【4-7 評価シート エビデンス総体】

診療ガイドライン	乳癌診療ガイドライン 薬物療法 2018年版
対象	HER2陰性転移・再発乳癌（女性）
介入	分子標的治療薬（ベバシズマブ）+化学療法
対照	化学療法

エビデンスの強さはRCTは"強（A）"からスタート、観察研究は弱（C）からスタート
* 各ドメインは"高（-2）"、"中/疑い（-1）"、"低（0）"の3段階
** エビデンスの強さは"強（A）"、"中（B）"、"弱（C）"、"非常に弱（D）"の4段階
*** 重要性はアウトカムの重要性（1～9）

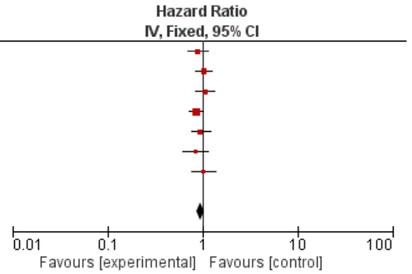
エビデンス総体

アウトカム	研究デザイン/研究数	バイアスリスク*	非一貫性*	不精確*	非直接性*	その他(出版バイアスなど)*	上昇要因(観察研究)*	リスク人数（アウトカム率） 対照群分母	対照群分子	(%)	介入群分母	介入群分子	(%)	効果指標(種類)	効果指標統合値	信頼区間	エビデンスの強さ**	重要性***	コメント
OS	RCT/7	-1	0	0	0	0		1710	-	-	2625	-	-	HR	0.95	0.87-1.03	強(A)	9	有意水準に達しない
PFS	RCT/8	-1	-1	0	0	0		1804	-	-	2722	-	-	HR	0.72	0.67-0.77	中(B)	7	Beva群で有意にPFS良好。異質性ありの判定であるが、全体の傾向は同じでありこのSRをそのまま採用。
ORR	RCT/8	-1	-1	0	0	-1		1476	399	27	2179	924	42.4	RR	1.47	1.26-1.71	中(B)	7	Beva群で有意にORR良好。異質性ありの判定であるが、全体の傾向は同じでありこのSRをそのまま採用。
QOL	RCT/2																	7	2試験のQOL評価の指標が異なるのでMA, 定量的SRは困難。
Toxicity(therapy discontinuation)	RCT/8	-1	-1	-1	0	-1		1743	208	11.9	2709	423	15.6	RR	1.43	1.06-1.93	中(B)	7	Beva群で有意にToxicity(therapy discontinuation)が高い。MBCでは効果があり投与期間が長いほどToxicity(therapy discontinuation)の頻度が高くなる傾向にあり、データの解釈に留意すべきである。
Toxicity(G3以上)	RCT/5	-1	0	0	0	-1		1093	329	30.1	2019	824	40.8	RR	1.43	1.25-1.64	中(B)	7	Beva群で有意にToxicity(グレード3以上)が高い。

コメント（該当するセルに記入）

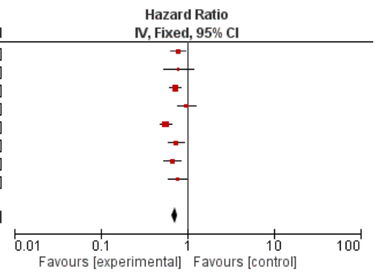
Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
Brufsky 2011 (RIBBON-2)	-0.1054	0.121	12.7%	0.90 [0.71, 1.14]
Miles 2010 (AVADO)	0.0392	0.1029	17.6%	1.04 [0.85, 1.27]
Miller 2005 (AVF2119g)	0.0677	0.1174	13.5%	1.07 [0.85, 1.35]
Miller 2007 (E2100)	-0.1508	0.0836	26.6%	0.86 [0.73, 1.01]
Minckwitz 2014 (TANIA)	-0.0408	0.1192	13.1%	0.96 [0.76, 1.21]
Robert 2011 (RIBBON-1 Cape cohort)	-0.1625	0.1528	8.0%	0.85 [0.63, 1.15]
Robert 2011 (RIBBON-1 T+Anthra cohort)	0.0296	0.1484	8.5%	1.03 [0.77, 1.38]
Total (95% CI)			**100.0%**	**0.95 [0.87, 1.03]**

Heterogeneity: Chi² = 4.25, df = 6 (P = 0.64); I² = 0%
Test for overall effect: Z = 1.24 (P = 0.22)



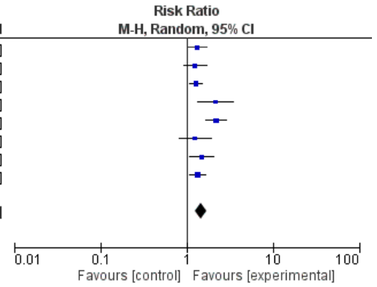
Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
Brufsky 2011 (RIBBON-2)	-0.2485	0.1009	13.1%	0.78 [0.64, 0.95]
Martin 2011	-0.2357	0.2037	3.2%	0.79 [0.53, 1.18]
Miles 2010 (AVADO)	-0.3147	0.0752	23.5%	0.73 [0.63, 0.85]
Miller 2005 (AVF2119g)	-0.0202	0.123	8.8%	0.98 [0.77, 1.25]
Miller 2007 (E2100)	-0.5798	0.0786	21.5%	0.56 [0.48, 0.65]
Minckwitz 2014 (TANIA)	-0.2877	0.1054	12.0%	0.75 [0.61, 0.92]
Robert 2011 (RIBBON-1 Cape cohort)	-0.3857	0.1176	9.6%	0.68 [0.54, 0.86]
Robert 2011 (RIBBON-1 T+Anthra cohort)	-0.2614	0.1273	8.2%	0.77 [0.60, 0.99]
Total (95% CI)			**100.0%**	**0.72 [0.67, 0.77]**

Heterogeneity: Chi² = 18.02, df = 7 (P = 0.01); I² = 61%
Test for overall effect: Z = 9.15 (P < 0.00001)



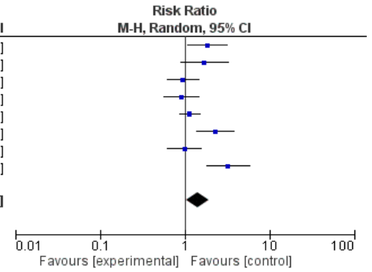
Study or Subgroup	Beva+CTx Events	Beva+CTx Total	CTx Events	CTx Total	Weight	Risk Ratio M-H, Random, 95% CI
Brufsky 2011 (RIBBON-2)	143	362	53	179	13.9%	1.33 [1.03, 1.73]
Martin 2011	50	97	39	94	11.9%	1.24 [0.91, 1.69]
Miles 2010 (AVADO)	243	407	96	207	18.3%	1.29 [1.09, 1.52]
Miller 2005 (AVF2119g)	46	232	21	230	6.9%	2.17 [1.34, 3.52]
Miller 2007 (E2100)	112	229	54	243	13.4%	2.20 [1.68, 2.88]
Minckwitz 2014 (TANIA)	38	182	31	185	8.1%	1.25 [0.81, 1.91]
Robert 2011 (RIBBON-1 Cape cohort)	115	325	38	161	11.6%	1.50 [1.09, 2.05]
Robert 2011 (RIBBON-1 T+Anthra cohort)	177	345	67	177	15.9%	1.36 [1.09, 1.68]
Total (95% CI)		**2179**		**1476**	**100.0%**	**1.47 [1.26, 1.71]**
Total events	924		399			

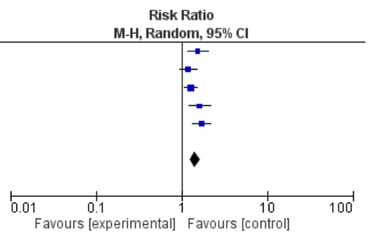
Heterogeneity: Tau² = 0.03; Chi² = 16.21, df = 7 (P = 0.02); I² = 57%
Test for overall effect: Z = 5.00 (P < 0.00001)



Study or Subgroup	Beva+CTx Events	Beva+CTx Total	CTx Events	CTx Total	Weight	Risk Ratio M-H, Random, 95% CI
Brufsky 2011 (RIBBON-2)	61	458	16	221	11.8%	1.84 [1.09, 3.11]
Martin 2011	22	96	12	89	10.1%	1.70 [0.89, 3.23]
Miles 2010 (AVADO)	58	499	28	231	13.6%	0.96 [0.63, 1.46]
Miller 2005 (AVF2119g)	28	229	29	215	12.5%	0.91 [0.56, 1.47]
Miller 2007 (E2100)	82	365	68	346	15.9%	1.14 [0.86, 1.52]
Minckwitz 2014 (TANIA)	45	245	19	238	12.2%	2.30 [1.39, 3.81]
Robert 2011 (RIBBON-1 Cape cohort)	48	404	24	201	13.0%	1.00 [0.63, 1.58]
Robert 2011 (RIBBON-1 T+Anthra cohort)	79	413	12	202	10.9%	3.22 [1.80, 5.77]
Total (95% CI)		**2709**		**1743**	**100.0%**	**1.43 [1.06, 1.93]**
Total events	423		208			

Heterogeneity: Tau² = 0.13; Chi² = 23.00, df = 7 (P = 0.002); I² = 70%
Test for overall effect: Z = 2.33 (P = 0.02)



Study or Subgroup	Beva+CTx Events	Beva+CTx Total	CTx Events	CTx Total	Weight	Risk Ratio M-H, Random, 95% CI
Brufsky 2011 (RIBBON-2)	161	458	50	221	16.6%	1.55 [1.18, 2.04]
Miles 2010 (AVADO)	187	499	72	231	21.6%	1.20 [0.96, 1.50]
Minckwitz 2014 (TANIA)	145	245	109	238	28.1%	1.29 [1.09, 1.54]
Robert 2011 (RIBBON-1 Cape cohort)	143	404	44	201	15.2%	1.62 [1.21, 2.17]
Robert 2011 (RIBBON-1 T+Anthra cohort)	188	413	54	202	18.6%	1.70 [1.32, 2.19]
Total (95% CI)		**2019**		**1093**	**100.0%**	**1.43 [1.25, 1.64]**
Total events	824		329			

Heterogeneity: Tau² = 0.01; Chi² = 6.56, df = 4 (P = 0.16); I² = 39%
Test for overall effect: Z = 5.16 (P < 0.00001)