Recurrent or Metastatic Breast Cancer in North America, Western Europe, and Australia: Results of the Phase III EMBRACE Study

Vahdat LT[1], Twelves CJ[2], Seegobin S[3], Dutcus CE[4], Wanders J[3], Cortes J[5]

[1]Weill Cornell Medical College, New York, NY; [2]Leeds Institute of Molecular Medicine, St. James's University Hospital, Leeds, United Kingdom; [3]Eisai Ltd, Hatfield, United Kingdom; [4]Eisai Inc, Woodcliff Lake, NJ; [5]Vall d'Hebron University Hospital, Barcelona, Spain

Málaga 2011 SEOM

Study Overview

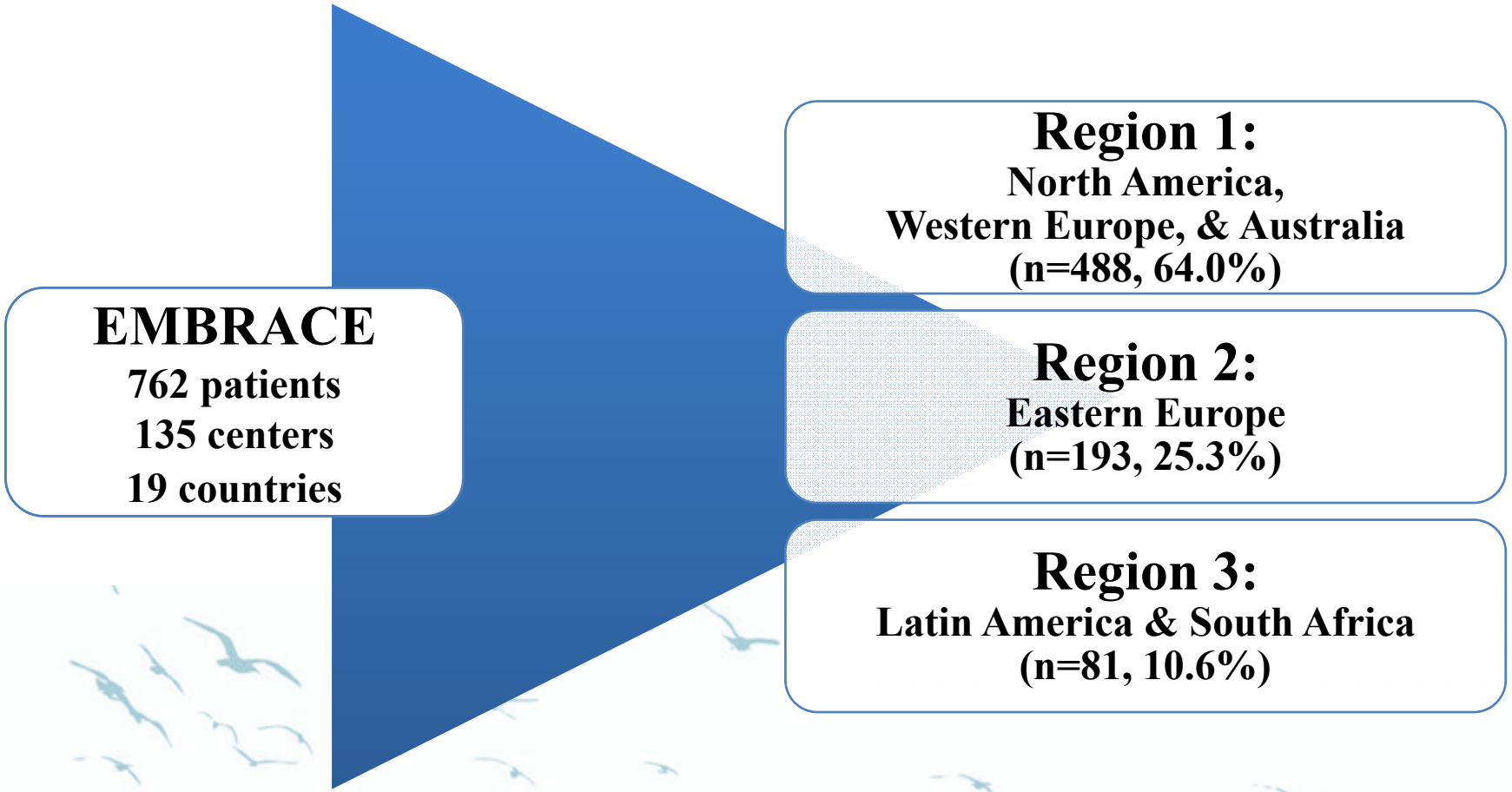
Eribulin for Patients with Metastatic Breast Cancer in Region 1

- **EMBRACE was a multi-centre, phase III, open-label clinical trial in patients with advanced breast cancer who had received two to five prior chemotherapy regimens**
  - **Prior chemotherapy regimens had to include an anthracycline and a taxane unless contraindicated**
  - **At least two regimens had to have been given for locally recurrent or metastatic disease**
- **All patients were randomised (2:1) to receive eribulin or treatment of physician's choice (TPC)**
  - **Eribulin dosed at 1.23 mg/m^2 IV over 2-5 minutes every 21 days on days 1 & 8**
  - **TPC dosed according to standard local practice**

Eribulin 1.23 mg/m^2 equivalent to Eribulin Mesylate 1.4 mg/m^2

Geographic Stratification

Eribulin for Patients with Metastatic Breast Cancer in Region 1



Region 1 was pre-defined as patients from Australia, Belgium, Canada, France, Germany, Italy, Spain, Switzerland, UK, & USA

Baseline Patient Characteristics

Eribulin for Patients with Metastatic Breast Cancer in Region 1

		Eribulin n=325	TPC n=163
Mean Time Since Original Diagnosis, (yrs)		7.4	7.3
Mean Age at Original Diagnosis, (yrs)		48.7	49.1
Incidence of Visceral Disease at Enrollment, n (%)		276 (84.9)	140 (85.9)
Number of Organs Involved, n (%)	1 2 3 or more	53 (16.3) 125 (38.5) 146 (44.9)	25 (15.3) 54 (33.1) 84 (51.5)
ER Status, n (%)	Positive	230 (70.8)	121 (74.2)
PR Status, n (%)	Positive	173 (53.2)	82 (50.3)
HER2/neu Status, n (%)	Positive	49 (15.1)	24 (14.7)

Prior Chemotherapy Regimens

Eribulin for Patients with Metastatic Breast Cancer in Region 1

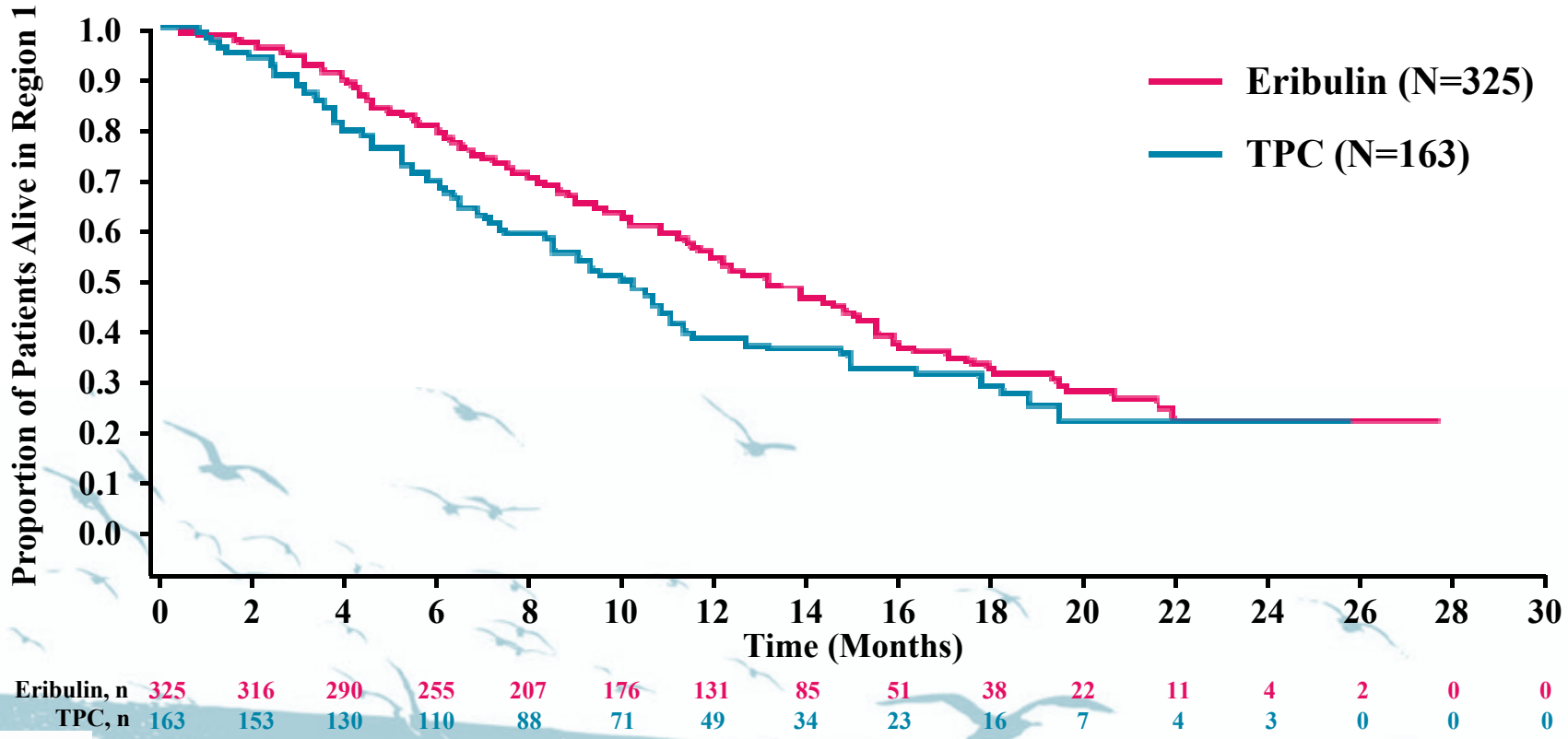
		Eribulin n=325	TPC n=163
Number of Prior Chemotherapy Regimens, n (%)	1	0 (0.0)	0 (0.0)
	2	31 (9.5)	13 (8.0)
	3	109 (33.5)	49 (30.1)
	4	117 (36.0)	55 (33.7)
	5	60 (18.5)	38 (23.3)
	≥6	6 (1.8)	7 (4.3)
Number of Patients Refractory to:	Taxane	249 (76.6)	128 (78.5)
	Anthracyclines	158 (48.6)	96 (58.9)
	Capecitabine	238 (73.2)	118 (72.4)
TPC (selected prior to randomisation)	Vinorelbine		45 (27.6)
	Taxanes		33 (20.2)
	Gemcitabine		27 (16.6)
	Capecitabine		22 (13.5)
	Anthracyclines		20 (12.3)
	Hormonal Therapy		1 (0.6)
	Other		15 (9.2)

Overall Survival in Region 1 Patients

Eribulin for Patients with Metastatic Breast Cancer in Region 1

Median overall survival for patients in Region 1 was significantly longer with eribulin therapy

- **Eribulin (13.1 months) vs. TPC (10.0 months)**
- **Hazard Ratio: 0.724; 95% CI: 0.568-0.924; p=0.009**



Estimation of Overall Survival in overall EMBRACE trial was based on the occurrence of 411 events out of a total study population of 762
Actual analyses of EMBRACE performed after a total of 422 events

Response to Eribulin Treatment

Eribulin for Patients with Metastatic Breast Cancer in Region 1

- **Best overall response was assessed by independent review, with significant benefit for eribulin on Objective Response Rate (ORR, defined as CR + PR)**
  - **Eribulin 11.8% vs. TPC 5.1%; *p*=0.025**
- **An overall Clinical Benefit Rate (CBR, defined as CR + PR + SD >6mos) was also demonstrated for eribulin compared with TPC**
  - **Eribulin 19.7% vs. TPC 13.8%**

Response Category	Eribulin n=305 n (%)	TPC n=138 n (%)
Complete Response (CR)	1 (0.3)	0 (0.0)
Partial Response (PR)	35 (11.5)	7 (5.1)
Stable Disease (SD)	125 (41.0)	56 (40.6)
Progressive Disease (PD)	135 (44.3)	73 (52.9)
Not Evaluable (NE)	9 (3.0)	2 (1.4)

Safety & Tolerability Assessment

Adverse Event Profile of Eribulin in the EMBRACE Study

- **Serious adverse events were seen in 25.0% of all eribulin-treated patients and 25.9% of all TPC-treated patients**
  - **The most common SAEs in the eribulin treatment group were febrile neutropenia (4.2%) and neutropenia (1.8%)**

- **Treatment-related adverse events**
  - **Neutropenia (grade 3/4) occurred in 59% of patients treated with eribulin**
  - **Peripheral neuropathy was reported for 34.2% of eribulin patients**
    - **Grade 3, 8.1% ; Grade 4, 0.3%**
    - **Most common AE leading to discontinuation in eribulin patient (4.8%)**

- **The safety pattern for the TPC groups in the total patient population appeared to be similar to that expected for use of each drug class**

Adapted from: Cortes J et al., Lancet. 2011 Mar 12;377(9769):914-23

Conclusions

Eribulin for Patients with Metastatic Breast Cancer in Region 1

- **Eribulin significantly increased Overall Survival in patients with heavily pretreated, advanced breast cancer in North America, Western Europe, and Australia**
- **The safety profile of eribulin was consistent with that observed in Phase II studies**
- **The clinical benefits of eribulin in this Phase III study were achieved with a manageable toxicity profile**

Presentation based on original poster presented at the
33rd Annual San Antonio Breast Cancer Symposium, San Antonio, TX,
December 8-12, 2010

Acknowledgements

- We would like to thank all of the patients, as well as the investigators and their teams, who participated in the EMBRACE study
- Editorial support was provided by The Medicine Group and was funded by Eisai Inc, Woodcliff Lake, NJ

Recurrent or Metastatic Breast Cancer in North America, Western Europe, and Australia: Results of the Phase III EMBRACE Study

Back-up Slides

Vahdat LT[1], Twelves CJ[2], Seegobin S[3], Dutcus CE[4], Wanders J[3], Cortes J[5]

[1]Weill Cornell Medical College, New York, NY; [2]Leeds Institute of Molecular Medicine, St. James's University Hospital, Leeds, United Kingdom; [3]Eisai Ltd, Hatfield, United Kingdom; [4]Eisai Inc, Woodcliff Lake, NJ; [5]Vall d'Hebron University Hospital, Barcelona, Spain

Málaga 2011 SEOM

Demographic Profile

Eribulin for Patients with Metastatic Breast Cancer in Region 1

	Eribulin n=325	TPC n=163
Age at Consent (yrs)		
Mean	**56**	**56.3**
Height (cm)		
Mean	**162**	**161.2**
Race, n (%)		
White	**301 (92.6)**	**148 (90.8)**
Black	**15 (4.6)**	**8 (4.9)**
Asian/Pacific Islander	**2 (0.6)**	**2 (1.2)**
Other	**7 (2.2)**	**5 (3.1)**
Reproductive Status, n (%)		
Fertile	**27 (8.3)**	**11 (6.7)**
Post-Menopausal	**244 (75.1)**	**128 (78.5)**
Surgically Sterile	**51 (15.7)**	**24 (14.7)**
Infertile	**3 (0.9)**	**0 (0.0)**