SUPPLEMENTARY SECTION

Efficacy of eribulin for metastatic breast cancer based on localization of specific secondary metastases: a post hoc analysis

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SUPPLEMENTARY SECTION

Online Resource Supplemental Fig. 1 Summary of overall survival in patients with MBC (a) and progression-free survival (b), by site of lesions at baseline (Study 305)

a Events/N				Median (Months)				
Subgroup	Eribulin	TPC		HR (95%CI)	Eribulin	TPC	P value	
Overall	274/508	148/254	H	0.809 (0.660-0.991)	13.1	10.6	0.0407	
Bone metastases	165/306	93/158	<u> </u>	0.815 (0.632–1.051)	12.5	10.5	0.1136	
Liver metastases	166/296	97/159		0.743 (0.578–0.955)	12.2	10.1	0.0197	
Lung metastases	104/197	52/95	<u> </u>	0.970 (0.695–1.354)	11.8	10.7	0.8595	
Lymph nodes metastases	121/220	72/118	⊢	0.831 (0.621–1.113)	11.1	10.1	0.2133	
Chest wall/breast/ skin metastases	64/118	43/64	⊢	0.706 (0.479–1.039)	13.1	8.7	0.0762	
		Favor	s eribulin Fa	vors TPC				
			0.5 1	1.5 2 2.5 3				
b	Even	te/N						
(220)		13/14			Median	(Months)		
Subgroup	Eribulin	TPC		HR (95%CI)	Median (Eribulin	(Months) TPC	P value	
Subgroup Overall			⊢	HR (95%CI) 0.757 (0.638–0.900)	about the particular of		P value 0.0015	
pper-100-000 € 700-0000 € 7	Eribulin	TPC		,	Eribulin	TPC	1 11-11-11-1	
Overall	Eribulin 429/508	TPC 206/254		0.757 (0.638–0.900)	Eribulin 3.6	TPC 2.2	0.0015	
Overall Bone metastases	Eribulin 429/508 264/306	TPC 206/254 129/158	H-1	0.757 (0.638–0.900) 0.749 (0.606–0.926)	3.6 3.7	2.2 2.1	0.0015	
Overall Bone metastases Liver metastases	Eribulin 429/508 264/306 261/296	TPC 206/254 129/158 130/159	H-1	0.757 (0.638–0.900) 0.749 (0.606–0.926) 0.652 (0.527–0.806)	3.6 3.7 3.7	2.2 2.1 2.0	0.0015 0.0072 < .0001	
Overall Bone metastases Liver metastases Lung metastases	Eribulin 429/508 264/306 261/296 165/197	TPC 206/254 129/158 130/159 80/95	H-1	0.757 (0.638–0.900) 0.749 (0.606–0.926) 0.652 (0.527–0.806) 0.926 (0.707–1.213)	3.6 3.7 3.7 2.8	2.2 2.1 2.0 2.2	0.0015 0.0072 < .0001 0.5772	

In Study 305, patients randomized to eribulin had a nominally significant difference in overall survival compared with patients randomized to TPC in the overall population (a). Patients with liver metastases also had nominally significant differences in overall survival when randomized to eribulin compared with TPC. (b) Overall, patients randomized to eribulin had a nominally significant difference in progression-free survival compared with TPC. Patients with bone, liver, lymph node and chest wall/breast/skin metastases also had better progression-free survival with eribulin compared with control.

For the overall population, HR value and 2-sided 95% CIs were computed using Cox models with treatment as a covariate with HER2/neu status, prior capecitabine treatment, and geographical region as strata. Nominal *P* value was based on log-rank test. No strata were used for analyses in subgroups.

CI, confidence interval; HR, hazard ratio; TPC, treatment of physician's choice.

Online Resource Supplemental Fig. 2 Summary of overall survival in patients with MBC (a) and progression-free survival (b), by site of lesions at baseline (Study 301)

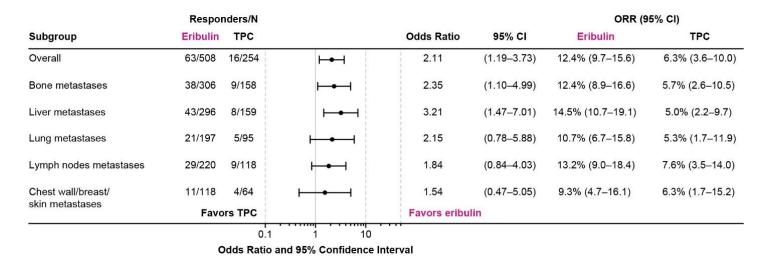
а	Ev	/ents/N		Median (Months)			
Subgroup	Eribulin	Capecitabine		HR (95%CI)	Eribulin	Capecitabine	P value
Overall	446/554	459/548	100	0.879 (0.770-1.003)	15.9	14.5	0.0560
Bone metastases	244/299	272/308	⊢	0.767 (0.645–0.912)	16.4	13.5	0.0026
Liver metastases	212/247	233/271	H	0.901 (0.748–1.085)	14.4	12.7	0.2714
Lung metastases	228/279	237/280	 	0.850 (0.709-1.020)	15.8	13.5	0.0814
Lymph nodes metastases	215/268	236/274	⊢	0.832 (0.692-1.002)	15.8	13.4	0.0522
Chest wall/breast/ skin metastases	165/201	169/198		0.832 (0.671–1.031)	16.4	12.4	0.0931
		Favors e	ribulin Fa	vors capecitabine			
		C	.5 1 1	.5 2 2.5 3			
b Events/N				Median (Months)			
Subgroup	Eribulin	Capecitabine		HR (95%CI)	Eribulin	Capecitabine	P value
Overall	470/554	468/548	H	0.977 (0.857–1.114)	4.2	4.1	0.7361
Bone metastases	245/299	258/308	 	0.831 (0.697–0.990)	4.3	4.0	0.0387
Liver metastases	220/247	228/271	 -	1.102 (0.915–1.327)	4.0	4.0	0.3103
	240/279	244/280	H	1.018 (0.851–1.218)	4.1	3.5	0.8472
Lung metastases	210/210						
	234/268	244/274	+	1.041 (0.870–1.246)	4.1	3.7	0.6654
Lymph nodes metastases Chest wall/ breast/ skin metastases		244/274 178/198	 	1.041 (0.870–1.246) 0.980 (0.795–1.208)	4.1 3.5	3.7 3.1	0.6654 0.8408

In Study 301, (a) patients with bone metastases at baseline and randomized to eribulin had a nominally significant difference in overall survival compared with capecitabine. (b) Patients with bone metastases randomized to eribulin also had a nominally significant dfference in progression-free survival compared with capecitabine.

For the overall population, HR values and 2-sided 95% CIs were computed using Cox models with treatment as a covariate with HER2/neu status and geographical region as strata. Nominal *P* values was based on log-rank test and stratified as noted above. No strata were used for analyses in subgroups.

CI, confidence interval; HR, hazard ratio; MBC, metastatic breast cancer.

Online Resource Supplemental Fig. 3 Summary of tumor response as assessed by investigators per RECIST version 1.0, by site of lesions at baseline (Study 305)



In Study 305, a nominally significant difference in the overall response rate was observed for the overall population, patients with bone metastases, and patients with liver metastases for the eribulin group compared with the TPC group.

For the overall population, the odds ratio and its 95% CIs were computed using the Cochran-Mantel-Haenszel test with HER2/neu status, prior capecitabine treatment, and geographical region as strata. No strata were used for analyses in subgroups.

CI, confidence interval; HR, hazard ratio; ORR, objective response rate; RECIST, Response Evaluation Criteria In Solid Tumors; TPC, treatment of physician's choice.

Online Resource Supplemental Fig. 4 Summary of tumor response as assessed by investigators per RECIST version 1.0, by site of lesions at baseline (Study 301)

	Responders/N					ORR (95% CI)	
Subgroup	Eribulin	Capecitabine		Odds Ratio	95%CI	Eribulin	Capecitabine
Overall	89/554	109/548	H • H	0.77	(0.57–1.05)	16.1% (13.1–19.4)	19.9% (16.6–23.5)
Bone metastases	48/299	60/308	I • I	0.79	(0.52–1.20)	16.1% (12.1–20.7)	19.5% (15.2–24.4)
Liver metastases	50/247	63/271	⊢• -I	0.84	(0.55–1.27)	20.2% (15.4–25.8)	23.2% (18.4–28.7)
Lung metastases	46/279	52/280	⊢ •-H	0.87	(0.56–1.34)	16.5% (12.3–21.4)	18.6% (14.2–23.6)
Lymph nodes metastases	54/268	62/274	⊢• -I	0.86	(0.57–1.30)	20.1% (15.5–25.5)	22.6% (17.8–28.0)
Chest wall/breast/ skin metastases	30/201	36/198	⊢• ⊢	0.79	(0.46–1.34)	14.9% (10.3–20.6)	18.2% (13.1–24.3)
	Favors eribulin			Favors cap	Favors capecitabine		

Odds Ratio and 95% Confidence Interval

In Study 301, none of the observed differences in the overall response rate were nominally significant.

For the overall population, the odds ratio and its 95% CIs were calculated using the Cochran-Mantel-Haenszel test with HER2/neu status and geographical region as strata. No strata were used for analyses in subgroups.

CI, confidence interval; HR, hazard ratio; ORR, objective response rate; RECIST, Response Evaluation Criteria In Solid Tumors.