

## Electronic Supplementary Material

**Supplemental Table 1.** Demographic and baseline characteristics by NLR group.

Characteristic, n (%)	Eribulin (n=475)		TPC <sup>a</sup> (n=238)	
	NLR <3 (n=230)	NLR ≥3 (n=245)	NLR <3 (n=114)	NLR ≥3 (n=124)
Geographical region				
North America/Western	130 (57)	184 (75)	68 (60)	92 (74)
Europe/Australia				
Eastern Europe	70 (30)	37 (15)	31 (27)	20 (16)
Latin America/South Africa	30 (13)	24 (10)	15 (13)	12 (10)
HER2 status				
Positive	40 (17)	38 (16)	16 (14)	20 (16)
Negative	163 (71)	190 (78)	89 (78)	96 (77)
Unknown	27 (12)	17 (7)	9 (8)	8 (6)
Prior capecitabine treatment				
Yes	164 (71)	188 (77)	82 (72)	99 (80)
No	66 (29)	57 (23)	32 (28)	25 (20)
ECOG performance status				
0	112 (49)	92 (38)	54 (47)	46 (37)
≥1	117 (51)	146 (60)	60 (53)	75 (60)
Age group				
<65 years	197 (86)	188 (77)	95 (83)	91 (73)
≥65 years	33 (14)	57 (23)	19 (17)	33 (27)
ER status				
Positive	152 (66)	169 (69)	78 (68)	86 (69)
Negative	63 (27)	71 (29)	31 (27)	36 (29)
Unknown	15 (7)	5 (2)	5 (4)	2 (2)
PgR status				
Positive	114 (50)	128 (52)	57 (50)	59 (48)
Negative	84 (37)	101 (41)	43 (38)	54 (44)
Unknown	32 (14)	16 (7)	14 (12)	11 (9)
HR status				
Positive	157 (68)	175 (71)	84 (74)	87 (70)
Negative	54 (23)	63 (26)	25 (22)	34 (27)

Unknown	19 (8)	7 (3)	5 (4)	3 (2)
Triple negative				
Triple negative	41 (18)	47 (19)	21 (18)	28 (23)
Non-triple negative	189 (82)	198 (81)	93 (82)	96 (77)
Site of disease				
Visceral disease	188 (82)	202 (82)	88 (77)	111 (90)
Non-visceral disease	42 (18)	42 (17)	24 (21)	13 (10)
Number of organs involved				
$\leq 2$	185 (80)	166 (68)	82 (72)	73 (59)
$> 2$	45 (20)	78 (32)	30 (26)	51 (41)
Number of prior chemotherapy regimens				
$\leq 3$	121 (53)	99 (40)	56 (49)	47 (38)
$> 3$	107 (47)	146 (60)	57 (50)	77 (62)
Number of prior chemotherapy regimens for locally advanced or metastatic disease				
$\leq 3$	185 (80)	180 (73)	83 (73)	84 (68)
$> 3$	45 (20)	65 (27)	30 (26)	40 (32)
Refractory to taxanes <sup>b</sup>				
Yes	173 (75)	207 (84)	91 (80)	102 (82)
No	57 (25)	38 (16)	23 (20)	22 (18)

<sup>a</sup>TPC was defined as any single-agent chemotherapy, or hormonal or biological therapy, approved for the treatment of cancer.

<sup>b</sup>Disease progression on or within 6 months of taxane treatment.

ECOG, Eastern Cooperative Oncology Group; ER, oestrogen receptor; HER2, human epidermal growth factor receptor-2; HR, hormone receptor; NLR, neutrophil-to-lymphocyte ratio; PgR, progesterone receptor; TPC, treatment of physician's choice.

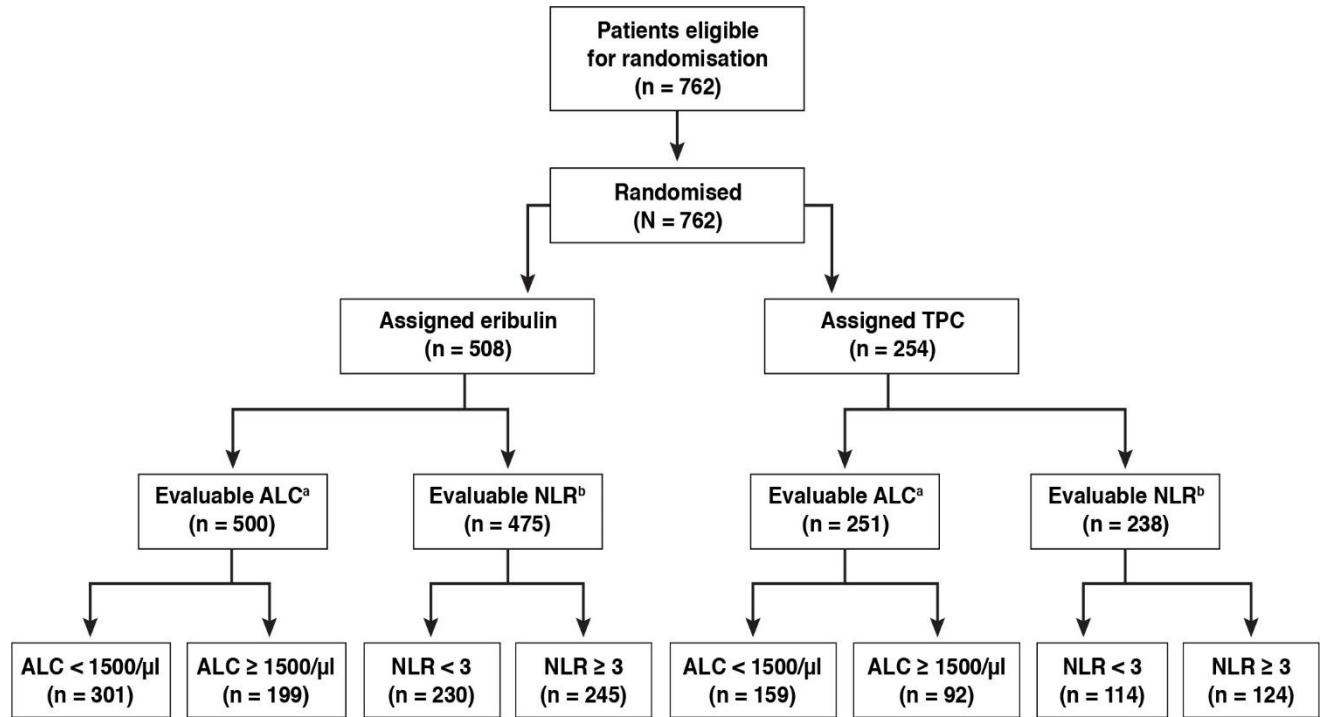
**Supplemental Table 2.** Cut-off value of ALC as a predictive factor of the effect of eribulin on OS.

<b>ALC Cut-off (/<math>\mu</math>l)</b>	<b>Treatment</b>	<b><i>n</i></b>	<b>Median (months)</b>	<b>HR (Eribulin/TPC)</b>	<b>95% CI (Lower)</b>	<b>95% CI (Upper)</b>	<b>Interaction <i>P</i>-value</b>
≥1300	Eribulin	258	15.0	0.743	0.578	0.957	0.3982
	TPC	131	11.4				
<1300	Eribulin	242	11.1	0.865	0.673	1.112	
	TPC	120	9.1				
≥1400	Eribulin	234	15.7	0.641	0.490	0.840	0.0136
	TPC	112	11.4				
<1400	Eribulin	266	11.1	0.993	0.783	1.258	
	TPC	139	10.1				
≥1500	Eribulin	199	15.6	0.586	0.437	0.784	0.0031
	TPC	92	11.4				
<1500	Eribulin	301	11.6	1.002	0.800	1.253	
	TPC	159	10.3				
≥1600	Eribulin	172	15.7	0.578	0.418	0.799	0.0042
	TPC	72	10.5				
<1600	Eribulin	328	11.8	0.964	0.780	1.193	
	TPC	179	10.7				
≥1700	Eribulin	149	15.7	0.633	0.444	0.903	0.0326
	TPC	62	10.5				
<1700	Eribulin	351	12.3	0.907	0.739	1.114	
	TPC	189	10.7				
≥1800	Eribulin	130	14.9	0.629	0.425	0.931	0.0681
	TPC	51	10.5				
<1800	Eribulin	370	12.5	0.873	0.715	1.066	
	TPC	200	10.7				

ALC, absolute lymphocyte count; CI, confidence interval; HR, hazard ratio; OS, overall survival; TPC, treatment of physician's choice.

## Electronic Supplementary Material

**Supplemental Fig. 1** CONSORT diagram of study population in EMBRACE



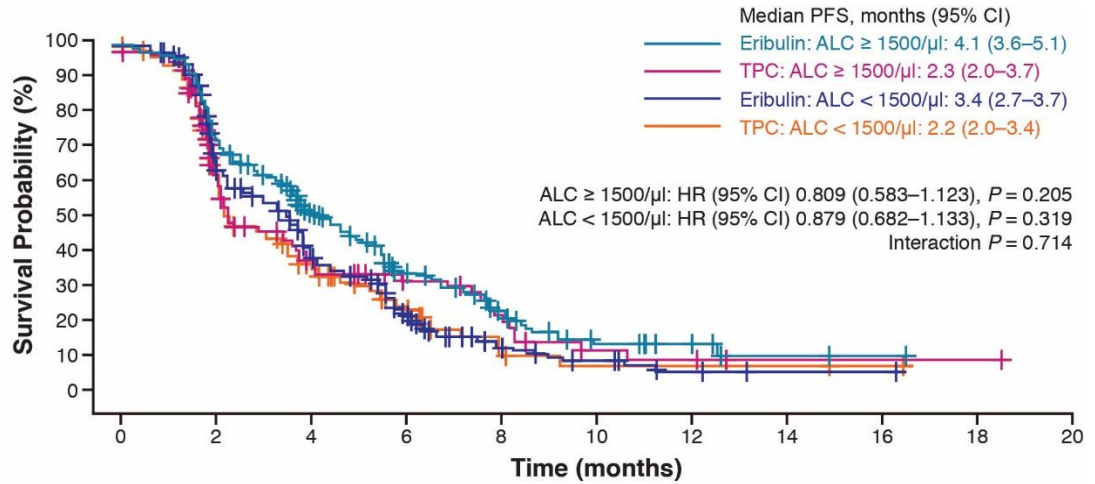
<sup>a</sup>Data from 8 patients in the eribulin arm and 3 patients in the TPC arm were omitted due to missing baseline ALCs.

<sup>b</sup>Data from 33 patients in eribulin arm and 16 patients in the TPC arm were omitted due to missing baseline NLRs.

ALC, absolute lymphocyte count; NLR, neutrophil-to-lymphocyte ratio; TPC, treatment of physician's choice.

**Supplemental Fig. 2** Interaction between treatment and baseline ALC (<1500/ $\mu$ l/  $\geq$ 1500/ $\mu$ l) on PFS

(Independent review)

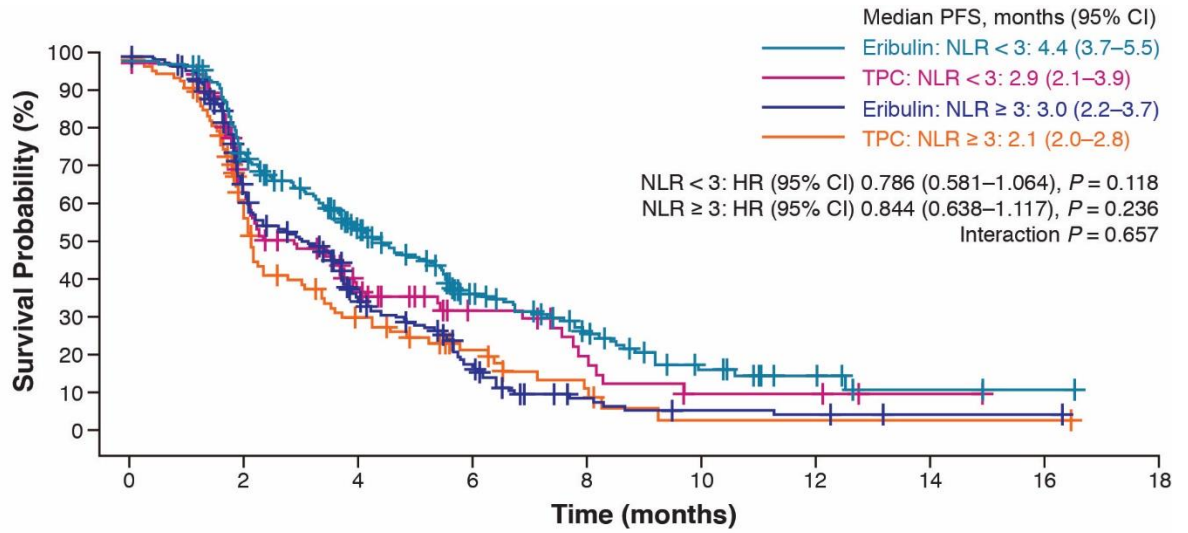


**Number of Patients at Risk**

ALC $\geq$ 1500/ $\mu$ l: Eribulin	199	127	79	41	22	10	6	2	1	0	0
ALC $\geq$ 1500/ $\mu$ l: TPC	92	50	25	17	11	4	3	1	1	1	0
ALC < 1500/ $\mu$ l: Eribulin	301	176	89	41	15	8	3	1	1	0	0
ALC < 1500/ $\mu$ l: TPC	159	70	36	15	5	2	2	2	1	0	0

ALC, absolute lymphocyte count; CI, confidence interval; HR, hazard ratio; PFS, progression-free survival; TPC, treatment of physician's choice.

**Supplemental Fig. 3** Interaction between treatment and baseline NLR (<3/≥3) on PFS (Independent review)



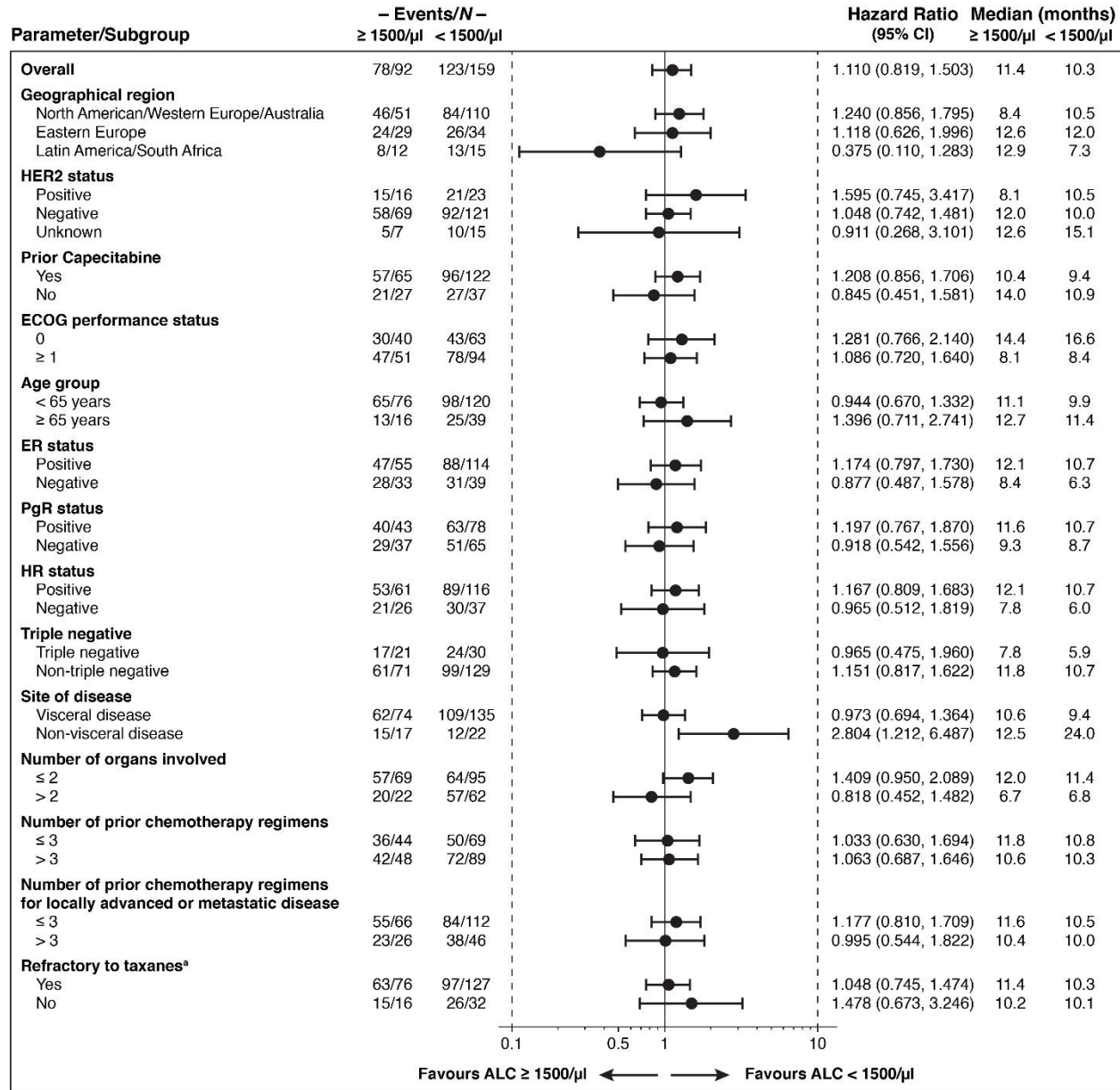
**Number of Patients at Risk**

NLR < 3: Eribulin	230	156	98	51	28	13	6	2	1	0
NLR < 3: TPC	114	60	31	15	8	3	3	1	0	0
NLR ≥ 3: Eribulin	245	134	63	27	8	4	3	1	1	0
NLR ≥ 3: TPC	124	53	23	12	5	1	1	1	1	0

CI, confidence interval; HR, hazard ratio; NLR, neutrophil-to-lymphocyte ratio; PFS, progression-free survival; TPC, treatment of physician’s choice.

**Supplemental Fig. 4** Forest plot for baseline ALC (<1500/ $\mu$ l vs  $\geq$ 1500/ $\mu$ l) effects on OS for the

TPC arm



<sup>a</sup>Disease progression on or within 6 months of taxane treatment.

ALC, absolute lymphocyte count; CI, confidence interval; ER, oestrogen receptor; HR, hormone receptor; OS, overall survival; PgR, progesterone receptor; TPC, treatment of physician's choice.