Test for overall effect: Z = 1.12 (P = 0.26)<br/>Test for subgroup differences: Chi² = 19.68, df = 1 (P &lt; 0.00001), I² = 94.9%</td></tr></tbody></table> |                                           |                                     |                          |                                                                                                                                                                                                                                                                                             | Study or Subgroup                 | log[Hazard Ratio] | SE | Weight | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI | <b>1.2.1 Anthra containing regimens vs CMF</b> |  |  |  |  |  | Ackland SP 2001 | 0 | 0 |  | Not estimable |  | Aisner J 1987 | 0 | 0 |  | Not estimable |  | Bull JM 1978 | 0 | 0 |  | Not estimable |  | Cummings FJ 1981 | 0 | 0 |  | Not estimable |  | Erkisi M 1997 | 0 | 0 |  | Not estimable |  | Falkson G 1991 | 0 | 0 |  | Not estimable |  | Smalley RV 1983 | 0 | 0 |  | Not estimable |  | Tormey C 1984 | 0 | 0 |  | Not estimable |  | <b>Subtotal (95% CI)</b> |  |  |  | <b>Not estimable</b> |  | Heterogeneity: Not applicable<br>Test for overall effect: Not applicable |  |  |  |  |  | <b>1.2.2 Anthra containing regimens vs Taxane</b> |  |  |  |  |  | Denise A 2009 | 0 | 0 |  | Not estimable |  | Katsumata N 2009 | 0 | 0 |  | Not estimable |  | Prodaens R 2000 | -0.5108 | 0.1139 | 18.7% | 0.60 [0.48, 0.75] |  | Sledge GW 2003 | 0 | 0 |  | Not estimable |  | Sparano JA 2009 | 0 | 0 |  | Not estimable |  | <b>Subtotal (95% CI)</b> |  |  | <b>18.7%</b> | <b>0.60 [0.48, 0.75]</b> |  | Heterogeneity: Not applicable<br>Test for overall effect: Z = 4.48 (P < 0.00001) |  |  |  |  |  | <b>1.2.3 Anthra containing regimens vs Anthra+Taxane</b> |  |  |  |  |  | Biganzoli L 2002 | 0.0583 | 0.1248 | 15.5% | 1.06 [0.83, 1.35] |  | Bonnetterre J. 2004 | 0 | 0 |  | Not estimable |  | Bontenbal M. 2005 | 0.4055 | 0.1445 | 11.6% | 1.50 [1.13, 1.99] |  | Jassem J 2001 | 0 | 0 |  | Not estimable |  | Langley RE. 2005 | -0.0672 | 0.0757 | 42.2% | 0.94 [0.81, 1.08] |  | Lyman GH 2004 | 0 | 0 |  | Not estimable |  | Nabholtz JM. 2003 | 0 | 0 |  | Not estimable |  | Zielinski C 2005 | 0.1044 | 0.1422 | 12.0% | 1.11 [0.84, 1.47] |  | <b>Subtotal (95% CI)</b> |  |  | <b>81.3%</b> | <b>1.05 [0.94, 1.17]</b> |  | Heterogeneity: Chi² = 8.60, df = 3 (P = 0.04); I² = 65%<br>Test for overall effect: Z = 0.91 (P = 0.37) |  |  |  |  |  | <b>Total (95% CI)</b> 100.0% 0.95 [0.86, 1.04] |  |  |  |  |  | Heterogeneity: Chi² = 28.28, df = 4 (P < 0.0001); I² = 86%<br>Test for overall effect: Z = 1.12 (P = 0.26)<br>Test for subgroup differences: Chi² = 19.68, df = 1 (P < 0.00001), I² = 94.9% |  |  |  |  |  |
|                                                                                                                                                                                             | Study or Subgroup                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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                                                                                              | Hazard Ratio<br>IV, Fixed, 95% CI |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |   |   |  |               |  |              |   |   |  |               |  |                  |   |   |  |               |  |               |   |   |  |               |  |                |   |   |  |               |  |                 |   |   |  |               |  |               |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                                                   |  |  |  |  |  |               |   |   |  |               |  |                  |   |   |  |               |  |           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                                                    |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
|                                                                                                                                                                                             | <b>1.2.1 Anthra containing regimens vs CMF</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           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                                                    |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
|                                                                                                                                                                                             | Ackland SP 2001                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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                                                    |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
|                                                                                                                                                                                             | Aisner J 1987                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            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                                                    |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
|                                                                                                                                                                                             | Bull JM 1978                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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|                                                                                                                                                                                             | Erkisi M 1997                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            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                                                    |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
|                                                                                                                                                                                             | Falkson G 1991                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           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                                                    |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
|                                                                                                                                                                                             | Smalley RV 1983                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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|                                                                                                                                                                                             | <b>1.2.2 Anthra containing regimens vs Taxane</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| Sledge GW 2003                                                                                                                                                                              | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| Sparano JA 2009                                                                                                                                                                             | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| <b>Subtotal (95% CI)</b>                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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| Heterogeneity: Not applicable<br>Test for overall effect: Z = 4.48 (P < 0.00001)                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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| <b>1.2.3 Anthra containing regimens vs Anthra+Taxane</b>                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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| Biganzoli L 2002                                                                                                                                                                            | 0.0583                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 0.1248                                    | 15.5%                               | 1.06 [0.83, 1.35]        |                                                                                                                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |   |   |  |               |  |              |   |   |  |               |  |                  |   |   |  |               |  |               |   |   |  |               |  |                |   |   |  |               |  |                 |   |   |  |               |  |               |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                                                   |  |  |  |  |  |               |   |   |  |               |  |                  |   |   |  |               |  |                 |         |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                          |  |  |              |                          |  |                                                                                  |  |  |  |  |  |                                                          |  |  |  |  |  |                  |        |        |       |                   |  |                     |   |   |  |               |  |                   |        |        |       |                   |  |               |   |   |  |               |  |                  |         |        |       |                   |  |               |   |   |  |               |  |                   |   |   |  |               |  |                  |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
| Bonnetterre J. 2004                                                                                                                                                                         | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 0                                         |                                     | Not estimable            |                                                                                                                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |   |   |  |               |  |              |   |   |  |               |  |                  |   |   |  |               |  |               |   |   |  |               |  |                |   |   |  |               |  |                 |   |   |  |               |  |               |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                                                   |  |  |  |  |  |               |   |   |  |               |  |                  |   |   |  |               |  |                 |         |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                          |  |  |              |                          |  |                                                                                  |  |  |  |  |  |                                                          |  |  |  |  |  |                  |        |        |       |                   |  |                     |   |   |  |               |  |                   |        |        |       |                   |  |               |   |   |  |               |  |                  |         |        |       |                   |  |               |   |   |  |               |  |                   |   |   |  |               |  |                  |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
| Bontenbal M. 2005                                                                                                                                                                           | 0.4055                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 0.1445                                    | 11.6%                               | 1.50 [1.13, 1.99]        |                                                                                                                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |   |   |  |               |  |              |   |   |  |               |  |                  |   |   |  |               |  |               |   |   |  |               |  |                |   |   |  |               |  |                 |   |   |  |               |  |               |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                                                   |  |  |  |  |  |               |   |   |  |               |  |                  |   |   |  |               |  |                 |         |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                          |  |  |              |                          |  |                                                                                  |  |  |  |  |  |                                                          |  |  |  |  |  |                  |        |        |       |                   |  |                     |   |   |  |               |  |                   |        |        |       |                   |  |               |   |   |  |               |  |                  |         |        |       |                   |  |               |   |   |  |               |  |                   |   |   |  |               |  |                  |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
| Jassem J 2001                                                                                                                                                                               | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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                                                                                              |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |   |   |  |               |  |              |   |   |  |               |  |                  |   |   |  |               |  |               |   |   |  |               |  |                |   |   |  |               |  |                 |   |   |  |               |  |               |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                                                   |  |  |  |  |  |               |   |   |  |               |  |                  |   |   |  |               |  |                 |         |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                          |  |  |              |                          |  |                                                                                  |  |  |  |  |  |                                                          |  |  |  |  |  |                  |        |        |       |                   |  |                     |   |   |  |               |  |                   |        |        |       |                   |  |               |   |   |  |               |  |                  |         |        |       |                   |  |               |   |   |  |               |  |                   |   |   |  |               |  |                  |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
| Langley RE. 2005                                                                                                                                                                            | -0.0672                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 0.0757                                    | 42.2%                               | 0.94 [0.81, 1.08]        |                                                                                                                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |   |   |  |               |  |              |   |   |  |               |  |                  |   |   |  |               |  |               |   |   |  |               |  |                |   |   |  |               |  |                 |   |   |  |               |  |               |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                                                   |  |  |  |  |  |               |   |   |  |               |  |                  |   |   |  |               |  |                 |         |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                          |  |  |              |                          |  |                                                                                  |  |  |  |  |  |                                                          |  |  |  |  |  |                  |        |        |       |                   |  |                     |   |   |  |               |  |                   |        |        |       |                   |  |               |   |   |  |               |  |                  |         |        |       |                   |  |               |   |   |  |               |  |                   |   |   |  |               |  |                  |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
| Lyman GH 2004                                                                                                                                                                               | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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                                                                                              |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |   |   |  |               |  |              |   |   |  |               |  |                  |   |   |  |               |  |               |   |   |  |               |  |                |   |   |  |               |  |                 |   |   |  |               |  |               |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                                                   |  |  |  |  |  |               |   |   |  |               |  |                  |   |   |  |               |  |                 |         |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                          |  |  |              |                          |  |                                                                                  |  |  |  |  |  |                                                          |  |  |  |  |  |                  |        |        |       |                   |  |                     |   |   |  |               |  |                   |        |        |       |                   |  |               |   |   |  |               |  |                  |         |        |       |                   |  |               |   |   |  |               |  |                   |   |   |  |               |  |                  |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
| Nabholtz JM. 2003                                                                                                                                                                           | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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                                                                                              |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |   |   |  |               |  |              |   |   |  |               |  |                  |   |   |  |               |  |               |   |   |  |               |  |                |   |   |  |               |  |                 |   |   |  |               |  |               |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                                                   |  |  |  |  |  |               |   |   |  |               |  |                  |   |   |  |               |  |                 |         |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                          |  |  |              |                          |  |                                                                                  |  |  |  |  |  |                                                          |  |  |  |  |  |                  |        |        |       |                   |  |                     |   |   |  |               |  |                   |        |        |       |                   |  |               |   |   |  |               |  |                  |         |        |       |                   |  |               |   |   |  |               |  |                   |   |   |  |               |  |                  |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
| Zielinski C 2005                                                                                                                                                                            | 0.1044                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 0.1422                                    | 12.0%                               | 1.11 [0.84, 1.47]        |                                                                                                                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |   |   |  |               |  |              |   |   |  |               |  |                  |   |   |  |               |  |               |   |   |  |               |  |                |   |   |  |               |  |                 |   |   |  |               |  |               |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                                                   |  |  |  |  |  |               |   |   |  |               |  |                  |   |   |  |               |  |                 |         |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                          |  |  |              |                          |  |                                                                                  |  |  |  |  |  |                                                          |  |  |  |  |  |                  |        |        |       |                   |  |                     |   |   |  |               |  |                   |        |        |       |                   |  |               |   |   |  |               |  |                  |         |        |       |                   |  |               |   |   |  |               |  |                   |   |   |  |               |  |                  |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                           | <b>81.3%</b>                        | <b>1.05 [0.94, 1.17]</b> |                                                                                                                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                                |  |  |  |  |  |                 |   |   |  |               |  |               |   |   |  |               |  |              |   |   |  |               |  |                  |   |   |  |               |  |               |   |   |  |               |  |                |   |   |  |               |  |                 |   |   |  |               |  |               |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                                                   |  |  |  |  |  |               |   |   |  |               |  |                  |   |   |  |               |  |                 |         |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                          |  |  |              |                          |  |                                                                                  |  |  |  |  |  |                                                          |  |  |  |  |  |                  |        |        |       |                   |  |                     |   |   |  |               |  |                   |        |        |       |                   |  |               |   |   |  |               |  |                  |         |        |       |                   |  |               |   |   |  |               |  |                   |   |   |  |               |  |                  |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
| Heterogeneity: Chi² = 8.60, df = 3 (P = 0.04); I² = 65%<br>Test for overall effect: Z = 0.91 (P = 0.37)                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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                                                    |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
| <b>Total (95% CI)</b> 100.0% 0.95 [0.86, 1.04]                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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                                                    |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
| Heterogeneity: Chi² = 28.28, df = 4 (P < 0.0001); I² = 86%<br>Test for overall effect: Z = 1.12 (P = 0.26)<br>Test for subgroup differences: Chi² = 19.68, df = 1 (P < 0.00001), I² = 94.9% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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      |         |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                          |  |  |              |                          |  |                                                                                  |  |  |  |  |  |                                                          |  |  |  |  |  |                  |        |        |       |                   |  |                     |   |   |  |               |  |                   |        |        |       |                   |  |               |   |   |  |               |  |                  |         |        |       |                   |  |               |   |   |  |               |  |                   |   |   |  |               |  |                  |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                                |  |  |  |  |  |                                                                                                                                                                                             |  |  |  |  |  |
| コメント： 1試験のみの結果でアンスラサイクリンはタキサンと比較しPFSを延長した。またアンスラサイクリン+タキサンとは差は認めない。                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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| Funnel plot                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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| メタリグレーション                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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【4-9 メタアナリシス】

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| P                                                                                                             | HER2陰性転移・再発乳癌（女性）                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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| C                                                                                                             | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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| 研究デザイン                                                                                                        | RCT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 文献数                                       | 20                                 | コード    | Ackland SP 2001, Falkson G 1991, Erkisi M 1997, Tormey C 1984, Smalley RV 1983, Cummings FJ 1981, Aisner J 1987, Bull JM 1978, Katsumata N 2009, Sledge GW 2003, Prodaens R 2000, Denise A 2009, Zielinski C 2005, Biganzoli L 2002, Jassem J 2001, Nabholtz JM. 2003, Bonnetterre J. 2004, |                   |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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| モデル                                                                                                           | Random Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 方法                                        | Mantel-Haenszel method (RevMan5.3) |        |                                                                                                                                                                                                                                                                                             |                   |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |                 |    |    |    |    |      |                   |  |               |    |     |    |     |      |                   |  |                   |  |     |  |     |       |                   |  |              |     |  |     |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |                                               |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |               |    |    |    |    |      |                   |  |                  |    |     |    |     |      |                   |  |                 |    |     |    |     |      |                   |  |                |    |     |    |     |      |                   |  |                 |   |   |   |   |  |               |  |                   |  |     |  |     |       |                   |  |              |     |  |     |  |  |  |  |                                                   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| 効果指標                                                                                                          | Risk Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 統合値                                       | 0.98 ( 0.85 - 1.12 ) P= 0.73       |        |                                                                                                                                                                                                                                                                                             |                   |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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| Forest plot                                                                                                   | <table><thead><tr><th>Study or Subgroup</th><th>Events</th><th>Total</th><th>Events</th><th>Total</th><th>Weight</th><th>M-H, Random, 95% CI</th><th>Risk Ratio<br/>M-H, Random, 95% CI</th></tr></thead><tbody><tr><td colspan="8">1.3.1 Anthra containing regimens vs CMF</td></tr><tr><td>Ackland SP 2001</td><td>127</td><td>223</td><td>109</td><td>237</td><td>7.1%</td><td>1.24 [1.04, 1.48]</td><td></td></tr><tr><td>Aisner J 1987</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Bull JM 1978</td><td>31</td><td>38</td><td>25</td><td>40</td><td>6.0%</td><td>1.31 [0.98, 1.73]</td><td></td></tr><tr><td>Cummings FJ 1981</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Erkisi M 1997</td><td>17</td><td>30</td><td>21</td><td>30</td><td>4.9%</td><td>0.81 [0.55, 1.20]</td><td></td></tr><tr><td>Falkson G 1991</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Smalley RV 1983</td><td>38</td><td>75</td><td>20</td><td>75</td><td>4.5%</td><td>1.90 [1.23, 2.94]</td><td></td></tr><tr><td>Tormey C 1984</td><td>76</td><td>107</td><td>97</td><td>195</td><td>7.0%</td><td>1.43 [1.19, 1.72]</td><td></td></tr><tr><td>Subtotal (95% CI)</td><td></td><td>473</td><td></td><td>577</td><td>29.6%</td><td>1.29 [1.07, 1.56]</td><td></td></tr><tr><td>Total events</td><td>289</td><td></td><td>272</td><td></td><td></td><td></td><td></td></tr><tr><td colspan="8">Heterogeneity: Tau<sup>2</sup> = 0.03; Chi<sup>2</sup> = 9.85, df = 4 (P = 0.04); I<sup>2</sup> = 59%</td></tr><tr><td colspan="8">Test for overall effect: Z = 2.66 (P = 0.008)</td></tr><tr><td colspan="8">1.3.2 Anthra containing regimens vs Taxane</td></tr><tr><td>Denise A 2009</td><td>14</td><td>50</td><td>16</td><td>52</td><td>3.2%</td><td>0.91 [0.50, 1.66]</td><td></td></tr><tr><td>Katsumata N 2009</td><td>42</td><td>146</td><td>59</td><td>147</td><td>5.6%</td><td>0.72 [0.52, 0.99]</td><td></td></tr><tr><td>Prodaens R 2000</td><td>67</td><td>165</td><td>42</td><td>166</td><td>5.6%</td><td>1.60 [1.17, 2.21]</td><td></td></tr><tr><td>Sledge GW 2003</td><td>81</td><td>224</td><td>78</td><td>229</td><td>6.4%</td><td>1.06 [0.83, 1.36]</td><td></td></tr><tr><td>Sparano JA 2009</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Subtotal (95% CI)</td><td></td><td>585</td><td></td><td>594</td><td>20.9%</td><td>1.04 [0.73, 1.48]</td><td></td></tr><tr><td>Total events</td><td>204</td><td></td><td>195</td><td></td><td></td><td></td><td></td></tr><tr><td colspan="8">Heterogeneity: Tau<sup>2</sup> = 0.09; Chi<sup>2</sup> = 12.35, df = 3 (P = 0.006); I<sup>2</sup> = 76%</td></tr><tr><td colspan="8">Test for overall effect: Z = 0.22 (P = 0.83)</td></tr><tr><td colspan="8">1.3.3 Anthra containing regimens vs Anthra+Taxane</td></tr><tr><td>Biganzoli L 2002</td><td>74</td><td>137</td><td>80</td><td>138</td><td>6.8%</td><td>0.93 [0.76, 1.15]</td><td></td></tr><tr><td>Bonnetterre J. 2004</td><td>23</td><td>67</td><td>41</td><td>65</td><td>5.0%</td><td>0.54 [0.37, 0.80]</td><td></td></tr><tr><td>Bontenbal M. 2005</td><td>40</td><td>107</td><td>63</td><td>109</td><td>5.9%</td><td>0.65 [0.48, 0.87]</td><td></td></tr><tr><td>Jassem J 2001</td><td>73</td><td>133</td><td>91</td><td>134</td><td>7.0%</td><td>0.81 [0.67, 0.98]</td><td></td></tr><tr><td>Langley RE. 2005</td><td>186</td><td>343</td><td>221</td><td>347</td><td>7.6%</td><td>0.85 [0.75, 0.97]</td><td></td></tr><tr><td>Lyman GH 2004</td><td>18</td><td>45</td><td>14</td><td>46</td><td>3.5%</td><td>1.31 [0.75, 2.31]</td><td></td></tr><tr><td>Nabholtz JM. 2003</td><td>101</td><td>215</td><td>126</td><td>214</td><td>7.1%</td><td>0.80 [0.67, 0.96]</td><td></td></tr><tr><td>Zielinski C 2005</td><td>66</td><td>129</td><td>71</td><td>114</td><td>6.7%</td><td>0.82 [0.66, 1.02]</td><td></td></tr><tr><td>Subtotal (95% CI)</td><td></td><td>1176</td><td></td><td>1167</td><td>49.5%</td><td>0.81 [0.73, 0.90]</td><td></td></tr><tr><td>Total events</td><td>581</td><td></td><td>707</td><td></td><td></td><td></td><td></td></tr><tr><td colspan="8">Heterogeneity: Tau<sup>2</sup> = 0.01; Chi<sup>2</sup> = 11.57, df = 7 (P = 0.12); I<sup>2</sup> = 40%</td></tr><tr><td colspan="8">Test for overall effect: Z = 4.02 (P &lt; 0.0001)</td></tr><tr><td>Total (95% CI)</td><td></td><td>2234</td><td></td><td>2338</td><td>100.0%</td><td>0.98 [0.85, 1.12]</td><td></td></tr><tr><td>Total events</td><td>1074</td><td></td><td>1174</td><td></td><td></td><td></td><td></td></tr><tr><td colspan="8">Heterogeneity: Tau<sup>2</sup> = 0.06; Chi<sup>2</sup> = 82.94, df = 16 (P &lt; 0.00001); I<sup>2</sup> = 81%</td></tr><tr><td colspan="8">Test for overall effect: Z = 0.34 (P = 0.73)</td></tr><tr><td colspan="8">Test for subgroup differences: Chi<sup>2</sup> = 18.79, df = 2 (P &lt; 0.0001), I<sup>2</sup> = 89.4%</td></tr></tbody></table> |                                           |                                    |        |                                                                                                                                                                                                                                                                                             | Study or Subgroup | Events              | Total                             | Events | Total | Weight | M-H, Random, 95% CI | Risk Ratio<br>M-H, Random, 95% CI | 1.3.1 Anthra containing regimens vs CMF |  |  |  |  |  |  |  | Ackland SP 2001 | 127 | 223 | 109 | 237 | 7.1% | 1.24 [1.04, 1.48] |  | Aisner J 1987 | 0 | 0 | 0 | 0 |  | Not estimable |  | Bull JM 1978 | 31 | 38 | 25 | 40 | 6.0% | 1.31 [0.98, 1.73] |  | Cummings FJ 1981 | 0 | 0 | 0 | 0 |  | Not estimable |  | Erkisi M 1997 | 17 | 30 | 21 | 30 | 4.9% | 0.81 [0.55, 1.20] |  | Falkson G 1991 | 0 | 0 | 0 | 0 |  | Not estimable |  | Smalley RV 1983 | 38 | 75 | 20 | 75 | 4.5% | 1.90 [1.23, 2.94] |  | Tormey C 1984 | 76 | 107 | 97 | 195 | 7.0% | 1.43 [1.19, 1.72] |  | Subtotal (95% CI) |  | 473 |  | 577 | 29.6% | 1.29 [1.07, 1.56] |  | Total events | 289 |  | 272 |  |  |  |  | Heterogeneity: Tau <sup>2</sup> = 0.03; Chi <sup>2</sup> = 9.85, df = 4 (P = 0.04); I <sup>2</sup> = 59% |  |  |  |  |  |  |  | Test for overall effect: Z = 2.66 (P = 0.008) |  |  |  |  |  |  |  | 1.3.2 Anthra containing regimens vs Taxane |  |  |  |  |  |  |  | Denise A 2009 | 14 | 50 | 16 | 52 | 3.2% | 0.91 [0.50, 1.66] |  | Katsumata N 2009 | 42 | 146 | 59 | 147 | 5.6% | 0.72 [0.52, 0.99] |  | Prodaens R 2000 | 67 | 165 | 42 | 166 | 5.6% | 1.60 [1.17, 2.21] |  | Sledge GW 2003 | 81 | 224 | 78 | 229 | 6.4% | 1.06 [0.83, 1.36] |  | Sparano JA 2009 | 0 | 0 | 0 | 0 |  | Not estimable |  | Subtotal (95% CI) |  | 585 |  | 594 | 20.9% | 1.04 [0.73, 1.48] |  | Total events | 204 |  | 195 |  |  |  |  | Heterogeneity: Tau <sup>2</sup> = 0.09; Chi <sup>2</sup> = 12.35, df = 3 (P = 0.006); I <sup>2</sup> = 76% |  |  |  |  |  |  |  | Test for overall effect: Z = 0.22 (P = 0.83) |  |  |  |  |  |  |  | 1.3.3 Anthra containing regimens vs Anthra+Taxane |  |  |  |  |  |  |  | Biganzoli L 2002 | 74 | 137 | 80 | 138 | 6.8% | 0.93 [0.76, 1.15] |  | Bonnetterre J. 2004 | 23 | 67 | 41 | 65 | 5.0% | 0.54 [0.37, 0.80] |  | Bontenbal M. 2005 | 40 | 107 | 63 | 109 | 5.9% | 0.65 [0.48, 0.87] |  | Jassem J 2001 | 73 | 133 | 91 | 134 | 7.0% | 0.81 [0.67, 0.98] |  | Langley RE. 2005 | 186 | 343 | 221 | 347 | 7.6% | 0.85 [0.75, 0.97] |  | Lyman GH 2004 | 18 | 45 | 14 | 46 | 3.5% | 1.31 [0.75, 2.31] |  | Nabholtz JM. 2003 | 101 | 215 | 126 | 214 | 7.1% | 0.80 [0.67, 0.96] |  | Zielinski C 2005 | 66 | 129 | 71 | 114 | 6.7% | 0.82 [0.66, 1.02] |  | Subtotal (95% CI) |  | 1176 |  | 1167 | 49.5% | 0.81 [0.73, 0.90] |  | Total events | 581 |  | 707 |  |  |  |  | Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 11.57, df = 7 (P = 0.12); I <sup>2</sup> = 40% |  |  |  |  |  |  |  | Test for overall effect: Z = 4.02 (P < 0.0001) |  |  |  |  |  |  |  | Total (95% CI) |  | 2234 |  | 2338 | 100.0% | 0.98 [0.85, 1.12] |  | Total events | 1074 |  | 1174 |  |  |  |  | Heterogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 82.94, df = 16 (P < 0.00001); I <sup>2</sup> = 81% |  |  |  |  |  |  |  | Test for overall effect: Z = 0.34 (P = 0.73) |  |  |  |  |  |  |  | Test for subgroup differences: Chi <sup>2</sup> = 18.79, df = 2 (P < 0.0001), I <sup>2</sup> = 89.4% |  |  |  |  |  |  |  |
|                                                                                                               | Study or Subgroup                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Events                                    | Total                              | Events | Total                                                                                                                                                                                                                                                                                       | Weight            | M-H, Random, 95% CI | Risk Ratio<br>M-H, Random, 95% CI |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |                 |    |    |    |    |      |                   |  |               |    |     |    |     |      |                   |  |                   |  |     |  |     |       |                   |  |              |     |  |     |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |                                               |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |               |    |    |    |    |      |                   |  |                  |    |     |    |     |      |                   |  |                 |    |     |    |     |      |                   |  |                |    |     |    |     |      |                   |  |                 |   |   |   |   |  |               |  |                   |  |     |  |     |       |                   |  |              |     |  |     |  |  |  |  |                                                   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      |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |                |  |      |  |      |        |                   |  |              |      |  |      |  |  |  |  |                                                                                                               |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                      |  |  |  |  |  |  |  |
|                                                                                                               | 1.3.1 Anthra containing regimens vs CMF                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                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|                                                                                                               | Ackland SP 2001                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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|                                                                                                               | Aisner J 1987                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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|                                                                                                               | Bull JM 1978                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 31                                        | 38                                 | 25     | 40                                                                                                                                                                                                                                                                                          | 6.0%              | 1.31 [0.98, 1.73]   |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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|                                                                                                               | Cummings FJ 1981                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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|                                                                                                               | Erkisi M 1997                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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|                                                                                                               | Falkson G 1991                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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|                                                                                                               | Smalley RV 1983                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 38                                        | 75                                 | 20     | 75                                                                                                                                                                                                                                                                                          | 4.5%              | 1.90 [1.23, 2.94]   |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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| Tormey C 1984                                                                                                 | 76                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 107                                       | 97                                 | 195    | 7.0%                                                                                                                                                                                                                                                                                        | 1.43 [1.19, 1.72] |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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| Subtotal (95% CI)                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 473                                       |                                    | 577    | 29.6%                                                                                                                                                                                                                                                                                       | 1.29 [1.07, 1.56] |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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| Total events                                                                                                  | 289                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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| Heterogeneity: Tau <sup>2</sup> = 0.03; Chi <sup>2</sup> = 9.85, df = 4 (P = 0.04); I <sup>2</sup> = 59%      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| Test for overall effect: Z = 2.66 (P = 0.008)                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| 1.3.2 Anthra containing regimens vs Taxane                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| Denise A 2009                                                                                                 | 14                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 50                                        | 16                                 | 52     | 3.2%                                                                                                                                                                                                                                                                                        | 0.91 [0.50, 1.66] |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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| Katsumata N 2009                                                                                              | 42                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 146                                       | 59                                 | 147    | 5.6%                                                                                                                                                                                                                                                                                        | 0.72 [0.52, 0.99] |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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| Prodaens R 2000                                                                                               | 67                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 165                                       | 42                                 | 166    | 5.6%                                                                                                                                                                                                                                                                                        | 1.60 [1.17, 2.21] |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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| Sledge GW 2003                                                                                                | 81                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 224                                       | 78                                 | 229    | 6.4%                                                                                                                                                                                                                                                                                        | 1.06 [0.83, 1.36] |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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| Sparano JA 2009                                                                                               | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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| Subtotal (95% CI)                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 585                                       |                                    | 594    | 20.9%                                                                                                                                                                                                                                                                                       | 1.04 [0.73, 1.48] |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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| Total events                                                                                                  | 204                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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| Heterogeneity: Tau <sup>2</sup> = 0.09; Chi <sup>2</sup> = 12.35, df = 3 (P = 0.006); I <sup>2</sup> = 76%    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| Test for overall effect: Z = 0.22 (P = 0.83)                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| 1.3.3 Anthra containing regimens vs Anthra+Taxane                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| Biganzoli L 2002                                                                                              | 74                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 137                                       | 80                                 | 138    | 6.8%                                                                                                                                                                                                                                                                                        | 0.93 [0.76, 1.15] |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                   |  |  |  |  |  |  |  |                  |    |     |    |     |      |                   |  |                     |    |    |    |    |      |                   |  |                   |    |     |    |     |      |                   |  |               |    |     |    |     |      |                   |  |                  |     |     |     |     |      |                   |  |               |    |    |    |    |      |                   |  |                   |     |     |     |     |      |                   |  |                  |    |     |    |     |      |                   |  |                   |  |      |  |      |       |                   |  |              |     |  |     |  |  |  |  |                                                                                                     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| Bonnetterre J. 2004                                                                                           | 23                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 67                                        | 41                                 | 65     | 5.0%                                                                                                                                                                                                                                                                                        | 0.54 [0.37, 0.80] |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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| Bontenbal M. 2005                                                                                             | 40                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 107                                       | 63                                 | 109    | 5.9%                                                                                                                                                                                                                                                                                        | 0.65 [0.48, 0.87] |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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| Jassem J 2001                                                                                                 | 73                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 133                                       | 91                                 | 134    | 7.0%                                                                                                                                                                                                                                                                                        | 0.81 [0.67, 0.98] |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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| Langley RE. 2005                                                                                              | 186                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 343                                       | 221                                | 347    | 7.6%                                                                                                                                                                                                                                                                                        | 0.85 [0.75, 0.97] |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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| Lyman GH 2004                                                                                                 | 18                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 45                                        | 14                                 | 46     | 3.5%                                                                                                                                                                                                                                                                                        | 1.31 [0.75, 2.31] |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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| Nabholtz JM. 2003                                                                                             | 101                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 215                                       | 126                                | 214    | 7.1%                                                                                                                                                                                                                                                                                        | 0.80 [0.67, 0.96] |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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| Zielinski C 2005                                                                                              | 66                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 129                                       | 71                                 | 114    | 6.7%                                                                                                                                                                                                                                                                                        | 0.82 [0.66, 1.02] |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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| Subtotal (95% CI)                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 1176                                      |                                    | 1167   | 49.5%                                                                                                                                                                                                                                                                                       | 0.81 [0.73, 0.90] |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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| Total events                                                                                                  | 581                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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| Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 11.57, df = 7 (P = 0.12); I <sup>2</sup> = 40%     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| Test for overall effect: Z = 4.02 (P < 0.0001)                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| Total (95% CI)                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 2234                                      |                                    | 2338   | 100.0%                                                                                                                                                                                                                                                                                      | 0.98 [0.85, 1.12] |                     |                                   |        |       |        |                     |                                   |                                         |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |               |   |   |   |   |  |               |  |              |    |    |    |    |      |                   |  |                  |   |   |   |   |  |               |  |               |    |    |    |    |      |                   |  |                |   |   |   |   |  |               |  |   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| Total events                                                                                                  | 1074                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| Heterogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 82.94, df = 16 (P < 0.00001); I <sup>2</sup> = 81% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| Test for overall effect: Z = 0.34 (P = 0.73)                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| Test for subgroup differences: Chi <sup>2</sup> = 18.79, df = 2 (P < 0.0001), I <sup>2</sup> = 89.4%          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| コメント： アンスラサイクリンはCMFに対してORRが良好である。またタキサンに対しては同等で、アンスラサイクリン+タキサンに対しては有意に低い結果であった。                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| Funnel plot                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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              |    |    |    |    |      |                   |  |               |    |     |    |     |      |                   |  |                   |  |     |  |     |       |                   |  |              |     |  |     |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |                                               |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |               |    |    |    |    |      |                   |  |                  |    |     |    |     |      |                   |  |                 |    |     |    |     |      |                   |  |                |    |     |    |     |      |                   |  |                 |   |   |   |   |  |               |  |                   |  |     |  |     |       |                   |  |              |     |  |     |  |  |  |  |                                                   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| コメント：                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| その他の解析                                                                                                        | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| メタリグレーション                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| 感度分析                                                                                                          | コメント：                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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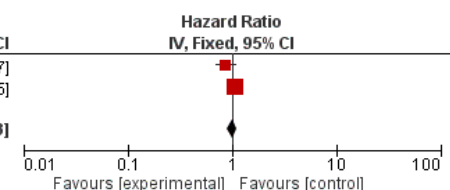
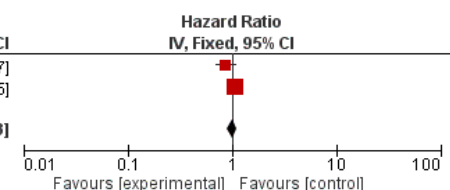
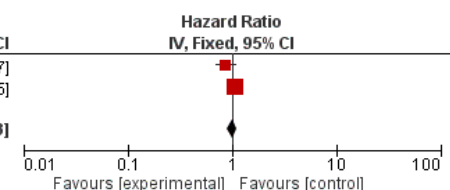
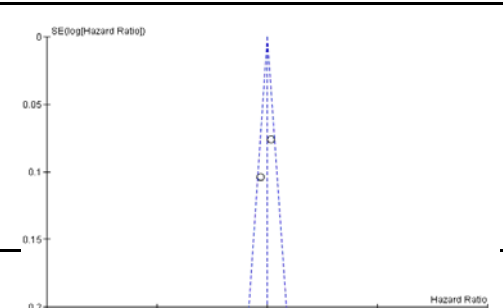
## 【4-9 メタアナリシス】

| CQ                                                                                                      |                          | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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| P                                                                                                       | HER2陰性転移・再発乳癌（女性）        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                | I     | アンスラサイクリンを含むレジメン                                                                                                                                                                                                                                                                                  |                     |                          |  |                |  |        |            |  |            |  |        |       |        |       |                     |                     |                                                |  |  |  |  |  |  |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |              |   |   |   |   |  |               |  |  |  |                  |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                |   |   |   |   |  |               |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                   |  |   |  |   |  |               |  |  |  |              |   |  |   |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |                                         |  |  |  |  |  |  |  |  |  |                                                   |  |  |  |  |  |  |  |  |  |               |   |   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| C                                                                                                       | その他のレジメン                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                | O     | Toxicity (therapy discontinuation)                                                                                                                                                                                                                                                                |                     |                          |  |                |  |        |            |  |            |  |        |       |        |       |                     |                     |                                                |  |  |  |  |  |  |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |              |   |   |   |   |  |               |  |  |  |                  |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                |   |   |   |   |  |               |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                   |  |   |  |   |  |               |  |  |  |              |   |  |   |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |                                         |  |  |  |  |  |  |  |  |  |                                                   |  |  |  |  |  |  |  |  |  |               |   |   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| 研究デザイン                                                                                                  |                          | RCT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 文献数            | 20    | コード<br>Ackland SP 2001, Falkson G 1991, Erkisi M 1997, Tormey C 1984, Smalley RV 1983, Cummings FJ 1981, Aisner J 1987, Bull JM 1978, Katsumata N 2009, Sledge GW 2003, Prodaens R 2000, Denise A 2009, Zielinski C 2005, Biganzoli L 2002, Jassem J 2001, Nabholtz JM. 2003, Bonneterre J. 2004, |                     |                          |  |                |  |        |            |  |            |  |        |       |        |       |                     |                     |                                                |  |  |  |  |  |  |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |              |   |   |   |   |  |               |  |  |  |                  |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                |   |   |   |   |  |               |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                   |  |   |  |   |  |               |  |  |  |              |   |  |   |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |                                         |  |  |  |  |  |  |  |  |  |                                                   |  |  |  |  |  |  |  |  |  |               |   |   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| モデル                                                                                                     |                          | Random Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 方法             |       | Mantel-Haenszel method (RevMan5.3)                                                                                                                                                                                                                                                                |                     |                          |  |                |  |        |            |  |            |  |        |       |        |       |                     |                     |                                                |  |  |  |  |  |  |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |              |   |   |   |   |  |               |  |  |  |                  |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                |   |   |   |   |  |               |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                   |  |   |  |   |  |               |  |  |  |              |   |  |   |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |                                         |  |  |  |  |  |  |  |  |  |                                                   |  |  |  |  |  |  |  |  |  |               |   |   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| 効果指標                                                                                                    |                          | Risk Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 統合値            |       | 0.58 ( 0.45 – 0.74 ) P< 0.0001                                                                                                                                                                                                                                                                    |                     |                          |  |                |  |        |            |  |            |  |        |       |        |       |                     |                     |                                                |  |  |  |  |  |  |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |              |   |   |   |   |  |               |  |  |  |                  |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                |   |   |   |   |  |               |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                   |  |   |  |   |  |               |  |  |  |              |   |  |   |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |                                         |  |  |  |  |  |  |  |  |  |                                                   |  |  |  |  |  |  |  |  |  |               |   |   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| Forest plot                                                                                             |                          | <table><thead><tr><th rowspan="2">Study or Subgroup</th><th colspan="2">Antra containing regimen</th><th colspan="2">Other regimens</th><th rowspan="2">Weight</th><th colspan="2">Risk Ratio</th><th colspan="2">Risk Ratio</th></tr><tr><th>Events</th><th>Total</th><th>Events</th><th>Total</th><th>M-H, Random, 95% CI</th><th>M-H, Random, 95% CI</th></tr></thead><tbody><tr><td colspan="10"><b>1.4.1 Anthra containing regimens vs CMF</b></td></tr><tr><td>Ackland SP 2001</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td><td></td><td></td></tr><tr><td>Aisner J 1987</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td><td></td><td></td></tr><tr><td>Bull JM 1978</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td><td></td><td></td></tr><tr><td>Cummings FJ 1981</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td><td></td><td></td></tr><tr><td>Erkisi M 1997</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td><td></td><td></td></tr><tr><td>Falkson G 1991</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td><td></td><td></td></tr><tr><td>Smalley RV 1983</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td><td></td><td></td></tr><tr><td>Tormey C 1984</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td><td></td><td></td></tr><tr><td>Subtotal (95% CI)</td><td></td><td>0</td><td></td><td>0</td><td></td><td>Not estimable</td><td></td><td></td><td></td></tr><tr><td>Total events</td><td>0</td><td></td><td>0</td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td colspan="10">Heterogeneity: Not applicable</td></tr><tr><td colspan="10">Test for overall effect: Not applicable</td></tr><tr><td colspan="10"><b>1.4.2 Anthra containing regimens vs Taxane</b></td></tr><tr><td>Denise A 2009</td><td>5</td><td>50</td><td>6</td><td>52</td><td>5.2%</td><td>0.87 [0.28, 2.66]</td><td></td><td></td><td></td></tr><tr><td>Katsumata N 2009</td><td>2</td><td>146</td><td>2</td><td>147</td><td>1.7%</td><td>1.01 [0.14, 7.05]</td><td></td><td></td><td></td></tr><tr><td>Prodaens R 2000</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td><td></td><td></td></tr><tr><td>Sledge GW 2003</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td><td></td><td></td></tr><tr><td>Sparano JA 2009</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td><td></td><td></td></tr><tr><td>Subtotal (95% CI)</td><td></td><td>196</td><td></td><td>199</td><td>6.9%</td><td>0.90 [0.34, 2.38]</td><td></td><td></td><td></td></tr><tr><td>Total events</td><td>7</td><td></td><td>8</td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td colspan="10">Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 0.02, df = 1 (P = 0.90); I<sup>2</sup> = 0%</td></tr><tr><td colspan="10">Test for overall effect: Z = 0.21 (P = 0.83)</td></tr><tr><td colspan="10"><b>1.4.3 Anthra containing regimens vs Anthra+Taxane</b></td></tr><tr><td>Biganzoli L 2002</td><td>36</td><td>135</td><td>66</td><td>136</td><td>60.1%</td><td>0.55 [0.40, 0.76]</td><td></td><td></td><td></td></tr><tr><td>Bonneterre J. 2004</td><td>2</td><td>72</td><td>5</td><td>70</td><td>2.5%</td><td>0.39 [0.08, 1.94]</td><td></td><td></td><td></td></tr><tr><td>Bontenbal M. 2005</td><td>5</td><td>107</td><td>10</td><td>109</td><td>6.0%</td><td>0.51 [0.18, 1.44]</td><td></td><td></td><td></td></tr><tr><td>Jassem J 2001</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td><td></td><td></td></tr><tr><td>Langley RE. 2005</td><td>18</td><td>96</td><td>29</td><td>94</td><td>24.5%</td><td>0.61 [0.36, 1.02]</td><td></td><td></td><td></td></tr><tr><td>Lyman GH 2004</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td><td></td><td></td></tr><tr><td>Nabholtz JM. 2003</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td><td></td><td></td></tr><tr><td>Zielinski C 2005</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td><td></td><td></td></tr><tr><td>Subtotal (95% CI)</td><td></td><td>410</td><td></td><td>409</td><td>93.1%</td><td>0.56 [0.43, 0.72]</td><td></td><td></td><td></td></tr><tr><td>Total events</td><td>61</td><td></td><td>110</td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td colspan="10">Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 0.34, df = 3 (P = 0.95); I<sup>2</sup> = 0%</td></tr><tr><td colspan="10">Test for overall effect: Z = 4.35 (P &lt; 0.0001)</td></tr><tr><td colspan="10"><b>Total (95% CI)</b></td></tr><tr><td></td><td>68</td><td>606</td><td></td><td>608</td><td>100.0%</td><td>0.58 [0.45, 0.74]</td><td></td><td></td><td></td></tr><tr><td>Total events</td><td>68</td><td></td><td>118</td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td colspan="10">Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 1.23, df = 5 (P = 0.94); I<sup>2</sup> = 0%</td></tr><tr><td colspan="10">Test for overall effect: Z = 4.25 (P &lt; 0.0001)</td></tr><tr><td colspan="10">Test for subgroup differences: Chi<sup>2</sup> = 0.88, df = 1 (P = 0.35), I<sup>2</sup> = 0%</td></tr></tbody></table> <div><p>コメント： アンスラサイクリンとタキサンのToxicityは同等であるが、アンスラサイクリン+タキサンは有意に悪い。</p></div> |                |       |                                                                                                                                                                                                                                                                                                   | Study or Subgroup   | Antra containing regimen |  | Other regimens |  | Weight | Risk Ratio |  | Risk Ratio |  | Events | Total | Events | Total | M-H, Random, 95% CI | M-H, Random, 95% CI | <b>1.4.1 Anthra containing regimens vs CMF</b> |  |  |  |  |  |  |  |  |  | Ackland SP 2001 | 0 | 0 | 0 | 0 |  | Not estimable |  |  |  | Aisner J 1987 | 0 | 0 | 0 | 0 |  | Not estimable |  |  |  | Bull JM 1978 | 0 | 0 | 0 | 0 |  | Not estimable |  |  |  | Cummings FJ 1981 | 0 | 0 | 0 | 0 |  | Not estimable |  |  |  | Erkisi M 1997 | 0 | 0 | 0 | 0 |  | Not estimable |  |  |  | Falkson G 1991 | 0 | 0 | 0 | 0 |  | Not estimable |  |  |  | Smalley RV 1983 | 0 | 0 | 0 | 0 |  | Not estimable |  |  |  | Tormey C 1984 | 0 | 0 | 0 | 0 |  | Not estimable |  |  |  | Subtotal (95% CI) |  | 0 |  | 0 |  | Not estimable |  |  |  | Total events | 0 |  | 0 |  |  |  |  |  |  | Heterogeneity: Not applicable |  |  |  |  |  |  |  |  |  | Test for overall effect: Not applicable |  |  |  |  |  |  |  |  |  | <b>1.4.2 Anthra containing regimens vs Taxane</b> |  |  |  |  |  |  |  |  |  | Denise A 2009 | 5 | 50 | 6 | 52 | 5.2% | 0.87 [0.28, 2.66] |  |  |  | Katsumata N 2009 | 2 | 146 | 2 | 147 | 1.7% | 1.01 [0.14, 7.05] |  |  |  | Prodaens R 2000 | 0 | 0 | 0 | 0 |  | Not estimable |  |  |  | Sledge GW 2003 | 0 | 0 | 0 | 0 |  | Not estimable |  |  |  | Sparano JA 2009 | 0 | 0 | 0 | 0 |  | Not estimable |  |  |  | Subtotal (95% CI) |  | 196 |  | 199 | 6.9% | 0.90 [0.34, 2.38] |  |  |  | Total events | 7 |  | 8 |  |  |  |  |  |  | Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.02, df = 1 (P = 0.90); I <sup>2</sup> = 0% |  |  |  |  |  |  |  |  |  | Test for overall effect: Z = 0.21 (P = 0.83) |  |  |  |  |  |  |  |  |  | <b>1.4.3 Anthra containing regimens vs Anthra+Taxane</b> |  |  |  |  |  |  |  |  |  | Biganzoli L 2002 | 36 | 135 | 66 | 136 | 60.1% | 0.55 [0.40, 0.76] |  |  |  | Bonneterre J. 2004 | 2 | 72 | 5 | 70 | 2.5% | 0.39 [0.08, 1.94] |  |  |  | Bontenbal M. 2005 | 5 | 107 | 10 | 109 | 6.0% | 0.51 [0.18, 1.44] |  |  |  | Jassem J 2001 | 0 | 0 | 0 | 0 |  | Not estimable |  |  |  | Langley RE. 2005 | 18 | 96 | 29 | 94 | 24.5% | 0.61 [0.36, 1.02] |  |  |  | Lyman GH 2004 | 0 | 0 | 0 | 0 |  | Not estimable |  |  |  | Nabholtz JM. 2003 | 0 | 0 | 0 | 0 |  | Not estimable |  |  |  | Zielinski C 2005 | 0 | 0 | 0 | 0 |  | Not estimable |  |  |  | Subtotal (95% CI) |  | 410 |  | 409 | 93.1% | 0.56 [0.43, 0.72] |  |  |  | Total events | 61 |  | 110 |  |  |  |  |  |  | Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.34, df = 3 (P = 0.95); I <sup>2</sup> = 0% |  |  |  |  |  |  |  |  |  | Test for overall effect: Z = 4.35 (P < 0.0001) |  |  |  |  |  |  |  |  |  | <b>Total (95% CI)</b> |  |  |  |  |  |  |  |  |  |  | 68 | 606 |  | 608 | 100.0% | 0.58 [0.45, 0.74] |  |  |  | Total events | 68 |  | 118 |  |  |  |  |  |  | Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 1.23, df = 5 (P = 0.94); I <sup>2</sup> = 0% |  |  |  |  |  |  |  |  |  | Test for overall effect: Z = 4.25 (P < 0.0001) |  |  |  |  |  |  |  |  |  | Test for subgroup differences: Chi <sup>2</sup> = 0.88, df = 1 (P = 0.35), I <sup>2</sup> = 0% |  |  |  |  |  |  |  |  |  |
| Study or Subgroup                                                                                       | Antra containing regimen |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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|                                                                                                         | Events                   | Total                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Events         | Total |                                                                                                                                                                                                                                                                                                   | M-H, Random, 95% CI | M-H, Random, 95% CI      |  |                |  |        |            |  |            |  |        |       |        |       |                     |                     |                                                |  |  |  |  |  |  |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |              |   |   |   |   |  |               |  |  |  |                  |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                |   |   |   |   |  |               |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                   |  |   |  |   |  |               |  |  |  |              |   |  |   |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |                                         |  |  |  |  |  |  |  |  |  |                                                   |  |  |  |  |  |  |  |  |  |               |   |   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| <b>1.4.1 Anthra containing regimens vs CMF</b>                                                          |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| Ackland SP 2001                                                                                         | 0                        | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 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| Aisner J 1987                                                                                           | 0                        | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 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| Bull JM 1978                                                                                            | 0                        | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 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| Cummings FJ 1981                                                                                        | 0                        | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 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| Erkisi M 1997                                                                                           | 0                        | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 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| Falkson G 1991                                                                                          | 0                        | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 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| Smalley RV 1983                                                                                         | 0                        | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 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| Tormey C 1984                                                                                           | 0                        | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 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| Heterogeneity: Not applicable                                                                           |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| Test for overall effect: Not applicable                                                                 |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| Katsumata N 2009                                                                                        | 2                        | 146                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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| Prodaens R 2000                                                                                         | 0                        | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 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| Sledge GW 2003                                                                                          | 0                        | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 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| Sparano JA 2009                                                                                         | 0                        | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 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| Subtotal (95% CI)                                                                                       |                          | 196                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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    |  |            |  |        |       |        |       |                     |                     |                                                |  |  |  |  |  |  |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |              |   |   |   |   |  |               |  |  |  |                  |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                |   |   |   |   |  |               |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                   |  |   |  |   |  |               |  |  |  |              |   |  |   |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |                                         |  |  |  |  |  |  |  |  |  |                                                   |  |  |  |  |  |  |  |  |  |               |   |   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| Total events                                                                                            | 7                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.02, df = 1 (P = 0.90); I <sup>2</sup> = 0% |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| Test for overall effect: Z = 0.21 (P = 0.83)                                                            |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| <b>1.4.3 Anthra containing regimens vs Anthra+Taxane</b>                                                |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| Biganzoli L 2002                                                                                        | 36                       | 135                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 66             | 136   | 60.1%                                                                                                                                                                                                                                                                                             | 0.55 [0.40, 0.76]   |                          |  |                |  |        |            |  |            |  |        |       |        |       |                     |                     |                                                |  |  |  |  |  |  |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |              |   |   |   |   |  |               |  |  |  |                  |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                |   |   |   |   |  |               |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                   |  |   |  |   |  |               |  |  |  |              |   |  |   |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |                                         |  |  |  |  |  |  |  |  |  |                                                   |  |  |  |  |  |  |  |  |  |               |   |   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| Bonneterre J. 2004                                                                                      | 2                        | 72                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 5              | 70    | 2.5%                                                                                                                                                                                                                                                                                              | 0.39 [0.08, 1.94]   |                          |  |                |  |        |            |  |            |  |        |       |        |       |                     |                     |                                                |  |  |  |  |  |  |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |              |   |   |   |   |  |               |  |  |  |                  |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                |   |   |   |   |  |               |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                   |  |   |  |   |  |               |  |  |  |              |   |  |   |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |                                         |  |  |  |  |  |  |  |  |  |                                                   |  |  |  |  |  |  |  |  |  |               |   |   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| Bontenbal M. 2005                                                                                       | 5                        | 107                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 10             | 109   | 6.0%                                                                                                                                                                                                                                                                                              | 0.51 [0.18, 1.44]   |                          |  |                |  |        |            |  |            |  |        |       |        |       |                     |                     |                                                |  |  |  |  |  |  |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |              |   |   |   |   |  |               |  |  |  |                  |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                |   |   |   |   |  |               |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                   |  |   |  |   |  |               |  |  |  |              |   |  |   |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |                                         |  |  |  |  |  |  |  |  |  |                                                   |  |  |  |  |  |  |  |  |  |               |   |   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                                                                |  |  |  |  |  |  |  |  |  |
| Jassem J 2001                                                                                           | 0                        | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 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| Langley RE. 2005                                                                                        | 18                       | 96                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                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    |  |            |  |        |       |        |       |                     |                     |                                                |  |  |  |  |  |  |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |              |   |   |   |   |  |               |  |  |  |                  |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                |   |   |   |   |  |               |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                   |  |   |  |   |  |               |  |  |  |              |   |  |   |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |                                         |  |  |  |  |  |  |  |  |  |                                                   |  |  |  |  |  |  |  |  |  |               |   |   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| Lyman GH 2004                                                                                           | 0                        | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 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| Nabholtz JM. 2003                                                                                       | 0                        | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 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| Zielinski C 2005                                                                                        | 0                        | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 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| Subtotal (95% CI)                                                                                       |                          | 410                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                | 409   | 93.1%                                                                                                                                                                                                                                                                                             | 0.56 [0.43, 0.72]   |                          |  |                |  |        |            |  |            |  |        |       |        |       |                     |                     |                                                |  |  |  |  |  |  |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |              |   |   |   |   |  |               |  |  |  |                  |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                |   |   |   |   |  |               |  |  |  |                 |   |   |   |   |  |               |  |  |  |               |   |   |   |   |  |               |  |  |  |                   |  |   |  |   |  |               |  |  |  |              |   |  |   |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |  |  |                                         |  |  |  |  |  |  |  |  |  |                                                   |  |  |  |  |  |  |  |  |  |               |   |   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| Total events                                                                                            | 61                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.34, df = 3 (P = 0.95); I <sup>2</sup> = 0% |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| Test for overall effect: Z = 4.35 (P < 0.0001)                                                          |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| <b>Total (95% CI)</b>                                                                                   |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| Total events                                                                                            | 68                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 1.23, df = 5 (P = 0.94); I <sup>2</sup> = 0% |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| Test for overall effect: Z = 4.25 (P < 0.0001)                                                          |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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|  |  |                  |    |    |    |    |       |                   |  |  |  |               |   |   |   |   |  |               |  |  |  |                   |   |   |   |   |  |               |  |  |  |                  |   |   |   |   |  |               |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |     |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |  |    |     |  |     |        |                   |  |  |  |              |    |  |     |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |  |                                                                                                |  |  |  |  |  |  |  |  |  |
| Test for subgroup differences: Chi <sup>2</sup> = 0.88, df = 1 (P = 0.35), I <sup>2</sup> = 0%          |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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                                                                |  |  |  |  |  |  |  |  |  |
| Funnel plot                                                                                             |                          | <div><p>SE(log(RR))</p><p>0.2</p><p>0.4</p><p>0.6</p><p>0.8</p><p>1</p><p>0.01 0.1 1 10 100</p><p>RR</p><p>Subgroups</p><p>○ Anthra containing regimens vs CMF</p><p>◇ Anthra containing regimens vs Taxane</p><p>■ Anthra containing regimens vs Anthra+Taxane</p></div> <p>コメント：</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            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| その他の解析                                                                                                  |                          | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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| メタリグレーション                                                                                               |                          | コメント：                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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|  |  |                  |    |    |    |    |       |                   |  |  |  |               |   |   |   |   |  |               |  |  |  |                   |   |   |   |   |  |               |  |  |  |                  |   |   |   |   |  |               |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |     |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |  |    |     |  |     |        |                   |  |  |  |              |    |  |     |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |  |                                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| 感度分析                                                                                                    |                          | コメント：                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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                                                                |  |  |  |  |  |  |  |  |  |

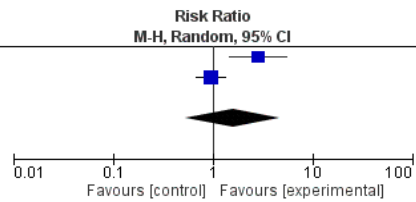
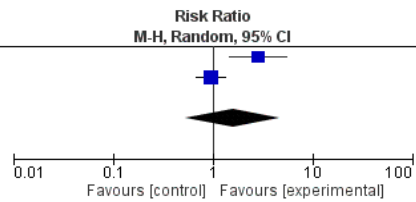
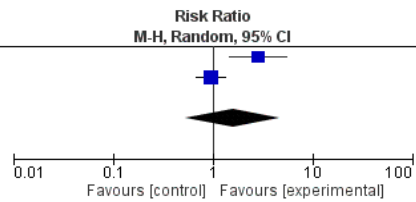
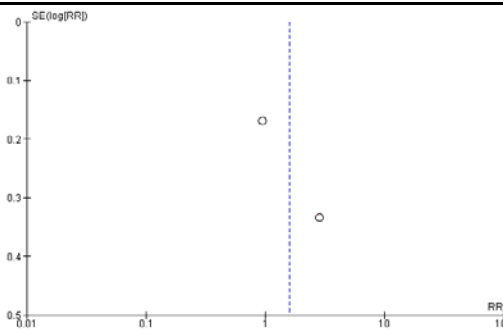
【4-9 メタアナリシス】

| CQ                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | HER2陰性転移・再発乳癌に対する二次以降の化学療法として何が推奨されるか？ |       |                                     |                                             |                                |                   |    |        |                                |                                |                           |         |        |       |                   |  |                    |         |        |       |                   |                |  |  |  |                          |                                                        |  |  |  |  |                                               |  |  |  |  |
|--------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|-------|-------------------------------------|---------------------------------------------|--------------------------------|-------------------|----|--------|--------------------------------|--------------------------------|---------------------------|---------|--------|-------|-------------------|--|--------------------|---------|--------|-------|-------------------|----------------|--|--|--|--------------------------|--------------------------------------------------------|--|--|--|--|-----------------------------------------------|--|--|--|--|
| P                                                      | HER2陰性転移・再発乳癌（女性）                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                        |       | I                                   | エリブリン                                       |                                |                   |    |        |                                |                                |                           |         |        |       |                   |  |                    |         |        |       |                   |                |  |  |  |                          |                                                        |  |  |  |  |                                               |  |  |  |  |
| C                                                      | その他の化学療法                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        |       | O                                   | OS                                          |                                |                   |    |        |                                |                                |                           |         |        |       |                   |  |                    |         |        |       |                   |                |  |  |  |                          |                                                        |  |  |  |  |                                               |  |  |  |  |
| 研究デザイン                                                 | RCT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 文献数                                    | 2     | コード                                 | Kaufman 2015(301), Cortes 2011(EMBRACE 305) |                                |                   |    |        |                                |                                |                           |         |        |       |                   |  |                    |         |        |       |                   |                |  |  |  |                          |                                                        |  |  |  |  |                                               |  |  |  |  |
|                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                        |       |                                     |                                             |                                |                   |    |        |                                |                                |                           |         |        |       |                   |  |                    |         |        |       |                   |                |  |  |  |                          |                                                        |  |  |  |  |                                               |  |  |  |  |
| モデル                                                    | Fixed Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 方法                                     |       | Inverse Variance method (RevMan5.3) |                                             |                                |                   |    |        |                                |                                |                           |         |        |       |                   |  |                    |         |        |       |                   |                |  |  |  |                          |                                                        |  |  |  |  |                                               |  |  |  |  |
| 効果指標                                                   | Hazard Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 統合値                                    |       | 0.86 ( 0.77 – 0.96 ) P= 0.008       |                                             |                                |                   |    |        |                                |                                |                           |         |        |       |                   |  |                    |         |        |       |                   |                |  |  |  |                          |                                                        |  |  |  |  |                                               |  |  |  |  |
| Forest plot                                            | <table><thead><tr><th>Study or Subgroup</th><th>log[Hazard Ratio]</th><th>SE</th><th>Weight</th><th>Hazard Ratio IV, Fixed, 95% CI</th><th>Hazard Ratio IV, Fixed, 95% CI</th></tr></thead><tbody><tr><td>Cortes 2011 (EMBRACE 305)</td><td>-0.2107</td><td>0.1045</td><td>29.8%</td><td>0.81 [0.66, 0.99]</td><td rowspan="3"></td></tr><tr><td>Kaufman 2015 (301)</td><td>-0.1278</td><td>0.0681</td><td>70.2%</td><td>0.88 [0.77, 1.01]</td></tr><tr><td colspan="4">Total (95% CI)</td><td>100.0% 0.86 [0.77, 0.96]</td></tr><tr><td colspan="5">Heterogeneity: Chi² = 0.44, df = 1 (P = 0.51); I² = 0%</td></tr><tr><td colspan="5">Test for overall effect: Z = 2.67 (P = 0.008)</td></tr></tbody></table> |                                        |       |                                     |                                             | Study or Subgroup              | log[Hazard Ratio] | SE | Weight | Hazard Ratio IV, Fixed, 95% CI | Hazard Ratio IV, Fixed, 95% CI | Cortes 2011 (EMBRACE 305) | -0.2107 | 0.1045 | 29.8% | 0.81 [0.66, 0.99] |  | Kaufman 2015 (301) | -0.1278 | 0.0681 | 70.2% | 0.88 [0.77, 1.01] | Total (95% CI) |  |  |  | 100.0% 0.86 [0.77, 0.96] | Heterogeneity: Chi² = 0.44, df = 1 (P = 0.51); I² = 0% |  |  |  |  | Test for overall effect: Z = 2.67 (P = 0.008) |  |  |  |  |
|                                                        | Study or Subgroup                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | log[Hazard Ratio]                      | SE    | Weight                              | Hazard Ratio IV, Fixed, 95% CI              | Hazard Ratio IV, Fixed, 95% CI |                   |    |        |                                |                                |                           |         |        |       |                   |  |                    |         |        |       |                   |                |  |  |  |                          |                                                        |  |  |  |  |                                               |  |  |  |  |
| Cortes 2011 (EMBRACE 305)                              | -0.2107                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 0.1045                                 | 29.8% | 0.81 [0.66, 0.99]                   |                                             |                                |                   |    |        |                                |                                |                           |         |        |       |                   |  |                    |         |        |       |                   |                |  |  |  |                          |                                                        |  |  |  |  |                                               |  |  |  |  |
| Kaufman 2015 (301)                                     | -0.1278                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 0.0681                                 | 70.2% | 0.88 [0.77, 1.01]                   |                                             |                                |                   |    |        |                                |                                |                           |         |        |       |                   |  |                    |         |        |       |                   |                |  |  |  |                          |                                                        |  |  |  |  |                                               |  |  |  |  |
| Total (95% CI)                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                        |       | 100.0% 0.86 [0.77, 0.96]            |                                             |                                |                   |    |        |                                |                                |                           |         |        |       |                   |  |                    |         |        |       |                   |                |  |  |  |                          |                                                        |  |  |  |  |                                               |  |  |  |  |
| Heterogeneity: Chi² = 0.44, df = 1 (P = 0.51); I² = 0% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                        |       |                                     |                                             |                                |                   |    |        |                                |                                |                           |         |        |       |                   |  |                    |         |        |       |                   |                |  |  |  |                          |                                                        |  |  |  |  |                                               |  |  |  |  |
| Test for overall effect: Z = 2.67 (P = 0.008)          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                        |       |                                     |                                             |                                |                   |    |        |                                |                                |                           |         |        |       |                   |  |                    |         |        |       |                   |                |  |  |  |                          |                                                        |  |  |  |  |                                               |  |  |  |  |
| コメント： Eribulin群で有意にOSが良好。                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                        |       |                                     |                                             |                                |                   |    |        |                                |                                |                           |         |        |       |                   |  |                    |         |        |       |                   |                |  |  |  |                          |                                                        |  |  |  |  |                                               |  |  |  |  |
| Funnel plot                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                        |       |                                     |                                             |                                |                   |    |        |                                |                                |                           |         |        |       |                   |  |                    |         |        |       |                   |                |  |  |  |                          |                                                        |  |  |  |  |                                               |  |  |  |  |
|                                                        | コメント：                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                        |       |                                     |                                             |                                |                   |    |        |                                |                                |                           |         |        |       |                   |  |                    |         |        |       |                   |                |  |  |  |                          |                                                        |  |  |  |  |                                               |  |  |  |  |
| その他の解析                                                 | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                        |       |                                     | コメント：                                       |                                |                   |    |        |                                |                                |                           |         |        |       |                   |  |                    |         |        |       |                   |                |  |  |  |                          |                                                        |  |  |  |  |                                               |  |  |  |  |
| メタリグレーション                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                        |       |                                     |                                             |                                |                   |    |        |                                |                                |                           |         |        |       |                   |  |                    |         |        |       |                   |                |  |  |  |                          |                                                        |  |  |  |  |                                               |  |  |  |  |
| 感度分析                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                        |       |                                     |                                             |                                |                   |    |        |                                |                                |                           |         |        |       |                   |  |                    |         |        |       |                   |                |  |  |  |                          |                                                        |  |  |  |  |                                               |  |  |  |  |

【4-9 メタアナリシス】

| CQ                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | HER2陰性転移・再発乳癌に対する二次以降の化学療法として何が推奨されるか？ |                                     |                                |                                                                                     |                   |                   |    |        |                                |                                |                           |         |        |       |                   |                                                                                     |                    |       |        |       |                   |                |  |  |  |        |                   |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |
|---------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|-------------------------------------|--------------------------------|-------------------------------------------------------------------------------------|-------------------|-------------------|----|--------|--------------------------------|--------------------------------|---------------------------|---------|--------|-------|-------------------|-------------------------------------------------------------------------------------|--------------------|-------|--------|-------|-------------------|----------------|--|--|--|--------|-------------------|---------------------------------------------------------|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|
| P                                                       | HER2陰性転移・再発乳癌（女性）                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                        |                                     | I                              | エリブリン                                                                               |                   |                   |    |        |                                |                                |                           |         |        |       |                   |                                                                                     |                    |       |        |       |                   |                |  |  |  |        |                   |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |
| C                                                       | その他の化学療法                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                        |                                     | O                              | PFS                                                                                 |                   |                   |    |        |                                |                                |                           |         |        |       |                   |                                                                                     |                    |       |        |       |                   |                |  |  |  |        |                   |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |
| 研究デザイン                                                  | RCT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 文献数                                    | 2                                   | コード                            | Kaufman 2015(301), Cortes 2011(EMBRACE 305)                                         |                   |                   |    |        |                                |                                |                           |         |        |       |                   |                                                                                     |                    |       |        |       |                   |                |  |  |  |        |                   |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |
| モデル                                                     | Fixed Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 方法                                     | Inverse Variance method (RevMan5.3) |                                |                                                                                     |                   |                   |    |        |                                |                                |                           |         |        |       |                   |                                                                                     |                    |       |        |       |                   |                |  |  |  |        |                   |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |
| 効果指標                                                    | Hazard Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 統合値                                    | 1.00 ( 0.89 – 1.13 ) P= 0.99        |                                |                                                                                     |                   |                   |    |        |                                |                                |                           |         |        |       |                   |                                                                                     |                    |       |        |       |                   |                |  |  |  |        |                   |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |
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| Study or Subgroup                                       | log[Hazard Ratio]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | SE                                     | Weight                              | Hazard Ratio IV, Fixed, 95% CI | Hazard Ratio IV, Fixed, 95% CI                                                      |                   |                   |    |        |                                |                                |                           |         |        |       |                   |                                                                                     |                    |       |        |       |                   |                |  |  |  |        |                   |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |
| Cortes 2011 (EMBRACE 305)                               | -0.1393                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 0.1037                                 | 35.1%                               | 0.87 [0.71, 1.07]              |  |                   |                   |    |        |                                |                                |                           |         |        |       |                   |                                                                                     |                    |       |        |       |                   |                |  |  |  |        |                   |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |
| Kaufman 2015 (301)                                      | 0.077                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 0.0763                                 | 64.9%                               | 1.08 [0.93, 1.25]              |                                                                                     |                   |                   |    |        |                                |                                |                           |         |        |       |                   |                                                                                     |                    |       |        |       |                   |                |  |  |  |        |                   |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |
| Total (95% CI)                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                        |                                     | 100.0%                         |                                                                                     | 1.00 [0.89, 1.13] |                   |    |        |                                |                                |                           |         |        |       |                   |                                                                                     |                    |       |        |       |                   |                |  |  |  |        |                   |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |
| Heterogeneity: Chi² = 2.82, df = 1 (P = 0.09); I² = 65% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                        |                                     |                                |                                                                                     |                   |                   |    |        |                                |                                |                           |         |        |       |                   |                                                                                     |                    |       |        |       |                   |                |  |  |  |        |                   |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |
| Test for overall effect: Z = 0.02 (P = 0.99)            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                        |                                     |                                |                                                                                     |                   |                   |    |        |                                |                                |                           |         |        |       |                   |                                                                                     |                    |       |        |       |                   |                |  |  |  |        |                   |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |
| Funnel plot                                             |  <p>コメント：</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                        |                                     |                                |                                                                                     |                   |                   |    |        |                                |                                |                           |         |        |       |                   |                                                                                     |                    |       |        |       |                   |                |  |  |  |        |                   |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |
| その他の解析                                                  | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                        |                                     |                                | コメント：                                                                               |                   |                   |    |        |                                |                                |                           |         |        |       |                   |                                                                                     |                    |       |        |       |                   |                |  |  |  |        |                   |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |
| メタリグレーション                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                        |                                     |                                |                                                                                     |                   |                   |    |        |                                |                                |                           |         |        |       |                   |                                                                                     |                    |       |        |       |                   |                |  |  |  |        |                   |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |
| 感度分析                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                        |                                     |                                |                                                                                     |                   |                   |    |        |                                |                                |                           |         |        |       |                   |                                                                                     |                    |       |        |       |                   |                |  |  |  |        |                   |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |

【4-9 メタアナリシス】

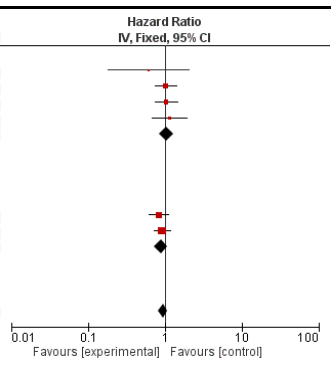
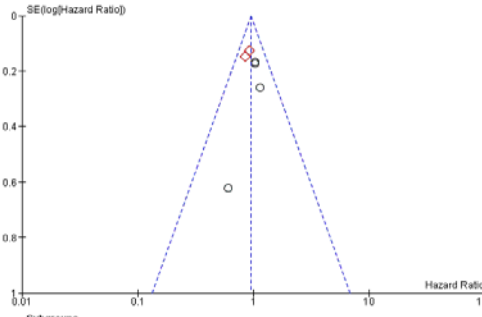
| CQ                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | HER2陰性転移・再発乳癌に対する二次以降の化学療法として何が推奨されるか？ |                                    |       |                                             |                     |                                                                                     |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
|-----------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|------------------------------------|-------|---------------------------------------------|---------------------|-------------------------------------------------------------------------------------|--|--------|--|--------|------------|--|--------|-------|--------|-------|---------------------|---------------------|---------------------------|----|-----|----|-----|-------|-------------------|-------------------------------------------------------------------------------------|--------------------|----|-----|----|-----|-------|-------------------|----------------|------|--|-----|--|--------|-------------------|--------------|-----|--|----|--|--|--|--|-----------------------------------------------------------------------|--|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|--|
| P                                                                     | HER2陰性転移・再発乳癌（女性）                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                        |                                    | I     | エリブリン                                       |                     |                                                                                     |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| C                                                                     | その他の化学療法                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                        |                                    | O     | ORR                                         |                     |                                                                                     |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| 研究デザイン                                                                | RCT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 文献数                                    | 2                                  | コード   | Kaufman 2015(301), Cortes 2011(EMBRACE 305) |                     |                                                                                     |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| モデル                                                                   | Random Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 方法                                     | Mantel-Haenszel method (RevMan5.3) |       |                                             |                     |                                                                                     |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| 効果指標                                                                  | Risk Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 統合値                                    | 1.59 ( 0.54 - 4.69 ) P= 0.40       |       |                                             |                     |                                                                                     |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Forest plot                                                           | <table><thead><tr><th rowspan="2">Study or Subgroup</th><th colspan="2">Eribulin</th><th colspan="2">Others</th><th rowspan="2">Weight</th><th colspan="2">Risk Ratio</th></tr><tr><th>Events</th><th>Total</th><th>Events</th><th>Total</th><th>M-H, Random, 95% CI</th><th>M-H, Random, 95% CI</th></tr></thead><tbody><tr><td>Cortes 2011 (EMBRACE 305)</td><td>57</td><td>508</td><td>10</td><td>254</td><td>46.6%</td><td>2.85 [1.48, 5.49]</td><td rowspan="3"></td></tr><tr><td>Kaufman 2015 (301)</td><td>61</td><td>554</td><td>63</td><td>548</td><td>53.4%</td><td>0.96 [0.69, 1.33]</td></tr><tr><td>Total (95% CI)</td><td colspan="2">1062</td><td colspan="2">802</td><td>100.0%</td><td>1.59 [0.54, 4.69]</td></tr><tr><td>Total events</td><td colspan="2">118</td><td colspan="2">73</td><td></td><td></td><td></td></tr><tr><td colspan="7">Heterogeneity: Tau² = 0.54; Chi² = 8.71, df = 1 (P = 0.003); I² = 89%</td></tr><tr><td colspan="7">Test for overall effect: Z = 0.84 (P = 0.40)</td></tr></tbody></table> |                                        |                                    |       |                                             | Study or Subgroup   | Eribulin                                                                            |  | Others |  | Weight | Risk Ratio |  | Events | Total | Events | Total | M-H, Random, 95% CI | M-H, Random, 95% CI | Cortes 2011 (EMBRACE 305) | 57 | 508 | 10 | 254 | 46.6% | 2.85 [1.48, 5.49] |  | Kaufman 2015 (301) | 61 | 554 | 63 | 548 | 53.4% | 0.96 [0.69, 1.33] | Total (95% CI) | 1062 |  | 802 |  | 100.0% | 1.59 [0.54, 4.69] | Total events | 118 |  | 73 |  |  |  |  | Heterogeneity: Tau² = 0.54; Chi² = 8.71, df = 1 (P = 0.003); I² = 89% |  |  |  |  |  |  | Test for overall effect: Z = 0.84 (P = 0.40) |  |  |  |  |  |  |
| Study or Subgroup                                                     | Eribulin                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                        | Others                             |       | Weight                                      |                     | Risk Ratio                                                                          |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
|                                                                       | Events                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Total                                  | Events                             | Total |                                             | M-H, Random, 95% CI | M-H, Random, 95% CI                                                                 |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Cortes 2011 (EMBRACE 305)                                             | 57                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 508                                    | 10                                 | 254   | 46.6%                                       | 2.85 [1.48, 5.49]   |  |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Kaufman 2015 (301)                                                    | 61                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 554                                    | 63                                 | 548   | 53.4%                                       | 0.96 [0.69, 1.33]   |                                                                                     |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Total (95% CI)                                                        | 1062                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                        | 802                                |       | 100.0%                                      | 1.59 [0.54, 4.69]   |                                                                                     |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Total events                                                          | 118                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        | 73                                 |       |                                             |                     |                                                                                     |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Heterogeneity: Tau² = 0.54; Chi² = 8.71, df = 1 (P = 0.003); I² = 89% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                        |                                    |       |                                             |                     |                                                                                     |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Test for overall effect: Z = 0.84 (P = 0.40)                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                        |                                    |       |                                             |                     |                                                                                     |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| コメント： 有意水準に達しない。2試験で異なる結果であった。                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                        |                                    |       |                                             |                     |                                                                                     |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Funnel plot                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        |                                    |       |                                             |                     |                                                                                     |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| コメント：                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                        |                                    |       |                                             |                     |                                                                                     |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| その他の解析                                                                | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                        |                                    |       | コメント：                                       |                     |                                                                                     |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| メタリグレーション                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                        |                                    |       |                                             |                     |                                                                                     |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| 感度分析                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                        |                                    |       |                                             |                     |                                                                                     |  |        |  |        |            |  |        |       |        |       |                     |                     |                           |    |     |    |     |       |                   |                                                                                     |                    |    |     |    |     |       |                   |                |      |  |     |  |        |                   |              |     |  |    |  |  |  |  |                                                                       |  |  |  |  |  |  |                                              |  |  |  |  |  |  |

【4-9 メタアナリシス】

| CQ                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | HER2陰性転移・再発乳癌に対する二次以降の化学療法として何が推奨されるか？ |                                    |            |                                             |                   |                     |  |                                   |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |
|---------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|------------------------------------|------------|---------------------------------------------|-------------------|---------------------|--|-----------------------------------|--|--------|------------|--|-----------------------------------|--------|-------|--------|-------|-------------|--------|---------------------------|----|-----|----|-----|-------|------|--------------|--|--------------------|----|-----|----|-----|-------|------|--------------|-----------------------|--|-------------|--|------------|---------------|-------------|---------------------|-------------------------------------------|--|--|--|--|--|--|--|--|---------------------------------------------------------------------------------------------------------|--|--|--|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|--|--|--|
| P                                                                                                       | HER2陰性転移・再発乳癌（女性）                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                        |                                    | I          | エリブリン                                       |                   |                     |  |                                   |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |
| C                                                                                                       | その他の化学療法                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                        |                                    | O          | Toxicity(therapy discontinuation)           |                   |                     |  |                                   |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |
| 研究デザイン                                                                                                  | RCT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 文献数                                    | 2                                  | コード        | Kaufman 2015(301), Cortes 2011(EMBRACE 305) |                   |                     |  |                                   |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |
| モデル                                                                                                     | Random Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 方法                                     | Mantel-Haenszel method (RevMan5.3) |            |                                             |                   |                     |  |                                   |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |
| 効果指標                                                                                                    | Risk Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 統合値                                    | 0.81 ( 0.62 – 1.06 ) P= 0.12       |            |                                             |                   |                     |  |                                   |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |
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| Study or Subgroup                                                                                       | Eribulin                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                        | Others                             |            | Weight                                      |                   | Risk Ratio          |  | Risk Ratio<br>M-H, Random, 95% CI |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |
|                                                                                                         | Events                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Total                                  | Events                             | Total      |                                             | M-H, Random       | 95% CI              |  |                                   |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |
| Cortes 2011 (EMBRACE 305)                                                                               | 67                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 503                                    | 38                                 | 247        | 51.3%                                       | 0.87              | [0.60, 1.25]        |  |                                   |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |
| Kaufman 2015 (301)                                                                                      | 43                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 544                                    | 57                                 | 546        | 48.7%                                       | 0.76              | [0.52, 1.10]        |  |                                   |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |
| <b>Total (95% CI)</b>                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | <b>1047</b>                            |                                    | <b>793</b> | <b>100.0%</b>                               | <b>0.81</b>       | <b>[0.62, 1.06]</b> |  |                                   |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |
| Total events: 110 (Eribulin), 95 (Others)                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                        |                                    |            |                                             |                   |                     |  |                                   |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |
| Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.25, df = 1 (P = 0.62); I <sup>2</sup> = 0% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                        |                                    |            |                                             |                   |                     |  |                                   |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |
| Test for overall effect: Z = 1.56 (P = 0.12)                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                        |                                    |            |                                             |                   |                     |  |                                   |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |
|                                                                                                         | コメント： 有意水準に達しない。                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                        |                                    |            |                                             |                   |                     |  |                                   |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |
| Funnel plot                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                        |                                    |            |                                             |                   |                     |  |                                   |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |
|                                                                                                         | コメント：                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                        |                                    |            |                                             |                   |                     |  |                                   |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |
| その他の解析                                                                                                  | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                        |                                    |            | コメント：                                       |                   |                     |  |                                   |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |
| メタリグレーション                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                        |                                    |            |                                             |                   |                     |  |                                   |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |
| 感度分析                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                        |                                    |            |                                             |                   |                     |  |                                   |  |        |            |  |                                   |        |       |        |       |             |        |                           |    |     |    |     |       |      |              |  |                    |    |     |    |     |       |      |              |                       |  |             |  |            |               |             |                     |                                           |  |  |  |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |



【4-9 メタアナリシス】

| CQ                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |                                     |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
|------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|-------------------------------------|-------------------|----------------------------------------------------------------------------------------------------|-----------------------------------|-------------------|----|--------|-----------------------------------|-----------------------------------|--------------------------------------------------------|--|--|--|--|--|-----------------|---------|--------|------|-------------------|--|--------------|--------|--------|-------|-------------------|--|------------------|--------|--------|-------|-------------------|--|--------------------|--------|--------|------|-------------------|--|-------------------|--|--|-------|-------------------|--|--------------------------------------------------------|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|--------------------------------------------|--|--|--|--|--|------------------|---------|--------|-------|-------------------|--|-------------|---------|--------|-------|-------------------|--|-------------------|--|--|-------|-------------------|--|--------------------------------------------------------|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|-----------------------|--|--|--|--|--|--|--|--|--|--------|-------------------|--------------------------------------------------------|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|---------------------------------------------------------------------------|--|--|--|--|--|
| P                                                                            | HER2陰性転移・再発乳癌(女性)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                           | I                                   | カペシタビンを含むレジメン     |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| C                                                                            | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           | O                                   | OS                |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| 研究デザイン                                                                       | RCT (1st)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 文献数                                       | 6                                   | コード               | Smorenburg CH 2014, Mavroudis D 2010, Bachelot T 2011, Luck HJ 2013, Lam SW 2014, Hatscheck T 2012 |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
|                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| モデル                                                                          | Fixed Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 方法                                        | Inverse Variance method (RevMan5.3) |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| 効果指標                                                                         | Hazard Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 統合値                                       | 0.95 ( 0.82 – 1.09 ) P= 0.46        |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| Forest plot                                                                  | <table><thead><tr><th>Study or Subgroup</th><th>log[Hazard Ratio]</th><th>SE</th><th>Weight</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th></tr></thead><tbody><tr><td colspan="6"><b>2.1.1 Cape ± Regimen A vs Regimen B ± Regimen A</b></td></tr><tr><td>Bachelot T 2011</td><td>-0.4943</td><td>0.6227</td><td>1.3%</td><td>0.61 [0.18, 2.07]</td><td></td></tr><tr><td>Luck HJ 2013</td><td>0.0296</td><td>0.1687</td><td>17.9%</td><td>1.03 [0.74, 1.43]</td><td></td></tr><tr><td>Mavroudis D 2010</td><td>0.0392</td><td>0.1736</td><td>16.9%</td><td>1.04 [0.74, 1.46]</td><td></td></tr><tr><td>Smorenburg CH 2014</td><td>0.1398</td><td>0.2606</td><td>7.5%</td><td>1.15 [0.69, 1.92]</td><td></td></tr><tr><td>Subtotal (95% CI)</td><td></td><td></td><td>43.7%</td><td>1.04 [0.84, 1.28]</td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 0.89, df = 3 (P = 0.83); I² = 0%</td></tr><tr><td colspan="6">Test for overall effect: Z = 0.34 (P = 0.74)</td></tr><tr><td colspan="6"><b>2.1.2 Cape + Regimen A vs Regimen A</b></td></tr><tr><td>Hatscheck T 2012</td><td>-0.1744</td><td>0.1468</td><td>23.7%</td><td>0.84 [0.63, 1.12]</td><td></td></tr><tr><td>Lam SW 2014</td><td>-0.0834</td><td>0.1251</td><td>32.6%</td><td>0.92 [0.72, 1.18]</td><td></td></tr><tr><td>Subtotal (95% CI)</td><td></td><td></td><td>56.3%</td><td>0.89 [0.73, 1.07]</td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 0.22, df = 1 (P = 0.64); I² = 0%</td></tr><tr><td colspan="6">Test for overall effect: Z = 1.28 (P = 0.20)</td></tr><tr><td colspan="6"><b>Total (95% CI)</b></td></tr><tr><td colspan="4"></td><td>100.0%</td><td>0.95 [0.82, 1.09]</td></tr><tr><td colspan="6">Heterogeneity: Chi² = 2.31, df = 5 (P = 0.80); I² = 0%</td></tr><tr><td colspan="6">Test for overall effect: Z = 0.74 (P = 0.46)</td></tr><tr><td colspan="6">Test for subarouo differences: Chi² = 1.21, df = 1 (P = 0.27), I² = 17.1%</td></tr></tbody></table>  |                                           |                                     |                   |                                                                                                    | Study or Subgroup                 | log[Hazard Ratio] | SE | Weight | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI | <b>2.1.1 Cape ± Regimen A vs Regimen B ± Regimen A</b> |  |  |  |  |  | Bachelot T 2011 | -0.4943 | 0.6227 | 1.3% | 0.61 [0.18, 2.07] |  | Luck HJ 2013 | 0.0296 | 0.1687 | 17.9% | 1.03 [0.74, 1.43] |  | Mavroudis D 2010 | 0.0392 | 0.1736 | 16.9% | 1.04 [0.74, 1.46] |  | Smorenburg CH 2014 | 0.1398 | 0.2606 | 7.5% | 1.15 [0.69, 1.92] |  | Subtotal (95% CI) |  |  | 43.7% | 1.04 [0.84, 1.28] |  | Heterogeneity: Chi² = 0.89, df = 3 (P = 0.83); I² = 0% |  |  |  |  |  | Test for overall effect: Z = 0.34 (P = 0.74) |  |  |  |  |  | <b>2.1.2 Cape + Regimen A vs Regimen A</b> |  |  |  |  |  | Hatscheck T 2012 | -0.1744 | 0.1468 | 23.7% | 0.84 [0.63, 1.12] |  | Lam SW 2014 | -0.0834 | 0.1251 | 32.6% | 0.92 [0.72, 1.18] |  | Subtotal (95% CI) |  |  | 56.3% | 0.89 [0.73, 1.07] |  | Heterogeneity: Chi² = 0.22, df = 1 (P = 0.64); I² = 0% |  |  |  |  |  | Test for overall effect: Z = 1.28 (P = 0.20) |  |  |  |  |  | <b>Total (95% CI)</b> |  |  |  |  |  |  |  |  |  | 100.0% | 0.95 [0.82, 1.09] | Heterogeneity: Chi² = 2.31, df = 5 (P = 0.80); I² = 0% |  |  |  |  |  | Test for overall effect: Z = 0.74 (P = 0.46) |  |  |  |  |  | Test for subarouo differences: Chi² = 1.21, df = 1 (P = 0.27), I² = 17.1% |  |  |  |  |  |
|                                                                              | Study or Subgroup                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | log[Hazard Ratio]                         | SE                                  | Weight            | Hazard Ratio<br>IV, Fixed, 95% CI                                                                  | Hazard Ratio<br>IV, Fixed, 95% CI |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| <b>2.1.1 Cape ± Regimen A vs Regimen B ± Regimen A</b>                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| Bachelot T 2011                                                              | -0.4943                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 0.6227                                    | 1.3%                                | 0.61 [0.18, 2.07] |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| Luck HJ 2013                                                                 | 0.0296                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 0.1687                                    | 17.9%                               | 1.03 [0.74, 1.43] |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| Mavroudis D 2010                                                             | 0.0392                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 0.1736                                    | 16.9%                               | 1.04 [0.74, 1.46] |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| Smorenburg CH 2014                                                           | 0.1398                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 0.2606                                    | 7.5%                                | 1.15 [0.69, 1.92] |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| Subtotal (95% CI)                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           | 43.7%                               | 1.04 [0.84, 1.28] |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| Heterogeneity: Chi² = 0.89, df = 3 (P = 0.83); I² = 0%                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| Test for overall effect: Z = 0.34 (P = 0.74)                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| <b>2.1.2 Cape + Regimen A vs Regimen A</b>                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| Hatscheck T 2012                                                             | -0.1744                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 0.1468                                    | 23.7%                               | 0.84 [0.63, 1.12] |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| Lam SW 2014                                                                  | -0.0834                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 0.1251                                    | 32.6%                               | 0.92 [0.72, 1.18] |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| Subtotal (95% CI)                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           | 56.3%                               | 0.89 [0.73, 1.07] |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| Heterogeneity: Chi² = 0.22, df = 1 (P = 0.64); I² = 0%                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| Test for overall effect: Z = 1.28 (P = 0.20)                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| <b>Total (95% CI)</b>                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
|                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     | 100.0%            | 0.95 [0.82, 1.09]                                                                                  |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| Heterogeneity: Chi² = 2.31, df = 5 (P = 0.80); I² = 0%                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| Test for overall effect: Z = 0.74 (P = 0.46)                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| Test for subarouo differences: Chi² = 1.21, df = 1 (P = 0.27), I² = 17.1%    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| コメント: カペシタビンは他の1次治療(アンスラサイクリン、タキサン)に対して有意性を示していない。また、他の化学療法に追加することでOSを改善しない。 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| Funnel plot                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |                                     |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
|                                                                              | コメント:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                           |                                     |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| その他の解析                                                                       | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                           |                                     |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| メタリグレーション                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
| 感度分析                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                   |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |
|                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     | コメント:             |                                                                                                    |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |        |      |                   |  |              |        |        |       |                   |  |                  |        |        |       |                   |  |                    |        |        |      |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |        |       |                   |  |                   |  |  |       |                   |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |        |                   |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                                                           |  |  |  |  |  |

【4-9 メタアナリシス】

| CQ                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |                                     |                                   |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|-------------------------------------|-----------------------------------|----------------------------------------------------------------------------------|-------------------|-------------------|----|--------|-----------------------------------|-----------------------------------|--------------------------------------------------------|--|--|--|--|--|-----------------|---------|-------|------|-------------------|--|--------------|------|--------|-------|-------------------|--|------------------|---|---|--|---------------|--|--------------------|--------|--------|------|-------------------|--|--------------------------|--|--|--------------|--------------------------|--|---------------------------------------------------------------------------------------------------------|--|--|--|--|--|--------------------------------------------|--|--|--|--|--|------------------|---------|--------|-------|-------------------|--|-------------|---------|-------|-------|-------------------|--|--------------------------|--|--|--------------|--------------------------|--|-----------------------------------------------------------------------------------------------------------|--|--|--|--|--|-----------------------|--|--|---------------|--------------------------|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|--|
| P                                                                                                                                                                                         | HER2陰性転移・再発乳癌（女性）                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                           | I                                   | カペシタビンを含むレジメン                     |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| C                                                                                                                                                                                         | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                           | O                                   | PFS                               |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| 研究デザイン                                                                                                                                                                                    | RCT (1st)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 文献数                                       | 5                                   | コード                               | Smorenburg CH 2014, Bachelot T 2011, Luck HJ 2013, Lam SW 2014, Hatscheck T 2012 |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| モデル                                                                                                                                                                                       | Fixed Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 方法                                        | Inverse Variance method (RevMan5.3) |                                   |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| 効果指標                                                                                                                                                                                      | Hazard Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 統合値                                       | 0.82 ( 0.71 – 0.93 ) P= 0.003       |                                   |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| Forest plot                                                                                                                                                                               | <table><thead><tr><th>Study or Subgroup</th><th>log[Hazard Ratio]</th><th>SE</th><th>Weight</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th></tr></thead><tbody><tr><td colspan="6"><b>2.2.1 Cape ± Regimen A vs Regimen B ± Regimen A</b></td></tr><tr><td>Bachelot T 2011</td><td>-0.1508</td><td>0.247</td><td>7.6%</td><td>0.86 [0.53, 1.40]</td><td></td></tr><tr><td>Luck HJ 2013</td><td>0.01</td><td>0.1318</td><td>26.7%</td><td>1.01 [0.78, 1.31]</td><td></td></tr><tr><td>Mavroudis D 2010</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Smorenburg CH 2014</td><td>0.3853</td><td>0.2391</td><td>8.1%</td><td>1.47 [0.92, 2.35]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>42.3%</b></td><td><b>1.05 [0.86, 1.29]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 2.72, df = 2 (P = 0.26); I² = 26%<br/>Test for overall effect: Z = 0.51 (P = 0.61)</td></tr><tr><td colspan="6"><b>2.2.2 Cape + Regimen A vs Regimen A</b></td></tr><tr><td>Hatscheck T 2012</td><td>-0.1744</td><td>0.1308</td><td>27.1%</td><td>0.84 [0.65, 1.09]</td><td></td></tr><tr><td>Lam SW 2014</td><td>-0.5798</td><td>0.123</td><td>30.6%</td><td>0.56 [0.44, 0.71]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>57.7%</b></td><td><b>0.68 [0.57, 0.81]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 5.10, df = 1 (P = 0.02); I² = 80%<br/>Test for overall effect: Z = 4.35 (P &lt; 0.0001)</td></tr><tr><td><b>Total (95% CI)</b></td><td></td><td></td><td><b>100.0%</b></td><td><b>0.82 [0.71, 0.93]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 18.14, df = 4 (P = 0.001); I² = 78%<br/>Test for overall effect: Z = 2.97 (P = 0.003)<br/>Test for subgroup differences: Chi² = 10.33, df = 1 (P = 0.001), I² = 90.3%</td></tr></tbody></table> |                                           |                                     |                                   |                                                                                  | Study or Subgroup | log[Hazard Ratio] | SE | Weight | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI | <b>2.2.1 Cape ± Regimen A vs Regimen B ± Regimen A</b> |  |  |  |  |  | Bachelot T 2011 | -0.1508 | 0.247 | 7.6% | 0.86 [0.53, 1.40] |  | Luck HJ 2013 | 0.01 | 0.1318 | 26.7% | 1.01 [0.78, 1.31] |  | Mavroudis D 2010 | 0 | 0 |  | Not estimable |  | Smorenburg CH 2014 | 0.3853 | 0.2391 | 8.1% | 1.47 [0.92, 2.35] |  | <b>Subtotal (95% CI)</b> |  |  | <b>42.3%</b> | <b>1.05 [0.86, 1.29]</b> |  | Heterogeneity: Chi² = 2.72, df = 2 (P = 0.26); I² = 26%<br>Test for overall effect: Z = 0.51 (P = 0.61) |  |  |  |  |  | <b>2.2.2 Cape + Regimen A vs Regimen A</b> |  |  |  |  |  | Hatscheck T 2012 | -0.1744 | 0.1308 | 27.1% | 0.84 [0.65, 1.09] |  | Lam SW 2014 | -0.5798 | 0.123 | 30.6% | 0.56 [0.44, 0.71] |  | <b>Subtotal (95% CI)</b> |  |  | <b>57.7%</b> | <b>0.68 [0.57, 0.81]</b> |  | Heterogeneity: Chi² = 5.10, df = 1 (P = 0.02); I² = 80%<br>Test for overall effect: Z = 4.35 (P < 0.0001) |  |  |  |  |  | <b>Total (95% CI)</b> |  |  | <b>100.0%</b> | <b>0.82 [0.71, 0.93]</b> |  | Heterogeneity: Chi² = 18.14, df = 4 (P = 0.001); I² = 78%<br>Test for overall effect: Z = 2.97 (P = 0.003)<br>Test for subgroup differences: Chi² = 10.33, df = 1 (P = 0.001), I² = 90.3% |  |  |  |  |  |
| Study or Subgroup                                                                                                                                                                         | log[Hazard Ratio]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | SE                                        | Weight                              | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI                                                |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| <b>2.2.1 Cape ± Regimen A vs Regimen B ± Regimen A</b>                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                     |                                   |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| Bachelot T 2011                                                                                                                                                                           | -0.1508                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 0.247                                     | 7.6%                                | 0.86 [0.53, 1.40]                 |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| Luck HJ 2013                                                                                                                                                                              | 0.01                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 0.1318                                    | 26.7%                               | 1.01 [0.78, 1.31]                 |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| Mavroudis D 2010                                                                                                                                                                          | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0                                         |                                     | Not estimable                     |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| Smorenburg CH 2014                                                                                                                                                                        | 0.3853                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 0.2391                                    | 8.1%                                | 1.47 [0.92, 2.35]                 |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           | <b>42.3%</b>                        | <b>1.05 [0.86, 1.29]</b>          |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| Heterogeneity: Chi² = 2.72, df = 2 (P = 0.26); I² = 26%<br>Test for overall effect: Z = 0.51 (P = 0.61)                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                     |                                   |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| <b>2.2.2 Cape + Regimen A vs Regimen A</b>                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                     |                                   |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| Hatscheck T 2012                                                                                                                                                                          | -0.1744                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 0.1308                                    | 27.1%                               | 0.84 [0.65, 1.09]                 |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| Lam SW 2014                                                                                                                                                                               | -0.5798                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 0.123                                     | 30.6%                               | 0.56 [0.44, 0.71]                 |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           | <b>57.7%</b>                        | <b>0.68 [0.57, 0.81]</b>          |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| Heterogeneity: Chi² = 5.10, df = 1 (P = 0.02); I² = 80%<br>Test for overall effect: Z = 4.35 (P < 0.0001)                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                     |                                   |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| <b>Total (95% CI)</b>                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           | <b>100.0%</b>                       | <b>0.82 [0.71, 0.93]</b>          |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| Heterogeneity: Chi² = 18.14, df = 4 (P = 0.001); I² = 78%<br>Test for overall effect: Z = 2.97 (P = 0.003)<br>Test for subgroup differences: Chi² = 10.33, df = 1 (P = 0.001), I² = 90.3% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                     |                                   |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| コメント： カペシタビンは他の1次治療(アンスラサイクリン、タキサン)に対して有意性を示していない。一方で、他の化学療法に追加することで有意にPFSを改善する。                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                     |                                   |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| Funnel plot                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                     |                                   |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| コメント：                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                     |                                   |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| その他の解析                                                                                                                                                                                    | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                           |                                     |                                   |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| メタリグレーション                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                     |                                   |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |
| 感度分析                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                     |                                   |                                                                                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |                 |         |       |      |                   |  |              |      |        |       |                   |  |                  |   |   |  |               |  |                    |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                                            |  |  |  |  |  |                  |         |        |       |                   |  |             |         |       |       |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                           |  |  |  |  |  |

【4-9 メタアナリシス】

| CQ                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |                                    |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
|----------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|------------------------------------|---------------|----------------------------------------------------------------------------------------------------|--------------------------|-----------------------------------|-----------------------------------|----------------|--|--------|-----------------------------------|-----------------------------------|--------|-------|--------|-------|--------------------------------------------------------|--|--|--|--|--|--|--|-----------------|----|----|----|----|------|-------------------|--|--------------|----|-----|----|-----|-------|-------------------|------------------|----|-----|----|-----|-------|-------------------|--------------------|---|----|---|----|------|-------------------|--------------------------|--|------------|--|------------|--------------|--------------------------|----------------------|--|--|--|--|--|--|--|---------------------------------------------------------------------|--|--|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|--|--|--------------------------------------------|--|--|--|--|--|--|--|------------------|----|-----|----|-----|-------|-------------------|--|-------------|-----|-----|----|-----|-------|-------------------|--------------------------|--|------------|--|------------|--------------|--------------------------|----------------------|--|--|--|--|--|--|--|---------------------------------------------------------------------|--|--|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|--|--|-----------------------|--|--|--|--|--|--|--|--|--|------------|--|------------|---------------|--------------------------|--|----------------------|--|--|--|--|--|--|--|---------------------------------------------------------------------|--|--|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|--|--|------------------------------------------------------------------------|--|--|--|--|--|--|--|
| P                                                                                                  | HER2陰性転移・再発乳癌（女性）                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                           | I                                  | カペシタビンを含むレジメン |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| C                                                                                                  | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                           | O                                  | ORR           |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| 研究デザイン                                                                                             | RCT (1st)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 文献数                                       | 6                                  | コード           | Smorenburg CH 2014, Mavroudis D 2010, Bachelot T 2011, Luck HJ 2013, Lam SW 2014, Hatscheck T 2012 |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| モデル                                                                                                | Random Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 方法                                        | Mantel-Haenszel method (RevMan5.3) |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| 効果指標                                                                                               | Risk Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 統合値                                       | 1.14 ( 1.03 – 1.27 ) P= 0.01       |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| Forest plot                                                                                        | <table><thead><tr><th rowspan="2">Study or Subgroup</th><th colspan="2">Cape containing regimens</th><th colspan="2">Other regimens</th><th rowspan="2">Weight</th><th rowspan="2">Risk Ratio<br/>M-H, Random, 95% CI</th><th rowspan="2">Risk Ratio<br/>M-H, Random, 95% CI</th></tr><tr><th>Events</th><th>Total</th><th>Events</th><th>Total</th></tr></thead><tbody><tr><td colspan="8"><b>2.3.1 Cape ± Regimen A vs Regimen B ± Regimen A</b></td></tr><tr><td>Bachelot T 2011</td><td>21</td><td>33</td><td>17</td><td>35</td><td>6.1%</td><td>1.31 [0.85, 2.01]</td><td rowspan="5"></td></tr><tr><td>Luck HJ 2013</td><td>79</td><td>169</td><td>71</td><td>170</td><td>19.4%</td><td>1.12 [0.88, 1.42]</td></tr><tr><td>Mavroudis D 2010</td><td>72</td><td>145</td><td>60</td><td>141</td><td>17.5%</td><td>1.17 [0.91, 1.50]</td></tr><tr><td>Smorenburg CH 2014</td><td>6</td><td>38</td><td>7</td><td>40</td><td>1.1%</td><td>0.90 [0.33, 2.44]</td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td><b>385</b></td><td></td><td><b>386</b></td><td><b>44.1%</b></td><td><b>1.16 [0.99, 1.36]</b></td></tr><tr><td colspan="8">Total events 178 155</td></tr><tr><td colspan="8">Heterogeneity: Tau² = 0.00; Chi² = 0.65, df = 3 (P = 0.89); I² = 0%</td></tr><tr><td colspan="8">Test for overall effect: Z = 1.79 (P = 0.07)</td></tr><tr><td colspan="8"><b>2.3.2 Cape ± Regimen A vs Regimen A</b></td></tr><tr><td>Hatscheck T 2012</td><td>78</td><td>144</td><td>64</td><td>143</td><td>20.0%</td><td>1.21 [0.96, 1.53]</td><td rowspan="3"></td></tr><tr><td>Lam SW 2014</td><td>100</td><td>156</td><td>92</td><td>156</td><td>36.0%</td><td>1.09 [0.91, 1.30]</td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td><b>300</b></td><td></td><td><b>299</b></td><td><b>55.9%</b></td><td><b>1.13 [0.98, 1.30]</b></td></tr><tr><td colspan="8">Total events 178 156</td></tr><tr><td colspan="8">Heterogeneity: Tau² = 0.00; Chi² = 0.52, df = 1 (P = 0.47); I² = 0%</td></tr><tr><td colspan="8">Test for overall effect: Z = 1.69 (P = 0.09)</td></tr><tr><td colspan="8"><b>Total (95% CI)</b></td></tr><tr><td></td><td></td><td><b>685</b></td><td></td><td><b>685</b></td><td><b>100.0%</b></td><td><b>1.14 [1.03, 1.27]</b></td><td></td></tr><tr><td colspan="8">Total events 356 311</td></tr><tr><td colspan="8">Heterogeneity: Tau² = 0.00; Chi² = 1.20, df = 5 (P = 0.94); I² = 0%</td></tr><tr><td colspan="8">Test for overall effect: Z = 2.46 (P = 0.01)</td></tr><tr><td colspan="8">Test for subgroup differences: Chi² = 0.05, df = 1 (P = 0.83); I² = 0%</td></tr></tbody></table> |                                           |                                    |               |                                                                                                    | Study or Subgroup        | Cape containing regimens          |                                   | Other regimens |  | Weight | Risk Ratio<br>M-H, Random, 95% CI | Risk Ratio<br>M-H, Random, 95% CI | Events | Total | Events | Total | <b>2.3.1 Cape ± Regimen A vs Regimen B ± Regimen A</b> |  |  |  |  |  |  |  | Bachelot T 2011 | 21 | 33 | 17 | 35 | 6.1% | 1.31 [0.85, 2.01] |  | Luck HJ 2013 | 79 | 169 | 71 | 170 | 19.4% | 1.12 [0.88, 1.42] | Mavroudis D 2010 | 72 | 145 | 60 | 141 | 17.5% | 1.17 [0.91, 1.50] | Smorenburg CH 2014 | 6 | 38 | 7 | 40 | 1.1% | 0.90 [0.33, 2.44] | <b>Subtotal (95% CI)</b> |  | <b>385</b> |  | <b>386</b> | <b>44.1%</b> | <b>1.16 [0.99, 1.36]</b> | Total events 178 155 |  |  |  |  |  |  |  | Heterogeneity: Tau² = 0.00; Chi² = 0.65, df = 3 (P = 0.89); I² = 0% |  |  |  |  |  |  |  | Test for overall effect: Z = 1.79 (P = 0.07) |  |  |  |  |  |  |  | <b>2.3.2 Cape ± Regimen A vs Regimen A</b> |  |  |  |  |  |  |  | Hatscheck T 2012 | 78 | 144 | 64 | 143 | 20.0% | 1.21 [0.96, 1.53] |  | Lam SW 2014 | 100 | 156 | 92 | 156 | 36.0% | 1.09 [0.91, 1.30] | <b>Subtotal (95% CI)</b> |  | <b>300</b> |  | <b>299</b> | <b>55.9%</b> | <b>1.13 [0.98, 1.30]</b> | Total events 178 156 |  |  |  |  |  |  |  | Heterogeneity: Tau² = 0.00; Chi² = 0.52, df = 1 (P = 0.47); I² = 0% |  |  |  |  |  |  |  | Test for overall effect: Z = 1.69 (P = 0.09) |  |  |  |  |  |  |  | <b>Total (95% CI)</b> |  |  |  |  |  |  |  |  |  | <b>685</b> |  | <b>685</b> | <b>100.0%</b> | <b>1.14 [1.03, 1.27]</b> |  | Total events 356 311 |  |  |  |  |  |  |  | Heterogeneity: Tau² = 0.00; Chi² = 1.20, df = 5 (P = 0.94); I² = 0% |  |  |  |  |  |  |  | Test for overall effect: Z = 2.46 (P = 0.01) |  |  |  |  |  |  |  | Test for subgroup differences: Chi² = 0.05, df = 1 (P = 0.83); I² = 0% |  |  |  |  |  |  |  |
| Study or Subgroup                                                                                  | Cape containing regimens                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                           | Other regimens                     |               | Weight                                                                                             |                          | Risk Ratio<br>M-H, Random, 95% CI | Risk Ratio<br>M-H, Random, 95% CI |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
|                                                                                                    | Events                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Total                                     | Events                             | Total         |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| <b>2.3.1 Cape ± Regimen A vs Regimen B ± Regimen A</b>                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| Bachelot T 2011                                                                                    | 21                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 33                                        | 17                                 | 35            | 6.1%                                                                                               | 1.31 [0.85, 2.01]        |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| Luck HJ 2013                                                                                       | 79                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 169                                       | 71                                 | 170           | 19.4%                                                                                              | 1.12 [0.88, 1.42]        |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| Mavroudis D 2010                                                                                   | 72                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 145                                       | 60                                 | 141           | 17.5%                                                                                              | 1.17 [0.91, 1.50]        |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| Smorenburg CH 2014                                                                                 | 6                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 38                                        | 7                                  | 40            | 1.1%                                                                                               | 0.90 [0.33, 2.44]        |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | <b>385</b>                                |                                    | <b>386</b>    | <b>44.1%</b>                                                                                       | <b>1.16 [0.99, 1.36]</b> |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| Total events 178 155                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| Heterogeneity: Tau² = 0.00; Chi² = 0.65, df = 3 (P = 0.89); I² = 0%                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| Test for overall effect: Z = 1.79 (P = 0.07)                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| <b>2.3.2 Cape ± Regimen A vs Regimen A</b>                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| Hatscheck T 2012                                                                                   | 78                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 144                                       | 64                                 | 143           | 20.0%                                                                                              | 1.21 [0.96, 1.53]        |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| Lam SW 2014                                                                                        | 100                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 156                                       | 92                                 | 156           | 36.0%                                                                                              | 1.09 [0.91, 1.30]        |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | <b>300</b>                                |                                    | <b>299</b>    | <b>55.9%</b>                                                                                       | <b>1.13 [0.98, 1.30]</b> |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| Total events 178 156                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| Heterogeneity: Tau² = 0.00; Chi² = 0.52, df = 1 (P = 0.47); I² = 0%                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| Test for overall effect: Z = 1.69 (P = 0.09)                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| <b>Total (95% CI)</b>                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
|                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | <b>685</b>                                |                                    | <b>685</b>    | <b>100.0%</b>                                                                                      | <b>1.14 [1.03, 1.27]</b> |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| Total events 356 311                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| Heterogeneity: Tau² = 0.00; Chi² = 1.20, df = 5 (P = 0.94); I² = 0%                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| Test for overall effect: Z = 2.46 (P = 0.01)                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| Test for subgroup differences: Chi² = 0.05, df = 1 (P = 0.83); I² = 0%                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| コメント： カペシタビンは他の1次治療(アンスラサイクリン、タキサン)に対して有意性を示していない。また、他の化学療法に追加することでも有意性を示していないが、統合解析では有意にORRを改善する。 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| Funnel plot                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| コメント：                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| その他の解析                                                                                             | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                           |                                    |               | コメント：                                                                                              |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| メタリグレーション                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |
| 感度分析                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |               |                                                                                                    |                          |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                                        |  |  |  |  |  |  |  |                 |    |    |    |    |      |                   |  |              |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |                    |   |    |   |    |      |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |             |     |     |    |     |       |                   |                          |  |            |  |            |              |                          |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |            |  |            |               |                          |  |                      |  |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |  |

【4-9 メタアナリシス】

| CQ                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |                                     |                   |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|-------------------------------------|-------------------|---------------------------------------|-----------------------------------|-------------------|----|--------|-----------------------------------|-----------------------------------|--------------------------------------------------------|--|--|--|--|--|-------------|---|---|--|---------------|--|----------------|---|---|--|---------------|--|----------------|---|---|--|---------------|--|-------------------|--|--|--|---------------|--|--------------------------------------------------------------------------|--|--|--|--|--|--------------------------------------------|--|--|--|--|--|----------------------|---------|-------|-------|-------------------|--|-----------------|---------|--------|-------|-------------------|--|-------------------|--|--|--------|-------------------|--|--------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|--|----------------|--|--|--------|-------------------|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|--|
| P                                                                                                                                                                               | HER2陰性転移・再発乳癌（女性）                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                           | I                                   | カペシタビンを含むレジメン     |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| C                                                                                                                                                                               | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                           | O                                   | OS                |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| 研究デザイン                                                                                                                                                                          | RCT (2nd)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 文献数                                       | 2                                   | コード               | Yamamoto D 2017, Oshaughnessy JA 2002 |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
|                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |                                     |                   |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| モデル                                                                                                                                                                             | Fixed Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 方法                                        | Inverse Variance method (RevMan5.3) |                   |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| 効果指標                                                                                                                                                                            | Hazard Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 統合値                                       | 0.79 ( 0.65 – 0.97 ) P= 0.02        |                   |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| Forest plot                                                                                                                                                                     | <table><thead><tr><th>Study or Subgroup</th><th>log[Hazard Ratio]</th><th>SE</th><th>Weight</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th></tr></thead><tbody><tr><td colspan="6"><b>1.1.1 Cape ± Regimen A vs Regimen B ± Regimen A</b></td></tr><tr><td>Chan S 2009</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Pallis AG 2012</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Talbot DC 2002</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Subtotal (95% CI)</td><td></td><td></td><td></td><td>Not estimable</td><td></td></tr><tr><td colspan="6">Heterogeneity: Not applicable<br/>Test for overall effect: Not applicable</td></tr><tr><td colspan="6"><b>1.1.2 Cape + Regimen A vs Regimen A</b></td></tr><tr><td>Oshaughnessy JA 2002</td><td>-0.2485</td><td>0.109</td><td>86.4%</td><td>0.78 [0.63, 0.97]</td><td></td></tr><tr><td>Yamamoto D 2017</td><td>-0.1165</td><td>0.2742</td><td>13.6%</td><td>0.89 [0.52, 1.52]</td><td></td></tr><tr><td>Subtotal (95% CI)</td><td></td><td></td><td>100.0%</td><td>0.79 [0.65, 0.97]</td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi<sup>2</sup> = 0.20, df = 1 (P = 0.65); I<sup>2</sup> = 0%<br/>Test for overall effect: Z = 2.28 (P = 0.02)</td></tr><tr><td>Total (95% CI)</td><td></td><td></td><td>100.0%</td><td>0.79 [0.65, 0.97]</td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi<sup>2</sup> = 0.20, df = 1 (P = 0.65); I<sup>2</sup> = 0%<br/>Test for overall effect: Z = 2.28 (P = 0.02)<br/>Test for subgroup differences: Not applicable</td></tr></tbody></table> |                                           |                                     |                   |                                       | Study or Subgroup                 | log[Hazard Ratio] | SE | Weight | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI | <b>1.1.1 Cape ± Regimen A vs Regimen B ± Regimen A</b> |  |  |  |  |  | Chan S 2009 | 0 | 0 |  | Not estimable |  | Pallis AG 2012 | 0 | 0 |  | Not estimable |  | Talbot DC 2002 | 0 | 0 |  | Not estimable |  | Subtotal (95% CI) |  |  |  | Not estimable |  | Heterogeneity: Not applicable<br>Test for overall effect: Not applicable |  |  |  |  |  | <b>1.1.2 Cape + Regimen A vs Regimen A</b> |  |  |  |  |  | Oshaughnessy JA 2002 | -0.2485 | 0.109 | 86.4% | 0.78 [0.63, 0.97] |  | Yamamoto D 2017 | -0.1165 | 0.2742 | 13.6% | 0.89 [0.52, 1.52] |  | Subtotal (95% CI) |  |  | 100.0% | 0.79 [0.65, 0.97] |  | Heterogeneity: Chi <sup>2</sup> = 0.20, df = 1 (P = 0.65); I <sup>2</sup> = 0%<br>Test for overall effect: Z = 2.28 (P = 0.02) |  |  |  |  |  | Total (95% CI) |  |  | 100.0% | 0.79 [0.65, 0.97] |  | Heterogeneity: Chi <sup>2</sup> = 0.20, df = 1 (P = 0.65); I <sup>2</sup> = 0%<br>Test for overall effect: Z = 2.28 (P = 0.02)<br>Test for subgroup differences: Not applicable |  |  |  |  |  |
|                                                                                                                                                                                 | Study or Subgroup                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | log[Hazard Ratio]                         | SE                                  | Weight            | Hazard Ratio<br>IV, Fixed, 95% CI     | Hazard Ratio<br>IV, Fixed, 95% CI |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| <b>1.1.1 Cape ± Regimen A vs Regimen B ± Regimen A</b>                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |                                     |                   |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| Chan S 2009                                                                                                                                                                     | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 0                                         |                                     | Not estimable     |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| Pallis AG 2012                                                                                                                                                                  | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 0                                         |                                     | Not estimable     |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| Talbot DC 2002                                                                                                                                                                  | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 0                                         |                                     | Not estimable     |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| Subtotal (95% CI)                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |                                     | Not estimable     |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| Heterogeneity: Not applicable<br>Test for overall effect: Not applicable                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |                                     |                   |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| <b>1.1.2 Cape + Regimen A vs Regimen A</b>                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |                                     |                   |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| Oshaughnessy JA 2002                                                                                                                                                            | -0.2485                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 0.109                                     | 86.4%                               | 0.78 [0.63, 0.97] |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| Yamamoto D 2017                                                                                                                                                                 | -0.1165                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 0.2742                                    | 13.6%                               | 0.89 [0.52, 1.52] |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| Subtotal (95% CI)                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           | 100.0%                              | 0.79 [0.65, 0.97] |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| Heterogeneity: Chi <sup>2</sup> = 0.20, df = 1 (P = 0.65); I <sup>2</sup> = 0%<br>Test for overall effect: Z = 2.28 (P = 0.02)                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |                                     |                   |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| Total (95% CI)                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           | 100.0%                              | 0.79 [0.65, 0.97] |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| Heterogeneity: Chi <sup>2</sup> = 0.20, df = 1 (P = 0.65); I <sup>2</sup> = 0%<br>Test for overall effect: Z = 2.28 (P = 0.02)<br>Test for subgroup differences: Not applicable |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |                                     |                   |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| コメント: カペシタビンを他の化学療法に追加することで有意にOSを改善する。しかし、2試験のデータのみで試験間で結果が異なっていることから解釈に注意が必要である。                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |                                     |                   |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| Funnel plot                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |                                     |                   |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
|                                                                                                                                                                                 | コメント:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                           |                                     |                   |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| その他の解析                                                                                                                                                                          | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                           |                                     |                   |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| メタリグレーション                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |                                     |                   |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |
| 感度分析                                                                                                                                                                            | コメント:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                           |                                     |                   |                                       |                                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |   |   |  |               |  |                |   |   |  |               |  |                |   |   |  |               |  |                   |  |  |  |               |  |                                                                          |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |       |       |                   |  |                 |         |        |       |                   |  |                   |  |  |        |                   |  |                                                                                                                                |  |  |  |  |  |                |  |  |        |                   |  |                                                                                                                                                                                 |  |  |  |  |  |

【4-9 メタアナリシス】

| CQ                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |                                     |                                   |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|-------------------------------------|-----------------------------------|----------------------------------------------------|-------------------|-------------------|----|--------|-----------------------------------|-----------------------------------|--------------------------------------------------------|--|--|--|--|--|-------------|---------|--------|-------|-------------------|--|----------------|---|---|--|---------------|--|----------------|---|---|--|---------------|--|--------------------------|--|--|--------------|--------------------------|--|-------------------------------------------------------------------------------|--|--|--|--|--|--------------------------------------------|--|--|--|--|--|----------------------|---------|--------|-------|-------------------|--|-----------------|--------|--------|------|-------------------|--|--------------------------|--|--|--------------|--------------------------|--|-----------------------------------------------------------------------------------------------------------|--|--|--|--|--|-----------------------|--|--|---------------|--------------------------|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|--|
| P                                                                                                                                                                                       | HER2陰性転移・再発乳癌（女性）                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                           | I                                   | カペシタビンを含むレジメン                     |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| C                                                                                                                                                                                       | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           | O                                   | PFS                               |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| 研究デザイン                                                                                                                                                                                  | RCT (2nd)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 文献数                                       | 3                                   | コード                               | Chan S 2009, Yamamoto D 2017, Oshaughnessy JA 2002 |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| モデル                                                                                                                                                                                     | Fixed Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 方法                                        | Inverse Variance method (RevMan5.3) |                                   |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| 効果指標                                                                                                                                                                                    | Hazard Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 統合値                                       | 0.70 ( 0.62 – 0.80 ) P< 0.00001     |                                   |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| Forest plot                                                                                                                                                                             | <table><thead><tr><th>Study or Subgroup</th><th>log[Hazard Ratio]</th><th>SE</th><th>Weight</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th></tr></thead><tbody><tr><td colspan="6"><b>1.2.1 Cape ± Regimen A vs Regimen B ± Regimen A</b></td></tr><tr><td>Chan S 2009</td><td>-0.1863</td><td>0.1093</td><td>34.7%</td><td>0.83 [0.67, 1.03]</td><td></td></tr><tr><td>Pallis AG 2012</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Talbot DC 2002</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>34.7%</b></td><td><b>0.83 [0.67, 1.03]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Not applicable<br/>Test for overall effect: Z = 1.70 (P = 0.09)</td></tr><tr><td colspan="6"><b>1.2.2 Cape + Regimen A vs Regimen A</b></td></tr><tr><td>Oshaughnessy JA 2002</td><td>-0.4308</td><td>0.0852</td><td>57.1%</td><td>0.65 [0.55, 0.77]</td><td></td></tr><tr><td>Yamamoto D 2017</td><td>-0.478</td><td>0.2236</td><td>8.3%</td><td>0.62 [0.40, 0.96]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>65.3%</b></td><td><b>0.65 [0.55, 0.76]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 0.04, df = 1 (P = 0.84); I² = 0%<br/>Test for overall effect: Z = 5.49 (P &lt; 0.00001)</td></tr><tr><td><b>Total (95% CI)</b></td><td></td><td></td><td><b>100.0%</b></td><td><b>0.70 [0.62, 0.80]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 3.47, df = 2 (P = 0.18); I² = 42%<br/>Test for overall effect: Z = 5.44 (P &lt; 0.00001)<br/>Test for subgroup differences: Chi² = 3.43, df = 1 (P = 0.06), I² = 70.9%</td></tr></tbody></table> |                                           |                                     |                                   |                                                    | Study or Subgroup | log[Hazard Ratio] | SE | Weight | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI | <b>1.2.1 Cape ± Regimen A vs Regimen B ± Regimen A</b> |  |  |  |  |  | Chan S 2009 | -0.1863 | 0.1093 | 34.7% | 0.83 [0.67, 1.03] |  | Pallis AG 2012 | 0 | 0 |  | Not estimable |  | Talbot DC 2002 | 0 | 0 |  | Not estimable |  | <b>Subtotal (95% CI)</b> |  |  | <b>34.7%</b> | <b>0.83 [0.67, 1.03]</b> |  | Heterogeneity: Not applicable<br>Test for overall effect: Z = 1.70 (P = 0.09) |  |  |  |  |  | <b>1.2.2 Cape + Regimen A vs Regimen A</b> |  |  |  |  |  | Oshaughnessy JA 2002 | -0.4308 | 0.0852 | 57.1% | 0.65 [0.55, 0.77] |  | Yamamoto D 2017 | -0.478 | 0.2236 | 8.3% | 0.62 [0.40, 0.96] |  | <b>Subtotal (95% CI)</b> |  |  | <b>65.3%</b> | <b>0.65 [0.55, 0.76]</b> |  | Heterogeneity: Chi² = 0.04, df = 1 (P = 0.84); I² = 0%<br>Test for overall effect: Z = 5.49 (P < 0.00001) |  |  |  |  |  | <b>Total (95% CI)</b> |  |  | <b>100.0%</b> | <b>0.70 [0.62, 0.80]</b> |  | Heterogeneity: Chi² = 3.47, df = 2 (P = 0.18); I² = 42%<br>Test for overall effect: Z = 5.44 (P < 0.00001)<br>Test for subgroup differences: Chi² = 3.43, df = 1 (P = 0.06), I² = 70.9% |  |  |  |  |  |
| Study or Subgroup                                                                                                                                                                       | log[Hazard Ratio]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | SE                                        | Weight                              | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI                  |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| <b>1.2.1 Cape ± Regimen A vs Regimen B ± Regimen A</b>                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                                   |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| Chan S 2009                                                                                                                                                                             | -0.1863                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 0.1093                                    | 34.7%                               | 0.83 [0.67, 1.03]                 |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| Pallis AG 2012                                                                                                                                                                          | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 0                                         |                                     | Not estimable                     |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| Talbot DC 2002                                                                                                                                                                          | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 0                                         |                                     | Not estimable                     |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           | <b>34.7%</b>                        | <b>0.83 [0.67, 1.03]</b>          |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| Heterogeneity: Not applicable<br>Test for overall effect: Z = 1.70 (P = 0.09)                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                                   |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| <b>1.2.2 Cape + Regimen A vs Regimen A</b>                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                                   |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| Oshaughnessy JA 2002                                                                                                                                                                    | -0.4308                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 0.0852                                    | 57.1%                               | 0.65 [0.55, 0.77]                 |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| Yamamoto D 2017                                                                                                                                                                         | -0.478                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 0.2236                                    | 8.3%                                | 0.62 [0.40, 0.96]                 |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           | <b>65.3%</b>                        | <b>0.65 [0.55, 0.76]</b>          |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| Heterogeneity: Chi² = 0.04, df = 1 (P = 0.84); I² = 0%<br>Test for overall effect: Z = 5.49 (P < 0.00001)                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                                   |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| <b>Total (95% CI)</b>                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           | <b>100.0%</b>                       | <b>0.70 [0.62, 0.80]</b>          |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| Heterogeneity: Chi² = 3.47, df = 2 (P = 0.18); I² = 42%<br>Test for overall effect: Z = 5.44 (P < 0.00001)<br>Test for subgroup differences: Chi² = 3.43, df = 1 (P = 0.06), I² = 70.9% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                                   |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| コメント： カペシタビンを他の化学療法に追加することで有意にPFSを改善する。                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                                   |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| Funnel plot                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                                   |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| コメント：                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                                   |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| その他の解析                                                                                                                                                                                  | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                           |                                     |                                   |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| メタリグレーション                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                                   |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| 感度分析                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                                   |                                                    |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
|                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           |                                     |                                   | コメント：                                              |                   |                   |    |        |                                   |                                   |                                                        |  |  |  |  |  |             |         |        |       |                   |  |                |   |   |  |               |  |                |   |   |  |               |  |                          |  |  |              |                          |  |                                                                               |  |  |  |  |  |                                            |  |  |  |  |  |                      |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |

【4-9 メタアナリシス】

| CQ                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |        |                                    |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
|---------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|--------|------------------------------------|------------------------------------------------------------------------------------|---------------------|--------------------------|------------|----------------|------------|--------|------------|--|------------|--|--------|-------|--------|-------|---------------------|---------------------|--------------------------------------------------------|--|--|--|--|--|--|--|--|--|-------------|----|-----|----|-----|-------|-------------------|--|--|--|----------------|----|----|----|----|------|-------------------|--|--|--|----------------|---|----|---|----|------|-------------------|--|--|--|-------------------|--|-----|--|-----|-------|-------------------|--|--|--|--------------|----|--|----|--|--|--|--|--|--|---------------------------------------------------------------------|--|--|--|--|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|--|--|--|--|--------------------------------------------|--|--|--|--|--|--|--|--|--|----------------------|-----|-----|----|-----|-------|-------------------|--|--|--|-----------------|----|----|----|----|-------|-------------------|--|--|--|-------------------|--|-----|--|-----|-------|-------------------|--|--|--|--------------|-----|--|-----|--|--|--|--|--|--|----------------------------------------------------------------------|--|--|--|--|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|--|--|--|--|-----------------------|--|-----|--|-----|--------|-------------------|--|--|--|--------------|-----|--|-----|--|--|--|--|--|--|----------------------------------------------------------------------|--|--|--|--|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|--|--|--|--|---------------------------------------------------------------------------|--|--|--|--|--|--|--|--|--|
| P                                                                         | HER2陰性転移・再発乳癌（女性）                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                           |        | I                                  | カペシタビンを含むレジメン                                                                      |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| C                                                                         | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |        | O                                  | ORR                                                                                |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| 研究デザイン                                                                    | RCT (2nd)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 文献数                                       | 5      | コード                                | Chan S 2009, Pallis AG 2012, Talbot DC 2002, Yamamoto D 2017, Oshaughnessy JA 2002 |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
|                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                           |        |                                    |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| モデル                                                                       | Random Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 方法                                        |        | Mantel-Haenszel method (RevMan5.3) |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| 効果指標                                                                      | Risk Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 統合値                                       |        | 1.17 ( 1.00 - 1.37 ) P= 0.05       |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Forest plot                                                               | <table><thead><tr><th rowspan="2">Study or Subgroup</th><th colspan="2">Cape containing regimens</th><th colspan="2">Other regimens</th><th rowspan="2">Weight</th><th colspan="2">Risk Ratio</th><th colspan="2">Risk Ratio</th></tr><tr><th>Events</th><th>Total</th><th>Events</th><th>Total</th><th>M-H, Random, 95% CI</th><th>M-H, Random, 95% CI</th></tr></thead><tbody><tr><td colspan="10"><b>1.3.1 Cape ± Regimen A vs Regimen B ± Regimen A</b></td></tr><tr><td>Chan S 2009</td><td>48</td><td>152</td><td>49</td><td>153</td><td>19.6%</td><td>0.99 [0.71, 1.37]</td><td></td><td></td><td></td></tr><tr><td>Pallis AG 2012</td><td>18</td><td>74</td><td>21</td><td>74</td><td>7.9%</td><td>0.86 [0.50, 1.47]</td><td></td><td></td><td></td></tr><tr><td>Talbot DC 2002</td><td>8</td><td>22</td><td>5</td><td>19</td><td>2.7%</td><td>1.38 [0.54, 3.51]</td><td></td><td></td><td></td></tr><tr><td>Subtotal (95% CI)</td><td></td><td>248</td><td></td><td>246</td><td>30.2%</td><td>0.98 [0.75, 1.28]</td><td></td><td></td><td></td></tr><tr><td>Total events</td><td>74</td><td></td><td>75</td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td colspan="10">Heterogeneity: Tau² = 0.00; Chi² = 0.76, df = 2 (P = 0.68); I² = 0%</td></tr><tr><td colspan="10">Test for overall effect: Z = 0.15 (P = 0.88)</td></tr><tr><td colspan="10"><b>1.3.2 Cape + Regimen A vs Regimen A</b></td></tr><tr><td>Oshaughnessy JA 2002</td><td>107</td><td>255</td><td>77</td><td>256</td><td>33.8%</td><td>1.40 [1.10, 1.77]</td><td></td><td></td><td></td></tr><tr><td>Yamamoto D 2017</td><td>57</td><td>82</td><td>49</td><td>81</td><td>35.9%</td><td>1.15 [0.92, 1.44]</td><td></td><td></td><td></td></tr><tr><td>Subtotal (95% CI)</td><td></td><td>337</td><td></td><td>337</td><td>69.8%</td><td>1.26 [1.04, 1.54]</td><td></td><td></td><td></td></tr><tr><td>Total events</td><td>164</td><td></td><td>126</td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td colspan="10">Heterogeneity: Tau² = 0.01; Chi² = 1.47, df = 1 (P = 0.23); I² = 32%</td></tr><tr><td colspan="10">Test for overall effect: Z = 2.30 (P = 0.02)</td></tr><tr><td><b>Total (95% CI)</b></td><td></td><td>585</td><td></td><td>583</td><td>100.0%</td><td>1.17 [1.00, 1.37]</td><td></td><td></td><td></td></tr><tr><td>Total events</td><td>238</td><td></td><td>201</td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td colspan="10">Heterogeneity: Tau² = 0.00; Chi² = 4.58, df = 4 (P = 0.33); I² = 13%</td></tr><tr><td colspan="10">Test for overall effect: Z = 1.96 (P = 0.05)</td></tr><tr><td colspan="10">Test for subgroup differences: Chi² = 2.22, df = 1 (P = 0.14), I² = 54.9%</td></tr></tbody></table> |                                           |        |                                    |                                                                                    | Study or Subgroup   | Cape containing regimens |            | Other regimens |            | Weight | Risk Ratio |  | Risk Ratio |  | Events | Total | Events | Total | M-H, Random, 95% CI | M-H, Random, 95% CI | <b>1.3.1 Cape ± Regimen A vs Regimen B ± Regimen A</b> |  |  |  |  |  |  |  |  |  | Chan S 2009 | 48 | 152 | 49 | 153 | 19.6% | 0.99 [0.71, 1.37] |  |  |  | Pallis AG 2012 | 18 | 74 | 21 | 74 | 7.9% | 0.86 [0.50, 1.47] |  |  |  | Talbot DC 2002 | 8 | 22 | 5 | 19 | 2.7% | 1.38 [0.54, 3.51] |  |  |  | Subtotal (95% CI) |  | 248 |  | 246 | 30.2% | 0.98 [0.75, 1.28] |  |  |  | Total events | 74 |  | 75 |  |  |  |  |  |  | Heterogeneity: Tau² = 0.00; Chi² = 0.76, df = 2 (P = 0.68); I² = 0% |  |  |  |  |  |  |  |  |  | Test for overall effect: Z = 0.15 (P = 0.88) |  |  |  |  |  |  |  |  |  | <b>1.3.2 Cape + Regimen A vs Regimen A</b> |  |  |  |  |  |  |  |  |  | Oshaughnessy JA 2002 | 107 | 255 | 77 | 256 | 33.8% | 1.40 [1.10, 1.77] |  |  |  | Yamamoto D 2017 | 57 | 82 | 49 | 81 | 35.9% | 1.15 [0.92, 1.44] |  |  |  | Subtotal (95% CI) |  | 337 |  | 337 | 69.8% | 1.26 [1.04, 1.54] |  |  |  | Total events | 164 |  | 126 |  |  |  |  |  |  | Heterogeneity: Tau² = 0.01; Chi² = 1.47, df = 1 (P = 0.23); I² = 32% |  |  |  |  |  |  |  |  |  | Test for overall effect: Z = 2.30 (P = 0.02) |  |  |  |  |  |  |  |  |  | <b>Total (95% CI)</b> |  | 585 |  | 583 | 100.0% | 1.17 [1.00, 1.37] |  |  |  | Total events | 238 |  | 201 |  |  |  |  |  |  | Heterogeneity: Tau² = 0.00; Chi² = 4.58, df = 4 (P = 0.33); I² = 13% |  |  |  |  |  |  |  |  |  | Test for overall effect: Z = 1.96 (P = 0.05) |  |  |  |  |  |  |  |  |  | Test for subgroup differences: Chi² = 2.22, df = 1 (P = 0.14), I² = 54.9% |  |  |  |  |  |  |  |  |  |
|                                                                           | Study or Subgroup                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Cape containing regimens                  |        | Other regimens                     |                                                                                    |                     | Weight                   | Risk Ratio |                | Risk Ratio |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Events                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Total                                     | Events | Total                              | M-H, Random, 95% CI                                                                | M-H, Random, 95% CI |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| <b>1.3.1 Cape ± Regimen A vs Regimen B ± Regimen A</b>                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                           |        |                                    |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Chan S 2009                                                               | 48                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 152                                       | 49     | 153                                | 19.6%                                                                              | 0.99 [0.71, 1.37]   |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Pallis AG 2012                                                            | 18                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 74                                        | 21     | 74                                 | 7.9%                                                                               | 0.86 [0.50, 1.47]   |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Talbot DC 2002                                                            | 8                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 22                                        | 5      | 19                                 | 2.7%                                                                               | 1.38 [0.54, 3.51]   |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Subtotal (95% CI)                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 248                                       |        | 246                                | 30.2%                                                                              | 0.98 [0.75, 1.28]   |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Total events                                                              | 74                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                           | 75     |                                    |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Heterogeneity: Tau² = 0.00; Chi² = 0.76, df = 2 (P = 0.68); I² = 0%       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                           |        |                                    |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Test for overall effect: Z = 0.15 (P = 0.88)                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                           |        |                                    |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| <b>1.3.2 Cape + Regimen A vs Regimen A</b>                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                           |        |                                    |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Oshaughnessy JA 2002                                                      | 107                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 255                                       | 77     | 256                                | 33.8%                                                                              | 1.40 [1.10, 1.77]   |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Yamamoto D 2017                                                           | 57                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 82                                        | 49     | 81                                 | 35.9%                                                                              | 1.15 [0.92, 1.44]   |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Subtotal (95% CI)                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 337                                       |        | 337                                | 69.8%                                                                              | 1.26 [1.04, 1.54]   |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Total events                                                              | 164                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           | 126    |                                    |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Heterogeneity: Tau² = 0.01; Chi² = 1.47, df = 1 (P = 0.23); I² = 32%      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                           |        |                                    |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Test for overall effect: Z = 2.30 (P = 0.02)                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                           |        |                                    |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| <b>Total (95% CI)</b>                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 585                                       |        | 583                                | 100.0%                                                                             | 1.17 [1.00, 1.37]   |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Total events                                                              | 238                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           | 201    |                                    |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Heterogeneity: Tau² = 0.00; Chi² = 4.58, df = 4 (P = 0.33); I² = 13%      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                           |        |                                    |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Test for overall effect: Z = 1.96 (P = 0.05)                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                           |        |                                    |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Test for subgroup differences: Chi² = 2.22, df = 1 (P = 0.14), I² = 54.9% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                           |        |                                    |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| コメント： Cape群でORRはいい傾向にあるが有意水準には達しない。                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                           |        |                                    |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| Funnel plot                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                           |        |                                    |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
|                                                                           | コメント：                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                           |        |                                    |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| その他の解析                                                                    | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |        |                                    | コメント：                                                                              |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| メタリグレーション                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                           |        |                                    |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |
| 感度分析                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                           |        |                                    |                                                                                    |                     |                          |            |                |            |        |            |  |            |  |        |       |        |       |                     |                     |                                                        |  |  |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |  |  |                |    |    |    |    |      |                   |  |  |  |                |   |    |   |    |      |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |    |  |    |  |  |  |  |  |  |                                                                     |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                            |  |  |  |  |  |  |  |  |  |                      |     |     |    |     |       |                   |  |  |  |                 |    |    |    |    |       |                   |  |  |  |                   |  |     |  |     |       |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                       |  |     |  |     |        |                   |  |  |  |              |     |  |     |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |  |                                                                           |  |  |  |  |  |  |  |  |  |

【4-9 メタアナリシス】

|             |                   |                                           |     |   |                                |       |  |
|-------------|-------------------|-------------------------------------------|-----|---|--------------------------------|-------|--|
| CQ          |                   | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |     |   |                                |       |  |
| P           | HER2陰性転移・再発乳癌(女性) |                                           |     | I | カペシタビンを含むレジメン                  |       |  |
| C           | その他のレジメン          |                                           |     | O | QOL                            |       |  |
| 研究デザイン      |                   | RCT                                       | 文献数 |   | コード                            |       |  |
| モデル         |                   |                                           | 方法  |   |                                |       |  |
| 効果指標        |                   |                                           | 統合値 |   | (            -            ) P= |       |  |
| Forest plot |                   |                                           |     |   |                                |       |  |
|             |                   | コメント:                                     |     |   |                                |       |  |
| Funnel plot |                   |                                           |     |   |                                |       |  |
|             |                   | コメント:                                     |     |   |                                |       |  |
| その他の解析      |                   | 施行せず                                      |     |   |                                | コメント: |  |
| メタリグレーション   |                   |                                           |     |   |                                |       |  |
| 感度分析        |                   |                                           |     |   |                                |       |  |

#### 【4-9 メタアナリシス】

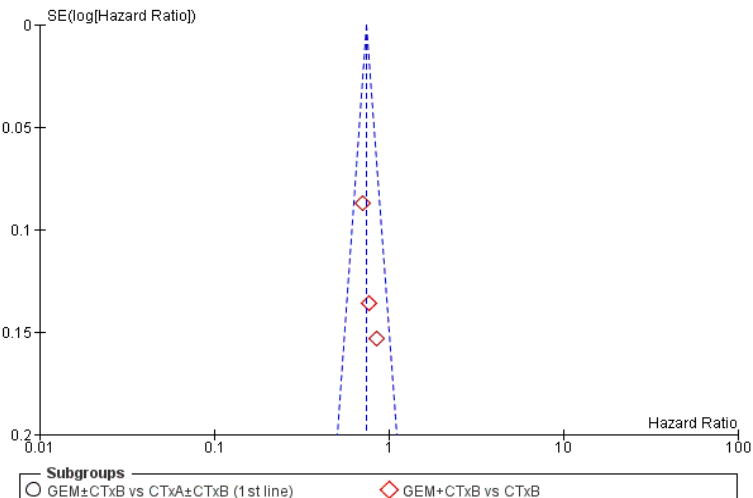
| CQ                                                                                                        |                          | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                |       |                                                                                                                                                           |                   |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
|-----------------------------------------------------------------------------------------------------------|--------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|-----------------------------------|--|----------------|--|--------|-----------------------------------|--------|-------|--------|-------|-----------------|----|----|---|----|-------|-------------------|-------------|----|-----|----|-----|-------|-------------------|------------------|----|-----|----|-----|-------|-------------------|-------------|----|-----|----|-----|-------|-------------------|------------------|---|-----|---|-----|------|-------------------|----------------|---|----|---|----|------|-------------------|--------------------|---|----|---|----|-------|-------------------|----------------|---|----|---|----|------|-------------------|-----------------|----|----|----|----|-------|-------------------|----------------|--|-----|--|-----|--|--------|-------------------|--------------|--|-----|--|-----|--|--|--|-----------------------------------------------------------------------------------------------------------|--|--|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|--|--|
| P                                                                                                         | HER2陰性転移・再発乳癌（女性）        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                | I     | カペシタビンを含むレジメン                                                                                                                                             |                   |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| C                                                                                                         | その他のレジメン                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                | O     | Toxicity(therapy discontinuation)                                                                                                                         |                   |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| 研究デザイン                                                                                                    |                          | RCT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 文献数            | 9     | コード<br>Smorenburg CH 2014, Mavroudis D 2010, Bachelot T 2011, Lam SW 2014, Hatscheck T 2012, Chan S 2009, Pallis AG 2012, Talbot DC 2002, Yamamoto D 2017 |                   |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| モデル                                                                                                       |                          | Random Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 方法             |       | Mantel-Haenszel method (RevMan5.3)                                                                                                                        |                   |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| 効果指標                                                                                                      |                          | Risk Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 統合値            |       | 1.18 ( 0.82 - 1.69 ) P= 0.37                                                                                                                              |                   |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| Forest plot                                                                                               |                          | <table><thead><tr><th rowspan="2">Study or Subgroup</th><th colspan="2">Cape containing regimens</th><th colspan="2">Other regimens</th><th rowspan="2">Weight</th><th rowspan="2">Risk Ratio<br/>M-H, Random, 95% CI</th></tr><tr><th>Events</th><th>Total</th><th>Events</th><th>Total</th></tr></thead><tbody><tr><td>Bachelot T 2011</td><td>13</td><td>33</td><td>6</td><td>35</td><td>10.5%</td><td>2.30 [0.99, 5.34]</td></tr><tr><td>Chan S 2009</td><td>41</td><td>152</td><td>20</td><td>153</td><td>17.2%</td><td>2.06 [1.27, 3.35]</td></tr><tr><td>Hatscheck T 2012</td><td>30</td><td>144</td><td>24</td><td>143</td><td>17.2%</td><td>1.24 [0.76, 2.01]</td></tr><tr><td>Lam SW 2014</td><td>28</td><td>156</td><td>23</td><td>156</td><td>16.8%</td><td>1.22 [0.73, 2.02]</td></tr><tr><td>Mavroudis D 2010</td><td>3</td><td>145</td><td>4</td><td>141</td><td>4.0%</td><td>0.73 [0.17, 3.20]</td></tr><tr><td>Pallis AG 2012</td><td>5</td><td>74</td><td>4</td><td>74</td><td>6.0%</td><td>1.26 [0.35, 4.47]</td></tr><tr><td>Smorenburg CH 2014</td><td>0</td><td>30</td><td>9</td><td>40</td><td>10.5%</td><td>0.94 [0.40, 2.17]</td></tr><tr><td>Talbot DC 2002</td><td>0</td><td>22</td><td>1</td><td>19</td><td>1.2%</td><td>0.28 [0.01, 6.72]</td></tr><tr><td>Yamamoto D 2017</td><td>15</td><td>62</td><td>27</td><td>61</td><td>15.7%</td><td>0.55 [0.32, 0.95]</td></tr><tr><td colspan="2">Total (95% CI)</td><td colspan="2">846</td><td colspan="2">842</td><td>100.0%</td><td>1.18 [0.82, 1.69]</td></tr><tr><td colspan="2">Total events</td><td colspan="2">143</td><td colspan="2">118</td><td colspan="2"></td></tr><tr><td colspan="8">Heterogeneity: Tau<sup>2</sup> = 0.13; Chi<sup>2</sup> = 16.39, df = 8 (P = 0.04); I<sup>2</sup> = 51%</td></tr><tr><td colspan="8">Test for overall effect: Z = 0.89 (P = 0.37)</td></tr></tbody></table> |                |       |                                                                                                                                                           | Study or Subgroup | Cape containing regimens          |  | Other regimens |  | Weight | Risk Ratio<br>M-H, Random, 95% CI | Events | Total | Events | Total | Bachelot T 2011 | 13 | 33 | 6 | 35 | 10.5% | 2.30 [0.99, 5.34] | Chan S 2009 | 41 | 152 | 20 | 153 | 17.2% | 2.06 [1.27, 3.35] | Hatscheck T 2012 | 30 | 144 | 24 | 143 | 17.2% | 1.24 [0.76, 2.01] | Lam SW 2014 | 28 | 156 | 23 | 156 | 16.8% | 1.22 [0.73, 2.02] | Mavroudis D 2010 | 3 | 145 | 4 | 141 | 4.0% | 0.73 [0.17, 3.20] | Pallis AG 2012 | 5 | 74 | 4 | 74 | 6.0% | 1.26 [0.35, 4.47] | Smorenburg CH 2014 | 0 | 30 | 9 | 40 | 10.5% | 0.94 [0.40, 2.17] | Talbot DC 2002 | 0 | 22 | 1 | 19 | 1.2% | 0.28 [0.01, 6.72] | Yamamoto D 2017 | 15 | 62 | 27 | 61 | 15.7% | 0.55 [0.32, 0.95] | Total (95% CI) |  | 846 |  | 842 |  | 100.0% | 1.18 [0.82, 1.69] | Total events |  | 143 |  | 118 |  |  |  | Heterogeneity: Tau <sup>2</sup> = 0.13; Chi <sup>2</sup> = 16.39, df = 8 (P = 0.04); I <sup>2</sup> = 51% |  |  |  |  |  |  |  | Test for overall effect: Z = 0.89 (P = 0.37) |  |  |  |  |  |  |  |
| Study or Subgroup                                                                                         | Cape containing regimens |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Other regimens |       | Weight                                                                                                                                                    |                   | Risk Ratio<br>M-H, Random, 95% CI |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
|                                                                                                           | Events                   | Total                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Events         | Total |                                                                                                                                                           |                   |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| Bachelot T 2011                                                                                           | 13                       | 33                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 6              | 35    | 10.5%                                                                                                                                                     | 2.30 [0.99, 5.34] |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| Chan S 2009                                                                                               | 41                       | 152                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 20             | 153   | 17.2%                                                                                                                                                     | 2.06 [1.27, 3.35] |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| Hatscheck T 2012                                                                                          | 30                       | 144                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 24             | 143   | 17.2%                                                                                                                                                     | 1.24 [0.76, 2.01] |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| Lam SW 2014                                                                                               | 28                       | 156                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 23             | 156   | 16.8%                                                                                                                                                     | 1.22 [0.73, 2.02] |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| Mavroudis D 2010                                                                                          | 3                        | 145                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 4              | 141   | 4.0%                                                                                                                                                      | 0.73 [0.17, 3.20] |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| Pallis AG 2012                                                                                            | 5                        | 74                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 4              | 74    | 6.0%                                                                                                                                                      | 1.26 [0.35, 4.47] |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| Smorenburg CH 2014                                                                                        | 0                        | 30                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 9              | 40    | 10.5%                                                                                                                                                     | 0.94 [0.40, 2.17] |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| Talbot DC 2002                                                                                            | 0                        | 22                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 1              | 19    | 1.2%                                                                                                                                                      | 0.28 [0.01, 6.72] |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| Yamamoto D 2017                                                                                           | 15                       | 62                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 27             | 61    | 15.7%                                                                                                                                                     | 0.55 [0.32, 0.95] |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| Total (95% CI)                                                                                            |                          | 846                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                | 842   |                                                                                                                                                           | 100.0%            | 1.18 [0.82, 1.69]                 |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| Total events                                                                                              |                          | 143                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                | 118   |                                                                                                                                                           |                   |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| Heterogeneity: Tau <sup>2</sup> = 0.13; Chi <sup>2</sup> = 16.39, df = 8 (P = 0.04); I <sup>2</sup> = 51% |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                |       |                                                                                                                                                           |                   |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| Test for overall effect: Z = 0.89 (P = 0.37)                                                              |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                |       |                                                                                                                                                           |                   |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| コメント：                                                                                                     |                          | 有意水準に達しない。異質性あり。                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                |       |                                                                                                                                                           |                   |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| Funnel plot                                                                                               |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                |       |                                                                                                                                                           |                   |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| コメント：                                                                                                     |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                |       |                                                                                                                                                           |                   |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| その他の解析                                                                                                    |                          | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                |       |                                                                                                                                                           |                   |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| メタリグレーション                                                                                                 |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                |       |                                                                                                                                                           |                   |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |
| 感度分析                                                                                                      |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                |       |                                                                                                                                                           |                   |                                   |  |                |  |        |                                   |        |       |        |       |                 |    |    |   |    |       |                   |             |    |     |    |     |       |                   |                  |    |     |    |     |       |                   |             |    |     |    |     |       |                   |                  |   |     |   |     |      |                   |                |   |    |   |    |      |                   |                    |   |    |   |    |       |                   |                |   |    |   |    |      |                   |                 |    |    |    |    |       |                   |                |  |     |  |     |  |        |                   |              |  |     |  |     |  |  |  |                                                                                                           |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |



【4-9 メタアナリシス】

| CQ                                                                                                                                                                                  |                   | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |               |                                   |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|-----------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|-------------------|-------------------|----|--------|-----------------------------------|-----------------------------------|-----------------------------------------------|--|--|--|--|--|--------------|---|---|--|---------------|--|----------------------------------------|---------|--------|------|-------------------|--|--------------------------|--|--|-------------|--------------------------|--|-------------------------------------------------------------------------------|--|--|--|--|--|-------------------------------|--|--|--|--|--|----------------|---------|--------|-------|-------------------|--|-------------------------------------|---------|--------|------|-------------------|--|----------------|--------|-----|-------|-------------------|--|-----------------|---------|--------|-------|-------------------|--|--------------------------|--|--|--------------|--------------------------|--|--------------------------------------------------------------------------------------------------------|--|--|--|--|--|-----------------------|--|--|---------------|--------------------------|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|--|
| P                                                                                                                                                                                   | HER2陰性転移・再発乳癌(女性) |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | I             | ゲムシタピンを含むレジメン                     |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| C                                                                                                                                                                                   | その他のレジメン          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | O             | OS                                |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| 研究デザイン                                                                                                                                                                              |                   | RCT(1st)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 文献数           | 6                                 | コード<br>Feher2005,Joensuu2012,Fountzilias G 2009 (GEM+DTX vs PTX+Cb),Fountzilias G 2009 (GEM+DTX vs PTX),Albain KS 2008,Nielsen DL 2011 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| モデル                                                                                                                                                                                 |                   | Fixed Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 方法            |                                   | Inverse Variance method (RevMan5.3)                                                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| 効果指標                                                                                                                                                                                |                   | Hazard Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 統合値           |                                   | 0.88 ( 0.77 - 1.00 ) P= 0.05                                                                                                           |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| Forest plot                                                                                                                                                                         |                   | <table><thead><tr><th>Study or Subgroup</th><th>log[Hazard Ratio]</th><th>SE</th><th>Weight</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th></tr></thead><tbody><tr><td colspan="6"><b>1.1.1 GEM±CTxB vs CTxA±CTxB (1st line)</b></td></tr><tr><td>Feher O 2005</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Fountzilias G 2009 (GEM+DTX vs PTX+Cb)</td><td>-0.4005</td><td>0.2383</td><td>7.7%</td><td>0.67 [0.42, 1.07]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>7.7%</b></td><td><b>0.67 [0.42, 1.07]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Not applicable<br/>Test for overall effect: Z = 1.68 (P = 0.09)</td></tr><tr><td colspan="6"><b>1.1.2 GEM+CTxB vs CTxB</b></td></tr><tr><td>Albain KS 2008</td><td>-0.1985</td><td>0.1031</td><td>41.0%</td><td>0.82 [0.67, 1.00]</td><td></td></tr><tr><td>Fountzilias G 2009 (GEM+DTX vs PTX)</td><td>-0.0943</td><td>0.2387</td><td>7.6%</td><td>0.91 [0.57, 1.45]</td><td></td></tr><tr><td>Joensuu H 2010</td><td>0.1044</td><td>0.2</td><td>10.9%</td><td>1.11 [0.75, 1.64]</td><td></td></tr><tr><td>Nielsen DL 2011</td><td>-0.0619</td><td>0.1152</td><td>32.8%</td><td>0.94 [0.75, 1.18]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>92.3%</b></td><td><b>0.90 [0.79, 1.03]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 2.06, df = 3 (P = 0.56); I² = 0%<br/>Test for overall effect: Z = 1.54 (P = 0.12)</td></tr><tr><td><b>Total (95% CI)</b></td><td></td><td></td><td><b>100.0%</b></td><td><b>0.88 [0.77, 1.00]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 3.47, df = 4 (P = 0.48); I² = 0%<br/>Test for overall effect: Z = 1.94 (P = 0.05)<br/>Test for subgroup differences: Chi² = 1.41, df = 1 (P = 0.23), I² = 29.3%</td></tr></tbody></table> |               |                                   |                                                                                                                                        | Study or Subgroup | log[Hazard Ratio] | SE | Weight | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI | <b>1.1.1 GEM±CTxB vs CTxA±CTxB (1st line)</b> |  |  |  |  |  | Feher O 2005 | 0 | 0 |  | Not estimable |  | Fountzilias G 2009 (GEM+DTX vs PTX+Cb) | -0.4005 | 0.2383 | 7.7% | 0.67 [0.42, 1.07] |  | <b>Subtotal (95% CI)</b> |  |  | <b>7.7%</b> | <b>0.67 [0.42, 1.07]</b> |  | Heterogeneity: Not applicable<br>Test for overall effect: Z = 1.68 (P = 0.09) |  |  |  |  |  | <b>1.1.2 GEM+CTxB vs CTxB</b> |  |  |  |  |  | Albain KS 2008 | -0.1985 | 0.1031 | 41.0% | 0.82 [0.67, 1.00] |  | Fountzilias G 2009 (GEM+DTX vs PTX) | -0.0943 | 0.2387 | 7.6% | 0.91 [0.57, 1.45] |  | Joensuu H 2010 | 0.1044 | 0.2 | 10.9% | 1.11 [0.75, 1.64] |  | Nielsen DL 2011 | -0.0619 | 0.1152 | 32.8% | 0.94 [0.75, 1.18] |  | <b>Subtotal (95% CI)</b> |  |  | <b>92.3%</b> | <b>0.90 [0.79, 1.03]</b> |  | Heterogeneity: Chi² = 2.06, df = 3 (P = 0.56); I² = 0%<br>Test for overall effect: Z = 1.54 (P = 0.12) |  |  |  |  |  | <b>Total (95% CI)</b> |  |  | <b>100.0%</b> | <b>0.88 [0.77, 1.00]</b> |  | Heterogeneity: Chi² = 3.47, df = 4 (P = 0.48); I² = 0%<br>Test for overall effect: Z = 1.94 (P = 0.05)<br>Test for subgroup differences: Chi² = 1.41, df = 1 (P = 0.23), I² = 29.3% |  |  |  |  |  |
| Study or Subgroup                                                                                                                                                                   | log[Hazard Ratio] | SE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Weight        | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI                                                                                                      |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| <b>1.1.1 GEM±CTxB vs CTxA±CTxB (1st line)</b>                                                                                                                                       |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |               |                                   |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| Feher O 2005                                                                                                                                                                        | 0                 | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |               | Not estimable                     |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| Fountzilias G 2009 (GEM+DTX vs PTX+Cb)                                                                                                                                              | -0.4005           | 0.2383                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 7.7%          | 0.67 [0.42, 1.07]                 |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                                                                                                                                            |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | <b>7.7%</b>   | <b>0.67 [0.42, 1.07]</b>          |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| Heterogeneity: Not applicable<br>Test for overall effect: Z = 1.68 (P = 0.09)                                                                                                       |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |               |                                   |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| <b>1.1.2 GEM+CTxB vs CTxB</b>                                                                                                                                                       |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |               |                                   |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| Albain KS 2008                                                                                                                                                                      | -0.1985           | 0.1031                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 41.0%         | 0.82 [0.67, 1.00]                 |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| Fountzilias G 2009 (GEM+DTX vs PTX)                                                                                                                                                 | -0.0943           | 0.2387                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 7.6%          | 0.91 [0.57, 1.45]                 |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| Joensuu H 2010                                                                                                                                                                      | 0.1044            | 0.2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 10.9%         | 1.11 [0.75, 1.64]                 |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| Nielsen DL 2011                                                                                                                                                                     | -0.0619           | 0.1152                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 32.8%         | 0.94 [0.75, 1.18]                 |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                                                                                                                                            |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | <b>92.3%</b>  | <b>0.90 [0.79, 1.03]</b>          |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| Heterogeneity: Chi² = 2.06, df = 3 (P = 0.56); I² = 0%<br>Test for overall effect: Z = 1.54 (P = 0.12)                                                                              |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |               |                                   |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| <b>Total (95% CI)</b>                                                                                                                                                               |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | <b>100.0%</b> | <b>0.88 [0.77, 1.00]</b>          |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| Heterogeneity: Chi² = 3.47, df = 4 (P = 0.48); I² = 0%<br>Test for overall effect: Z = 1.94 (P = 0.05)<br>Test for subgroup differences: Chi² = 1.41, df = 1 (P = 0.23), I² = 29.3% |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |               |                                   |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
|                                                                                                                                                                                     |                   | コメント: 有意水準に達しない                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |               |                                   |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| Funnel plot                                                                                                                                                                         |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |               |                                   |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
|                                                                                                                                                                                     |                   | コメント:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |               |                                   |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| その他の解析                                                                                                                                                                              |                   | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |               |                                   |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| メタリグレーション                                                                                                                                                                           |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |               |                                   |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |
| 感度分析                                                                                                                                                                                |                   | コメント:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |               |                                   |                                                                                                                                        |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |         |        |      |                   |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |         |        |      |                   |  |                |        |     |       |                   |  |                 |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                        |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                     |  |  |  |  |  |

【4-9 メタアナリシス】

| CQ                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |               |                                     |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|---------------|-------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|-------------------|-------------------|----|--------|-----------------------------------|-----------------------------------|-----------------------------------------------|--|--|--|--|--|--------------|---|---|--|---------------|--|----------------------------------------|---|---|--|---------------|--|--------------------------|--|--|--|----------------------|--|--------------------------------------------------------------------------|--|--|--|--|--|-------------------------------|--|--|--|--|--|----------------|---------|--------|-------|-------------------|--|-------------------------------------|---|---|--|---------------|--|----------------|---------|--------|-------|-------------------|--|-----------------|---------|--------|-------|-------------------|--|--------------------------|--|--|---------------|--------------------------|--|-----------------------------------------------------------------------------------------------------------|--|--|--|--|--|-----------------------|--|--|---------------|--------------------------|--|------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|--|
| P                                                                                                                                                          | HER2陰性転移・再発乳癌（女性）                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                           | I             | ゲムシタビンを含むレジメン                       |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| C                                                                                                                                                          | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                           | O             | PFS                                 |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| 研究デザイン                                                                                                                                                     | RCT(1st)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 文献数                                       | 6             | コード                                 | Feher2005,Joensuu2012,Fountzilias G 2009 (GEM+DTX vs PTX+Cb),Fountzilias G 2009 (GEM+DTX vs PTX),Albain KS 2008,Nielsen DL 2011 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| モデル                                                                                                                                                        | Fixed Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                           | 方法            | Inverse Variance method (RevMan5.3) |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| 効果指標                                                                                                                                                       | Hazard Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                           | 統合値           | 0.74 ( 0.65 – 0.85 ) P< 0.00001     |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| Forest plot                                                                                                                                                | <table><thead><tr><th>Study or Subgroup</th><th>log[Hazard Ratio]</th><th>SE</th><th>Weight</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th></tr></thead><tbody><tr><td colspan="6"><b>1.2.1 GEM±CTxB vs CTxA±CTxB (1st line)</b></td></tr><tr><td>Feher O 2005</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Fountzilias G 2009 (GEM+DTX vs PTX+Cb)</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td></td><td><b>Not estimable</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Not applicable<br/>Test for overall effect: Not applicable</td></tr><tr><td colspan="6"><b>1.2.2 GEM+CTxB vs CTxB</b></td></tr><tr><td>Albain KS 2008</td><td>-0.3567</td><td>0.0872</td><td>57.6%</td><td>0.70 [0.59, 0.83]</td><td></td></tr><tr><td>Fountzilias G 2009 (GEM+DTX vs PTX)</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Joensuu H 2010</td><td>-0.1625</td><td>0.1528</td><td>18.7%</td><td>0.85 [0.63, 1.15]</td><td></td></tr><tr><td>Nielsen DL 2011</td><td>-0.2614</td><td>0.1359</td><td>23.7%</td><td>0.77 [0.59, 1.00]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>100.0%</b></td><td><b>0.74 [0.65, 0.85]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 1.31, df = 2 (P = 0.52); I² = 0%<br/>Test for overall effect: Z = 4.50 (P &lt; 0.00001)</td></tr><tr><td><b>Total (95% CI)</b></td><td></td><td></td><td><b>100.0%</b></td><td><b>0.74 [0.65, 0.85]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 1.31, df = 2 (P = 0.52); I² = 0%<br/>Test for overall effect: Z = 4.50 (P &lt; 0.00001)<br/>Test for subgroup differences: Not applicable</td></tr></tbody></table> <p>コメント： ゲムシタビンを上乗せすることでPFSを有意に延長する</p> |                                           |               |                                     |                                                                                                                                 | Study or Subgroup | log[Hazard Ratio] | SE | Weight | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI | <b>1.2.1 GEM±CTxB vs CTxA±CTxB (1st line)</b> |  |  |  |  |  | Feher O 2005 | 0 | 0 |  | Not estimable |  | Fountzilias G 2009 (GEM+DTX vs PTX+Cb) | 0 | 0 |  | Not estimable |  | <b>Subtotal (95% CI)</b> |  |  |  | <b>Not estimable</b> |  | Heterogeneity: Not applicable<br>Test for overall effect: Not applicable |  |  |  |  |  | <b>1.2.2 GEM+CTxB vs CTxB</b> |  |  |  |  |  | Albain KS 2008 | -0.3567 | 0.0872 | 57.6% | 0.70 [0.59, 0.83] |  | Fountzilias G 2009 (GEM+DTX vs PTX) | 0 | 0 |  | Not estimable |  | Joensuu H 2010 | -0.1625 | 0.1528 | 18.7% | 0.85 [0.63, 1.15] |  | Nielsen DL 2011 | -0.2614 | 0.1359 | 23.7% | 0.77 [0.59, 1.00] |  | <b>Subtotal (95% CI)</b> |  |  | <b>100.0%</b> | <b>0.74 [0.65, 0.85]</b> |  | Heterogeneity: Chi² = 1.31, df = 2 (P = 0.52); I² = 0%<br>Test for overall effect: Z = 4.50 (P < 0.00001) |  |  |  |  |  | <b>Total (95% CI)</b> |  |  | <b>100.0%</b> | <b>0.74 [0.65, 0.85]</b> |  | Heterogeneity: Chi² = 1.31, df = 2 (P = 0.52); I² = 0%<br>Test for overall effect: Z = 4.50 (P < 0.00001)<br>Test for subgroup differences: Not applicable |  |  |  |  |  |
| Study or Subgroup                                                                                                                                          | log[Hazard Ratio]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | SE                                        | Weight        | Hazard Ratio<br>IV, Fixed, 95% CI   | Hazard Ratio<br>IV, Fixed, 95% CI                                                                                               |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| <b>1.2.1 GEM±CTxB vs CTxA±CTxB (1st line)</b>                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |               |                                     |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| Feher O 2005                                                                                                                                               | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0                                         |               | Not estimable                       |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| Fountzilias G 2009 (GEM+DTX vs PTX+Cb)                                                                                                                     | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0                                         |               | Not estimable                       |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |               | <b>Not estimable</b>                |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| Heterogeneity: Not applicable<br>Test for overall effect: Not applicable                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |               |                                     |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| <b>1.2.2 GEM+CTxB vs CTxB</b>                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |               |                                     |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| Albain KS 2008                                                                                                                                             | -0.3567                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 0.0872                                    | 57.6%         | 0.70 [0.59, 0.83]                   |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| Fountzilias G 2009 (GEM+DTX vs PTX)                                                                                                                        | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0                                         |               | Not estimable                       |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| Joensuu H 2010                                                                                                                                             | -0.1625                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 0.1528                                    | 18.7%         | 0.85 [0.63, 1.15]                   |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| Nielsen DL 2011                                                                                                                                            | -0.2614                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 0.1359                                    | 23.7%         | 0.77 [0.59, 1.00]                   |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           | <b>100.0%</b> | <b>0.74 [0.65, 0.85]</b>            |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| Heterogeneity: Chi² = 1.31, df = 2 (P = 0.52); I² = 0%<br>Test for overall effect: Z = 4.50 (P < 0.00001)                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |               |                                     |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| <b>Total (95% CI)</b>                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           | <b>100.0%</b> | <b>0.74 [0.65, 0.85]</b>            |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| Heterogeneity: Chi² = 1.31, df = 2 (P = 0.52); I² = 0%<br>Test for overall effect: Z = 4.50 (P < 0.00001)<br>Test for subgroup differences: Not applicable |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |               |                                     |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| Funnel plot                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                           |               |                                     |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| その他の解析                                                                                                                                                     | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                           |               |                                     |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| メタリグレーション                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |               |                                     |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |
| 感度分析                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |               |                                     |                                                                                                                                 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |              |   |   |  |               |  |                                        |   |   |  |               |  |                          |  |  |  |                      |  |                                                                          |  |  |  |  |  |                               |  |  |  |  |  |                |         |        |       |                   |  |                                     |   |   |  |               |  |                |         |        |       |                   |  |                 |         |        |       |                   |  |                          |  |  |               |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                            |  |  |  |  |  |

【4-9 メタアナリシス】

| CQ                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |        |                                    |                                                                                                                               |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|--------|------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|--------------------------|-------------------------|-----------------------------------|-----------------------------------|--|--------|-----------------------------------|-----------------------------------|--------|-------|--------|-------|-----------------------------------------------|--|--|--|--|--|--|--|--------------|----|-----|----|-----|-------|-------------------|--|---------------------------------------|----|-----|----|-----|-------|-------------------|-------------------|--|-----|--|-----|-------|-------------------|--------------|----|--|-----|--|--|--|--------------------------------------------------------------------------------------------------------------------------|--|--|--|--|--|--|-------------------------------|--|--|--|--|--|--|--|----------------|-----|-----|----|-----|-------|-------------------|--|------------------------------------|----|-----|----|-----|-------|-------------------|----------------|----|-----|----|-----|-------|-------------------|-----------------|----|-----|----|-----|-------|-------------------|-------------------|--|-----|--|-----|-------|-------------------|--------------|-----|--|-----|--|--|--|----------------------------------------------------------------------------------------------------------------------|--|--|--|--|--|--|-----------------------|--|------------|--|------------|---------------|--------------------------|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|--|--|
| P                                                                                                                                                                                                                          | HER2陰性転移・再発乳癌（女性）                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                           |        | I                                  | ゲムシタビンを含むレジメン                                                                                                                 |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| C                                                                                                                                                                                                                          | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |        | O                                  | ORR                                                                                                                           |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| 研究デザイン                                                                                                                                                                                                                     | RCT(1st)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 文献数                                       | 6      | コード                                | Feher2005,Joensuu2012,Fountzilas G 2009 (GEM+DTX vs PTX+Cb),Fountzilas G 2009 (GEM+DTX vs PTX),Albain KS 2008,Nielsen DL 2011 |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
|                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |        |                                    |                                                                                                                               |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| モデル                                                                                                                                                                                                                        | Random Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 方法                                        |        | Mantel-Haenszel method (RevMan5.3) |                                                                                                                               |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| 効果指標                                                                                                                                                                                                                       | Risk Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 統合値                                       |        | 0.99 ( 0.73 – 1.34 ) P= 0.38       |                                                                                                                               |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| Forest plot                                                                                                                                                                                                                | <table><thead><tr><th rowspan="2">Study or Subgroup</th><th colspan="2">GEM containing regimens</th><th colspan="2">Other regimens</th><th rowspan="2">Weight</th><th rowspan="2">Risk Ratio<br/>M-H, Random, 95% CI</th><th rowspan="2">Risk Ratio<br/>M-H, Random, 95% CI</th></tr><tr><th>Events</th><th>Total</th><th>Events</th><th>Total</th></tr></thead><tbody><tr><td colspan="8"><b>1.3.1 GEM±CTxB vs CTxA±CTxB (1st line)</b></td></tr><tr><td>Feher O 2005</td><td>30</td><td>183</td><td>75</td><td>186</td><td>15.2%</td><td>0.41 [0.28, 0.59]</td><td rowspan="6"></td></tr><tr><td>Fountzilas G 2009 (GEM+DTX vs PTX+Cb)</td><td>66</td><td>144</td><td>52</td><td>136</td><td>16.8%</td><td>1.20 [0.91, 1.58]</td></tr><tr><td>Subtotal (95% CI)</td><td></td><td>327</td><td></td><td>322</td><td>32.0%</td><td>0.70 [0.24, 2.07]</td></tr><tr><td>Total events</td><td>96</td><td></td><td>127</td><td></td><td></td><td></td></tr><tr><td colspan="7">Heterogeneity: Tau² = 0.58; Chi² = 21.64, df = 1 (P &lt; 0.00001); I² = 95%<br/>Test for overall effect: Z = 0.64 (P = 0.52)</td></tr><tr><td colspan="8"><b>1.3.2 GEM+CTxB vs CTxB</b></td></tr><tr><td>Albain KS 2008</td><td>110</td><td>266</td><td>69</td><td>263</td><td>17.3%</td><td>1.58 [1.23, 2.02]</td><td rowspan="6"></td></tr><tr><td>Fountzilas G 2009 (GEM+DTX vs PTX)</td><td>66</td><td>144</td><td>67</td><td>136</td><td>17.3%</td><td>0.93 [0.73, 1.19]</td></tr><tr><td>Joensuu H 2010</td><td>75</td><td>115</td><td>71</td><td>122</td><td>18.0%</td><td>1.12 [0.92, 1.37]</td></tr><tr><td>Nielsen DL 2011</td><td>41</td><td>114</td><td>36</td><td>106</td><td>15.3%</td><td>1.06 [0.74, 1.52]</td></tr><tr><td>Subtotal (95% CI)</td><td></td><td>639</td><td></td><td>627</td><td>68.0%</td><td>1.15 [0.92, 1.45]</td></tr><tr><td>Total events</td><td>292</td><td></td><td>243</td><td></td><td></td><td></td></tr><tr><td colspan="7">Heterogeneity: Tau² = 0.04; Chi² = 9.48, df = 3 (P = 0.02); I² = 68%<br/>Test for overall effect: Z = 1.23 (P = 0.22)</td></tr><tr><td><b>Total (95% CI)</b></td><td></td><td><b>966</b></td><td></td><td><b>949</b></td><td><b>100.0%</b></td><td><b>0.99 [0.73, 1.34]</b></td><td></td></tr><tr><td colspan="7">Total events 388 370<br/>Heterogeneity: Tau² = 0.12; Chi² = 37.87, df = 5 (P &lt; 0.00001); I² = 87%<br/>Test for overall effect: Z = 0.07 (P = 0.95)<br/>Test for subgroup differences: Chi² = 0.78, df = 1 (P = 0.38), I² = 0%</td></tr></tbody></table> |                                           |        |                                    |                                                                                                                               | Study or Subgroup        | GEM containing regimens |                                   | Other regimens                    |  | Weight | Risk Ratio<br>M-H, Random, 95% CI | Risk Ratio<br>M-H, Random, 95% CI | Events | Total | Events | Total | <b>1.3.1 GEM±CTxB vs CTxA±CTxB (1st line)</b> |  |  |  |  |  |  |  | Feher O 2005 | 30 | 183 | 75 | 186 | 15.2% | 0.41 [0.28, 0.59] |  | Fountzilas G 2009 (GEM+DTX vs PTX+Cb) | 66 | 144 | 52 | 136 | 16.8% | 1.20 [0.91, 1.58] | Subtotal (95% CI) |  | 327 |  | 322 | 32.0% | 0.70 [0.24, 2.07] | Total events | 96 |  | 127 |  |  |  | Heterogeneity: Tau² = 0.58; Chi² = 21.64, df = 1 (P < 0.00001); I² = 95%<br>Test for overall effect: Z = 0.64 (P = 0.52) |  |  |  |  |  |  | <b>1.3.2 GEM+CTxB vs CTxB</b> |  |  |  |  |  |  |  | Albain KS 2008 | 110 | 266 | 69 | 263 | 17.3% | 1.58 [1.23, 2.02] |  | Fountzilas G 2009 (GEM+DTX vs PTX) | 66 | 144 | 67 | 136 | 17.3% | 0.93 [0.73, 1.19] | Joensuu H 2010 | 75 | 115 | 71 | 122 | 18.0% | 1.12 [0.92, 1.37] | Nielsen DL 2011 | 41 | 114 | 36 | 106 | 15.3% | 1.06 [0.74, 1.52] | Subtotal (95% CI) |  | 639 |  | 627 | 68.0% | 1.15 [0.92, 1.45] | Total events | 292 |  | 243 |  |  |  | Heterogeneity: Tau² = 0.04; Chi² = 9.48, df = 3 (P = 0.02); I² = 68%<br>Test for overall effect: Z = 1.23 (P = 0.22) |  |  |  |  |  |  | <b>Total (95% CI)</b> |  | <b>966</b> |  | <b>949</b> | <b>100.0%</b> | <b>0.99 [0.73, 1.34]</b> |  | Total events 388 370<br>Heterogeneity: Tau² = 0.12; Chi² = 37.87, df = 5 (P < 0.00001); I² = 87%<br>Test for overall effect: Z = 0.07 (P = 0.95)<br>Test for subgroup differences: Chi² = 0.78, df = 1 (P = 0.38), I² = 0% |  |  |  |  |  |  |
|                                                                                                                                                                                                                            | Study or Subgroup                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | GEM containing regimens                   |        | Other regimens                     |                                                                                                                               |                          | Weight                  | Risk Ratio<br>M-H, Random, 95% CI | Risk Ratio<br>M-H, Random, 95% CI |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| Events                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Total                                     | Events | Total                              |                                                                                                                               |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| <b>1.3.1 GEM±CTxB vs CTxA±CTxB (1st line)</b>                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |        |                                    |                                                                                                                               |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| Feher O 2005                                                                                                                                                                                                               | 30                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 183                                       | 75     | 186                                | 15.2%                                                                                                                         | 0.41 [0.28, 0.59]        |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| Fountzilas G 2009 (GEM+DTX vs PTX+Cb)                                                                                                                                                                                      | 66                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 144                                       | 52     | 136                                | 16.8%                                                                                                                         | 1.20 [0.91, 1.58]        |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| Subtotal (95% CI)                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 327                                       |        | 322                                | 32.0%                                                                                                                         | 0.70 [0.24, 2.07]        |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| Total events                                                                                                                                                                                                               | 96                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                           | 127    |                                    |                                                                                                                               |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| Heterogeneity: Tau² = 0.58; Chi² = 21.64, df = 1 (P < 0.00001); I² = 95%<br>Test for overall effect: Z = 0.64 (P = 0.52)                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |        |                                    |                                                                                                                               |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| <b>1.3.2 GEM+CTxB vs CTxB</b>                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |        |                                    |                                                                                                                               |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| Albain KS 2008                                                                                                                                                                                                             | 110                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 266                                       | 69     | 263                                | 17.3%                                                                                                                         | 1.58 [1.23, 2.02]        |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| Fountzilas G 2009 (GEM+DTX vs PTX)                                                                                                                                                                                         | 66                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 144                                       | 67     | 136                                | 17.3%                                                                                                                         | 0.93 [0.73, 1.19]        |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| Joensuu H 2010                                                                                                                                                                                                             | 75                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 115                                       | 71     | 122                                | 18.0%                                                                                                                         | 1.12 [0.92, 1.37]        |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| Nielsen DL 2011                                                                                                                                                                                                            | 41                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 114                                       | 36     | 106                                | 15.3%                                                                                                                         | 1.06 [0.74, 1.52]        |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| Subtotal (95% CI)                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 639                                       |        | 627                                | 68.0%                                                                                                                         | 1.15 [0.92, 1.45]        |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| Total events                                                                                                                                                                                                               | 292                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                           | 243    |                                    |                                                                                                                               |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| Heterogeneity: Tau² = 0.04; Chi² = 9.48, df = 3 (P = 0.02); I² = 68%<br>Test for overall effect: Z = 1.23 (P = 0.22)                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |        |                                    |                                                                                                                               |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| <b>Total (95% CI)</b>                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | <b>966</b>                                |        | <b>949</b>                         | <b>100.0%</b>                                                                                                                 | <b>0.99 [0.73, 1.34]</b> |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| Total events 388 370<br>Heterogeneity: Tau² = 0.12; Chi² = 37.87, df = 5 (P < 0.00001); I² = 87%<br>Test for overall effect: Z = 0.07 (P = 0.95)<br>Test for subgroup differences: Chi² = 0.78, df = 1 (P = 0.38), I² = 0% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |        |                                    |                                                                                                                               |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| コメント： 有意水準に達しない                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |        |                                    |                                                                                                                               |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| Funnel plot                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |        |                                    |                                                                                                                               |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
|                                                                                                                                                                                                                            | コメント：                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |        |                                    |                                                                                                                               |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| その他の解析                                                                                                                                                                                                                     | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |        |                                    |                                                                                                                               |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| メタリグレッション                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |        |                                    |                                                                                                                               |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |
| 感度分析                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |        |                                    |                                                                                                                               |                          |                         |                                   |                                   |  |        |                                   |                                   |        |       |        |       |                                               |  |  |  |  |  |  |  |              |    |     |    |     |       |                   |  |                                       |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |    |  |     |  |  |  |                                                                                                                          |  |  |  |  |  |  |                               |  |  |  |  |  |  |  |                |     |     |    |     |       |                   |  |                                    |    |     |    |     |       |                   |                |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                                      |  |  |  |  |  |  |                       |  |            |  |            |               |                          |  |                                                                                                                                                                                                                            |  |  |  |  |  |  |

【4-9 メタアナリシス】

| CQ                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |               |                                     |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
|--------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|---------------|-------------------------------------|--------------------------------------------------------------------|-------------------|-------------------|----|--------|-----------------------------------|-----------------------------------|-----------------------------------------------|--|--|--|--|--|-------------|---|---|--|---------------|--|--------------------------|--|--|--|----------------------|--|-------------------------------|--|--|--|--|--|-----------------------------------------|--|--|--|--|--|------------------------------------------|--|--|--|--|--|---------------|--------|--------|-------|-------------------|--|-----------------|---------|--------|-------|-------------------|--|-----------------------|---|---|--|---------------|--|--------------------------|--|--|---------------|--------------------------|--|--------------------------------------------------------|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|-----------------------|--|--|---------------|--------------------------|--|--------------------------------------------------------|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|-----------------------------------------------|--|--|--|--|--|
| P                                                      | HER2陰性転移・再発乳癌(女性)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                           | I             | ゲムシタビンを含むレジメン                       |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| C                                                      | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           | O             | OS                                  |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| 研究デザイン                                                 | RCT(2nd)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 文献数                                       | 4             | コード                                 | Chan S 2009, Nielsen DL 2011, Papadimitriou CA 2009, Martin M 2007 |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| モデル                                                    | Fixed Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 方法                                        |               | Inverse Variance method (RevMan5.3) |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| 効果指標                                                   | Hazard Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 統合値                                       |               | 0.98 ( 0.82 – 1.17 ) P= 0.80        |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Forest plot                                            | <table><thead><tr><th>Study or Subgroup</th><th>log[Hazard Ratio]</th><th>SE</th><th>Weight</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th></tr></thead><tbody><tr><td colspan="6"><b>2.1.1 GEM±CTxB vs CTxA±CTxB (2nd line)</b></td></tr><tr><td>Chan S 2009</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td></td><td><b>Not estimable</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Not applicable</td></tr><tr><td colspan="6">Test for overall effect: Not applicable</td></tr><tr><td colspan="6"><b>2.1.2 GEM+CTxB vs CTxB (2nd line)</b></td></tr><tr><td>Martin M 2007</td><td>0.0392</td><td>0.1468</td><td>38.1%</td><td>1.04 [0.78, 1.39]</td><td></td></tr><tr><td>Nielsen DL 2011</td><td>-0.0619</td><td>0.1152</td><td>61.9%</td><td>0.94 [0.75, 1.18]</td><td></td></tr><tr><td>Papadimitriou CA 2009</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>100.0%</b></td><td><b>0.98 [0.82, 1.17]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 0.29, df = 1 (P = 0.59); I² = 0%</td></tr><tr><td colspan="6">Test for overall effect: Z = 0.26 (P = 0.80)</td></tr><tr><td><b>Total (95% CI)</b></td><td></td><td></td><td><b>100.0%</b></td><td><b>0.98 [0.82, 1.17]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 0.29, df = 1 (P = 0.59); I² = 0%</td></tr><tr><td colspan="6">Test for overall effect: Z = 0.26 (P = 0.80)</td></tr><tr><td colspan="6">Test for subgroup differences: Not applicable</td></tr></tbody></table> |                                           |               |                                     |                                                                    | Study or Subgroup | log[Hazard Ratio] | SE | Weight | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI | <b>2.1.1 GEM±CTxB vs CTxA±CTxB (2nd line)</b> |  |  |  |  |  | Chan S 2009 | 0 | 0 |  | Not estimable |  | <b>Subtotal (95% CI)</b> |  |  |  | <b>Not estimable</b> |  | Heterogeneity: Not applicable |  |  |  |  |  | Test for overall effect: Not applicable |  |  |  |  |  | <b>2.1.2 GEM+CTxB vs CTxB (2nd line)</b> |  |  |  |  |  | Martin M 2007 | 0.0392 | 0.1468 | 38.1% | 1.04 [0.78, 1.39] |  | Nielsen DL 2011 | -0.0619 | 0.1152 | 61.9% | 0.94 [0.75, 1.18] |  | Papadimitriou CA 2009 | 0 | 0 |  | Not estimable |  | <b>Subtotal (95% CI)</b> |  |  | <b>100.0%</b> | <b>0.98 [0.82, 1.17]</b> |  | Heterogeneity: Chi² = 0.29, df = 1 (P = 0.59); I² = 0% |  |  |  |  |  | Test for overall effect: Z = 0.26 (P = 0.80) |  |  |  |  |  | <b>Total (95% CI)</b> |  |  | <b>100.0%</b> | <b>0.98 [0.82, 1.17]</b> |  | Heterogeneity: Chi² = 0.29, df = 1 (P = 0.59); I² = 0% |  |  |  |  |  | Test for overall effect: Z = 0.26 (P = 0.80) |  |  |  |  |  | Test for subgroup differences: Not applicable |  |  |  |  |  |
| Study or Subgroup                                      | log[Hazard Ratio]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | SE                                        | Weight        | Hazard Ratio<br>IV, Fixed, 95% CI   | Hazard Ratio<br>IV, Fixed, 95% CI                                  |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| <b>2.1.1 GEM±CTxB vs CTxA±CTxB (2nd line)</b>          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |               |                                     |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Chan S 2009                                            | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 0                                         |               | Not estimable                       |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |               | <b>Not estimable</b>                |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Heterogeneity: Not applicable                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |               |                                     |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Test for overall effect: Not applicable                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |               |                                     |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| <b>2.1.2 GEM+CTxB vs CTxB (2nd line)</b>               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |               |                                     |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Martin M 2007                                          | 0.0392                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 0.1468                                    | 38.1%         | 1.04 [0.78, 1.39]                   |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Nielsen DL 2011                                        | -0.0619                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0.1152                                    | 61.9%         | 0.94 [0.75, 1.18]                   |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Papadimitriou CA 2009                                  | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 0                                         |               | Not estimable                       |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           | <b>100.0%</b> | <b>0.98 [0.82, 1.17]</b>            |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Heterogeneity: Chi² = 0.29, df = 1 (P = 0.59); I² = 0% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |               |                                     |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Test for overall effect: Z = 0.26 (P = 0.80)           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |               |                                     |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| <b>Total (95% CI)</b>                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           | <b>100.0%</b> | <b>0.98 [0.82, 1.17]</b>            |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Heterogeneity: Chi² = 0.29, df = 1 (P = 0.59); I² = 0% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |               |                                     |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Test for overall effect: Z = 0.26 (P = 0.80)           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |               |                                     |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Test for subgroup differences: Not applicable          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |               |                                     |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| コメント: 有意水準に達しない                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |               |                                     |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Funnel plot                                            | <br>コメント:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                           |               |                                     |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| その他の解析                                                 | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |               |                                     |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| メタリグレーション                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           |               |                                     |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| 感度分析                                                   | コメント:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |               |                                     |                                                                    |                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |   |   |  |               |  |                          |  |  |  |                      |  |                               |  |  |  |  |  |                                         |  |  |  |  |  |                                          |  |  |  |  |  |               |        |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |

【4-9 メタアナリシス】

| CQ                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |               |                                     |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
|------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|---------------|-------------------------------------|--------------------------------------------------------------------|-----------------------------------|-------------------|----|--------|-----------------------------------|-----------------------------------|-----------------------------------------------|--|--|--|--|--|-------------|--------|--------|-------|-------------------|--|--------------------------|--|--|--------------|--------------------------|--|-------------------------------|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|------------------------------------------|--|--|--|--|--|---------------|---------|--------|-------|-------------------|--|-----------------|---------|--------|-------|-------------------|--|-----------------------|---|---|--|---------------|--|--------------------------|--|--|--------------|--------------------------|--|--------------------------------------------------------|--|--|--|--|--|------------------------------------------------|--|--|--|--|--|-----------------------|--|--|---------------|--------------------------|--|-----------------------------------------------------------|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|------------------------------------------------------------------------------|--|--|--|--|--|
| P                                                                            | HER2陰性転移・再発乳癌(女性)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           | I             | ゲムシタビンを含むレジメン                       |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| C                                                                            | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           | O             | PFS                                 |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| 研究デザイン                                                                       | RCT(2nd)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 文献数                                       | 4             | コード                                 | Chan S 2009, Nielsen DL 2011, Papadimitriou CA 2009, Martin M 2007 |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
|                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                           |               |                                     |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| モデル                                                                          | Fixed Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 方法                                        |               | Inverse Variance method (RevMan5.3) |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| 効果指標                                                                         | Hazard Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 統合値                                       |               | 0.89 ( 0.77 - 1.03 ) P= 0.12        |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| Forest plot                                                                  | <table><thead><tr><th>Study or Subgroup</th><th>log[Hazard Ratio]</th><th>SE</th><th>Weight</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th></tr></thead><tbody><tr><td colspan="6"><b>2.2.1 GEM±CTxB vs CTxA±CTxB (2nd line)</b></td></tr><tr><td>Chan S 2009</td><td>0.1823</td><td>0.1139</td><td>42.6%</td><td>1.20 [0.96, 1.50]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>42.6%</b></td><td><b>1.20 [0.96, 1.50]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Not applicable</td></tr><tr><td colspan="6">Test for overall effect: Z = 1.60 (P = 0.11)</td></tr><tr><td colspan="6"><b>2.2.2 GEM±CTxB vs CTxB (2nd line)</b></td></tr><tr><td>Martin M 2007</td><td>-0.4155</td><td>0.1417</td><td>27.5%</td><td>0.66 [0.50, 0.87]</td><td></td></tr><tr><td>Nielsen DL 2011</td><td>-0.2614</td><td>0.1359</td><td>29.9%</td><td>0.77 [0.59, 1.00]</td><td></td></tr><tr><td>Papadimitriou CA 2009</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>57.4%</b></td><td><b>0.72 [0.59, 0.87]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 0.62, df = 1 (P = 0.43); I² = 0%</td></tr><tr><td colspan="6">Test for overall effect: Z = 3.42 (P = 0.0006)</td></tr><tr><td><b>Total (95% CI)</b></td><td></td><td></td><td><b>100.0%</b></td><td><b>0.89 [0.77, 1.03]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 12.47, df = 2 (P = 0.002); I² = 84%</td></tr><tr><td colspan="6">Test for overall effect: Z = 1.55 (P = 0.12)</td></tr><tr><td colspan="6">Test for subgroup differences: Chi² = 11.85, df = 1 (P = 0.0006), I² = 91.6%</td></tr></tbody></table> |                                           |               |                                     |                                                                    | Study or Subgroup                 | log[Hazard Ratio] | SE | Weight | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI | <b>2.2.1 GEM±CTxB vs CTxA±CTxB (2nd line)</b> |  |  |  |  |  | Chan S 2009 | 0.1823 | 0.1139 | 42.6% | 1.20 [0.96, 1.50] |  | <b>Subtotal (95% CI)</b> |  |  | <b>42.6%</b> | <b>1.20 [0.96, 1.50]</b> |  | Heterogeneity: Not applicable |  |  |  |  |  | Test for overall effect: Z = 1.60 (P = 0.11) |  |  |  |  |  | <b>2.2.2 GEM±CTxB vs CTxB (2nd line)</b> |  |  |  |  |  | Martin M 2007 | -0.4155 | 0.1417 | 27.5% | 0.66 [0.50, 0.87] |  | Nielsen DL 2011 | -0.2614 | 0.1359 | 29.9% | 0.77 [0.59, 1.00] |  | Papadimitriou CA 2009 | 0 | 0 |  | Not estimable |  | <b>Subtotal (95% CI)</b> |  |  | <b>57.4%</b> | <b>0.72 [0.59, 0.87]</b> |  | Heterogeneity: Chi² = 0.62, df = 1 (P = 0.43); I² = 0% |  |  |  |  |  | Test for overall effect: Z = 3.42 (P = 0.0006) |  |  |  |  |  | <b>Total (95% CI)</b> |  |  | <b>100.0%</b> | <b>0.89 [0.77, 1.03]</b> |  | Heterogeneity: Chi² = 12.47, df = 2 (P = 0.002); I² = 84% |  |  |  |  |  | Test for overall effect: Z = 1.55 (P = 0.12) |  |  |  |  |  | Test for subgroup differences: Chi² = 11.85, df = 1 (P = 0.0006), I² = 91.6% |  |  |  |  |  |
|                                                                              | Study or Subgroup                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | log[Hazard Ratio]                         | SE            | Weight                              | Hazard Ratio<br>IV, Fixed, 95% CI                                  | Hazard Ratio<br>IV, Fixed, 95% CI |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| <b>2.2.1 GEM±CTxB vs CTxA±CTxB (2nd line)</b>                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                           |               |                                     |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| Chan S 2009                                                                  | 0.1823                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 0.1139                                    | 42.6%         | 1.20 [0.96, 1.50]                   |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                           | <b>42.6%</b>  | <b>1.20 [0.96, 1.50]</b>            |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| Heterogeneity: Not applicable                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                           |               |                                     |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| Test for overall effect: Z = 1.60 (P = 0.11)                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                           |               |                                     |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| <b>2.2.2 GEM±CTxB vs CTxB (2nd line)</b>                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                           |               |                                     |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| Martin M 2007                                                                | -0.4155                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 0.1417                                    | 27.5%         | 0.66 [0.50, 0.87]                   |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| Nielsen DL 2011                                                              | -0.2614                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 0.1359                                    | 29.9%         | 0.77 [0.59, 1.00]                   |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| Papadimitriou CA 2009                                                        | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 0                                         |               | Not estimable                       |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                           | <b>57.4%</b>  | <b>0.72 [0.59, 0.87]</b>            |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| Heterogeneity: Chi² = 0.62, df = 1 (P = 0.43); I² = 0%                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                           |               |                                     |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| Test for overall effect: Z = 3.42 (P = 0.0006)                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                           |               |                                     |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| <b>Total (95% CI)</b>                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                           | <b>100.0%</b> | <b>0.89 [0.77, 1.03]</b>            |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| Heterogeneity: Chi² = 12.47, df = 2 (P = 0.002); I² = 84%                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                           |               |                                     |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| Test for overall effect: Z = 1.55 (P = 0.12)                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                           |               |                                     |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| Test for subgroup differences: Chi² = 11.85, df = 1 (P = 0.0006), I² = 91.6% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                           |               |                                     |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| コメント: 全体では有意水準に達しない。ゲムシタビンを上乗せする試験ではPFSを延長する。                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                           |               |                                     |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| Funnel plot                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                           |               |                                     |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
|                                                                              | コメント:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                           |               |                                     |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| その他の解析                                                                       | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |               |                                     |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| メタリグレーション                                                                    | コメント:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                           |               |                                     |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |
| 感度分析                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                           |               |                                     |                                                                    |                                   |                   |    |        |                                   |                                   |                                               |  |  |  |  |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                               |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |               |         |        |       |                   |  |                 |         |        |       |                   |  |                       |   |   |  |               |  |                          |  |  |              |                          |  |                                                        |  |  |  |  |  |                                                |  |  |  |  |  |                       |  |  |               |                          |  |                                                           |  |  |  |  |  |                                              |  |  |  |  |  |                                                                              |  |  |  |  |  |

【4-9 メタアナリシス】

| CQ                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |       |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
|------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|-------|------------------------------------|--------------------------------------------------------------------|-------------------|-----------------------------------|-----------------------------------|--------------------------|-------|--------|-----------------------------------|-----------------------------------|----------------------------------------|--|--|--|--|--|--|--|-------------|----|-----|----|-----|-------|-------------------|--|-------------------|--|-----|--|-----|-------|-------------------|--------------|----|--|----|--|--|--|-------------------------------|--|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|--|-----------------------------------|--|--|--|--|--|--|--|---------------|----|-----|----|-----|-------|-------------------|-----------------|----|-----|----|-----|-------|-------------------|-----------------------|----|----|---|----|------|-------------------|-------------------|--|-----|--|-----|-------|-------------------|--------------|----|--|----|--|--|--|---------------------------------------------------------------------|--|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|--|----------------|--|-----|--|-----|--------|-------------------|--------------|-----|--|-----|--|--|--|---------------------------------------------------------------------|--|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|--|------------------------------------------------------------------------|--|--|--|--|--|--|
| P                                                                      | HER2陰性転移・再発乳癌（女性）                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                           |       | I                                  | ゲムシタピンを含むレジメン                                                      |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| C                                                                      | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                           |       | O                                  | ORR                                                                |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| 研究デザイン                                                                 | RCT(2nd)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 文献数                                       | 4     | コード                                | Chan S 2009, Nielsen DL 2011, Papadimitriou CA 2009, Martin M 2007 |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
|                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |       |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| モデル                                                                    | Random Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 方法                                        |       | Mantel-Haenszel method (RevMan5.3) |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| 効果指標                                                                   | Risk Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 統合値                                       |       | 1.14 ( 0.93 – 1.39 ) P= 0.19       |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| Forest plot                                                            | <table><thead><tr><th>Study or Subgroup</th><th>GEM containing regimens<br/>Events</th><th>Total</th><th>Other regimens<br/>Events</th><th>Total</th><th>Weight</th><th>Risk Ratio<br/>M-H, Random, 95% CI</th><th>Risk Ratio<br/>M-H, Random, 95% CI</th></tr></thead><tbody><tr><td colspan="8">2.3.1 GEM±CTxB vs CTxA±CTxB (2nd line)</td></tr><tr><td>Chan S 2009</td><td>49</td><td>153</td><td>48</td><td>152</td><td>36.5%</td><td>1.01 [0.73, 1.41]</td><td rowspan="5"></td></tr><tr><td>Subtotal (95% CI)</td><td></td><td>153</td><td></td><td>152</td><td>36.5%</td><td>1.01 [0.73, 1.41]</td></tr><tr><td>Total events</td><td>49</td><td></td><td>48</td><td></td><td></td><td></td></tr><tr><td colspan="7">Heterogeneity: Not applicable</td></tr><tr><td colspan="7">Test for overall effect: Z = 0.08 (P = 0.93)</td></tr><tr><td colspan="8">2.3.2 GEM+CTxB vs CTxB (2nd line)</td></tr><tr><td>Martin M 2007</td><td>45</td><td>125</td><td>33</td><td>126</td><td>28.1%</td><td>1.37 [0.94, 2.00]</td></tr><tr><td>Nielsen DL 2011</td><td>41</td><td>114</td><td>36</td><td>106</td><td>30.3%</td><td>1.06 [0.74, 1.52]</td></tr><tr><td>Paradimitriou CA 2009</td><td>11</td><td>40</td><td>6</td><td>32</td><td>5.1%</td><td>1.47 [0.61, 3.53]</td></tr><tr><td>Subtotal (95% CI)</td><td></td><td>279</td><td></td><td>264</td><td>63.5%</td><td>1.22 [0.95, 1.57]</td></tr><tr><td>Total events</td><td>97</td><td></td><td>75</td><td></td><td></td><td></td></tr><tr><td colspan="7">Heterogeneity: Tau² = 0.00; Chi² = 1.15, df = 2 (P = 0.56); I² = 0%</td></tr><tr><td colspan="7">Test for overall effect: Z = 1.56 (P = 0.12)</td></tr><tr><td>Total (95% CI)</td><td></td><td>432</td><td></td><td>416</td><td>100.0%</td><td>1.14 [0.93, 1.39]</td></tr><tr><td>Total events</td><td>146</td><td></td><td>123</td><td></td><td></td><td></td></tr><tr><td colspan="7">Heterogeneity: Tau² = 0.00; Chi² = 1.92, df = 3 (P = 0.59); I² = 0%</td></tr><tr><td colspan="7">Test for overall effect: Z = 1.30 (P = 0.19)</td></tr><tr><td colspan="7">Test for subgroup differences: Chi² = 0.77, df = 1 (P = 0.38), I² = 0%</td></tr></tbody></table> |                                           |       |                                    |                                                                    | Study or Subgroup | GEM containing regimens<br>Events | Total                             | Other regimens<br>Events | Total | Weight | Risk Ratio<br>M-H, Random, 95% CI | Risk Ratio<br>M-H, Random, 95% CI | 2.3.1 GEM±CTxB vs CTxA±CTxB (2nd line) |  |  |  |  |  |  |  | Chan S 2009 | 49 | 153 | 48 | 152 | 36.5% | 1.01 [0.73, 1.41] |  | Subtotal (95% CI) |  | 153 |  | 152 | 36.5% | 1.01 [0.73, 1.41] | Total events | 49 |  | 48 |  |  |  | Heterogeneity: Not applicable |  |  |  |  |  |  | Test for overall effect: Z = 0.08 (P = 0.93) |  |  |  |  |  |  | 2.3.2 GEM+CTxB vs CTxB (2nd line) |  |  |  |  |  |  |  | Martin M 2007 | 45 | 125 | 33 | 126 | 28.1% | 1.37 [0.94, 2.00] | Nielsen DL 2011 | 41 | 114 | 36 | 106 | 30.3% | 1.06 [0.74, 1.52] | Paradimitriou CA 2009 | 11 | 40 | 6 | 32 | 5.1% | 1.47 [0.61, 3.53] | Subtotal (95% CI) |  | 279 |  | 264 | 63.5% | 1.22 [0.95, 1.57] | Total events | 97 |  | 75 |  |  |  | Heterogeneity: Tau² = 0.00; Chi² = 1.15, df = 2 (P = 0.56); I² = 0% |  |  |  |  |  |  | Test for overall effect: Z = 1.56 (P = 0.12) |  |  |  |  |  |  | Total (95% CI) |  | 432 |  | 416 | 100.0% | 1.14 [0.93, 1.39] | Total events | 146 |  | 123 |  |  |  | Heterogeneity: Tau² = 0.00; Chi² = 1.92, df = 3 (P = 0.59); I² = 0% |  |  |  |  |  |  | Test for overall effect: Z = 1.30 (P = 0.19) |  |  |  |  |  |  | Test for subgroup differences: Chi² = 0.77, df = 1 (P = 0.38), I² = 0% |  |  |  |  |  |  |
|                                                                        | Study or Subgroup                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | GEM containing regimens<br>Events         | Total | Other regimens<br>Events           | Total                                                              | Weight            | Risk Ratio<br>M-H, Random, 95% CI | Risk Ratio<br>M-H, Random, 95% CI |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| 2.3.1 GEM±CTxB vs CTxA±CTxB (2nd line)                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |       |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| Chan S 2009                                                            | 49                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 153                                       | 48    | 152                                | 36.5%                                                              | 1.01 [0.73, 1.41] |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| Subtotal (95% CI)                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 153                                       |       | 152                                | 36.5%                                                              | 1.01 [0.73, 1.41] |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| Total events                                                           | 49                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                           | 48    |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| Heterogeneity: Not applicable                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |       |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| Test for overall effect: Z = 0.08 (P = 0.93)                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |       |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| 2.3.2 GEM+CTxB vs CTxB (2nd line)                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |       |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| Martin M 2007                                                          | 45                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 125                                       | 33    | 126                                | 28.1%                                                              | 1.37 [0.94, 2.00] |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| Nielsen DL 2011                                                        | 41                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 114                                       | 36    | 106                                | 30.3%                                                              | 1.06 [0.74, 1.52] |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| Paradimitriou CA 2009                                                  | 11                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 40                                        | 6     | 32                                 | 5.1%                                                               | 1.47 [0.61, 3.53] |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| Subtotal (95% CI)                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 279                                       |       | 264                                | 63.5%                                                              | 1.22 [0.95, 1.57] |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| Total events                                                           | 97                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                           | 75    |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| Heterogeneity: Tau² = 0.00; Chi² = 1.15, df = 2 (P = 0.56); I² = 0%    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |       |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| Test for overall effect: Z = 1.56 (P = 0.12)                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |       |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| Total (95% CI)                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 432                                       |       | 416                                | 100.0%                                                             | 1.14 [0.93, 1.39] |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| Total events                                                           | 146                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                           | 123   |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| Heterogeneity: Tau² = 0.00; Chi² = 1.92, df = 3 (P = 0.59); I² = 0%    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |       |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| Test for overall effect: Z = 1.30 (P = 0.19)                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |       |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| Test for subgroup differences: Chi² = 0.77, df = 1 (P = 0.38), I² = 0% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |       |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| コメント： 有意水準に達しない                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |       |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| Funnel plot                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |       |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
|                                                                        | コメント：                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                           |       |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| その他の解析                                                                 | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                           |       |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| メタリグレーション                                                              | コメント：                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                           |       |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |
| 感度分析                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |       |                                    |                                                                    |                   |                                   |                                   |                          |       |        |                                   |                                   |                                        |  |  |  |  |  |  |  |             |    |     |    |     |       |                   |  |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                               |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                   |  |  |  |  |  |  |  |               |    |     |    |     |       |                   |                 |    |     |    |     |       |                   |                       |    |    |   |    |      |                   |                   |  |     |  |     |       |                   |              |    |  |    |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                |  |     |  |     |        |                   |              |     |  |     |  |  |  |                                                                     |  |  |  |  |  |  |                                              |  |  |  |  |  |  |                                                                        |  |  |  |  |  |  |

【4-9 メタアナリシス】

| CQ                                                                                                       |                         | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                |                                    |                                                                                                                                                                                           |                     |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
|----------------------------------------------------------------------------------------------------------|-------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|--------------------------------|--|----------------|--|--------|------------|--|--------|-------|--------|-------|---------------------|--------------------------------|----------------|----|-----|----|-----|-------|-------------------|--|-------------|----|-----|----|-----|-------|-------------------|--------------|----|-----|----|-----|-------|-------------------|-------------------------------------|----|-----|----|-----|-------|-------------------|----------------------------------------|----|-----|---|-----|------|-------------------|----------------|---|---|---|---|--|---------------|---------------|---|-----|---|-----|------|-------------------|-----------------|----|-----|----|-----|-------|-------------------|-----------------------|---|---|---|---|--|---------------|----------------|--|------|--|------|--------|-------------------|---------------------|--|--|--|--|--|--|----------------------------------------------------------------------------------------------------------|--|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|--|
| P                                                                                                        | HER2陰性転移・再発乳癌（女性）       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | I              | ゲムシタピンを含むレジメン                      |                                                                                                                                                                                           |                     |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| C                                                                                                        | その他のレジメン                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | O              | Toxicity (therapy discontinuation) |                                                                                                                                                                                           |                     |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| 研究デザイン                                                                                                   |                         | RCT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 文献数            | 9                                  | コード<br>Feher2005,Joensuu2012,Fountzilias G 2009 (GEM+DTX vs PTX+Cb),Fountzilias G 2009 (GEM+DTX vs PTX),Albain KS 2008,Nielsen DL 2011, Chan S 2009, Papadimitriou CA 2009, Martin M 2007 |                     |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| モデル                                                                                                      |                         | Random Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 方法             |                                    | Mantel-Haenszel method (RevMan5.3)                                                                                                                                                        |                     |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| 効果指標                                                                                                     |                         | Risk Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 統合値            |                                    | 0.77 ( 0.55 – 1.09 ) P= 0.15                                                                                                                                                              |                     |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Forest plot                                                                                              |                         | <table><thead><tr><th rowspan="2">Study or Subgroup</th><th colspan="2">GEM containing regimens</th><th colspan="2">Other regimens</th><th rowspan="2">Weight</th><th colspan="2">Risk Ratio</th></tr><tr><th>Events</th><th>Total</th><th>Events</th><th>Total</th><th>M-H, Random, 95% CI</th><th>Risk Ratio M-H, Random, 95% CI</th></tr></thead><tbody><tr><td>Albain KS 2008</td><td>18</td><td>266</td><td>13</td><td>263</td><td>15.1%</td><td>1.37 [0.68, 2.74]</td><td rowspan="10"></td></tr><tr><td>Chan S 2009</td><td>20</td><td>153</td><td>41</td><td>152</td><td>21.8%</td><td>0.48 [0.30, 0.79]</td></tr><tr><td>Feher O 2005</td><td>12</td><td>198</td><td>17</td><td>199</td><td>14.6%</td><td>0.71 [0.35, 1.45]</td></tr><tr><td>Fountzilias G 2009 (GEM+DTX vs PTX)</td><td>11</td><td>144</td><td>12</td><td>136</td><td>12.9%</td><td>0.87 [0.40, 1.90]</td></tr><tr><td>Fountzilias G 2009 (GEM+DTX vs PTX+Cb)</td><td>11</td><td>144</td><td>6</td><td>136</td><td>9.6%</td><td>1.73 [0.66, 4.55]</td></tr><tr><td>Joensuu H 2010</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td></tr><tr><td>Martin M 2007</td><td>4</td><td>125</td><td>6</td><td>126</td><td>6.4%</td><td>0.67 [0.19, 2.32]</td></tr><tr><td>Nielsen DL 2011</td><td>18</td><td>170</td><td>30</td><td>167</td><td>19.7%</td><td>0.59 [0.34, 1.02]</td></tr><tr><td>Paradimitriou CA 2009</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td></tr><tr><td>Total (95% CI)</td><td></td><td>1200</td><td></td><td>1179</td><td>100.0%</td><td>0.77 [0.55, 1.09]</td></tr><tr><td colspan="7">Total events 94 125</td></tr><tr><td colspan="7">Heterogeneity: Tau<sup>2</sup> = 0.08; Chi<sup>2</sup> = 9.78, df = 6 (P = 0.13); I<sup>2</sup> = 39%</td></tr><tr><td colspan="7">Test for overall effect: Z = 1.46 (P = 0.15)</td></tr></tbody></table> |                |                                    |                                                                                                                                                                                           | Study or Subgroup   | GEM containing regimens        |  | Other regimens |  | Weight | Risk Ratio |  | Events | Total | Events | Total | M-H, Random, 95% CI | Risk Ratio M-H, Random, 95% CI | Albain KS 2008 | 18 | 266 | 13 | 263 | 15.1% | 1.37 [0.68, 2.74] |  | Chan S 2009 | 20 | 153 | 41 | 152 | 21.8% | 0.48 [0.30, 0.79] | Feher O 2005 | 12 | 198 | 17 | 199 | 14.6% | 0.71 [0.35, 1.45] | Fountzilias G 2009 (GEM+DTX vs PTX) | 11 | 144 | 12 | 136 | 12.9% | 0.87 [0.40, 1.90] | Fountzilias G 2009 (GEM+DTX vs PTX+Cb) | 11 | 144 | 6 | 136 | 9.6% | 1.73 [0.66, 4.55] | Joensuu H 2010 | 0 | 0 | 0 | 0 |  | Not estimable | Martin M 2007 | 4 | 125 | 6 | 126 | 6.4% | 0.67 [0.19, 2.32] | Nielsen DL 2011 | 18 | 170 | 30 | 167 | 19.7% | 0.59 [0.34, 1.02] | Paradimitriou CA 2009 | 0 | 0 | 0 | 0 |  | Not estimable | Total (95% CI) |  | 1200 |  | 1179 | 100.0% | 0.77 [0.55, 1.09] | Total events 94 125 |  |  |  |  |  |  | Heterogeneity: Tau <sup>2</sup> = 0.08; Chi <sup>2</sup> = 9.78, df = 6 (P = 0.13); I <sup>2</sup> = 39% |  |  |  |  |  |  | Test for overall effect: Z = 1.46 (P = 0.15) |  |  |  |  |  |  |
| Study or Subgroup                                                                                        | GEM containing regimens |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Other regimens |                                    | Weight                                                                                                                                                                                    |                     | Risk Ratio                     |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
|                                                                                                          | Events                  | Total                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Events         | Total                              |                                                                                                                                                                                           | M-H, Random, 95% CI | Risk Ratio M-H, Random, 95% CI |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Albain KS 2008                                                                                           | 18                      | 266                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 13             | 263                                | 15.1%                                                                                                                                                                                     | 1.37 [0.68, 2.74]   |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Chan S 2009                                                                                              | 20                      | 153                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 41             | 152                                | 21.8%                                                                                                                                                                                     | 0.48 [0.30, 0.79]   |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Feher O 2005                                                                                             | 12                      | 198                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 17             | 199                                | 14.6%                                                                                                                                                                                     | 0.71 [0.35, 1.45]   |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Fountzilias G 2009 (GEM+DTX vs PTX)                                                                      | 11                      | 144                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 12             | 136                                | 12.9%                                                                                                                                                                                     | 0.87 [0.40, 1.90]   |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Fountzilias G 2009 (GEM+DTX vs PTX+Cb)                                                                   | 11                      | 144                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 6              | 136                                | 9.6%                                                                                                                                                                                      | 1.73 [0.66, 4.55]   |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Joensuu H 2010                                                                                           | 0                       | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 0              | 0                                  |                                                                                                                                                                                           | Not estimable       |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Martin M 2007                                                                                            | 4                       | 125                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 6              | 126                                | 6.4%                                                                                                                                                                                      | 0.67 [0.19, 2.32]   |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Nielsen DL 2011                                                                                          | 18                      | 170                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 30             | 167                                | 19.7%                                                                                                                                                                                     | 0.59 [0.34, 1.02]   |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Paradimitriou CA 2009                                                                                    | 0                       | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 0              | 0                                  |                                                                                                                                                                                           | Not estimable       |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Total (95% CI)                                                                                           |                         | 1200                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                | 1179                               | 100.0%                                                                                                                                                                                    | 0.77 [0.55, 1.09]   |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Total events 94 125                                                                                      |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                |                                    |                                                                                                                                                                                           |                     |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Heterogeneity: Tau <sup>2</sup> = 0.08; Chi <sup>2</sup> = 9.78, df = 6 (P = 0.13); I <sup>2</sup> = 39% |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                |                                    |                                                                                                                                                                                           |                     |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Test for overall effect: Z = 1.46 (P = 0.15)                                                             |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                |                                    |                                                                                                                                                                                           |                     |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| コメント:                                                                                                    |                         | 有意水準に達しない                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                |                                    |                                                                                                                                                                                           |                     |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Funnel plot                                                                                              |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                |                                    |                                                                                                                                                                                           |                     |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| コメント:                                                                                                    |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                |                                    |                                                                                                                                                                                           |                     |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| その他の解析                                                                                                   |                         | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                | コメント:                              |                                                                                                                                                                                           |                     |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| メタリグレーション                                                                                                |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                |                                    |                                                                                                                                                                                           |                     |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| 感度分析                                                                                                     |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                |                                    |                                                                                                                                                                                           |                     |                                |  |                |  |        |            |  |        |       |        |       |                     |                                |                |    |     |    |     |       |                   |  |             |    |     |    |     |       |                   |              |    |     |    |     |       |                   |                                     |    |     |    |     |       |                   |                                        |    |     |   |     |      |                   |                |   |   |   |   |  |               |               |   |     |   |     |      |                   |                 |    |     |    |     |       |                   |                       |   |   |   |   |  |               |                |  |      |  |      |        |                   |                     |  |  |  |  |  |  |                                                                                                          |  |  |  |  |  |  |                                              |  |  |  |  |  |  |

【4-9 メタアナリシス】

| CQ                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |               |                                     |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |       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-----------|--------|--------|-------|-------------------|--|--------------------------|--|--|--------------|--------------------------|--|------------------------------------------------------------------------------------|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|-----------------------------|--|--|--|--|--|----------|---------|--------|------|-------------------|--|----------------|---------|--------|------|-------------------|--|-------------|--------|--------|------|-------------------|--|----------|---------|--------|------|-------------------|--|---------|--------|-------|------|-------------------|--|--------------------------|--|--|--------------|--------------------------|--|---------------------------------------------------------------------------------|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|-----------------------|--|--|---------------|--------------------------|--|------------------------------------------------------------------------------------|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|------------------------------------------------------------------------------------------------|--|--|--|--|--|
| P                                                                                              | HER2陰性転移・再発乳癌（女性）                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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            |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |       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| C                                                                                              | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| 研究デザイン                                                                                         | RCT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 文献数                                       | 17            | コード                                 | ECOG E1193 (A), EU-93011, 306 Study Group, AGO, Blohmer, Bonneterre, CECOG BM1, EORTC 10961, Jassem, Lyman, Nabholtz, UKCCCR AB01, ANZ TITG, ECOG E1193 (B), EORTC 10923, JCOG9802, Yardley |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |       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|                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| モデル                                                                                            | Fixed Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                           | 方法            | Inverse Variance method (RevMan5.3) |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |       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                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| 効果指標                                                                                           | Hazard Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                           | 統合値           | 0.94 ( 0.88 - 1.01 ) P= 0.09        |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Forest plot                                                                                    | <table><thead><tr><th>Study or Subgroup</th><th>log[Hazard Ratio]</th><th>SE</th><th>Weight</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th></tr></thead><tbody><tr><td colspan="6"><b>1.1.1 Taxane+CTxA vs CTxA</b></td></tr><tr><td>ECOG E1193 (A)</td><td>-0.0202</td><td>0.123</td><td>8.7%</td><td>0.98 [0.77, 1.25]</td><td></td></tr><tr><td>EU-93011</td><td>-0.0202</td><td>0.1717</td><td>4.4%</td><td>0.98 [0.70, 1.37]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>13.1%</b></td><td><b>0.98 [0.81, 1.19]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi<sup>2</sup> = 0.00, df = 1 (P = 1.00); I<sup>2</sup> = 0%</td></tr><tr><td colspan="6">Test for overall effect: Z = 0.20 (P = 0.84)</td></tr><tr><td colspan="6"><b>1.1.2 Taxane+CTxA vs CTxB</b></td></tr><tr><td>306 Study Group</td><td>-0.1165</td><td>0.1082</td><td>11.2%</td><td>0.89 [0.72, 1.10]</td><td></td></tr><tr><td>AGO</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Blohmer</td><td>-0.4155</td><td>0.1842</td><td>3.9%</td><td>0.66 [0.46, 0.95]</td><td></td></tr><tr><td>Bonneterre</td><td>-0.1985</td><td>0.2324</td><td>2.4%</td><td>0.82 [0.52, 1.29]</td><td></td></tr><tr><td>CECOG BM1</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>EORTC 10961</td><td>0.1044</td><td>0.1483</td><td>6.0%</td><td>1.11 [0.83, 1.48]</td><td></td></tr><tr><td>Jassem</td><td>-0.3857</td><td>0.1369</td><td>7.0%</td><td>0.68 [0.52, 0.89]</td><td></td></tr><tr><td>Lyman</td><td>0.7275</td><td>0.2413</td><td>2.3%</td><td>2.07 [1.29, 3.32]</td><td></td></tr><tr><td>Nabholtz</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>UKCCCR AB01</td><td>0.0198</td><td>0.0812</td><td>19.9%</td><td>1.02 [0.87, 1.20]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>52.6%</b></td><td><b>0.94 [0.85, 1.03]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi<sup>2</sup> = 22.85, df = 6 (P = 0.0008); I<sup>2</sup> = 74%</td></tr><tr><td colspan="6">Test for overall effect: Z = 1.31 (P = 0.19)</td></tr><tr><td colspan="6"><b>1.1.3 Taxane vs CTxA</b></td></tr><tr><td>ANZ TITG</td><td>-0.2877</td><td>0.1582</td><td>5.2%</td><td>0.75 [0.55, 1.02]</td><td></td></tr><tr><td>ECOG E1193 (B)</td><td>-0.0834</td><td>0.1251</td><td>8.4%</td><td>0.92 [0.72, 1.18]</td><td></td></tr><tr><td>EORTC 10923</td><td>0.1133</td><td>0.1289</td><td>7.9%</td><td>1.12 [0.87, 1.44]</td><td></td></tr><tr><td>JCOG9802</td><td>-0.1744</td><td>0.1154</td><td>9.8%</td><td>0.84 [0.67, 1.05]</td><td></td></tr><tr><td>Yardley</td><td>0.1989</td><td>0.209</td><td>3.0%</td><td>1.22 [0.81, 1.84]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>34.3%</b></td><td><b>0.93 [0.83, 1.05]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi<sup>2</sup> = 6.40, df = 4 (P = 0.17); I<sup>2</sup> = 38%</td></tr><tr><td colspan="6">Test for overall effect: Z = 1.15 (P = 0.25)</td></tr><tr><td colspan="3"><b>Total (95% CI)</b></td><td><b>100.0%</b></td><td><b>0.94 [0.88, 1.01]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi<sup>2</sup> = 29.45, df = 13 (P = 0.006); I<sup>2</sup> = 56%</td></tr><tr><td colspan="6">Test for overall effect: Z = 1.69 (P = 0.09)</td></tr><tr><td colspan="6">Test for subgroup differences: Chi<sup>2</sup> = 0.20, df = 2 (P = 0.91), I<sup>2</sup> = 0%</td></tr></tbody></table> <p>コメント： タキサンと他の1次治療(アンスラサイクリン)に有意差を認めない。</p> |                                           |               |                                     |                                                                                                                                                                                             | Study or Subgroup                 | log[Hazard Ratio] | SE | Weight | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI | <b>1.1.1 Taxane+CTxA vs CTxA</b> |  |  |  |  |  | ECOG E1193 (A) | -0.0202 | 0.123 | 8.7% | 0.98 [0.77, 1.25] |  | EU-93011 | -0.0202 | 0.1717 | 4.4% | 0.98 [0.70, 1.37] |  | <b>Subtotal (95% CI)</b> |  |  | <b>13.1%</b> | <b>0.98 [0.81, 1.19]</b> |  | Heterogeneity: Chi <sup>2</sup> = 0.00, df = 1 (P = 1.00); I <sup>2</sup> = 0% |  |  |  |  |  | Test for overall effect: Z = 0.20 (P = 0.84) |  |  |  |  |  | <b>1.1.2 Taxane+CTxA vs CTxB</b> |  |  |  |  |  | 306 Study Group | -0.1165 | 0.1082 | 11.2% | 0.89 [0.72, 1.10] |  | AGO | 0 | 0 |  | Not estimable |  | Blohmer | -0.4155 | 0.1842 | 3.9% | 0.66 [0.46, 0.95] |  | Bonneterre | -0.1985 | 0.2324 | 2.4% | 0.82 [0.52, 1.29] |  | CECOG BM1 | 0 | 0 |  | Not estimable |  | EORTC 10961 | 0.1044 | 0.1483 | 6.0% | 1.11 [0.83, 1.48] |  | Jassem | -0.3857 | 0.1369 | 7.0% | 0.68 [0.52, 0.89] |  | Lyman | 0.7275 | 0.2413 | 2.3% | 2.07 [1.29, 3.32] |  | Nabholtz | 0 | 0 |  | Not estimable |  | UKCCCR AB01 | 0.0198 | 0.0812 | 19.9% | 1.02 [0.87, 1.20] |  | <b>Subtotal (95% CI)</b> |  |  | <b>52.6%</b> | <b>0.94 [0.85, 1.03]</b> |  | Heterogeneity: Chi <sup>2</sup> = 22.85, df = 6 (P = 0.0008); I <sup>2</sup> = 74% |  |  |  |  |  | Test for overall effect: Z = 1.31 (P = 0.19) |  |  |  |  |  | <b>1.1.3 Taxane vs CTxA</b> |  |  |  |  |  | ANZ TITG | -0.2877 | 0.1582 | 5.2% | 0.75 [0.55, 1.02] |  | ECOG E1193 (B) | -0.0834 | 0.1251 | 8.4% | 0.92 [0.72, 1.18] |  | EORTC 10923 | 0.1133 | 0.1289 | 7.9% | 1.12 [0.87, 1.44] |  | JCOG9802 | -0.1744 | 0.1154 | 9.8% | 0.84 [0.67, 1.05] |  | Yardley | 0.1989 | 0.209 | 3.0% | 1.22 [0.81, 1.84] |  | <b>Subtotal (95% CI)</b> |  |  | <b>34.3%</b> | <b>0.93 [0.83, 1.05]</b> |  | Heterogeneity: Chi <sup>2</sup> = 6.40, df = 4 (P = 0.17); 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|                                                                                                | Study or Subgroup                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | log[Hazard Ratio]                         | SE            | Weight                              | Hazard Ratio<br>IV, Fixed, 95% CI                                                                                                                                                           | Hazard Ratio<br>IV, Fixed, 95% CI |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |       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                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| <b>1.1.1 Taxane+CTxA vs CTxA</b>                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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      |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| ECOG E1193 (A)                                                                                 | -0.0202                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 0.123                                     | 8.7%          | 0.98 [0.77, 1.25]                   |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |       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                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| EU-93011                                                                                       | -0.0202                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 0.1717                                    | 4.4%          | 0.98 [0.70, 1.37]                   |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |       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                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                           | <b>13.1%</b>  | <b>0.98 [0.81, 1.19]</b>            |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |       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                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Heterogeneity: Chi <sup>2</sup> = 0.00, df = 1 (P = 1.00); I <sup>2</sup> = 0%                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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      |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Test for overall effect: Z = 0.20 (P = 0.84)                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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      |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| <b>1.1.2 Taxane+CTxA vs CTxB</b>                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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      |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| 306 Study Group                                                                                | -0.1165                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 0.1082                                    | 11.2%         | 0.89 [0.72, 1.10]                   |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| AGO                                                                                            | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 0                                         |               | Not estimable                       |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Blohmer                                                                                        | -0.4155                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 0.1842                                    | 3.9%          | 0.66 [0.46, 0.95]                   |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Bonneterre                                                                                     | -0.1985                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 0.2324                                    | 2.4%          | 0.82 [0.52, 1.29]                   |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| CECOG BM1                                                                                      | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 0                                         |               | Not estimable                       |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| EORTC 10961                                                                                    | 0.1044                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 0.1483                                    | 6.0%          | 1.11 [0.83, 1.48]                   |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Jassem                                                                                         | -0.3857                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 0.1369                                    | 7.0%          | 0.68 [0.52, 0.89]                   |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Lyman                                                                                          | 0.7275                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 0.2413                                    | 2.3%          | 2.07 [1.29, 3.32]                   |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Nabholtz                                                                                       | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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            |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| UKCCCR AB01                                                                                    | 0.0198                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 0.0812                                    | 19.9%         | 1.02 [0.87, 1.20]                   |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                           | <b>52.6%</b>  | <b>0.94 [0.85, 1.03]</b>            |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |       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                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Heterogeneity: Chi <sup>2</sup> = 22.85, df = 6 (P = 0.0008); I <sup>2</sup> = 74%             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Test for overall effect: Z = 1.31 (P = 0.19)                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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      |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| <b>1.1.3 Taxane vs CTxA</b>                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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      |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| ANZ TITG                                                                                       | -0.2877                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 0.1582                                    | 5.2%          | 0.75 [0.55, 1.02]                   |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| ECOG E1193 (B)                                                                                 | -0.0834                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 0.1251                                    | 8.4%          | 0.92 [0.72, 1.18]                   |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| EORTC 10923                                                                                    | 0.1133                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 0.1289                                    | 7.9%          | 1.12 [0.87, 1.44]                   |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| JCOG9802                                                                                       | -0.1744                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 0.1154                                    | 9.8%          | 0.84 [0.67, 1.05]                   |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Yardley                                                                                        | 0.1989                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 0.209                                     | 3.0%          | 1.22 [0.81, 1.84]                   |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                             |  |  |  |  |  |          |         |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |      |                   |  |         |        |       |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                    |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                           | <b>34.3%</b>  | <b>0.93 [0.83, 1.05]</b>            |                                                                                                                                                                                             |                                   |                   |    |        |                                   |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |       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                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Heterogeneity: Chi <sup>2</sup> = 6.40, df = 4 (P = 0.17); I <sup>2</sup> = 38%                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Test for overall effect: Z = 1.15 (P = 0.25)                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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| <b>Total (95% CI)</b>                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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            |                                   |                                  |  |  |  |  |  |                |         |       |      |                   |  |          |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                |  |  |  |  |  |                                              |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |       |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |   |   |  |               |  |             |        |        |      |                   |  |        |         |        |      |                   |  |       |        |        |      |                   |  |          |   |   |  |               |  |       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                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Heterogeneity: Chi <sup>2</sup> = 29.45, df = 13 (P = 0.006); I <sup>2</sup> = 56%             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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| Test for overall effect: Z = 1.69 (P = 0.09)                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Test for subgroup differences: Chi <sup>2</sup> = 0.20, df = 2 (P = 0.91), I <sup>2</sup> = 0% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Funnel plot                                                                                    | <p>コメント：</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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| その他の解析                                                                                         | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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| メタリグレーション                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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| 感度分析                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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## 【4-9 メタアナリシス】

| CQ                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |                                     |                          |                                                                                                                                                                                             |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          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--------|--------|------|-------------------|--|----------------|---------|--------|------|-------------------|--|-------------|--------|--------|------|-------------------|--|----------|---------|--------|-------|-------------------|--|---------|---------|--------|------|-------------------|--|--------------------------|--|--|--------------|--------------------------|--|-----------------------------------------------------------------------------------------------------------|--|--|--|--|--|-----------------------|--|--|---------------|--------------------------|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|--|
| P                                                                                                                                                                                       | HER2陰性転移・再発乳癌(女性)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            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| C                                                                                                                                                                                       | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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| 研究デザイン                                                                                                                                                                                  | RCT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 文献数                                       | 17                                  | コード                      | ECOG E1193 (A), EU-93011, 306 Study Group, AGO, Blohmer, Bonneterre, CECOG BM1, EORTC 10961, Jassem, Lyman, Nabholtz, UKCCCR AB01, ANZ TITG, ECOG E1193 (B), EORTC 10923, JCOG9802, Yardley |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |      |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |         |        |      |                   |  |             |         |        |      |                   |  |        |         |      |      |                   |  |       |   |   |  |               |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                             |  |  |  |  |  |          |    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| モデル                                                                                                                                                                                     | Fixed Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 方法                                        | Inverse Variance method (RevMan5.3) |                          |                                                                                                                                                                                             |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          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| 効果指標                                                                                                                                                                                    | Hazard Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 統合値                                       | 0.98 ( 0.91 - 1.05 ) P= 0.51        |                          |                                                                                                                                                                                             |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |      |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |         |        |      |                   |  |             |         |        |      |                   |  |        |         |      |      |                   |  |       |   |   |  |               |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                             |  |  |  |  |  |          |        |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |       |                   |  |         |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| Forest plot                                                                                                                                                                             | <table><thead><tr><th>Study or Subgroup</th><th>log[Hazard Ratio]</th><th>SE</th><th>Weight</th><th>Hazard Ratio IV, Fixed, 95% CI</th><th>Hazard Ratio IV, Fixed, 95% CI</th></tr></thead><tbody><tr><td colspan="6"><b>1.2.1 Taxane+CTxA vs CTxA</b></td></tr><tr><td>ECOG E1193 (A)</td><td>-0.0305</td><td>0.1245</td><td>7.5%</td><td>0.97 [0.76, 1.24]</td><td></td></tr><tr><td>EU-93011</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>7.5%</b></td><td><b>0.97 [0.76, 1.24]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Not applicable<br/>Test for overall effect: Z = 0.24 (P = 0.81)</td></tr><tr><td colspan="6"><b>1.2.2 Taxane+CTxA vs CTxB</b></td></tr><tr><td>306 Study Group</td><td>-0.2744</td><td>0.1122</td><td>9.2%</td><td>0.76 [0.61, 0.95]</td><td></td></tr><tr><td>AGO</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Blohmer</td><td>-0.0202</td><td>0.1503</td><td>5.1%</td><td>0.98 [0.73, 1.32]</td><td></td></tr><tr><td>Bonneterre</td><td>-0.1054</td><td>0.1901</td><td>3.2%</td><td>0.90 [0.62, 1.31]</td><td></td></tr><tr><td>CECOG BM1</td><td>-0.1165</td><td>0.1373</td><td>6.1%</td><td>0.89 [0.68, 1.16]</td><td></td></tr><tr><td>EORTC 10961</td><td>-0.0619</td><td>0.1221</td><td>7.8%</td><td>0.94 [0.74, 1.19]</td><td></td></tr><tr><td>Jassem</td><td>-0.2877</td><td>0.14</td><td>5.9%</td><td>0.75 [0.57, 0.99]</td><td></td></tr><tr><td>Lyman</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Nabholtz</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>UKCCCR AB01</td><td>0.0677</td><td>0.0771</td><td>19.5%</td><td>1.07 [0.92, 1.24]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>56.8%</b></td><td><b>0.92 [0.85, 1.01]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 9.14, df = 6 (P = 0.17); I² = 34%<br/>Test for overall effect: Z = 1.77 (P = 0.08)</td></tr><tr><td colspan="6"><b>1.2.3 Taxane vs CTxA</b></td></tr><tr><td>ANZ TITG</td><td>0.1655</td><td>0.1439</td><td>5.6%</td><td>1.18 [0.89, 1.56]</td><td></td></tr><tr><td>ECOG E1193 (B)</td><td>-0.0834</td><td>0.1251</td><td>7.4%</td><td>0.92 [0.72, 1.18]</td><td></td></tr><tr><td>EORTC 10923</td><td>0.4383</td><td>0.1139</td><td>8.9%</td><td>1.55 [1.24, 1.94]</td><td></td></tr><tr><td>JCOG9802</td><td>-0.1165</td><td>0.1011</td><td>11.3%</td><td>0.89 [0.73, 1.09]</td><td></td></tr><tr><td>Yardley</td><td>-0.1393</td><td>0.2157</td><td>2.5%</td><td>0.87 [0.57, 1.33]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>35.7%</b></td><td><b>1.07 [0.96, 1.20]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 16.74, df = 4 (P = 0.002); I² = 76%<br/>Test for overall effect: Z = 1.26 (P = 0.21)</td></tr><tr><td><b>Total (95% CI)</b></td><td></td><td></td><td><b>100.0%</b></td><td><b>0.98 [0.91, 1.05]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 30.23, df = 12 (P = 0.003); I² = 60%<br/>Test for overall effect: Z = 0.65 (P = 0.51)<br/>Test for subgroup differences: Chi² = 4.35, df = 2 (P = 0.11), I² = 54.0%</td></tr></tbody></table> |                                           |                                     |                          |                                                                                                                                                                                             | Study or Subgroup              | log[Hazard Ratio] | SE | Weight | Hazard Ratio IV, Fixed, 95% CI | Hazard Ratio IV, Fixed, 95% CI | <b>1.2.1 Taxane+CTxA vs CTxA</b> |  |  |  |  |  | ECOG E1193 (A) | -0.0305 | 0.1245 | 7.5% | 0.97 [0.76, 1.24] |  | EU-93011 | 0 | 0 |  | Not estimable |  | <b>Subtotal (95% CI)</b> |  |  | <b>7.5%</b> | <b>0.97 [0.76, 1.24]</b> |  | Heterogeneity: Not applicable<br>Test for overall effect: Z = 0.24 (P = 0.81) |  |  |  |  |  | <b>1.2.2 Taxane+CTxA vs CTxB</b> |  |  |  |  |  | 306 Study Group | -0.2744 | 0.1122 | 9.2% | 0.76 [0.61, 0.95] |  | AGO | 0 | 0 |  | Not estimable |  | Blohmer | -0.0202 | 0.1503 | 5.1% | 0.98 [0.73, 1.32] |  | Bonneterre | -0.1054 | 0.1901 | 3.2% | 0.90 [0.62, 1.31] |  | CECOG BM1 | -0.1165 | 0.1373 | 6.1% | 0.89 [0.68, 1.16] |  | EORTC 10961 | -0.0619 | 0.1221 | 7.8% | 0.94 [0.74, 1.19] |  | Jassem | -0.2877 | 0.14 | 5.9% | 0.75 [0.57, 0.99] |  | Lyman | 0 | 0 |  | Not estimable |  | Nabholtz | 0 | 0 |  | Not estimable |  | UKCCCR AB01 | 0.0677 | 0.0771 | 19.5% | 1.07 [0.92, 1.24] |  | <b>Subtotal (95% CI)</b> |  |  | <b>56.8%</b> | <b>0.92 [0.85, 1.01]</b> |  | Heterogeneity: Chi² = 9.14, df = 6 (P = 0.17); I² = 34%<br>Test for overall effect: Z = 1.77 (P = 0.08) |  |  |  |  |  | <b>1.2.3 Taxane vs CTxA</b> |  |  |  |  |  | ANZ TITG | 0.1655 | 0.1439 | 5.6% | 1.18 [0.89, 1.56] |  | ECOG E1193 (B) | -0.0834 | 0.1251 | 7.4% | 0.92 [0.72, 1.18] |  | EORTC 10923 | 0.4383 | 0.1139 | 8.9% | 1.55 [1.24, 1.94] |  | JCOG9802 | -0.1165 | 0.1011 | 11.3% | 0.89 [0.73, 1.09] |  | Yardley | -0.1393 | 0.2157 | 2.5% | 0.87 [0.57, 1.33] |  | <b>Subtotal (95% CI)</b> |  |  | <b>35.7%</b> | <b>1.07 [0.96, 1.20]</b> |  | Heterogeneity: Chi² = 16.74, df = 4 (P = 0.002); I² = 76%<br>Test for overall effect: Z = 1.26 (P = 0.21) |  |  |  |  |  | <b>Total (95% CI)</b> |  |  | <b>100.0%</b> | <b>0.98 [0.91, 1.05]</b> |  | Heterogeneity: Chi² = 30.23, df = 12 (P = 0.003); I² = 60%<br>Test for overall effect: Z = 0.65 (P = 0.51)<br>Test for subgroup differences: Chi² = 4.35, df = 2 (P = 0.11), I² = 54.0% |  |  |  |  |  |
|                                                                                                                                                                                         | Study or Subgroup                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | log[Hazard Ratio]                         | SE                                  | Weight                   | Hazard Ratio IV, Fixed, 95% CI                                                                                                                                                              | Hazard Ratio IV, Fixed, 95% CI |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |      |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |         |        |      |                   |  |             |         |        |      |                   |  |        |         |      |      |                   |  |       |   |   |  |               |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                             |  |  |  |  |  |          |    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|                                                                                                                                                                                         | <b>1.2.1 Taxane+CTxA vs CTxA</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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|                                                                                                                                                                                         | ECOG E1193 (A)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | -0.0305                                   | 0.1245                              | 7.5%                     | 0.97 [0.76, 1.24]                                                                                                                                                                           |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |      |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |         |        |      |                   |  |             |         |        |      |                   |  |        |         |      |      |                   |  |       |   |   |  |               |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                             |  |  |  |  |  |          |    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|                                                                                                                                                                                         | EU-93011                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0                                         | 0                                   |                          | Not estimable                                                                                                                                                                               |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |      |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |         |        |      |                   |  |             |         |        |      |                   |  |        |         |      |      |                   |  |       |   |   |  |               |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                             |  |  |  |  |  |          |    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|                                                                                                                                                                                         | <b>Subtotal (95% CI)</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                           |                                     | <b>7.5%</b>              | <b>0.97 [0.76, 1.24]</b>                                                                                                                                                                    |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |      |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |         |        |      |                   |  |             |         |        |      |                   |  |        |         |      |      |                   |  |       |   |   |  |               |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                             |  |  |  |  |  |          |    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|                                                                                                                                                                                         | Heterogeneity: Not applicable<br>Test for overall effect: Z = 0.24 (P = 0.81)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                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|                                                                                                                                                                                         | <b>1.2.2 Taxane+CTxA vs CTxB</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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|                                                                                                                                                                                         | 306 Study Group                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | -0.2744                                   | 0.1122                              | 9.2%                     | 0.76 [0.61, 0.95]                                                                                                                                                                           |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |      |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |         |        |      |                   |  |             |         |        |      |                   |  |        |         |      |      |                   |  |       |   |   |  |               |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                             |  |  |  |  |  |          |    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|                                                                                                                                                                                         | AGO                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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|  |  |             |                          |  |                                                                               |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |      |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |         |        |      |                   |  |             |         |        |      |                   |  |        |         |      |      |                   |  |       |   |   |  |               |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                             |  |  |  |  |  |          |    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| Blohmer                                                                                                                                                                                 | -0.0202                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 0.1503                                    | 5.1%                                | 0.98 [0.73, 1.32]        |                                                                                                                                                                                             |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |      |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |         |        |      |                   |  |             |         |        |      |                   |  |        |         |      |      |                   |  |       |   |   |  |               |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                             |  |  |  |  |  |          |        |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |       |                   |  |         |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| Bonneterre                                                                                                                                                                              | -0.1054                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 0.1901                                    | 3.2%                                | 0.90 [0.62, 1.31]        |                                                                                                                                                                                             |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |      |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |         |        |      |                   |  |             |         |        |      |                   |  |        |         |      |      |                   |  |       |   |   |  |               |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                             |  |  |  |  |  |          |    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| CECOG BM1                                                                                                                                                                               | -0.1165                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 0.1373                                    | 6.1%                                | 0.89 [0.68, 1.16]        |                                                                                                                                                                                             |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |      |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |         |        |      |                   |  |             |         |        |      |                   |  |        |         |      |      |                   |  |       |   |   |  |               |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                             |  |  |  |  |  |          |    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| EORTC 10961                                                                                                                                                                             | -0.0619                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 0.1221                                    | 7.8%                                | 0.94 [0.74, 1.19]        |                                                                                                                                                                                             |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |      |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |         |        |      |                   |  |             |         |        |      |                   |  |        |         |      |      |                   |  |       |   |   |  |               |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                             |  |  |  |  |  |          |    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| Jassem                                                                                                                                                                                  | -0.2877                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 0.14                                      | 5.9%                                | 0.75 [0.57, 0.99]        |                                                                                                                                                                                             |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          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| Lyman                                                                                                                                                                                   | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            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| Nabholtz                                                                                                                                                                                | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            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| UKCCCR AB01                                                                                                                                                                             | 0.0677                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 0.0771                                    | 19.5%                               | 1.07 [0.92, 1.24]        |                                                                                                                                                                                             |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          |  |  |             |                          |  |                                                                               |  |  |  |  |  |                                  |  |  |  |  |  |                 |         |        |      |                   |  |     |   |   |  |               |  |         |         |        |      |                   |  |            |         |        |      |                   |  |           |         |        |      |                   |  |             |         |        |      |                   |  |        |         |      |      |                   |  |       |   |   |  |               |  |          |   |   |  |               |  |             |        |        |       |                   |  |                          |  |  |              |                          |  |                                                                                                         |  |  |  |  |  |                             |  |  |  |  |  |          |    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| <b>Subtotal (95% CI)</b>                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                           | <b>56.8%</b>                        | <b>0.92 [0.85, 1.01]</b> |                                                                                                                                                                                             |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          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| Heterogeneity: Chi² = 9.14, df = 6 (P = 0.17); I² = 34%<br>Test for overall effect: Z = 1.77 (P = 0.08)                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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| <b>1.2.3 Taxane vs CTxA</b>                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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| ANZ TITG                                                                                                                                                                                | 0.1655                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 0.1439                                    | 5.6%                                | 1.18 [0.89, 1.56]        |                                                                                                                                                                                             |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          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| ECOG E1193 (B)                                                                                                                                                                          | -0.0834                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 0.1251                                    | 7.4%                                | 0.92 [0.72, 1.18]        |                                                                                                                                                                                             |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          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    |        |      |                   |  |                |         |        |      |                   |  |             |        |        |      |                   |  |          |         |        |       |                   |  |         |         |        |      |                   |  |                          |  |  |              |                          |  |                                                                                                           |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                                                                                                                         |  |  |  |  |  |
| EORTC 10923                                                                                                                                                                             | 0.4383                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 0.1139                                    | 8.9%                                | 1.55 [1.24, 1.94]        |                                                                                                                                                                                             |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          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| JCOG9802                                                                                                                                                                                | -0.1165                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 0.1011                                    | 11.3%                               | 0.89 [0.73, 1.09]        |                                                                                                                                                                                             |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          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| Yardley                                                                                                                                                                                 | -0.1393                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 0.2157                                    | 2.5%                                | 0.87 [0.57, 1.33]        |                                                                                                                                                                                             |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          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| <b>Subtotal (95% CI)</b>                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                           | <b>35.7%</b>                        | <b>1.07 [0.96, 1.20]</b> |                                                                                                                                                                                             |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          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| Heterogeneity: Chi² = 16.74, df = 4 (P = 0.002); I² = 76%<br>Test for overall effect: Z = 1.26 (P = 0.21)                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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| <b>Total (95% CI)</b>                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                           | <b>100.0%</b>                       | <b>0.98 [0.91, 1.05]</b> |                                                                                                                                                                                             |                                |                   |    |        |                                |                                |                                  |  |  |  |  |  |                |         |        |      |                   |  |          |   |   |  |               |  |                          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| Heterogeneity: Chi² = 30.23, df = 12 (P = 0.003); I² = 60%<br>Test for overall effect: Z = 0.65 (P = 0.51)<br>Test for subgroup differences: Chi² = 4.35, df = 2 (P = 0.11), I² = 54.0% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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| コメント： タキサンと他の1次治療(アンスラサイクリン)に有意差を認めない。                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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| Funnel plot                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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|                                                                                                                                                                                         | コメント：                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| その他の解析                                                                                                                                                                                  | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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| メタリグレーション                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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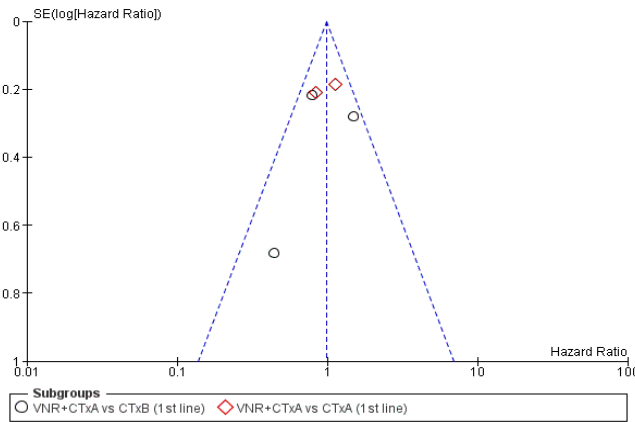
【4-9 メタアナリシス】

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| 研究デザイン                                                                                                       | RCT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           | 文献数        | 17                                 | コード           | ECOG E1193 (A), EU-93011, 306 Study Group, AGO, Blohmer, Bonneterre, CECOG BM1, EORTC 10961, Jassem, Lyman, Nabholtz, UKCCCR AB01, ANZ TITG, ECOG E1193 (B), EORTC 10923, JCOG9802, Yardley |                          |                           |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |              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| モデル                                                                                                          | Random Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           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|  |
| 効果指標                                                                                                         | Risk Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 統合値                                       |            | 1.16 ( 1.05 - 1.29 ) P= 0.004      |               |                                                                                                                                                                                             |                          |                           |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |                   |  |            |    |    |    |    |      |                   |  |           |    |     |    |     |      |                   |  |             |    |     |    |     |      |                   |  |        |    |     |    |     |      |                   |  |       |    |    |    |    |      |                   |  |          |     |     |     |     |      |                   |  |             |     |     |     |     |      |                   |  |                          |  |             |  |             |              |                          |  |              |     |  |     |  |  |  |  |                                                                                                           |  |  |  |  |  |  |  |  |                                                 |  |  |  |  |  |  |  |  |                             |  |  |  |  |  |  |  |  |          |    |     |    |    |      |                   |  |                |    |     |    |     |      |                   |  |             |    |     |    |     |      |                   |  |          |    |     |    |     |      |                   |  |         |    |    |    |    |      |                   |  |                          |  |            |  |            |              |                          |  |              |     |  |     |  |  |  |  |                                                                                                           |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                       |  |             |  |             |               |                          |  |              |      |  |      |  |  |  |  |                                                                                                              |  |  |  |  |  |  |  |  |                                               |  |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |  |
| Forest plot                                                                                                  | <table><thead><tr><th></th><th colspan="2">Taxane containing regimen</th><th colspan="2">Other regimens</th><th></th><th>Risk Ratio</th><th>Risk Ratio</th></tr><tr><th>Study or Subgroup</th><th>Events</th><th>Total</th><th>Events</th><th>Total</th><th>Weight</th><th>M-H, Random, 95% CI</th><th>M-H, Random, 95% CI</th></tr></thead><tbody><tr><td colspan="9"><b>1.3.1 Taxane+CTxA vs CTxA</b></td></tr><tr><td>ECOG E1193 (A)</td><td>108</td><td>230</td><td>41</td><td>112</td><td>6.0%</td><td>1.28 [0.97, 1.70]</td><td></td></tr><tr><td>EU-93011</td><td>44</td><td>87</td><td>20</td><td>86</td><td>3.6%</td><td>2.17 [1.41, 3.36]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td><b>317</b></td><td></td><td><b>198</b></td><td><b>9.6%</b></td><td><b>1.62 [0.97, 2.72]</b></td><td></td></tr><tr><td>Total events</td><td>152</td><td></td><td>61</td><td></td><td></td><td></td><td></td></tr><tr><td colspan="9">Heterogeneity: Tau<sup>2</sup> = 0.11; Chi<sup>2</sup> = 4.00, df = 1 (P = 0.05); I<sup>2</sup> = 75%</td></tr><tr><td colspan="9">Test for overall effect: Z = 1.84 (P = 0.07)</td></tr><tr><td colspan="9"><b>1.3.2 Taxane+CTxA vs CTxB</b></td></tr><tr><td>306 Study Group</td><td>124</td><td>191</td><td>100</td><td>199</td><td>8.4%</td><td>1.29 [1.09, 1.54]</td><td></td></tr><tr><td>AGO</td><td>94</td><td>204</td><td>81</td><td>198</td><td>7.2%</td><td>1.13 [0.90, 1.41]</td><td></td></tr><tr><td>Blohmer</td><td>59</td><td>125</td><td>47</td><td>111</td><td>5.9%</td><td>1.11 [0.84, 1.48]</td><td></td></tr><tr><td>Bonneterre</td><td>41</td><td>65</td><td>23</td><td>67</td><td>4.3%</td><td>1.84 [1.26, 2.69]</td><td></td></tr><tr><td>CECOG BM1</td><td>71</td><td>114</td><td>66</td><td>129</td><td>7.3%</td><td>1.22 [0.98, 1.52]</td><td></td></tr><tr><td>EORTC 10961</td><td>80</td><td>125</td><td>74</td><td>128</td><td>7.8%</td><td>1.11 [0.91, 1.35]</td><td></td></tr><tr><td>Jassem</td><td>81</td><td>122</td><td>69</td><td>129</td><td>7.7%</td><td>1.24 [1.01, 1.52]</td><td></td></tr><tr><td>Lyman</td><td>14</td><td>36</td><td>18</td><td>35</td><td>2.8%</td><td>0.76 [0.45, 1.27]</td><td></td></tr><tr><td>Nabholtz</td><td>133</td><td>238</td><td>106</td><td>237</td><td>8.2%</td><td>1.25 [1.04, 1.50]</td><td></td></tr><tr><td>UKCCCR AB01</td><td>221</td><td>347</td><td>186</td><td>343</td><td>9.5%</td><td>1.17 [1.04, 1.33]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td><b>1567</b></td><td></td><td><b>1576</b></td><td><b>69.2%</b></td><td><b>1.20 [1.12, 1.29]</b></td><td></td></tr><tr><td>Total events</td><td>918</td><td></td><td>770</td><td></td><td></td><td></td><td></td></tr><tr><td colspan="9">Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 10.17, df = 9 (P = 0.34); I<sup>2</sup> = 12%</td></tr><tr><td colspan="9">Test for overall effect: Z = 5.14 (P &lt; 0.00001)</td></tr><tr><td colspan="9"><b>1.3.3 Taxane vs CTxA</b></td></tr><tr><td>ANZ TITG</td><td>31</td><td>105</td><td>36</td><td>99</td><td>4.1%</td><td>0.81 [0.55, 1.20]</td><td></td></tr><tr><td>ECOG E1193 (B)</td><td>78</td><td>229</td><td>41</td><td>112</td><td>5.6%</td><td>0.93 [0.69, 1.26]</td><td></td></tr><tr><td>EORTC 10923</td><td>42</td><td>164</td><td>67</td><td>163</td><td>5.3%</td><td>0.62 [0.45, 0.86]</td><td></td></tr><tr><td>JCOG9802</td><td>40</td><td>147</td><td>29</td><td>146</td><td>3.8%</td><td>1.37 [0.90, 2.08]</td><td></td></tr><tr><td>Yardley</td><td>16</td><td>44</td><td>14</td><td>48</td><td>2.3%</td><td>1.25 [0.69, 2.25]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td><b>689</b></td><td></td><td><b>568</b></td><td><b>21.1%</b></td><td><b>0.92 [0.70, 1.22]</b></td><td></td></tr><tr><td>Total events</td><td>207</td><td></td><td>187</td><td></td><td></td><td></td><td></td></tr><tr><td colspan="9">Heterogeneity: Tau<sup>2</sup> = 0.06; Chi<sup>2</sup> = 10.41, df = 4 (P = 0.03); I<sup>2</sup> = 62%</td></tr><tr><td colspan="9">Test for overall effect: Z = 0.56 (P = 0.58)</td></tr><tr><td><b>Total (95% CI)</b></td><td></td><td><b>2573</b></td><td></td><td><b>2342</b></td><td><b>100.0%</b></td><td><b>1.16 [1.05, 1.29]</b></td><td></td></tr><tr><td>Total events</td><td>1277</td><td></td><td>1018</td><td></td><td></td><td></td><td></td></tr><tr><td colspan="9">Heterogeneity: Tau<sup>2</sup> = 0.02; Chi<sup>2</sup> = 40.13, df = 16 (P = 0.0007); I<sup>2</sup> = 60%</td></tr><tr><td colspan="9">Test for overall effect: Z = 2.91 (P = 0.004)</td></tr><tr><td colspan="9">Test for subgroup differences: Chi<sup>2</sup> = 4.65, df = 2 (P = 0.10), I<sup>2</sup> = 57.0%</td></tr></tbody></table> |                                           |            |                                    |               |                                                                                                                                                                                             |                          | Taxane containing regimen |  | Other regimens |  |  | Risk Ratio | Risk Ratio | Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | M-H, Random, 95% CI | <b>1.3.1 Taxane+CTxA vs CTxA</b> |  |  |  |  |  |  |  |  | ECOG E1193 (A) | 108 | 230 | 41 | 112 | 6.0% | 1.28 [0.97, 1.70] |  | EU-93011 | 44 | 87 | 20 | 86 | 3.6% | 2.17 [1.41, 3.36] |  | <b>Subtotal (95% CI)</b> |  | <b>317</b> |  | <b>198</b> | <b>9.6%</b> | <b>1.62 [0.97, 2.72]</b> |  | Total events | 152 |  | 61 |  |  |  |  | Heterogeneity: Tau <sup>2</sup> = 0.11; Chi <sup>2</sup> = 4.00, df = 1 (P = 0.05); I <sup>2</sup> = 75% |  |  |  |  |  |  |  |  | Test for overall effect: Z = 1.84 (P = 0.07) |  |  |  |  |  |  |  |  | <b>1.3.2 Taxane+CTxA vs CTxB</b> |  |  |  |  |  |  |  |  | 306 Study Group | 124 | 191 | 100 | 199 | 8.4% | 1.29 [1.09, 1.54] |  | AGO | 94 | 204 | 81 | 198 | 7.2% | 1.13 [0.90, 1.41] |  | Blohmer | 59 | 125 | 47 | 111 | 5.9% | 1.11 [0.84, 1.48] |  | Bonneterre | 41 | 65 | 23 | 67 | 4.3% | 1.84 [1.26, 2.69] |  | CECOG BM1 | 71 | 114 | 66 | 129 | 7.3% | 1.22 [0.98, 1.52] |  | EORTC 10961 | 80 | 125 | 74 | 128 | 7.8% | 1.11 [0.91, 1.35] |  | Jassem | 81 | 122 | 69 | 129 | 7.7% | 1.24 [1.01, 1.52] |  | Lyman | 14 | 36 | 18 | 35 | 2.8% | 0.76 [0.45, 1.27] |  | Nabholtz | 133 | 238 | 106 | 237 | 8.2% | 1.25 [1.04, 1.50] |  | UKCCCR AB01 | 221 | 347 | 186 | 343 | 9.5% | 1.17 [1.04, 1.33] |  | <b>Subtotal (95% CI)</b> |  | <b>1567</b> |  | <b>1576</b> | <b>69.2%</b> | <b>1.20 [1.12, 1.29]</b> |  | Total events | 918 |  | 770 |  |  |  |  | Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 10.17, df = 9 (P = 0.34); I <sup>2</sup> = 12% |  |  |  |  |  |  |  |  | Test for overall effect: Z = 5.14 (P < 0.00001) |  |  |  |  |  |  |  |  | <b>1.3.3 Taxane vs CTxA</b> |  |  |  |  |  |  |  |  | ANZ TITG | 31 | 105 | 36 | 99 | 4.1% | 0.81 [0.55, 1.20] |  | ECOG E1193 (B) | 78 | 229 | 41 | 112 | 5.6% | 0.93 [0.69, 1.26] |  | EORTC 10923 | 42 | 164 | 67 | 163 | 5.3% | 0.62 [0.45, 0.86] |  | JCOG9802 | 40 | 147 | 29 | 146 | 3.8% | 1.37 [0.90, 2.08] |  | Yardley | 16 | 44 | 14 | 48 | 2.3% | 1.25 [0.69, 2.25] |  | <b>Subtotal (95% CI)</b> |  | <b>689</b> |  | <b>568</b> | <b>21.1%</b> | <b>0.92 [0.70, 1.22]</b> |  | Total events | 207 |  | 187 |  |  |  |  | Heterogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 10.41, df = 4 (P = 0.03); I <sup>2</sup> = 62% |  |  |  |  |  |  |  |  | Test for overall effect: Z = 0.56 (P = 0.58) |  |  |  |  |  |  |  |  | <b>Total (95% CI)</b> |  | <b>2573</b> |  | <b>2342</b> | <b>100.0%</b> | <b>1.16 [1.05, 1.29]</b> |  | Total events | 1277 |  | 1018 |  |  |  |  | Heterogeneity: Tau <sup>2</sup> = 0.02; Chi <sup>2</sup> = 40.13, df = 16 (P = 0.0007); I <sup>2</sup> = 60% |  |  |  |  |  |  |  |  | Test for overall effect: Z = 2.91 (P = 0.004) |  |  |  |  |  |  |  |  | Test for subgroup differences: Chi <sup>2</sup> = 4.65, df = 2 (P = 0.10), I <sup>2</sup> = 57.0% |  |  |  |  |  |  |  |  |
|                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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  | Risk Ratio               | Risk Ratio                |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |                   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|                                                                                                              | Study or Subgroup                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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  | M-H, Random, 95% CI      | M-H, Random, 95% CI       |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |                   |  |            |    |    |    |    |      |                   |  |           |    |     |    |     |      |                   |  |             |    |     |    |     |      |                   |  |        |    |     |    |     |      |                   |  |       |    |    |    |    |      |                   |  |          |     |     |     |     |      |                   |  |             |     |     |     |     |      |                   |  |                          |  |             |  |             |              |                          |  |              |     |  |     |  |  |  |  |                                                                                                           |  |  |  |  |  |  |  |  |                                                 |  |  |  |  |  |  |  |  |                             |  |  |  |  |  |  |  |  |          |    |     |    |    |      |                   |  |                |    |     |    |     |      |                   |  |             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|  |
|                                                                                                              | <b>1.3.1 Taxane+CTxA vs CTxA</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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|  |
|                                                                                                              | ECOG E1193 (A)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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  | 1.28 [0.97, 1.70]        |                           |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |                   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|                                                                                                              | EU-93011                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                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  | 2.17 [1.41, 3.36]        |                           |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |                   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|                                                                                                              | <b>Subtotal (95% CI)</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                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  | <b>1.62 [0.97, 2.72]</b> |                           |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |                   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|                                                                                                              | Total events                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            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|  |
|                                                                                                              | Heterogeneity: Tau <sup>2</sup> = 0.11; Chi <sup>2</sup> = 4.00, df = 1 (P = 0.05); I <sup>2</sup> = 75%                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                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|  |
|                                                                                                              | Test for overall effect: Z = 1.84 (P = 0.07)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            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| <b>1.3.2 Taxane+CTxA vs CTxB</b>                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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| 306 Study Group                                                                                              | 124                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 191                                       | 100        | 199                                | 8.4%          | 1.29 [1.09, 1.54]                                                                                                                                                                           |                          |                           |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |                   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| AGO                                                                                                          | 94                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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| Blohmer                                                                                                      | 59                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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  |                          |                           |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |                   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| Bonneterre                                                                                                   | 41                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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  |                          |                           |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |                   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| CECOG BM1                                                                                                    | 71                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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  |                          |                           |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |                   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| EORTC 10961                                                                                                  | 80                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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| Jassem                                                                                                       | 81                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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  |                          |                           |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |                   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| Lyman                                                                                                        | 14                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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  |                          |                           |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |                   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| Nabholtz                                                                                                     | 133                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 238                                       | 106        | 237                                | 8.2%          | 1.25 [1.04, 1.50]                                                                                                                                                                           |                          |                           |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |                   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| UKCCCR AB01                                                                                                  | 221                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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|  |
| <b>Subtotal (95% CI)</b>                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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  |                          |                           |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |                   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|  |
| Total events                                                                                                 | 918                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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|  |
| Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 10.17, df = 9 (P = 0.34); I <sup>2</sup> = 12%    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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|  |
| Test for overall effect: Z = 5.14 (P < 0.00001)                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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| <b>1.3.3 Taxane vs CTxA</b>                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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|  |
| ANZ TITG                                                                                                     | 31                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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  |                          |                           |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |                   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|  |
| ECOG E1193 (B)                                                                                               | 78                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 229                                       | 41         | 112                                | 5.6%          | 0.93 [0.69, 1.26]                                                                                                                                                                           |                          |                           |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |                   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|  |
| EORTC 10923                                                                                                  | 42                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 164                                       | 67         | 163                                | 5.3%          | 0.62 [0.45, 0.86]                                                                                                                                                                         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| JCOG9802                                                                                                     | 40                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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  |                          |                           |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |                   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| Yardley                                                                                                      | 16                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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| <b>Subtotal (95% CI)</b>                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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  |                          |                           |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |                   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| Total events                                                                                                 | 207                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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|  |
| Heterogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 10.41, df = 4 (P = 0.03); I <sup>2</sup> = 62%    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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|  |
| Test for overall effect: Z = 0.56 (P = 0.58)                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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|  |
| <b>Total (95% CI)</b>                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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  |                          |                           |  |                |  |  |            |            |                   |        |       |        |       |        |                     |                     |                                  |  |  |  |  |  |  |  |  |                |     |     |    |     |      |                   |  |          |    |    |    |    |      |                   |  |                          |  |            |  |            |             |                          |  |              |     |  |    |  |  |  |  |                                                                                                          |  |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |  |                                  |  |  |  |  |  |  |  |  |                 |     |     |     |     |      |                   |  |     |    |     |    |     |      |                   |  |         |    |     |    |     |      |                   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|  |
| Total events                                                                                                 | 1277                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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|  |
| Heterogeneity: Tau <sup>2</sup> = 0.02; Chi <sup>2</sup> = 40.13, df = 16 (P = 0.0007); I <sup>2</sup> = 60% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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|  |
| Test for overall effect: Z = 2.91 (P = 0.004)                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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|  |
| Test for subgroup differences: Chi <sup>2</sup> = 4.65, df = 2 (P = 0.10), I <sup>2</sup> = 57.0%            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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| コメント： タキサンは他の1次治療(アンスラサイクリン)に対してORRを改善する。                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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| Funnel plot                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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|                                                                                                              | コメント：                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| その他の解析                                                                                                       | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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| メタリグレーション                                                                                                    | コメント：                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| 感度分析                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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【4-9 メタアナリシス】

| CQ                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |                                    |       |                                                                                                                                                                                             |                     |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
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| P                                                                                                       | HER2陰性転移・再発乳癌（女性）                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                           |                                    | I     | タキサンを含むレジメン                                                                                                                                                                                 |                     |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| C                                                                                                       | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                           |                                    | O     | Toxicity (therapy discontinuation)                                                                                                                                                          |                     |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| 研究デザイン                                                                                                  | RCT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 文献数                                       | 17                                 | コード   | ECOG E1193 (A), EU-93011, 306 Study Group, AGO, Blohmer, Bonneterre, CECOG BM1, EORTC 10961, Jassem, Lyman, Nabholtz, UKCCCR AB01, ANZ TITG, ECOG E1193 (B), EORTC 10923, JCOG9802, Yardley |                     |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| モデル                                                                                                     | Random Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 方法                                        | Mantel-Haenszel method (RevMan5.3) |       |                                                                                                                                                                                             |                     |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| 効果指標                                                                                                    | Risk Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 統合値                                       | 1.72 ( 1.28 - 2.31 ) P= 0.0003     |       |                                                                                                                                                                                             |                     |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| Forest plot                                                                                             | <table><thead><tr><th rowspan="2">Study or Subgroup</th><th colspan="2">Taxane containing regimen</th><th colspan="2">Other regimens</th><th rowspan="2">Weight</th><th colspan="2">Risk Ratio</th><th rowspan="2">Risk Ratio<br/>M-H, Random, 95% CI</th></tr><tr><th>Events</th><th>Total</th><th>Events</th><th>Total</th><th>M-H, Random, 95% CI</th><th>M-H, Random, 95% CI</th></tr></thead><tbody><tr><td>306 Study Group</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td colspan="2">Not estimable</td><td></td></tr><tr><td>AGO</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td colspan="2">Not estimable</td><td></td></tr><tr><td>ANZ TITG</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td colspan="2">Not estimable</td><td></td></tr><tr><td>Blohmer</td><td>11</td><td>125</td><td>6</td><td>111</td><td>9.5%</td><td colspan="2">1.63 [0.62, 4.26]</td><td></td></tr><tr><td>Bonneterre</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td colspan="2">Not estimable</td><td></td></tr><tr><td>CECOG BM1</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td colspan="2">Not estimable</td><td></td></tr><tr><td>ECOG E1193 (A)</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td colspan="2">Not estimable</td><td></td></tr><tr><td>ECOG E1193 (B)</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td colspan="2">Not estimable</td><td></td></tr><tr><td>EORTC 10923</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td colspan="2">Not estimable</td><td></td></tr><tr><td>EORTC 10961</td><td>66</td><td>136</td><td>36</td><td>135</td><td>81.2%</td><td colspan="2">1.82 [1.31, 2.53]</td><td></td></tr><tr><td>EU-93011</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td colspan="2">Not estimable</td><td></td></tr><tr><td>Jassem</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td colspan="2">Not estimable</td><td></td></tr><tr><td>JCOG9802</td><td>2</td><td>147</td><td>2</td><td>146</td><td>2.3%</td><td colspan="2">0.99 [0.14, 6.96]</td><td></td></tr><tr><td>Lyman</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td colspan="2">Not estimable</td><td></td></tr><tr><td>Nabholtz</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td colspan="2">Not estimable</td><td></td></tr><tr><td>UKCCCR AB01</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td colspan="2">Not estimable</td><td></td></tr><tr><td>Yardley</td><td>6</td><td>52</td><td>5</td><td>50</td><td>7.0%</td><td colspan="2">1.15 [0.38, 3.54]</td><td></td></tr><tr><td>Total (95% CI)</td><td></td><td>460</td><td></td><td>442</td><td>100.0%</td><td colspan="2">1.72 [1.28, 2.31]</td><td></td></tr><tr><td>Total events</td><td>85</td><td></td><td>49</td><td></td><td></td><td colspan="2"></td><td></td></tr><tr><td colspan="9">Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 0.93, df = 3 (P = 0.82); I<sup>2</sup> = 0%</td></tr><tr><td colspan="9">Test for overall effect: Z = 3.59 (P = 0.0003)</td></tr></tbody></table> |                                           |                                    |       |                                                                                                                                                                                             | Study or Subgroup   | Taxane containing regimen |  | Other regimens                    |  | Weight | Risk Ratio |  | Risk Ratio<br>M-H, Random, 95% CI | Events | Total | Events | Total | M-H, Random, 95% CI | M-H, Random, 95% CI | 306 Study Group | 0 | 0 | 0 | 0 |  | Not estimable |  |  | AGO | 0 | 0 | 0 | 0 |  | Not estimable |  |  | ANZ TITG | 0 | 0 | 0 | 0 |  | Not estimable |  |  | Blohmer | 11 | 125 | 6 | 111 | 9.5% | 1.63 [0.62, 4.26] |  |  | Bonneterre | 0 | 0 | 0 | 0 |  | Not estimable |  |  | CECOG BM1 | 0 | 0 | 0 | 0 |  | Not estimable |  |  | ECOG E1193 (A) | 0 | 0 | 0 | 0 |  | Not estimable |  |  | ECOG E1193 (B) | 0 | 0 | 0 | 0 |  | Not estimable |  |  | EORTC 10923 | 0 | 0 | 0 | 0 |  | Not estimable |  |  | EORTC 10961 | 66 | 136 | 36 | 135 | 81.2% | 1.82 [1.31, 2.53] |  |  | EU-93011 | 0 | 0 | 0 | 0 |  | Not estimable |  |  | Jassem | 0 | 0 | 0 | 0 |  | Not estimable |  |  | JCOG9802 | 2 | 147 | 2 | 146 | 2.3% | 0.99 [0.14, 6.96] |  |  | Lyman | 0 | 0 | 0 | 0 |  | Not estimable |  |  | Nabholtz | 0 | 0 | 0 | 0 |  | Not estimable |  |  | UKCCCR AB01 | 0 | 0 | 0 | 0 |  | Not estimable |  |  | Yardley | 6 | 52 | 5 | 50 | 7.0% | 1.15 [0.38, 3.54] |  |  | Total (95% CI) |  | 460 |  | 442 | 100.0% | 1.72 [1.28, 2.31] |  |  | Total events | 85 |  | 49 |  |  |  |  |  | Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.93, df = 3 (P = 0.82); I <sup>2</sup> = 0% |  |  |  |  |  |  |  |  | Test for overall effect: Z = 3.59 (P = 0.0003) |  |  |  |  |  |  |  |  |
| Study or Subgroup                                                                                       | Taxane containing regimen                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                           | Other regimens                     |       | Weight                                                                                                                                                                                      |                     | Risk Ratio                |  | Risk Ratio<br>M-H, Random, 95% CI |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
|                                                                                                         | Events                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Total                                     | Events                             | Total |                                                                                                                                                                                             | M-H, Random, 95% CI | M-H, Random, 95% CI       |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| 306 Study Group                                                                                         | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0                                         | 0                                  | 0     |                                                                                                                                                                                             | Not estimable       |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| AGO                                                                                                     | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0                                         | 0                                  | 0     |                                                                                                                                                                                             | Not estimable       |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| ANZ TITG                                                                                                | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0                                         | 0                                  | 0     |                                                                                                                                                                                             | Not estimable       |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| Blohmer                                                                                                 | 11                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 125                                       | 6                                  | 111   | 9.5%                                                                                                                                                                                        | 1.63 [0.62, 4.26]   |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| Bonneterre                                                                                              | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0                                         | 0                                  | 0     |                                                                                                                                                                                             | Not estimable       |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| CECOG BM1                                                                                               | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0                                         | 0                                  | 0     |                                                                                                                                                                                             | Not estimable       |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| ECOG E1193 (A)                                                                                          | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0                                         | 0                                  | 0     |                                                                                                                                                                                             | Not estimable       |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| ECOG E1193 (B)                                                                                          | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0                                         | 0                                  | 0     |                                                                                                                                                                                             | Not estimable       |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| EORTC 10923                                                                                             | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0                                         | 0                                  | 0     |                                                                                                                                                                                             | Not estimable       |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| EORTC 10961                                                                                             | 66                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 136                                       | 36                                 | 135   | 81.2%                                                                                                                                                                                       | 1.82 [1.31, 2.53]   |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| EU-93011                                                                                                | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0                                         | 0                                  | 0     |                                                                                                                                                                                             | Not estimable       |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| Jassem                                                                                                  | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0                                         | 0                                  | 0     |                                                                                                                                                                                             | Not estimable       |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| JCOG9802                                                                                                | 2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 147                                       | 2                                  | 146   | 2.3%                                                                                                                                                                                        | 0.99 [0.14, 6.96]   |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| Lyman                                                                                                   | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0                                         | 0                                  | 0     |                                                                                                                                                                                             | Not estimable       |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| Nabholtz                                                                                                | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0                                         | 0                                  | 0     |                                                                                                                                                                                             | Not estimable       |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| UKCCCR AB01                                                                                             | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0                                         | 0                                  | 0     |                                                                                                                                                                                             | Not estimable       |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| Yardley                                                                                                 | 6                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 52                                        | 5                                  | 50    | 7.0%                                                                                                                                                                                        | 1.15 [0.38, 3.54]   |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| Total (95% CI)                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 460                                       |                                    | 442   | 100.0%                                                                                                                                                                                      | 1.72 [1.28, 2.31]   |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| Total events                                                                                            | 85                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           | 49                                 |       |                                                                                                                                                                                             |                     |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.93, df = 3 (P = 0.82); I <sup>2</sup> = 0% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |       |                                                                                                                                                                                             |                     |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| Test for overall effect: Z = 3.59 (P = 0.0003)                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |       |                                                                                                                                                                                             |                     |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| コメント： タキサンは他の1次治療(アンスラサイクリン)に対してToxicityが高い。                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |       |                                                                                                                                                                                             |                     |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| Funnel plot                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |                                    |       |                                                                                                                                                                                             |                     |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| その他の解析                                                                                                  | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                           |                                    |       |                                                                                                                                                                                             |                     |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| メタリグレッション                                                                                               | コメント：                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                           |                                    |       |                                                                                                                                                                                             |                     |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |
| 感度分析                                                                                                    | コメント：                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                           |                                    |       |                                                                                                                                                                                             |                     |                           |  |                                   |  |        |            |  |                                   |        |       |        |       |                     |                     |                 |   |   |   |   |  |               |  |  |     |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |         |    |     |   |     |      |                   |  |  |            |   |   |   |   |  |               |  |  |           |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |                |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |             |    |     |    |     |       |                   |  |  |          |   |   |   |   |  |               |  |  |        |   |   |   |   |  |               |  |  |          |   |     |   |     |      |                   |  |  |       |   |   |   |   |  |               |  |  |          |   |   |   |   |  |               |  |  |             |   |   |   |   |  |               |  |  |         |   |    |   |    |      |                   |  |  |                |  |     |  |     |        |                   |  |  |              |    |  |    |  |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |  |                                                |  |  |  |  |  |  |  |  |

【4-9 メタアナリシス】

| CQ                                                                                             |                   | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |               |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
|------------------------------------------------------------------------------------------------|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|-----------------------------------|---------------------------------------------------------------------------------------|-------------------|-------------------|----|--------|-----------------------------------|-----------------------------------|------------------------------------------|--|--|--|--|--|----------------|--------|--------|-------|-------------------|--|--------------|---------|--------|-------|-------------------|--|-----------------|--------|--------|------|-------------------|--|--------------------------|--|--|--------------|--------------------------|--|---------------------------------------------------------------------------------|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|------------------------------------------|--|--|--|--|--|------------------|--------|--------|-------|-------------------|--|---------------|---------|--------|-------|-------------------|--|--------------------------|--|--|--------------|--------------------------|--|---------------------------------------------------------------------------------|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|-----------------------|--|--|---------------|--------------------------|--|---------------------------------------------------------------------------------|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|------------------------------------------------------------------------------------------------|--|--|--|--|--|
| P                                                                                              | HER2陰性転移・再発乳癌(女性) |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | I             | ビノレルビンを含むレジメン                     |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| C                                                                                              | その他のレジメン          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | O             | OS                                |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| 研究デザイン                                                                                         |                   | RCT(1st)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 文献数           | 5                                 | コード<br>Blajman C 1999, Namer M 2001, Riccardi A 2006, Norris B 2000, Ejlertsen B 2004 |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| モデル                                                                                            |                   | Fixed Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 方法            |                                   | Inverse Variance method (RevMan5.3)                                                   |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| 効果指標                                                                                           |                   | Hazard Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 統合値           |                                   | 0.98 ( 0.79 – 1.20 ) P= 0.82                                                          |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Forest plot                                                                                    |                   | <table><thead><tr><th>Study or Subgroup</th><th>log[Hazard Ratio]</th><th>SE</th><th>Weight</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th></tr></thead><tbody><tr><td colspan="6"><b>1.1.1 VNR+CTxA vs CTxB (1st line)</b></td></tr><tr><td>Blajman C 1999</td><td>0.3927</td><td>0.2791</td><td>14.5%</td><td>1.48 [0.86, 2.56]</td><td></td></tr><tr><td>Namer M 2001</td><td>-0.2395</td><td>0.2174</td><td>24.0%</td><td>0.79 [0.51, 1.21]</td><td></td></tr><tr><td>Riccardi A 2006</td><td>-0.821</td><td>0.6802</td><td>2.4%</td><td>0.44 [0.12, 1.67]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>40.9%</b></td><td><b>0.95 [0.69, 1.32]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi<sup>2</sup> = 4.56, df = 2 (P = 0.10); I<sup>2</sup> = 56%</td></tr><tr><td colspan="6">Test for overall effect: Z = 0.30 (P = 0.76)</td></tr><tr><td colspan="6"><b>1.1.2 VNR+CTxA vs CTxA (1st line)</b></td></tr><tr><td>Ejlertsen B 2004</td><td>0.1249</td><td>0.1846</td><td>33.2%</td><td>1.13 [0.79, 1.63]</td><td></td></tr><tr><td>Norris B 2000</td><td>-0.1767</td><td>0.2093</td><td>25.8%</td><td>0.84 [0.56, 1.26]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>59.1%</b></td><td><b>0.99 [0.76, 1.30]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi<sup>2</sup> = 1.17, df = 1 (P = 0.28); I<sup>2</sup> = 14%</td></tr><tr><td colspan="6">Test for overall effect: Z = 0.05 (P = 0.96)</td></tr><tr><td><b>Total (95% CI)</b></td><td></td><td></td><td><b>100.0%</b></td><td><b>0.98 [0.79, 1.20]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi<sup>2</sup> = 5.77, df = 4 (P = 0.22); I<sup>2</sup> = 31%</td></tr><tr><td colspan="6">Test for overall effect: Z = 0.23 (P = 0.82)</td></tr><tr><td colspan="6">Test for subgroup differences: Chi<sup>2</sup> = 0.04, df = 1 (P = 0.84), I<sup>2</sup> = 0%</td></tr></tbody></table> <p>コメント: 有意水準に達しない</p> |               |                                   |                                                                                       | Study or Subgroup | log[Hazard Ratio] | SE | Weight | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI | <b>1.1.1 VNR+CTxA vs CTxB (1st line)</b> |  |  |  |  |  | Blajman C 1999 | 0.3927 | 0.2791 | 14.5% | 1.48 [0.86, 2.56] |  | Namer M 2001 | -0.2395 | 0.2174 | 24.0% | 0.79 [0.51, 1.21] |  | Riccardi A 2006 | -0.821 | 0.6802 | 2.4% | 0.44 [0.12, 1.67] |  | <b>Subtotal (95% CI)</b> |  |  | <b>40.9%</b> | <b>0.95 [0.69, 1.32]</b> |  | Heterogeneity: Chi <sup>2</sup> = 4.56, df = 2 (P = 0.10); I <sup>2</sup> = 56% |  |  |  |  |  | Test for overall effect: Z = 0.30 (P = 0.76) |  |  |  |  |  | <b>1.1.2 VNR+CTxA vs CTxA (1st line)</b> |  |  |  |  |  | Ejlertsen B 2004 | 0.1249 | 0.1846 | 33.2% | 1.13 [0.79, 1.63] |  | Norris B 2000 | -0.1767 | 0.2093 | 25.8% | 0.84 [0.56, 1.26] |  | <b>Subtotal (95% CI)</b> |  |  | <b>59.1%</b> | <b>0.99 [0.76, 1.30]</b> |  | Heterogeneity: Chi <sup>2</sup> = 1.17, df = 1 (P = 0.28); I <sup>2</sup> = 14% |  |  |  |  |  | Test for overall effect: Z = 0.05 (P = 0.96) |  |  |  |  |  | <b>Total (95% CI)</b> |  |  | <b>100.0%</b> | <b>0.98 [0.79, 1.20]</b> |  | Heterogeneity: Chi <sup>2</sup> = 5.77, df = 4 (P = 0.22); I <sup>2</sup> = 31% |  |  |  |  |  | Test for overall effect: Z = 0.23 (P = 0.82) |  |  |  |  |  | Test for subgroup differences: Chi <sup>2</sup> = 0.04, df = 1 (P = 0.84), I <sup>2</sup> = 0% |  |  |  |  |  |
| Study or Subgroup                                                                              | log[Hazard Ratio] | SE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Weight        | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI                                                     |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| <b>1.1.1 VNR+CTxA vs CTxB (1st line)</b>                                                       |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |               |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Blajman C 1999                                                                                 | 0.3927            | 0.2791                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 14.5%         | 1.48 [0.86, 2.56]                 |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Namer M 2001                                                                                   | -0.2395           | 0.2174                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 24.0%         | 0.79 [0.51, 1.21]                 |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Riccardi A 2006                                                                                | -0.821            | 0.6802                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 2.4%          | 0.44 [0.12, 1.67]                 |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                                                       |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | <b>40.9%</b>  | <b>0.95 [0.69, 1.32]</b>          |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Heterogeneity: Chi <sup>2</sup> = 4.56, df = 2 (P = 0.10); I <sup>2</sup> = 56%                |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |               |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Test for overall effect: Z = 0.30 (P = 0.76)                                                   |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |               |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| <b>1.1.2 VNR+CTxA vs CTxA (1st line)</b>                                                       |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |               |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Ejlertsen B 2004                                                                               | 0.1249            | 0.1846                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 33.2%         | 1.13 [0.79, 1.63]                 |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Norris B 2000                                                                                  | -0.1767           | 0.2093                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 25.8%         | 0.84 [0.56, 1.26]                 |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                                                       |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | <b>59.1%</b>  | <b>0.99 [0.76, 1.30]</b>          |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Heterogeneity: Chi <sup>2</sup> = 1.17, df = 1 (P = 0.28); I <sup>2</sup> = 14%                |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |               |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Test for overall effect: Z = 0.05 (P = 0.96)                                                   |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |               |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| <b>Total (95% CI)</b>                                                                          |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | <b>100.0%</b> | <b>0.98 [0.79, 1.20]</b>          |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Heterogeneity: Chi <sup>2</sup> = 5.77, df = 4 (P = 0.22); I <sup>2</sup> = 31%                |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |               |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Test for overall effect: Z = 0.23 (P = 0.82)                                                   |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |               |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Test for subgroup differences: Chi <sup>2</sup> = 0.04, df = 1 (P = 0.84), I <sup>2</sup> = 0% |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |               |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| Funnel plot                                                                                    |                   |  <p>コメント:</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |               |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| その他の解析                                                                                         |                   | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |               |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| メタリグレーション                                                                                      |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |               |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |
| 感度分析                                                                                           |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |               |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |        |        |       |                   |  |              |         |        |       |                   |  |                 |        |        |      |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |        |        |       |                   |  |               |         |        |       |                   |  |                          |  |  |              |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                                                 |  |  |  |  |  |                                              |  |  |  |  |  |                                                                                                |  |  |  |  |  |

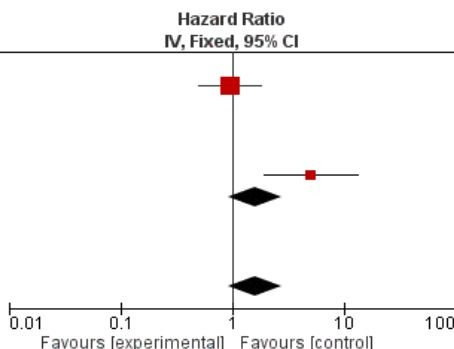
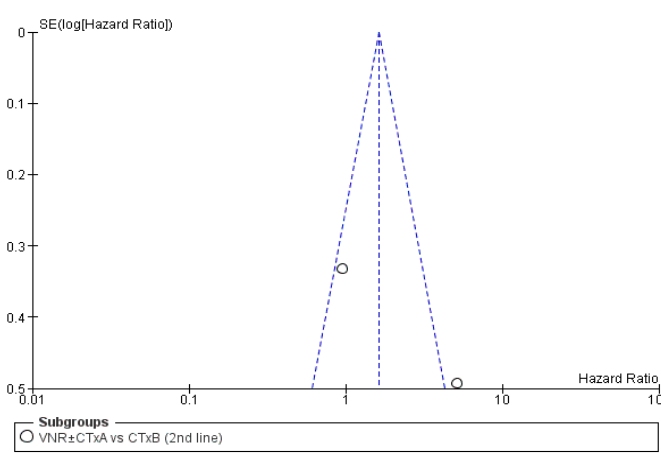
【4-9 メタアナリシス】

| CQ                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |              |                                     |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
|------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|--------------|-------------------------------------|-------------------------------------------------------------------------------|-----------------------------------|-------------------|----|--------|-----------------------------------|-----------------------------------|------------------------------------------|--|--|--|--|--|----------------|---------|--------|-------|-------------------|--|--------------|--------|--------|-------|-------------------|-----------------|--------|--------|------|-------------------|--------------------------|--|--|--------------|--------------------------|---------------------------------------------------------|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|------------------------------------------|--|--|--|--|--|------------------|---------|--------|-------|-------------------|--|---------------|---------|--------|-------|-------------------|--------------------------|--|--|--------------|--------------------------|--------------------------------------------------------|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|-----------------------|--|--|--|--|--|--|--|--|--|---------------|--------------------------|---------------------------------------------------------|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|------------------------------------------------------------------------|--|--|--|--|--|
| P                                                                      | HER2陰性転移・再発乳癌(女性)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                           | I            | ビノレルピンを含むレジメン                       |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| C                                                                      | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                           | O            | PFS                                 |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| 研究デザイン                                                                 | RCT(1st)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                           | 5            | コード                                 | Blajman C 1999, Namer M 2001, Riccardi A 2006, Norris B 2000, Ejlersen B 2004 |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
|                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 文献数                                       |              |                                     |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| モデル                                                                    | Fixed Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 方法                                        |              | Inverse Variance method (RevMan5.3) |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| 効果指標                                                                   | Hazard Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 統合値                                       |              | 0.78 ( 0.63 - 0.96 ) P= 0.02        |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| Forest plot                                                            | <table><thead><tr><th>Study or Subgroup</th><th>log[Hazard Ratio]</th><th>SE</th><th>Weight</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th></tr></thead><tbody><tr><td colspan="6"><b>1.2.1 VNR+CTxA vs CTxB (1st line)</b></td></tr><tr><td>Blajman C 1999</td><td>-0.3496</td><td>0.2791</td><td>14.2%</td><td>0.70 [0.41, 1.22]</td><td rowspan="4"></td></tr><tr><td>Namer M 2001</td><td>0.0573</td><td>0.2164</td><td>23.6%</td><td>1.06 [0.69, 1.62]</td></tr><tr><td>Riccardi A 2006</td><td>-0.821</td><td>0.4973</td><td>4.5%</td><td>0.44 [0.17, 1.17]</td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>42.3%</b></td><td><b>0.84 [0.61, 1.16]</b></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 3.23, df = 2 (P = 0.20); I² = 38%</td></tr><tr><td colspan="6">Test for overall effect: Z = 1.06 (P = 0.29)</td></tr><tr><td colspan="6"><b>1.2.2 VNR+CTxA vs CTxA (1st line)</b></td></tr><tr><td>Ejlertsen B 2004</td><td>-0.4339</td><td>0.1849</td><td>32.4%</td><td>0.65 [0.45, 0.93]</td><td rowspan="2"></td></tr><tr><td>Norris B 2000</td><td>-0.1416</td><td>0.2092</td><td>25.3%</td><td>0.87 [0.58, 1.31]</td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>57.7%</b></td><td><b>0.74 [0.56, 0.97]</b></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 1.10, df = 1 (P = 0.30); I² = 9%</td></tr><tr><td colspan="6">Test for overall effect: Z = 2.21 (P = 0.03)</td></tr><tr><td colspan="6"><b>Total (95% CI)</b></td></tr><tr><td colspan="4"></td><td><b>100.0%</b></td><td><b>0.78 [0.63, 0.96]</b></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 4.72, df = 4 (P = 0.32); I² = 15%</td></tr><tr><td colspan="6">Test for overall effect: Z = 2.37 (P = 0.02)</td></tr><tr><td colspan="6">Test for subgroup differences: Chi² = 0.39, df = 1 (P = 0.53), I² = 0%</td></tr></tbody></table> |                                           |              |                                     |                                                                               | Study or Subgroup                 | log[Hazard Ratio] | SE | Weight | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI | <b>1.2.1 VNR+CTxA vs CTxB (1st line)</b> |  |  |  |  |  | Blajman C 1999 | -0.3496 | 0.2791 | 14.2% | 0.70 [0.41, 1.22] |  | Namer M 2001 | 0.0573 | 0.2164 | 23.6% | 1.06 [0.69, 1.62] | Riccardi A 2006 | -0.821 | 0.4973 | 4.5% | 0.44 [0.17, 1.17] | <b>Subtotal (95% CI)</b> |  |  | <b>42.3%</b> | <b>0.84 [0.61, 1.16]</b> | Heterogeneity: Chi² = 3.23, df = 2 (P = 0.20); I² = 38% |  |  |  |  |  | Test for overall effect: Z = 1.06 (P = 0.29) |  |  |  |  |  | <b>1.2.2 VNR+CTxA vs CTxA (1st line)</b> |  |  |  |  |  | Ejlertsen B 2004 | -0.4339 | 0.1849 | 32.4% | 0.65 [0.45, 0.93] |  | Norris B 2000 | -0.1416 | 0.2092 | 25.3% | 0.87 [0.58, 1.31] | <b>Subtotal (95% CI)</b> |  |  | <b>57.7%</b> | <b>0.74 [0.56, 0.97]</b> | Heterogeneity: Chi² = 1.10, df = 1 (P = 0.30); I² = 9% |  |  |  |  |  | Test for overall effect: Z = 2.21 (P = 0.03) |  |  |  |  |  | <b>Total (95% CI)</b> |  |  |  |  |  |  |  |  |  | <b>100.0%</b> | <b>0.78 [0.63, 0.96]</b> | Heterogeneity: Chi² = 4.72, df = 4 (P = 0.32); I² = 15% |  |  |  |  |  | Test for overall effect: Z = 2.37 (P = 0.02) |  |  |  |  |  | Test for subgroup differences: Chi² = 0.39, df = 1 (P = 0.53), I² = 0% |  |  |  |  |  |
|                                                                        | Study or Subgroup                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | log[Hazard Ratio]                         | SE           | Weight                              | Hazard Ratio<br>IV, Fixed, 95% CI                                             | Hazard Ratio<br>IV, Fixed, 95% CI |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
|                                                                        | <b>1.2.1 VNR+CTxA vs CTxB (1st line)</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                           |              |                                     |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
|                                                                        | Blajman C 1999                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | -0.3496                                   | 0.2791       | 14.2%                               | 0.70 [0.41, 1.22]                                                             |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
|                                                                        | Namer M 2001                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 0.0573                                    | 0.2164       | 23.6%                               | 1.06 [0.69, 1.62]                                                             |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| Riccardi A 2006                                                        | -0.821                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0.4973                                    | 4.5%         | 0.44 [0.17, 1.17]                   |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           | <b>42.3%</b> | <b>0.84 [0.61, 1.16]</b>            |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| Heterogeneity: Chi² = 3.23, df = 2 (P = 0.20); I² = 38%                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |              |                                     |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| Test for overall effect: Z = 1.06 (P = 0.29)                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |              |                                     |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| <b>1.2.2 VNR+CTxA vs CTxA (1st line)</b>                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |              |                                     |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| Ejlertsen B 2004                                                       | -0.4339                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 0.1849                                    | 32.4%        | 0.65 [0.45, 0.93]                   |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| Norris B 2000                                                          | -0.1416                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 0.2092                                    | 25.3%        | 0.87 [0.58, 1.31]                   |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           | <b>57.7%</b> | <b>0.74 [0.56, 0.97]</b>            |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| Heterogeneity: Chi² = 1.10, df = 1 (P = 0.30); I² = 9%                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |              |                                     |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| Test for overall effect: Z = 2.21 (P = 0.03)                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |              |                                     |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| <b>Total (95% CI)</b>                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |              |                                     |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
|                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |              | <b>100.0%</b>                       | <b>0.78 [0.63, 0.96]</b>                                                      |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| Heterogeneity: Chi² = 4.72, df = 4 (P = 0.32); I² = 15%                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |              |                                     |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| Test for overall effect: Z = 2.37 (P = 0.02)                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |              |                                     |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| Test for subgroup differences: Chi² = 0.39, df = 1 (P = 0.53), I² = 0% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |              |                                     |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| コメント: ビノレルピンは他の1次化学療法に対して優位性はないが、上乗せすることでPFSを延長する。                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |              |                                     |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| Funnel plot                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |              |                                     |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
|                                                                        | コメント:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                           |              |                                     |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| その他の解析                                                                 | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |              |                                     |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| メタリグレーション                                                              | コメント:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                           |              |                                     |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |
| 感度分析                                                                   | コメント:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                           |              |                                     |                                                                               |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |                |         |        |       |                   |  |              |        |        |       |                   |                 |        |        |      |                   |                          |  |  |              |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                          |  |  |  |  |  |                  |         |        |       |                   |  |               |         |        |       |                   |                          |  |  |              |                          |                                                        |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |  |  |  |  |  |  |  |               |                          |                                                         |  |  |  |  |  |                                              |  |  |  |  |  |                                                                        |  |  |  |  |  |

【4-9 メタアナリシス】

| CQ                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |        |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
|---------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|--------|----------------|------------------------------------|-------------------------------------------------------------------------------|-------------------|-----------------------------------|-----------------------------------|----------------|--|--------|-----------------------------------|-----------------------------------|--------|-------|--------|-------|-------------------------------------|--|--|--|--|--|--|--|----------------|----|----|----|----|-------|-------------------|--|--------------|----|-----|----|-----|-------|-------------------|-----------------|---|---|---|---|--|---------------|-------------------|--|-----|--|-----|-------|-------------------|--------------|-----|--|-----|--|--|--|---------------------------------------------------------------------------------------------------------|--|--|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|--|--|------------------------------------------|--|--|--|--|--|--|--|------------------|----|-----|----|-----|-------|-------------------|--|---------------|----|-----|----|-----|-------|-------------------|-------------------|--|-----|--|-----|-------|-------------------|--------------|-----|--|-----|--|--|--|--|---------------------------------------------------------------------------------------------------------|--|--|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|--|--|----------------|--|-----|--|-----|--------|-------------------|--|--------------|-----|--|-----|--|--|--|--|---------------------------------------------------------------------------------------------------------|--|--|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|--|--|---------------------------------------------------------------------------------------------------|--|--|--|--|--|--|--|
| P                                                                                                       | HER2陰性転移・再発乳癌（女性）                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                           |        | I              | ビノレルピンを含むレジメン                      |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| C                                                                                                       | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                           |        | O              | ORR                                |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| 研究デザイン                                                                                                  | RCT(1st)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                           | 文献数    | 5              | コード                                | Blajman C 1999, Namer M 2001, Riccardi A 2006, Norris B 2000, Ejlersen B 2004 |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
|                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |        |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| モデル                                                                                                     | Random Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                           | 方法     |                | Mantel-Haenszel method (RevMan5.3) |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| 効果指標                                                                                                    | Risk Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                           | 統合値    |                | 1.09 ( 0.97 - 1.23 ) P= 0.13       |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Forest plot                                                                                             | <table><thead><tr><th rowspan="2">Study or Subgroup</th><th colspan="2">VNR containing regimens</th><th colspan="2">Other regimens</th><th rowspan="2">Weight</th><th rowspan="2">Risk Ratio<br/>M-H, Random, 95% CI</th><th rowspan="2">Risk Ratio<br/>M-H, Random, 95% CI</th></tr><tr><th>Events</th><th>Total</th><th>Events</th><th>Total</th></tr></thead><tbody><tr><td colspan="8"><b>1.3.1 VNR+CTxA vs CTxB (1st)</b></td></tr><tr><td>Blajman C 1999</td><td>64</td><td>85</td><td>63</td><td>85</td><td>45.0%</td><td>1.02 [0.85, 1.21]</td><td rowspan="5"></td></tr><tr><td>Namer M 2001</td><td>49</td><td>142</td><td>46</td><td>138</td><td>12.9%</td><td>1.04 [0.75, 1.44]</td></tr><tr><td>Riccardi A 2006</td><td>0</td><td>0</td><td>0</td><td>0</td><td></td><td>Not estimable</td></tr><tr><td>Subtotal (95% CI)</td><td></td><td>227</td><td></td><td>223</td><td>57.9%</td><td>1.02 [0.87, 1.19]</td></tr><tr><td>Total events</td><td>113</td><td></td><td>109</td><td></td><td></td><td></td></tr><tr><td colspan="8">Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 0.01, df = 1 (P = 0.91); I<sup>2</sup> = 0%</td></tr><tr><td colspan="8">Test for overall effect: Z = 0.25 (P = 0.80)</td></tr><tr><td colspan="8"><b>1.3.2 VNR+CTxA vs CTxA (1st line)</b></td></tr><tr><td>Ejlertsen B 2004</td><td>96</td><td>193</td><td>81</td><td>194</td><td>28.9%</td><td>1.19 [0.96, 1.48]</td><td rowspan="3"></td></tr><tr><td>Norris B 2000</td><td>55</td><td>145</td><td>44</td><td>144</td><td>13.3%</td><td>1.24 [0.90, 1.71]</td></tr><tr><td>Subtotal (95% CI)</td><td></td><td>338</td><td></td><td>338</td><td>42.1%</td><td>1.21 [1.01, 1.45]</td></tr><tr><td>Total events</td><td>151</td><td></td><td>125</td><td></td><td></td><td></td><td></td></tr><tr><td colspan="8">Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 0.04, df = 1 (P = 0.84); I<sup>2</sup> = 0%</td></tr><tr><td colspan="8">Test for overall effect: Z = 2.04 (P = 0.04)</td></tr><tr><td>Total (95% CI)</td><td></td><td>565</td><td></td><td>561</td><td>100.0%</td><td>1.09 [0.97, 1.23]</td><td></td></tr><tr><td>Total events</td><td>264</td><td></td><td>234</td><td></td><td></td><td></td><td></td></tr><tr><td colspan="8">Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 2.15, df = 3 (P = 0.54); I<sup>2</sup> = 0%</td></tr><tr><td colspan="8">Test for overall effect: Z = 1.51 (P = 0.13)</td></tr><tr><td colspan="8">Test for subgroup differences: Chi<sup>2</sup> = 1.92, df = 1 (P = 0.17), I<sup>2</sup> = 47.9%</td></tr></tbody></table> |                                           |        |                |                                    |                                                                               | Study or Subgroup | VNR containing regimens           |                                   | Other regimens |  | Weight | Risk Ratio<br>M-H, Random, 95% CI | Risk Ratio<br>M-H, Random, 95% CI | Events | Total | Events | Total | <b>1.3.1 VNR+CTxA vs CTxB (1st)</b> |  |  |  |  |  |  |  | Blajman C 1999 | 64 | 85 | 63 | 85 | 45.0% | 1.02 [0.85, 1.21] |  | Namer M 2001 | 49 | 142 | 46 | 138 | 12.9% | 1.04 [0.75, 1.44] | Riccardi A 2006 | 0 | 0 | 0 | 0 |  | Not estimable | Subtotal (95% CI) |  | 227 |  | 223 | 57.9% | 1.02 [0.87, 1.19] | Total events | 113 |  | 109 |  |  |  | Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.01, df = 1 (P = 0.91); I <sup>2</sup> = 0% |  |  |  |  |  |  |  | Test for overall effect: Z = 0.25 (P = 0.80) |  |  |  |  |  |  |  | <b>1.3.2 VNR+CTxA vs CTxA (1st line)</b> |  |  |  |  |  |  |  | Ejlertsen B 2004 | 96 | 193 | 81 | 194 | 28.9% | 1.19 [0.96, 1.48] |  | Norris B 2000 | 55 | 145 | 44 | 144 | 13.3% | 1.24 [0.90, 1.71] | Subtotal (95% CI) |  | 338 |  | 338 | 42.1% | 1.21 [1.01, 1.45] | Total events | 151 |  | 125 |  |  |  |  | Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.04, df = 1 (P = 0.84); I <sup>2</sup> = 0% |  |  |  |  |  |  |  | Test for overall effect: Z = 2.04 (P = 0.04) |  |  |  |  |  |  |  | Total (95% CI) |  | 565 |  | 561 | 100.0% | 1.09 [0.97, 1.23] |  | Total events | 264 |  | 234 |  |  |  |  | Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.15, df = 3 (P = 0.54); I <sup>2</sup> = 0% |  |  |  |  |  |  |  | Test for overall effect: Z = 1.51 (P = 0.13) |  |  |  |  |  |  |  | Test for subgroup differences: Chi <sup>2</sup> = 1.92, df = 1 (P = 0.17), I <sup>2</sup> = 47.9% |  |  |  |  |  |  |  |
|                                                                                                         | Study or Subgroup                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | VNR containing regimens                   |        | Other regimens |                                    | Weight                                                                        |                   | Risk Ratio<br>M-H, Random, 95% CI | Risk Ratio<br>M-H, Random, 95% CI |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Events                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Total                                     | Events | Total          |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| <b>1.3.1 VNR+CTxA vs CTxB (1st)</b>                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |        |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Blajman C 1999                                                                                          | 64                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 85                                        | 63     | 85             | 45.0%                              | 1.02 [0.85, 1.21]                                                             |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Namer M 2001                                                                                            | 49                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 142                                       | 46     | 138            | 12.9%                              | 1.04 [0.75, 1.44]                                                             |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Riccardi A 2006                                                                                         | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 0                                         | 0      | 0              |                                    | Not estimable                                                                 |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Subtotal (95% CI)                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 227                                       |        | 223            | 57.9%                              | 1.02 [0.87, 1.19]                                                             |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Total events                                                                                            | 113                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           | 109    |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.01, df = 1 (P = 0.91); I <sup>2</sup> = 0% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |        |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Test for overall effect: Z = 0.25 (P = 0.80)                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |        |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| <b>1.3.2 VNR+CTxA vs CTxA (1st line)</b>                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |        |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Ejlertsen B 2004                                                                                        | 96                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 193                                       | 81     | 194            | 28.9%                              | 1.19 [0.96, 1.48]                                                             |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Norris B 2000                                                                                           | 55                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 145                                       | 44     | 144            | 13.3%                              | 1.24 [0.90, 1.71]                                                             |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Subtotal (95% CI)                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 338                                       |        | 338            | 42.1%                              | 1.21 [1.01, 1.45]                                                             |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Total events                                                                                            | 151                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           | 125    |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.04, df = 1 (P = 0.84); I <sup>2</sup> = 0% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |        |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Test for overall effect: Z = 2.04 (P = 0.04)                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |        |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Total (95% CI)                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 565                                       |        | 561            | 100.0%                             | 1.09 [0.97, 1.23]                                                             |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Total events                                                                                            | 264                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           | 234    |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.15, df = 3 (P = 0.54); I <sup>2</sup> = 0% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |        |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Test for overall effect: Z = 1.51 (P = 0.13)                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |        |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Test for subgroup differences: Chi <sup>2</sup> = 1.92, df = 1 (P = 0.17), I <sup>2</sup> = 47.9%       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |        |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| コメント： ビノレルピンは他の1次化学療法に対して優位性はないが、上乗せすることでORRを改善する。                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |        |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| Funnel plot                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |        |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
|                                                                                                         | コメント：                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                           |        |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| その他の解析                                                                                                  | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                           |        |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| メタリグレーション                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |        |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
| 感度分析                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |        |                |                                    |                                                                               |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |
|                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                           |        |                |                                    | コメント：                                                                         |                   |                                   |                                   |                |  |        |                                   |                                   |        |       |        |       |                                     |  |  |  |  |  |  |  |                |    |    |    |    |       |                   |  |              |    |     |    |     |       |                   |                 |   |   |   |   |  |               |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                          |  |  |  |  |  |  |  |                  |    |     |    |     |       |                   |  |               |    |     |    |     |       |                   |                   |  |     |  |     |       |                   |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |     |  |     |  |  |  |  |                                                                                                         |  |  |  |  |  |  |  |                                              |  |  |  |  |  |  |  |                                                                                                   |  |  |  |  |  |  |  |

【4-9 メタアナリシス】

| CQ                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？ |               |                                     |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
|----------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|---------------|-------------------------------------|--------------------------------------------------------------------------------|-----------------------------------|-------------------|----|--------|-----------------------------------|-----------------------------------|------------------------------------------|--|--|--|--|--|---------------|--------|--------|-------|-------------------|--|----------------|---|---|--|---------------|--|-----------------|---|---|--|---------------|--|------------------|---|---|--|---------------|--|--------------|--------|--------|-------|--------------------|--|--------------------------|--|--|---------------|--------------------------|--|----------------------------------------------------------|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|-----------------------|--|--|---------------|--------------------------|--|----------------------------------------------------------|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|-----------------------------------------------|--|--|--|--|--|
| P                                                        | HER2陰性転移・再発乳癌(女性)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                           | I             | ビノレルビンを含むレジメン                       |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| C                                                        | その他のレジメン                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                           | O             | OS                                  |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| 研究デザイン                                                   | RCT(2nd)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 文献数                                       | 5             | コード                                 | Meier CR 2008, Verma S 2007, Palmieri C 2012, Pallis AG 2012, Stemmler HJ 2011 |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
|                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |               |                                     |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| モデル                                                      | Fixed Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 方法                                        |               | Inverse Variance method (RevMan5.3) |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| 効果指標                                                     | Hazard Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 統合値                                       |               | 1.61 ( 0.94 – 2.76 ) P= 0.08        |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Forest plot                                              | <table><thead><tr><th>Study or Subgroup</th><th>log[Hazard Ratio]</th><th>SE</th><th>Weight</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th></tr></thead><tbody><tr><td colspan="6"><b>2.1.1 VNR±CTxA vs CTxB (2nd line)</b></td></tr><tr><td>Meier CR 2008</td><td>-0.046</td><td>0.3312</td><td>68.8%</td><td>0.96 [0.50, 1.83]</td><td></td></tr><tr><td>Pallis AG 2012</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Palmieri C 2012</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Stemmler HJ 2011</td><td>0</td><td>0</td><td></td><td>Not estimable</td><td></td></tr><tr><td>Verma S 2007</td><td>1.6245</td><td>0.4913</td><td>31.2%</td><td>5.08 [1.94, 13.30]</td><td></td></tr><tr><td><b>Subtotal (95% CI)</b></td><td></td><td></td><td><b>100.0%</b></td><td><b>1.61 [0.94, 2.76]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 7.95, df = 1 (P = 0.005); I² = 87%</td></tr><tr><td colspan="6">Test for overall effect: Z = 1.73 (P = 0.08)</td></tr><tr><td><b>Total (95% CI)</b></td><td></td><td></td><td><b>100.0%</b></td><td><b>1.61 [0.94, 2.76]</b></td><td></td></tr><tr><td colspan="6">Heterogeneity: Chi² = 7.95, df = 1 (P = 0.005); I² = 87%</td></tr><tr><td colspan="6">Test for overall effect: Z = 1.73 (P = 0.08)</td></tr><tr><td colspan="6">Test for subgroup differences: Not applicable</td></tr></tbody></table>  |                                           |               |                                     |                                                                                | Study or Subgroup                 | log[Hazard Ratio] | SE | Weight | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI | <b>2.1.1 VNR±CTxA vs CTxB (2nd line)</b> |  |  |  |  |  | Meier CR 2008 | -0.046 | 0.3312 | 68.8% | 0.96 [0.50, 1.83] |  | Pallis AG 2012 | 0 | 0 |  | Not estimable |  | Palmieri C 2012 | 0 | 0 |  | Not estimable |  | Stemmler HJ 2011 | 0 | 0 |  | Not estimable |  | Verma S 2007 | 1.6245 | 0.4913 | 31.2% | 5.08 [1.94, 13.30] |  | <b>Subtotal (95% CI)</b> |  |  | <b>100.0%</b> | <b>1.61 [0.94, 2.76]</b> |  | Heterogeneity: Chi² = 7.95, df = 1 (P = 0.005); I² = 87% |  |  |  |  |  | Test for overall effect: Z = 1.73 (P = 0.08) |  |  |  |  |  | <b>Total (95% CI)</b> |  |  | <b>100.0%</b> | <b>1.61 [0.94, 2.76]</b> |  | Heterogeneity: Chi² = 7.95, df = 1 (P = 0.005); I² = 87% |  |  |  |  |  | Test for overall effect: Z = 1.73 (P = 0.08) |  |  |  |  |  | Test for subgroup differences: Not applicable |  |  |  |  |  |
|                                                          | Study or Subgroup                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | log[Hazard Ratio]                         | SE            | Weight                              | Hazard Ratio<br>IV, Fixed, 95% CI                                              | Hazard Ratio<br>IV, Fixed, 95% CI |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| <b>2.1.1 VNR±CTxA vs CTxB (2nd line)</b>                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |               |                                     |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Meier CR 2008                                            | -0.046                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 0.3312                                    | 68.8%         | 0.96 [0.50, 1.83]                   |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Pallis AG 2012                                           | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 0                                         |               | Not estimable                       |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Palmieri C 2012                                          | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 0                                         |               | Not estimable                       |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Stemmler HJ 2011                                         | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 0                                         |               | Not estimable                       |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Verma S 2007                                             | 1.6245                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 0.4913                                    | 31.2%         | 5.08 [1.94, 13.30]                  |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           | <b>100.0%</b> | <b>1.61 [0.94, 2.76]</b>            |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Heterogeneity: Chi² = 7.95, df = 1 (P = 0.005); I² = 87% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |               |                                     |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Test for overall effect: Z = 1.73 (P = 0.08)             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |               |                                     |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| <b>Total (95% CI)</b>                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           | <b>100.0%</b> | <b>1.61 [0.94, 2.76]</b>            |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Heterogeneity: Chi² = 7.95, df = 1 (P = 0.005); I² = 87% |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |               |                                     |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Test for overall effect: Z = 1.73 (P = 0.08)             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |               |                                     |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Test for subgroup differences: Not applicable            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |               |                                     |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| コメント: 有意水準に達しない。異質性高い。                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |               |                                     |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| Funnel plot                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                           |               |                                     |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
|                                                          | コメント:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                           |               |                                     |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| その他の解析                                                   | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                           |               |                                     |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| メタリグレーション                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |               |                                     |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |
| 感度分析                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                           |               |                                     |                                                                                |                                   |                   |    |        |                                   |                                   |                                          |  |  |  |  |  |               |        |        |       |                   |  |                |   |   |  |               |  |                 |   |   |  |               |  |                  |   |   |  |               |  |              |        |        |       |                    |  |                          |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                       |  |  |               |                          |  |                                                          |  |  |  |  |  |                                              |  |  |  |  |  |                                               |  |  |  |  |  |

【4-9 メタアナリシス】

| CQ                                                                                                                             |                   | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |        |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
|--------------------------------------------------------------------------------------------------------------------------------|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|-----------------------------------|---------------------------------------------------------------------------------------|-------------------|-------------------|----|--------|-----------------------------------|-----------------------------------|-----------------------------------|--|--|--|--|--|---------------|--------|--------|--------|-------------------|--|----------------|---|---|--|---------------|-----------------|---|---|--|---------------|------------------|---|---|--|---------------|--------------|---|---|--|---------------|--------------------------|--|--|--|---------------|--------------------------|-------------------------------------------------------------------------------|--|--|--|--|--|-----------------------|--|--|--|---------------|--------------------------|--------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|--|
| P                                                                                                                              | HER2陰性転移・再発乳癌(女性) |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | I      | ビノレルビンを含むレジメン                     |                                                                                       |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| C                                                                                                                              | その他のレジメン          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | O      | PFS                               |                                                                                       |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| 研究デザイン                                                                                                                         |                   | RCT(2nd)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 文献数    | 5                                 | コード<br>Meier CR 2008, Verma S 2007, Palmieri C 2012, Pallis AG 2012, Stemmler HJ 2011 |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| モデル                                                                                                                            |                   | Fixed Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 方法     |                                   | Inverse Variance method (RevMan5.3)                                                   |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| 効果指標                                                                                                                           |                   | Hazard Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 統合値    |                                   | 1.35 ( 0.71 – 2.60 ) P= 0.36                                                          |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| Forest plot                                                                                                                    |                   | <table><thead><tr><th>Study or Subgroup</th><th>log[Hazard Ratio]</th><th>SE</th><th>Weight</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th><th>Hazard Ratio<br/>IV, Fixed, 95% CI</th></tr></thead><tbody><tr><td colspan="6">2.2.1 VNR±CTxA vs CTxB (2nd line)</td></tr><tr><td>Meier CR 2008</td><td>0.3038</td><td>0.3319</td><td>100.0%</td><td>1.35 [0.71, 2.60]</td><td rowspan="5"></td></tr><tr><td>Pallis AG 2012</td><td>0</td><td>0</td><td></td><td>Not estimable</td></tr><tr><td>Palmieri C 2012</td><td>0</td><td>0</td><td></td><td>Not estimable</td></tr><tr><td>Stemmler HJ 2011</td><td>0</td><td>0</td><td></td><td>Not estimable</td></tr><tr><td>Verma S 2007</td><td>0</td><td>0</td><td></td><td>Not estimable</td></tr><tr><td colspan="4"><b>Subtotal (95% CI)</b></td><td><b>100.0%</b></td><td><b>1.35 [0.71, 2.60]</b></td></tr><tr><td colspan="6">Heterogeneity: Not applicable<br/>Test for overall effect: Z = 0.92 (P = 0.36)</td></tr><tr><td colspan="4"><b>Total (95% CI)</b></td><td><b>100.0%</b></td><td><b>1.35 [0.71, 2.60]</b></td></tr><tr><td colspan="6">Heterogeneity: Not applicable<br/>Test for overall effect: Z = 0.92 (P = 0.36)<br/>Test for subgroup differences: Not applicable</td></tr></tbody></table> |        |                                   |                                                                                       | Study or Subgroup | log[Hazard Ratio] | SE | Weight | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI | 2.2.1 VNR±CTxA vs CTxB (2nd line) |  |  |  |  |  | Meier CR 2008 | 0.3038 | 0.3319 | 100.0% | 1.35 [0.71, 2.60] |  | Pallis AG 2012 | 0 | 0 |  | Not estimable | Palmieri C 2012 | 0 | 0 |  | Not estimable | Stemmler HJ 2011 | 0 | 0 |  | Not estimable | Verma S 2007 | 0 | 0 |  | Not estimable | <b>Subtotal (95% CI)</b> |  |  |  | <b>100.0%</b> | <b>1.35 [0.71, 2.60]</b> | Heterogeneity: Not applicable<br>Test for overall effect: Z = 0.92 (P = 0.36) |  |  |  |  |  | <b>Total (95% CI)</b> |  |  |  | <b>100.0%</b> | <b>1.35 [0.71, 2.60]</b> | Heterogeneity: Not applicable<br>Test for overall effect: Z = 0.92 (P = 0.36)<br>Test for subgroup differences: Not applicable |  |  |  |  |  |
| Study or Subgroup                                                                                                              | log[Hazard Ratio] | SE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Weight | Hazard Ratio<br>IV, Fixed, 95% CI | Hazard Ratio<br>IV, Fixed, 95% CI                                                     |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| 2.2.1 VNR±CTxA vs CTxB (2nd line)                                                                                              |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |        |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| Meier CR 2008                                                                                                                  | 0.3038            | 0.3319                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 100.0% | 1.35 [0.71, 2.60]                 |                                                                                       |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| Pallis AG 2012                                                                                                                 | 0                 | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |        | Not estimable                     |                                                                                       |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| Palmieri C 2012                                                                                                                | 0                 | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |        | Not estimable                     |                                                                                       |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| Stemmler HJ 2011                                                                                                               | 0                 | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |        | Not estimable                     |                                                                                       |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| Verma S 2007                                                                                                                   | 0                 | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |        | Not estimable                     |                                                                                       |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| <b>Subtotal (95% CI)</b>                                                                                                       |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |        | <b>100.0%</b>                     | <b>1.35 [0.71, 2.60]</b>                                                              |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| Heterogeneity: Not applicable<br>Test for overall effect: Z = 0.92 (P = 0.36)                                                  |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |        |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| <b>Total (95% CI)</b>                                                                                                          |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |        | <b>100.0%</b>                     | <b>1.35 [0.71, 2.60]</b>                                                              |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| Heterogeneity: Not applicable<br>Test for overall effect: Z = 0.92 (P = 0.36)<br>Test for subgroup differences: Not applicable |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |        |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| コメント:                                                                                                                          |                   | 1試験しかデータが得られない。有意水準に達しない。                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |        |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| Funnel plot                                                                                                                    |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |        |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| コメント:                                                                                                                          |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |        |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| その他の解析                                                                                                                         |                   | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |        |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| メタリグレーション                                                                                                                      |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |        |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |
| 感度分析                                                                                                                           |                   | コメント:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |        |                                   |                                                                                       |                   |                   |    |        |                                   |                                   |                                   |  |  |  |  |  |               |        |        |        |                   |  |                |   |   |  |               |                 |   |   |  |               |                  |   |   |  |               |              |   |   |  |               |                          |  |  |  |               |                          |                                                                               |  |  |  |  |  |                       |  |  |  |               |                          |                                                                                                                                |  |  |  |  |  |



【4-9 メタアナリシス】

| CQ                                                                                                                                                                   |                         | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                |       |                                                                                |                     |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|-------|--------------------------------------------------------------------------------|---------------------|-----------------------------------|--|----------------|--|--------|------------|--|--------|-------|--------|-------|---------------------|-----------------------------------|-----------------------------------|--|--|--|--|--|--|--|---------------|----|----|----|----|-------|-------------------|--|----------------|----|----|----|----|-------|-------------------|-----------------|---|----|---|----|------|-------------------|------------------|----|----|----|----|-------|-------------------|--------------|---|----|---|----|--|---------------|-------------------|--|-----|--|-----|--------|-------------------|--|--------------|--|----|--|----|--|--|--|---------------------------------------------------------------------------------------------------------------------|--|--|--|--|--|--|--|----------------|--|-----|--|-----|--------|-------------------|--|--------------|--|----|--|----|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|--|--|--|
| P                                                                                                                                                                    | HER2陰性転移・再発乳癌(女性)       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                | I     | ビノレルビンを含むレジメン                                                                  |                     |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| C                                                                                                                                                                    | その他のレジメン                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                | O     | ORR                                                                            |                     |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| 研究デザイン                                                                                                                                                               |                         | RCT(2nd)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 文献数            | 5     | Meier CR 2008, Verma S 2007, Palmieri C 2012, Pallis AG 2012, Stemmler HJ 2011 |                     |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| モデル                                                                                                                                                                  |                         | Random Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 方法             |       | Mantel-Haenszel method (RevMan5.3)                                             |                     |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| 効果指標                                                                                                                                                                 |                         | Risk Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 統合値            |       | 0.96 ( 0.69 – 1.34 ) P= 0.82                                                   |                     |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| Forest plot                                                                                                                                                          |                         | <table><thead><tr><th rowspan="2">Study or Subgroup</th><th colspan="2">VNR containing regimens</th><th colspan="2">Other regimens</th><th rowspan="2">Weight</th><th colspan="2">Risk Ratio</th></tr><tr><th>Events</th><th>Total</th><th>Events</th><th>Total</th><th>M-H, Random, 95% CI</th><th>Risk Ratio<br/>M-H, Random, 95% CI</th></tr></thead><tbody><tr><td colspan="8">2.3.1 VNR±CTxA vs CTxB (2nd line)</td></tr><tr><td>Meier CR 2008</td><td>11</td><td>62</td><td>17</td><td>58</td><td>24.3%</td><td>0.61 [0.31, 1.18]</td><td rowspan="5"></td></tr><tr><td>Pallis AG 2012</td><td>21</td><td>74</td><td>18</td><td>74</td><td>36.9%</td><td>1.17 [0.68, 2.00]</td></tr><tr><td>Palmieri C 2012</td><td>1</td><td>18</td><td>2</td><td>17</td><td>2.1%</td><td>0.47 [0.05, 4.74]</td></tr><tr><td>Stemmler HJ 2011</td><td>16</td><td>41</td><td>17</td><td>49</td><td>36.7%</td><td>1.12 [0.65, 1.93]</td></tr><tr><td>Verma S 2007</td><td>0</td><td>45</td><td>0</td><td>68</td><td></td><td>Not estimable</td></tr><tr><td>Subtotal (95% CI)</td><td></td><td>240</td><td></td><td>266</td><td>100.0%</td><td>0.96 [0.69, 1.34]</td><td></td></tr><tr><td colspan="2">Total events</td><td>49</td><td></td><td>54</td><td></td><td></td><td></td></tr><tr><td colspan="8">Heterogeneity: Tau² = 0.00; Chi² = 3.04, df = 3 (P = 0.39); I² = 1%<br/>Test for overall effect: Z = 0.22 (P = 0.82)</td></tr><tr><td colspan="2">Total (95% CI)</td><td>240</td><td></td><td>266</td><td>100.0%</td><td>0.96 [0.69, 1.34]</td><td></td></tr><tr><td colspan="2">Total events</td><td>49</td><td></td><td>54</td><td></td><td></td><td></td></tr><tr><td colspan="8">Heterogeneity: Tau² = 0.00; Chi² = 3.04, df = 3 (P = 0.39); I² = 1%<br/>Test for overall effect: Z = 0.22 (P = 0.82)<br/>Test for subgroup differences: Not applicable</td></tr></tbody></table> <p>コメント: 有意水準に達しない</p> |                |       |                                                                                | Study or Subgroup   | VNR containing regimens           |  | Other regimens |  | Weight | Risk Ratio |  | Events | Total | Events | Total | M-H, Random, 95% CI | Risk Ratio<br>M-H, Random, 95% CI | 2.3.1 VNR±CTxA vs CTxB (2nd line) |  |  |  |  |  |  |  | Meier CR 2008 | 11 | 62 | 17 | 58 | 24.3% | 0.61 [0.31, 1.18] |  | Pallis AG 2012 | 21 | 74 | 18 | 74 | 36.9% | 1.17 [0.68, 2.00] | Palmieri C 2012 | 1 | 18 | 2 | 17 | 2.1% | 0.47 [0.05, 4.74] | Stemmler HJ 2011 | 16 | 41 | 17 | 49 | 36.7% | 1.12 [0.65, 1.93] | Verma S 2007 | 0 | 45 | 0 | 68 |  | Not estimable | Subtotal (95% CI) |  | 240 |  | 266 | 100.0% | 0.96 [0.69, 1.34] |  | Total events |  | 49 |  | 54 |  |  |  | Heterogeneity: Tau² = 0.00; Chi² = 3.04, df = 3 (P = 0.39); I² = 1%<br>Test for overall effect: Z = 0.22 (P = 0.82) |  |  |  |  |  |  |  | Total (95% CI) |  | 240 |  | 266 | 100.0% | 0.96 [0.69, 1.34] |  | Total events |  | 49 |  | 54 |  |  |  | Heterogeneity: Tau² = 0.00; Chi² = 3.04, df = 3 (P = 0.39); I² = 1%<br>Test for overall effect: Z = 0.22 (P = 0.82)<br>Test for subgroup differences: Not applicable |  |  |  |  |  |  |  |
| Study or Subgroup                                                                                                                                                    | VNR containing regimens |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Other regimens |       | Weight                                                                         |                     | Risk Ratio                        |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
|                                                                                                                                                                      | Events                  | Total                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Events         | Total |                                                                                | M-H, Random, 95% CI | Risk Ratio<br>M-H, Random, 95% CI |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| 2.3.1 VNR±CTxA vs CTxB (2nd line)                                                                                                                                    |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                |       |                                                                                |                     |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| Meier CR 2008                                                                                                                                                        | 11                      | 62                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 17             | 58    | 24.3%                                                                          | 0.61 [0.31, 1.18]   |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| Pallis AG 2012                                                                                                                                                       | 21                      | 74                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 18             | 74    | 36.9%                                                                          | 1.17 [0.68, 2.00]   |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| Palmieri C 2012                                                                                                                                                      | 1                       | 18                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 2              | 17    | 2.1%                                                                           | 0.47 [0.05, 4.74]   |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| Stemmler HJ 2011                                                                                                                                                     | 16                      | 41                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 17             | 49    | 36.7%                                                                          | 1.12 [0.65, 1.93]   |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| Verma S 2007                                                                                                                                                         | 0                       | 45                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 0              | 68    |                                                                                | Not estimable       |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| Subtotal (95% CI)                                                                                                                                                    |                         | 240                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                | 266   | 100.0%                                                                         | 0.96 [0.69, 1.34]   |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| Total events                                                                                                                                                         |                         | 49                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                | 54    |                                                                                |                     |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| Heterogeneity: Tau² = 0.00; Chi² = 3.04, df = 3 (P = 0.39); I² = 1%<br>Test for overall effect: Z = 0.22 (P = 0.82)                                                  |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                |       |                                                                                |                     |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| Total (95% CI)                                                                                                                                                       |                         | 240                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                | 266   | 100.0%                                                                         | 0.96 [0.69, 1.34]   |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| Total events                                                                                                                                                         |                         | 49                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                | 54    |                                                                                |                     |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| Heterogeneity: Tau² = 0.00; Chi² = 3.04, df = 3 (P = 0.39); I² = 1%<br>Test for overall effect: Z = 0.22 (P = 0.82)<br>Test for subgroup differences: Not applicable |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                |       |                                                                                |                     |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| Funnel plot                                                                                                                                                          |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                |       |                                                                                |                     |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| その他の解析                                                                                                                                                               |                         | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                |       |                                                                                |                     |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| メタリグレーション                                                                                                                                                            |                         | コメント:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                |       |                                                                                |                     |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |
| 感度分析                                                                                                                                                                 |                         | コメント:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                |       |                                                                                |                     |                                   |  |                |  |        |            |  |        |       |        |       |                     |                                   |                                   |  |  |  |  |  |  |  |               |    |    |    |    |       |                   |  |                |    |    |    |    |       |                   |                 |   |    |   |    |      |                   |                  |    |    |    |    |       |                   |              |   |    |   |    |  |               |                   |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                     |  |  |  |  |  |  |  |                |  |     |  |     |        |                   |  |              |  |    |  |    |  |  |  |                                                                                                                                                                      |  |  |  |  |  |  |  |

【4-9 メタアナリシス】

| CQ                                                                   |                   | HER2陰性転移・再発乳癌に対する一次・二次以降の化学療法として何が推奨されるか？                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |         |       |                                                                                                                                                                       |                     |                     |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
|----------------------------------------------------------------------|-------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|--|---------|--|--------|------------|--|--------|-------|--------|-------|---------------------|---------------------|------------------|----|-----|----|-----|-------|-------------------|--|---------------|----|----|----|----|-------|-------------------|---------------|----|-----|---|-----|-------|-------------------|----------------|---|----|---|----|-------|-------------------|----------------|--|-----|--|-----|--------|-------------------|--------------------|--|--|--|--|--|--|----------------------------------------------------------------------|--|--|--|--|--|--|----------------------------------------------|--|--|--|--|--|--|
| P                                                                    | HER2陰性転移・再発乳癌（女性） |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |         | I     | ビノレルビンを含むレジメン                                                                                                                                                         |                     |                     |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| C                                                                    | その他のレジメン          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |         | O     | Toxicity (therapy discontinuation)                                                                                                                                    |                     |                     |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| 研究デザイン                                                               |                   | RCT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 文献数     | 10    | コード<br>Blajman C 1999, Namer M 2001, Riccardi A 2006, Norris B 2000, Ejlertsen B 2004, Meier CR 2008, Verma S 2007, Palmieri C 2012, Pallis AG 2012, Stemmler HJ 2011 |                     |                     |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| モデル                                                                  |                   | Random Effect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 方法      |       | Mantel-Haenszel method (RevMan5.3)                                                                                                                                    |                     |                     |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| 効果指標                                                                 |                   | Risk Ratio                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 統合値     |       | 0.97 ( 0.51 - 1.84 ) P= 0.93                                                                                                                                          |                     |                     |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Forest plot                                                          |                   | <table><thead><tr><th rowspan="2">Study or Subgroup</th><th colspan="2">Experimental</th><th colspan="2">Control</th><th rowspan="2">Weight</th><th colspan="2">Risk Ratio</th></tr><tr><th>Events</th><th>Total</th><th>Events</th><th>Total</th><th>M-H, Random, 95% CI</th><th>M-H, Random, 95% CI</th></tr></thead><tbody><tr><td>Ejlertsen B 2004</td><td>17</td><td>193</td><td>23</td><td>194</td><td>31.1%</td><td>0.74 [0.41, 1.35]</td><td rowspan="5"></td></tr><tr><td>Meier CR 2008</td><td>13</td><td>95</td><td>21</td><td>97</td><td>30.1%</td><td>0.63 [0.34, 1.19]</td></tr><tr><td>Norris B 2000</td><td>17</td><td>151</td><td>6</td><td>149</td><td>23.0%</td><td>2.80 [1.13, 6.90]</td></tr><tr><td>Pallis AG 2012</td><td>4</td><td>74</td><td>5</td><td>74</td><td>15.8%</td><td>0.80 [0.22, 2.86]</td></tr><tr><td>Total (95% CI)</td><td></td><td>513</td><td></td><td>514</td><td>100.0%</td><td>0.97 [0.51, 1.84]</td></tr><tr><td colspan="7">Total events 51 55</td></tr><tr><td colspan="7">Heterogeneity: Tau² = 0.25; Chi² = 7.76, df = 3 (P = 0.05); I² = 61%</td></tr><tr><td colspan="7">Test for overall effect: Z = 0.09 (P = 0.93)</td></tr></tbody></table> <p>コメント： 有意水準に達しない</p> |         |       |                                                                                                                                                                       | Study or Subgroup   | Experimental        |  | Control |  | Weight | Risk Ratio |  | Events | Total | Events | Total | M-H, Random, 95% CI | M-H, Random, 95% CI | Ejlertsen B 2004 | 17 | 193 | 23 | 194 | 31.1% | 0.74 [0.41, 1.35] |  | Meier CR 2008 | 13 | 95 | 21 | 97 | 30.1% | 0.63 [0.34, 1.19] | Norris B 2000 | 17 | 151 | 6 | 149 | 23.0% | 2.80 [1.13, 6.90] | Pallis AG 2012 | 4 | 74 | 5 | 74 | 15.8% | 0.80 [0.22, 2.86] | Total (95% CI) |  | 513 |  | 514 | 100.0% | 0.97 [0.51, 1.84] | Total events 51 55 |  |  |  |  |  |  | Heterogeneity: Tau² = 0.25; Chi² = 7.76, df = 3 (P = 0.05); I² = 61% |  |  |  |  |  |  | Test for overall effect: Z = 0.09 (P = 0.93) |  |  |  |  |  |  |
| Study or Subgroup                                                    | Experimental      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Control |       | Weight                                                                                                                                                                |                     | Risk Ratio          |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
|                                                                      | Events            | Total                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Events  | Total |                                                                                                                                                                       | M-H, Random, 95% CI | M-H, Random, 95% CI |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Ejlertsen B 2004                                                     | 17                | 193                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 23      | 194   | 31.1%                                                                                                                                                                 | 0.74 [0.41, 1.35]   |                     |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Meier CR 2008                                                        | 13                | 95                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 21      | 97    | 30.1%                                                                                                                                                                 | 0.63 [0.34, 1.19]   |                     |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Norris B 2000                                                        | 17                | 151                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 6       | 149   | 23.0%                                                                                                                                                                 | 2.80 [1.13, 6.90]   |                     |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Pallis AG 2012                                                       | 4                 | 74                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 5       | 74    | 15.8%                                                                                                                                                                 | 0.80 [0.22, 2.86]   |                     |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Total (95% CI)                                                       |                   | 513                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |         | 514   | 100.0%                                                                                                                                                                | 0.97 [0.51, 1.84]   |                     |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Total events 51 55                                                   |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |         |       |                                                                                                                                                                       |                     |                     |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Heterogeneity: Tau² = 0.25; Chi² = 7.76, df = 3 (P = 0.05); I² = 61% |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |         |       |                                                                                                                                                                       |                     |                     |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Test for overall effect: Z = 0.09 (P = 0.93)                         |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |         |       |                                                                                                                                                                       |                     |                     |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| Funnel plot                                                          |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |         |       |                                                                                                                                                                       |                     |                     |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| その他の解析                                                               |                   | 施行せず                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |         |       |                                                                                                                                                                       |                     |                     |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| メタリグレーション                                                            |                   | コメント：                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |         |       |                                                                                                                                                                       |                     |                     |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |
| 感度分析                                                                 |                   | コメント：                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |         |       |                                                                                                                                                                       |                     |                     |  |         |  |        |            |  |        |       |        |       |                     |                     |                  |    |     |    |     |       |                   |  |               |    |    |    |    |       |                   |               |    |     |   |     |       |                   |                |   |    |   |    |       |                   |                |  |     |  |     |        |                   |                    |  |  |  |  |  |  |                                                                      |  |  |  |  |  |  |                                              |  |  |  |  |  |  |