MERIBEL STUDY: FIRST-LINE ERIBULIN FOR TAXANE-RESISTANT HER2[-] METASTATIC BREAST CANCER (MBC) PATIENTS (PTS)

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BACKGROUND

- Eribulin improved overall survival (OS) in ≥3 line treatment of MBC in anthracycline- and taxane-pretreated patients [1].
- Short disease-free interval (DFI) and prior taxane therapy have been associated with worse OS in pts receiving first-line chemotherapy for HER2[-] MBC in a large retrospective study [2].
- The aim of this trial is to evaluate the efficacy and safety of single agent eribulin as first-line chemotherapy for HER2[-] MBC pts with poor prognostic factors.

METHODS

- **Design:**

Phase II, multicenter, single arm, trial. Eribulin (1.23 mg/m2) as single-agent was administered on days 1 and 8 of 21 day cycles until progression or unacceptable toxicity.

- **Principal selection criteria:**

[1] HER2[-] pts with no prior chemotherapy for MBC.
[2] Prior taxane therapy (≥4 cycles) for early BC.
[3] Less than 36 months* (mo) between the last taxane cycle and distant relapse.
[4] RECIST v1.1 evaluable disease.
[5] No symptomatic brain involvement.

(*) Amendment to 48 mo.

- **Primary outcome:**

Primary outcome was time to progression (TTP) according to RECIST criteria guidelines (version 1.1).

- **Secondary outcomes:**

Secondary efficacy endpoints included:

- Progression-free survival (PFS)
- OS
- Clinical response assessed as best response according to RECIST criteria guidelines (version 1.1). We reported objective response rate (ORR), clinical benefit rate (CBR) -stabilization lasting 24 weeks- and median duration of response.
- We evaluated safety of eribulin in terms of adverse reactions according with common terminology criteria for adverse events (CTCAE) v4.

- **Sample size:**

We included 53 women between SEP/2013 to MAR/2015 across 12 sites and 2 countries. Patient characteristics are described in table 1.

Table 1. Patient characteristics

Characteristics	No. of patients (N=53)	%
Age, years		
Median	47	
Range	23 a 82.8	
Women	53	100.0
Ecog performance status		
0	27	50.9
1	26	49.1
Luminal phenotype (ER/PgR[+])	29	54.7
Triple (HER2/ER/PgR) negative	24	45.3
Prior hormone therapy		
Yes	21	39.6
(Neo) adjuvant setting	21	39.6
Metastatic setting	6	11.3
No	32	60.4
Refractory to treatment with:		
Taxane	53	100.0
Taxane and anthracycline	45	84.9
Disease free interval, months*		
Median	15.67	
Range	0.1 to 46.5	
Disease free interval		
>24 months	19	35.8
≤24 months	34	64.2
Stage at study entry		
Locally recurrent	3	5.7
Metastatic	50	94.3
No. of organs involved**		
1	28	52.8
2	19	35.8
≥3	6	11.3
Site of disease		
Visceral	28	52.8
Soft tissue	23	43.4
Most common metastatic sites		
Soft Tissue	23	43.4
Lung	21	39.6
Bone	18	34.0
Liver	14	26.4
Mediastine	3	5.7
Other sites	3	5.7

* The disease free interval is defined as the time from last taxane cycle until the first diagnosis of locally advanced or metastatic disease (radiologic or histologic diagnostic). That interval does not include the time between advance disease diagnosis and the date of inclusion in the study.
**Skin, lymph node, ipsi-/contralateral breast or other soft tissue involvement was scored as a single organ.

EFFICACY

The efficacy results are summarized in table 2 and figures 1 to 3.

Table 2. Efficacy analysis

Primary endpoint	events, n (%)	Median (95%CI)	
Time to progression (months)	36 (67.9%)	4.1 (3.2 to 6.6)	
Secondary endpoints			
Time to event	**events, n (%)**	**Median 95%CI**	**1-year PFS or OS rates**
Progression-free survival (months)	36 (67.9%)	4.1 (3.2 to 6.6)	16.2% (7 to 37.5)
Overall survival (months)	22 (41.5%)	Not achieved	68.3% (56.5 to 82.5)
Response evaluation	**events, n (%)**	**95%CI**	**Duration of response, range (months)**
Objective response rate	11 (20.8%)	(9.8 to 31.7%)	4.5 (2.1 to 20.9)
Clinical benefit rate	14 (26.4%)	(14.5 to 38.3%)	-

* The median follow-up was 12.7 mo (range 0.2 to 30.5).

Figure 1. Kaplan–Meier estimates of time to progression.

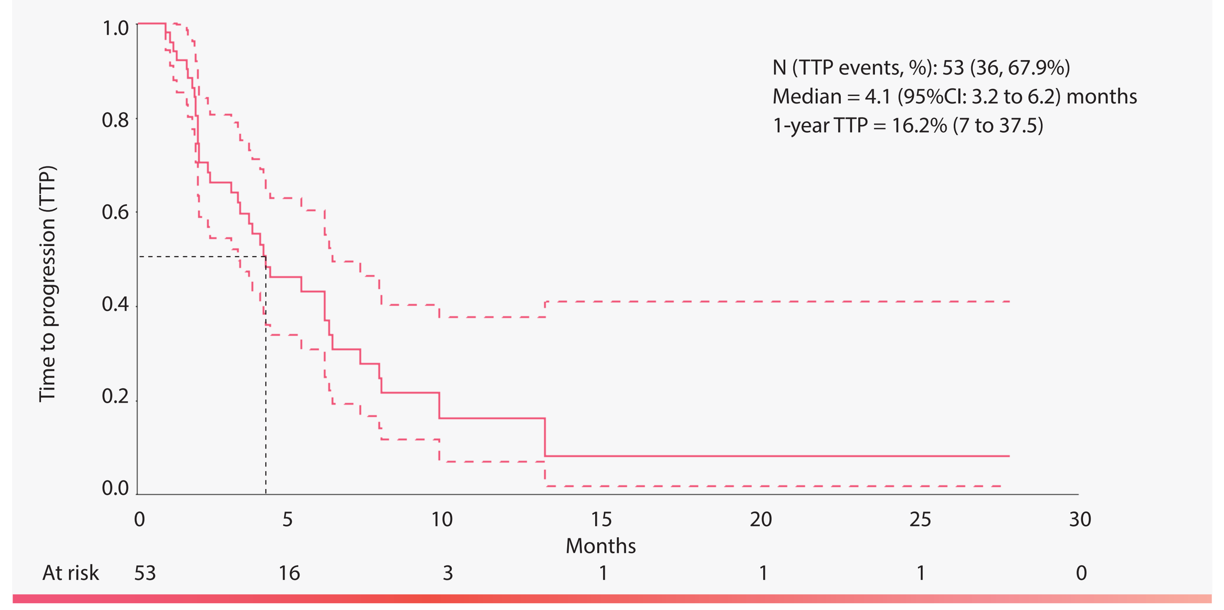


Figure 2. Kaplan–Meier estimates of overall survival.

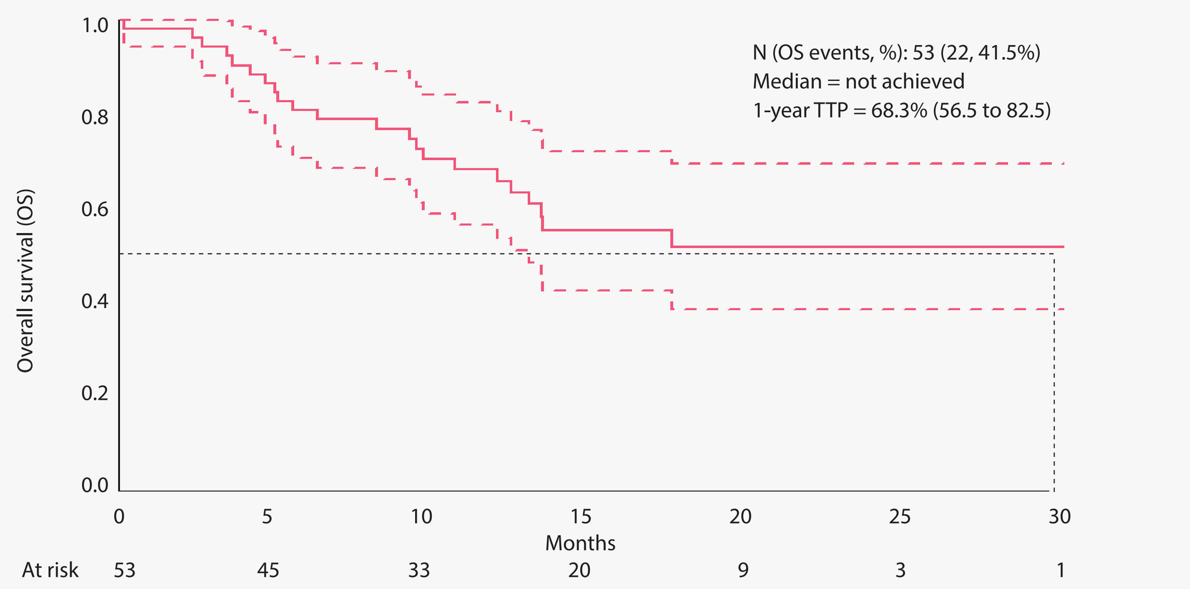
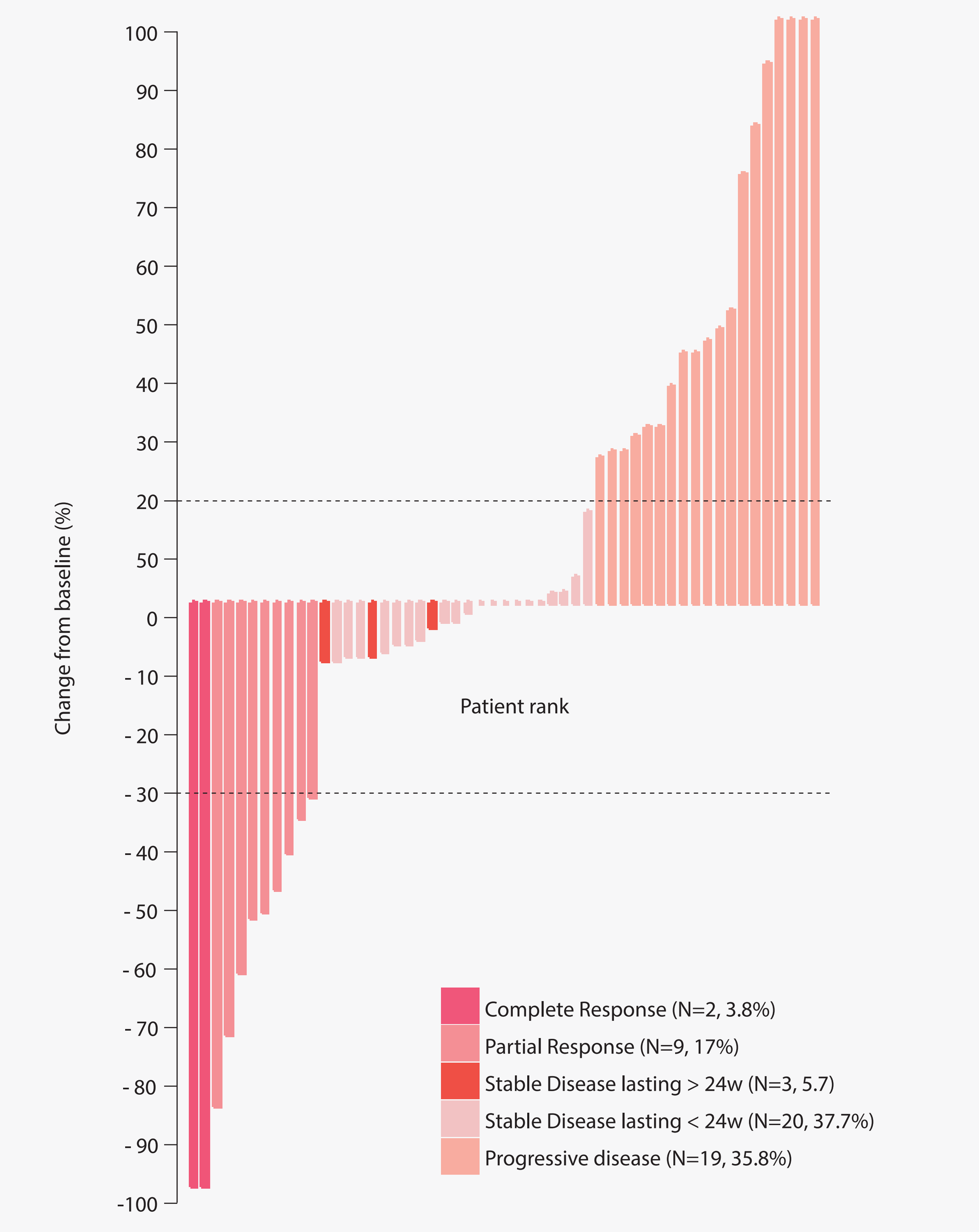


Figure 3. Waterfall plot of best percentage change from baseline in size of target tumour lesions.



SAFETY

- The median follow-up was 12.7 mo (range 0.2 to 30.5). Three patients were treated for more than one year with eribulin.
- The median number of cycles of eribulin administration was 4 (range 1 to 41) and the median relative dose intensity per week was 91.6 % (range 55 to 100 %).
- Dose reductions and interruptions were needed in 5 (9.4%) and 18 patients (34%), respectively.
- Toxicities related with eribulin are summarized in table 3.
- Serious adverse events were reported in 11 patients (20.8%). Eight patients (15.1%) were discontinued due to an adverse event. There was not any death due to eribulin toxicity.

Table 3. Related adverse events (AE) in the study

	Total		Grade 1-2		Grade 3		Grade 4	
Hematologic AE*	N	%	N	%	N	%	N	%
All	37	69.8	35	66.0	14	26.4	9	17.0
Neutropenia	31	58.5	30	56.6	10	18.9	9	17.0
Anemia	12	22.6	12	22.6	2	3.8	0	0.0
Febrile neutropenia	1	1.9	0	0.0	1	1.9	0	0.0
Thrombocytopenia	1	1.9	1	1.9	0	0.0	0	0.0
	Total (≥10% of patients)		**Grade 1-2**		**Grade 3**		**Grade 4 (all patients)**	
Nonhematologic AE*	N	%	N	%	N	%	N	%
All	39	73.6	39	73.6	14	26.4	4	7.5
Alopecia	18	34.0	18	34.0	0	0.0	0	0.0
Nausea	14	26.4	14	26.4	1	1.9	0	0.0
Constipation	11	20.8	10	18.9	2	3.8	0	0.0
Peripheral neuropathy	11	20.8	10	18.9	4	7.5	0	0.0
Anorexia	10	18.9	10	18.9	0	0.0	0	0.0
Asthenia	10	18.9	7	13.2	3	5.7	0	0.0
Abdominal pain	8	15.1	7	13.2	2	3.8	0	0.0
Paresthesia	7	13.2	7	13.2	1	1.9	0	0.0
Bone pain	6	11.3	5	9.4	2	3.8	0	0.0
Myalgia	6	11.3	5	9.4	1	1.9	0	0.0
Dry mouth	4	7.5	4	7.5	2	3.8	1	1.9
Alanine aminotransferase increased	2	3.8	1	1.9	1	1.9	1	1.9
Gamma glutamyl transferase increased	2	3.8	0	0.0	0	0.0	2	3.8
Thromboembolic event	1	1.9	0	0.0	0	0.0	1	1.9

*If a patient had two adverse events in the same system organ class or with the same preferred term with different Common Terminology Criteria for Adverse Events grades, the event with the highest grade was used for that patient.

CONCLUSIONS

Eribulin is active and safe as first-line therapy for aggressive taxane-resistant HER2[-] MBC pts.

Bibligraphy:
(1) Twelves C, Javier Cortes J, Vahdat L, Olivo M, He Y, Kaufman PA, and Awada A. Efficacy of eribulin in women with metastatic breast cancer: a pooled analysis of two phase 3 studies. Breast Cancer Res Treat. 2014; 148: 553–561.

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