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MEDICINE & DRUGS

FOCUS ON:

ERIBULINA MESILATO: UNA NUOVA PROSPETTIVA DI TRATTAMENTO DEL TUMORE DELLA MAMMELLA HER2-POSITIVO DOPO LA TERAPIA ANTI-HER2

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EFFECTIVENESS AND SAFETY OF ERIBULIN MESYLATE IN HEAVILY TREATED PATIENTS WITH HER2-POSITIVE LOCALLY ADVANCED OR METASTATIC BREAST CANCER: AN EXPLORATORY OBSERVATIONAL STUDY IN ITALY

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INTRODUZIONE AL MANOSCRITTO

Il **tumore della mammella** costituisce la **principale causa di mortalità femminile** tumore-dipendente in Europa e nel mondo[1] e, secondo stime dell'AIRTUM (Associazione Italiana Registro Tumori) per l'anno 2023, in Italia rappresenta il 30% di tutti i tumori diagnosticati nelle donne.[2]

L'**aumento dell'espressione di HER2,** implicato nell'attivazione aberrante di pathway coinvolti nella proliferazione cellulare, si registra **nel 15%-20% dei tumori della mammella**, ed è associato sia a una **maggiore aggressività** che a una **scarsa responsività** alle terapie tradizionali.[3,4] Nonostante l'introduzione nella pratica clinica di diverse terapie mirate abbia migliorato l'esito del trattamento del tumore della mammella HER2-positivo sia in termini di OS che di tasso di sopravvivenza a 5 anni, il fenomeno della **"resistenza"** continua a rappresentare un importante problema.[2,4]

L'**eribulina mesilato** è un analogo sintetico dell'alicondrina B, un macrolide polietere derivato da un potente inibitore naturale della mitosi.[5] L'eribulina esercita il suo **effetto citotossico** impedendo l'allungamento dei microtubuli e bloccando, quindi, la progressione del ciclo cellulare.[5] A differenza dei taxani che si legano esclusivamente alle molecole β di tubulina, l'eribulina **riconosce sia la tubulina β che l'interfaccia αβ**.[5] Nello **studio registrativo EMBRACE**,[6] la somministrazione di eribulina in pazienti con tumore della mammella localmente ricorrente o metastatico, precedentemente sottoposte a ≥2 e <5 linee di chemioterapia (compresi un'antraciclina e un taxano), è risultata in un **aumento significativo della OS** (mediana 13,2 mesi; IC 95% 12,1-14,4 mesi) rispetto al trattamento di scelta del medico (mediana 10,5 mesi; IC 95% 9,2-12,0 mesi; p=0,014). Un secondo trial clinico condotto qualche anno dopo ha rivelato la superiorità, sempre in termini di OS, dell'eribulina rispetto alla capecitabina, pur se in assenza di significatività statistica (HR 0,88; IC 95% 0,77-1,00; p=0,056).[7] Studi osservazionali hanno permesso di verificare la validità dell'eribulina nella pratica clinica, in pazienti con caratteristiche di malattia al basale differenti;[8-16] **tuttavia, i dati sull'utilizzo dell'eribulina** in pazienti con tumore della mammella HER2-positivo precedentemente trattate **rimangono limitati.**

L'obiettivo dello studio riportato di seguito è stato quello di analizzare la sicurezza e l'efficacia della sola eribulina in pazienti con tumore della mammella HER2-positivo localmente avanzato o metastatico, precedentemente trattate (≥2 linee) con agenti anti-HER2. La popolazione comprendeva un totale di 33 donne provenienti da 5 centri di oncologia italiani. Per quanto riguarda l'outcome primario di sicurezza, gli eventi avversi (EA) riscontrati con maggiore frequenza erano la neuropatia (69,7%), la neutropenia (54,5%), la nausea (42,4%) e l'alopecia (42,4%). Sette pazienti (21,2%) hanno riportato l'insorgenza di EA di Grado 3/4 (neutropenia [n=5], neuropatia [n=1], nausea [n=1]). Gli outcome secondari erano, invece, (1) la risposta oggettiva (OR), osservata nel 45,4% delle pazienti (IC 95% 28,1%-63,6%); (2) la mPFS, stimata a un valore pari a 4,4 mesi (IC 95% 3,3-7,3 mesi); (3) la OS, che corrispondeva a un valore mediano di 13,7 mesi (IC 95% 9,4-30,2 mesi) e, su un tempo mediano di follow-up di 38,1 mesi, a un tasso di mortalità pari a 54,6% PY (IC 95% 34,6%-81,9%); (4) la mPPS, pari a 11,0 mesi (IC 95% 7,1-28,9 mesi).

Nel complesso, questi dati suggeriscono che **l'eribulina per il trattamento di pazienti con tumore della mammella HER2-positivo localmente avanzato o metastatico in seguito a più linee di terapia anti-HER2, ha un profilo di sicurezza accettabile e un'efficacia paragonabile** (in termini di PFS e OS) **o superiore** (in termini di ORR) **ai risultati degli studi registrativi.** Studi aggiuntivi su campioni più ampi e adeguatamente rappresentativi di diverse tipologie di pazienti sarebbero auspicabili al fine di meglio definire il ruolo e le potenzialità dell'eribulina nella gestione del tumore della mammella HER2-positivo avanzato o metastatico.

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OBSERVATIONAL STUDY OF ERIBULIN IN ITALY

ABSTRACT

The goal of this exploratory, observational, retrospective study, conducted in 5 sites in Italy, was to evaluate the safety and efficacy of eribulin in patients with HER2-positive, locally advanced or metastatic breast cancer previously treated with anti-HER2 agents. Of the 33 participants (median age at diagnosis: 48.5 years), 8 (24.2%) had started a neoadjuvant therapy and 23 (69.7%) received an adjuvant therapy. In two thirds of patients eribulin was administered as 4th or 5th line of treatment. Adverse events (AEs) were reported in 31 patients (93.9%). The most common AEs were neuropathy (69.7% of patients), neutropenia (54.5%), nausea (42.4%) and alopecia (42.4%). Grade 3/4 AEs were reported in 7 patients (21.2%) and consisted of neutropenia in 5 patients, and neuropathy and nausea in 1 patient, respectively each. Two patients interrupted eribulin due to toxicity (grade 3-4 neutropenia in both cases). Objective tumor response was observed in 15 patients (45.4%). The median progression-free survival, overall survival (OS) and post-progression survival was 4.4 months (95% confidence interval [CI], 3.3-7.3 months), 13.7 months (95% CI, 9.4-30.2 months) and 11.0 months (95% CI, 7.1-28.9 months), respectively. The 1- and 2-year cumulative OS rates were 0.522 (95% CI, 0.371-0.733) and 0.391 (95% CI, 0.244-0.627), respectively. This study provides evidence of acceptable safety and satisfactory efficacy of eribulin in patients with HER2-positive, locally advanced or metastatic breast cancer previously treated with several lines of anti-HER2 agents.

KEY WORDS: *eribulin, HER2-positive, advanced or metastatic breast cancer*

INTRODUCTION

Breast cancer is the most commonly diagnosed cancer in women worldwide. In the year 2023, the incidence of breast cancer in Italy was estimated to be of 30% of all tumors in females, with a 5-year survival that has increased to 88% in recent years.[1] During the last decade, in contrast with an increasing incidence of breast cancer, mainly as a result of the introduction of mammography screening and of the increased ageing of population, the mortality rate has decreased, especially in younger age groups because of improved treatment and earlier detection.[2] Despite this fact, breast cancer is diagnosed in stage IV (metastatic breast cancer) in 6-7% of cases.[1] However, the availability of new antitumor drugs and supportive therapies, as well as the improved integration of systemic and local therapies, has led to substantial increases of overall survival (OS) in patients with metastatic disease.

The choice of the treatment for metastatic breast cancer is driven by the evaluation of the patient's biological profile and clinical characteristics. In recent years, the availability of new drugs for any breast cancer subtype has led to significant improvements of progression-free survival (PFS), objective tumor response and quality of life. Cyclin-dependent kinases (CDK) inhibitors for the hormone-sensitive forms, poly (ADP-ribose) polymerase (PARP) inhibitors in patients with triple- negative disease and BRCA mutations and anti-HER2 in case of human epidermal growth factor receptor 2 (HER2)-positive disease are the therapeutic classes that have substantially improved survival. Nonetheless, a significant proportion of patients undergoes progression and requires further lines of therapies.

Eribulin mesylate is a recently introduced drug approved for treatment of metastatic breast cancer. It is a synthetic halichondrin B derivative that acts by interfering with the microtubular growth, ultimately leading to apoptosis after prolonged mitotic blockage.[3] Following the pivotal phase III study EMBRACE Study 305,[4] eribulin was approved for the treatment of patients with locally advanced or metastatic breast cancer.

In the EMBRACE study, which was conducted in 762 women with locally recurrent or metastatic breast cancer who have previously received at least 2 and up to 5 chemotherapeutic regimens, including an anthracycline and a taxane, the treatment with eribulin was associated with a significantly longer OS (median 13.2 months) when compared with treatment of physician's choice (TPC: median 10.5 months; hazard ratio [HR] 0.81; 95% confidence interval [CI], 0.68–0.96; p=0.014). The most common adverse events (AEs, any grade) in the eribulin group were asthenia/fatigue (53.7%), neutropenia (51.7%), alopecia (44.5%), nausea (34.6%) and peripheral neuropathy (34.6%). The other pivotal Study E7389-G000-301,[5] which included 1.102 women with locally advanced or metastatic breast cancer, showed an improved OS with eribulin (median 15.9 months) compared to capecitabine (median 14.5 months; HR

0.88; 95% CI: 0.77–1.00; p=0.056), although the improvement was not statistically significant. The most common AEs with eribulin were neutropenia (54.2%), alopecia (34.6%), leukopenia (31.4%), global peripheral neuropathy (27.4%) and nausea (22.2%).

Observational studies performed in patients with advanced or metastatic breast cancer in a real-life setting have shown an efficacy and safety profile of eribulin that was in line with that reported in pivotal trials.[6-9] A substantial antitumour activity and an acceptable safety profile of eribulin have also been shown in elderly patients and in those with visceral disease.[10-12] Moreover, no harmful changes from baseline of quality of life scales were recorded during eribulin treatment.[13]

More recent observational studies have been conducted to review the safety and efficacy of eribulin in advanced breast cancers with different biological profiles. In a study performed in Spain in HER2- negative advanced breast cancer patients, the efficacy of eribulin was in line with that reported in pivotal trials, with a less incidence of grade 4 toxicity.[14] Similar findings were observed in an observational study conducted in Italy in elderly patients with HER2-negative metastatic breast cancer.[12]

Limited data are available on the effects of eribulin in metastatic HER2-positive breast cancer. In a randomised clinical trial, the combination of eribulin and lapatinib showed an acceptable safety profile with less toxicity observed with split-dose of eribulin compared to a 3-weekly dose.[15] In another single-centre study, treatment with the combination eribulin-trastuzumab was an effective and safe option with a low toxicity profile for high pre-treated HER2-positive patients with metastatic breast cancer.[16] This study was conducted to address further information on the safety and efficacy of eribulin as single agent in patients with HER2-positive, locally advanced or metastatic breast cancer previously treated with anti-HER2 drugs and managed according to common clinical practice in Italy.

MATERIALS AND METHODS

This is an exploratory, observational, retrospective, multicentre study conducted between January 2013 and January 2019 in 5 oncology centres in Italy.

The study population included women with a confirmed diagnosis of locally advanced or metastatic HER2-positive breast cancer who previously received at least two treatment line with an anti-HER2 regimen and at least one administration of eribulin mesylate. Information including breast cancer history, previous treatments, response to treatments and tumor biology was collected.

Eribulin mesylate 1.4 mg/m^2 (equivalent to eribulin 1.23 mg/m^2) was administered as an intravenous infusion over 2–5 min on day 1 and 8 of a 21-day cycle. The cycles were repeated until disease progression, unacceptable toxicity or withdrawal. A complete blood count and organ function test was performed before each cycle. Dose delays were planned to correspond with type and grade of observed toxicity, according to the summary of product characteristics. Concomitant medications such as granulocyte colony-stimulating factor, antiemetic drug, steroids and bisphosphonates were allowed.

The primary objective of the study was the incidence of AEs related to eribulin administration. AEs were recorded and graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) (version 5.0).[17]

The secondary objectives of the study were: objective tumor response; PFS, defined as time elapsing between the date of first administration of eribulin mesylate and the date of the first evidence of progression or death, whichever occurred first; OS, defined as time elapsing between the date of first administration of eribulin mesylate and the date of deaths due to any cause; and post-progression survival (PPS), defined as time elapsing between the date of the first evidence of progression and the date of death due to any cause. Treatment activity was assessed in accordance with the Response Evaluation Criteria In Solid Tumors (RECIST) criteria at CT scans. Data of patients not progressed at the last follow-up were considered as censored for PFS, and data of patients alive at the last follow- up were considered as censored for both OS and PPS. Additional objectives included the evaluation of eribulin treatment line in the therapeutic sequence and the frequency and reason for treatment interruption.

Sample characteristics were presented using descriptive statistics, i.e. median with range for numerical variables, and absolute frequencies and percentages for categorical variables. The analysis of AEs was performed in the safety population, defined as all patients who completed the treatment with eribulin or who were still in treatment but experienced an AE. The incidence of AEs was estimated by dividing the number of patients with an eribulin-related AE to the size of the safety population: the corresponding 95% confidence interval (CI) was estimated using the exact binomial method. Objective tumor response rate was estimated dividing the number of patients who reached an objective response during their therapeutic line by the size of the population: the corresponding 95% CI was estimated using the exact binomial method. Median time to objective response was estimated using only patients who reached the endpoint: the corresponding 95% CI was estimated using the Hodges-Lehman approach. PFS, OS and PPS were analysed using the Kaplan-Meier estimates. All statistical analyses were conducted using the statistical platform R (version 4.1).

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethical Committee of the coordinating Institution (Medical Oncology Unit, Cannizzaro Hospital, Catania, Italy, approval number 07/2020 CA and adopted by the satellite Centre. All patients signed an authorization form for the use of their data.

RESULTS

The overall sample included 33 women, who were evaluable for both safety and efficacy. **Table 1** shows the clinical characteristics of subjects and the lines of eribulin administration. The median age at diagnosis of the primitive breast cancer was 48.5 years (range: 34.9-72.8). The majority of patients had a ductal (28 patients, 84.8%) and grade 3 (18 patients, 54.4%) breast cancer. Eight (24.2%) patients performed a neoadjuvant therapy and 23 (69.7%) patients received an adjuvant regimen.

TABLE 1 • Clinical characteristics of subjects and the lines of eribulin mesylate administration

	N=33
Age at diagnosis for the primitive tumor (years), median (range)	48.5 (34.9-72.8)
Primitive tumor histology, n (%)	
Ductal	28 (84.8%)
Lobular	4 (12.1%)
Missing	1 (3.0%)
Grading, N (%)	
Grade 2	12 (36.4%)
Grade 3	18 (54.5%)
Missing	3 (9.1%)
Neoadjuvant chemotherapy, N (%)	8 (24.2%)
Antraciclines monotherapy	1 (3.0%)
Anthraciclines-taxanes	3 (9.1%)
Anthraciclines-taxanes-trastuzumab	4 (12.1%)
Taxanes-trastuzumab	1 (3.0%)
Adjuvant therapy, N (%)	23 (69.7%)
Antraciclines monotherapy	6 (18.2%)
Anthraciclines-taxanes-trastuzumab	8 (24.2%)
Anthraciclines-trastuzumab	5 (15.2%)
Taxanes-trastuzumab	2 (6.1%)
Trastuzumab monotherapy	7 (21.2%)
Age at diagnosis of metastatic disease (years), median (range)	52.9 (40.0-73.5)
Age at first-line therapy (years), median (range)	53.6 (40.0-73.5)
Age at start of eribulin treatment (years), median (range)	56.7 (43.5-78.6)
Interval from onset of metastatic disease to eribulin administration (years), median (range)	3.3 (1.3-9.6)
Eribulin line of therapy, N (%)	
3	4 (12.1%)
4	13 (39.4%)
5	9 (27.3%)
6	2 (6.1%)
7	2 (6.1%)
8	1 (3.0%)
9	1 (3.0%)
13	1 (3.0%)

N = number of patients

The median age at the beginning of eribulin treatment was 56.7 years (range: 43.5-78.6) while the median interval from onset of metastatic disease to eribulin administration was 3.3 years (range: 1.3-9.6). In two thirds of patients eribulin was administered as 4th or 5th line treatment.

Data collection ended on 06 December 2019 for the statistical analysis.

As primary objective, AEs were reported in 31 patients overall (93.9%). **Table 2** shows the frequency distribution of AEs. Neuropathy (23 patients, 69.7%), neutropenia (18 patients, 54.5%), nausea (14 patients, 42.4%) and alopecia (14 patients, 42.4%) were the most common AEs. The only other AE reported in more than 30% of patients was asthenia (10 patients, 30.3%). Overall, grade 3/4 AEs were reported in 7 patients (21.2%; 95% CI, 9.0-38.9%), and consisted of neutropenia in 5 patients (15.2% 95% CI, 5.1-31.9%), and neuropathy and nausea in 1 patient each (3.0%, 95% CI, 0.1-15.8%). With regard to the frequency of distribution of grade 3/4 AEs according to the line of eribulin therapy, neutropenia was reported in 2 cases when the drug was given as 4th line and in 1 case when given as 6th, 8th and later line; the case of neuropathy was reported when given as 7th line and the case of nausea was reported when given as 4th line.

TABLE 2 • Frequency distribution of adverse events

	N=33	
Adverse event	**N (%)**	**95% CI**
Neuropathy	23 (69.7%)	51.3-84.4%
Neutropenia	18 (54.5%)	36.4-71.9%
Nausea	14 (42.4%)	25.5-60.8%
Alopecia	14 (42.4%)	25.5-60.8%
Asthenia	10 (30.3%)	15.6-48.7%
Anaemia	6 (18.2%)	7.0-35.5%
Decreased appetite	4 (12.1%)	3.4-28.2%
Constipation	4 (12.1%)	3.4-28.2%
Dyspnea	2 (6.1%)	0.7-20.2%
Mucositis	2 (6.1%)	0.7-20.2%
Onychopathy	1 (3.0%)	0.1-15.8%
Vomiting	1 (3.0%)	0.1-15.8%

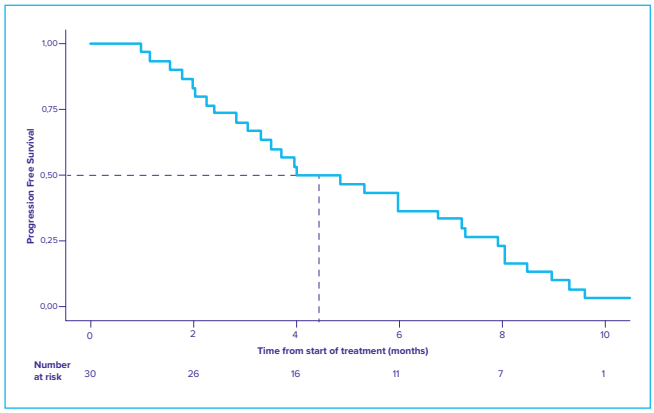
N = number of patients

Two patients interrupted eribulin administration due to toxicity (6.1%; 95% C.I., 0.7% to 20.2%), in particular grade 3/4 neutropenia.

As secondary objectives, objective tumor response was observed in 15 patients (45.4%, 95% CI, 28.1- 63.6%). The median time to response in those patients was 2.4 months (95% CI, 1.9-3.02 months).

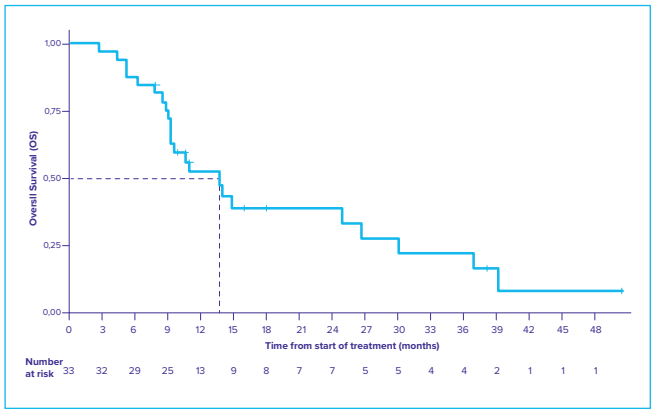
Since 3 patients did not present a valid disease progression date in correspondence of the eribulin line, data for PFS were available for 30 patients: all 30 patients underwent disease progression or died. The median PFS **(Figure 1)** was 4.4 months (95% CI, 3.3-7.3 months).

FIGURE 1 • Kaplan-Meier estimate of progression-free survival



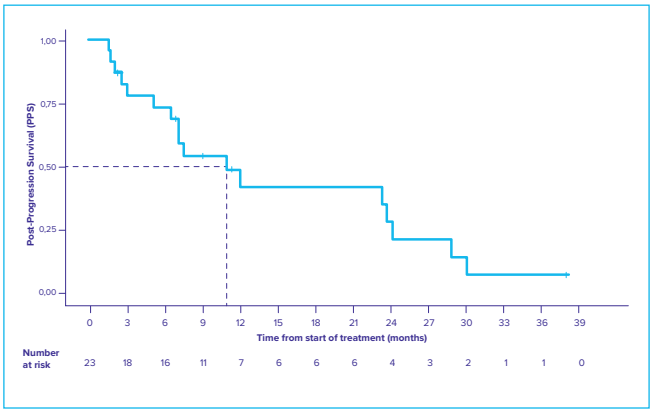
Data for OS were evaluable for all 33 patients. Over a median follow up of 38.1 months (range 2.8- 50.4 months), a total of 23 (69.7%) deaths were observed with an incidence rate of 54.6 deaths x 100 person-years (95% CI, 34.6 to 81.9). The median OS **(Figure 2)** was 13.7 months (95% CI, 9.4-30.2 months). The 1- and 2-year cumulative OS rates were 0.522 (95% CI, 0.371-0.733) and 0.391 (95% CI, 0.244-0.627), respectively.

FIGURE 2• Kaplan-Meier estimate of overall survival



Since for other 7 patients (in addition to the 3 patients not evaluable for PFS) progression event was due to death and not to disease progression, PPS was evaluable in 23 patients (69.7%). Overall, 17 patients (73.9% of evaluable patients) died following progressive disease. The median PPS **(Figure 3)** was 11.0 months (95% CI, 7.1-28.9 months).

FIGURE 3 • Kaplan-Meier estimate of post-progression survival



DISCUSSION

The main findings of this exploratory observational study in patients with HER2-positive breast cancer have shown that, overall, eribulin had an acceptable safety profile. The most common AEs are well known side effects reported with use of eribulin,[18] with a marginally increased rate in frequency of neuropathy, and a decreased rate of asthenia observed in this cohort of patients. Notably, there were no cases of anaemia or leukopenia, which are other two commonly reported haematological AEs with eribulin. Furthermore, grade 3/4 neutropenia was reported with a frequency (15.2%) that was greatly lower than that reported in the summary of product characteristics,[18] and discontinuation of eribulin treatment due to these AEs was required in only 6.1% of patients. In the analysis of frequency of adverse effects, it should be considered that the known labelled frequency distribution of AEs is mainly derived from randomised regulatory phase 2-3 trials, which included patient populations selected according to predetermined criteria. Therefore, data from a study conducted in a real-life setting in a less selected population in terms of number of previous lines of chemotherapy, comorbidities and associated treatment, as well as in terms of inclusion criteria for resolution of previous chemotherapy-induced toxicities, may not be consistent with findings from regulatory trials. Notably, the vast majority of participants in this study (i.e. approximately 90%) received eribulin as 4th or more line of therapy and in approximately half of patients eribulin was administered as 5th or more line, whereas the regulatory EMBRACE Study 305[4] included patients receiving 3-5 previous lines of chemotherapy and patients in the other regulatory E7389-G000-301 Study had received only ≤ 2 lines of chemotherapy based on study protocol.[5]

As concerning efficacy, 45.4% of patients in this cohort of patients achieved tumor response. The median PFS, OS and PPS were 4.4 months (95% CI, 3.3-7.3 months), 13.7 months (95% CI, 9.4-30.2 months) and 11.0 months (95% CI, 7.1-28.9 months), respectively. Therefore, the rate of tumor response observed in this study was higher than that reported in the overall eribu-

lin population included in regulatory trials,[4,5] whereas median PFS and OS was in line with that of phase III trials. A pooled analysis of the results of the two regulatory trials led to the conclusion that women with HER2-negative disease gained a significant survival benefit from eribulin,[19] which is of clinical relevance considering that patients with HER2-negative disease are estimated to represent about 85% of women with metastatic breast cancer.[20] However, in the interpretation of data it should be considered that only a minority of breast cancer patients that took part in the two regulatory trials were HER2-positive (i.e. approximately 15%) and that HER2 positivity resulted to be associated with reduced OS compared to the overall population or to HER2-negative patients. Therefore, the results of efficacy in this study showed that treatment with eribilin was associated not only to higher response rate, but also to prolonged survival compared to HER2 patients of the EMBRACE Study 305[4] and to comparable survival with that reported in HER2 patients of E7389-G000-301 Study,[5] which excluded patients with advanced or metastatic breast cancer that had received 3 or more lines of chemotherapy.

There are few published studies with eribulin in which only advanced and/or metastatic HER2-positive breast cancer patients were included. The safety results of the randomised trial that compared two dose regimens of eribulin in patients with trastuzumab-pretreated HER-2-positive metastatic breast cancer[15] showed higher rates of grade 3/4 neutropenia than that reported in the present study and 39% of grade 3/4 leukopenia. In another recent trial conducted in Japan,[21] triple therapy with eribulin, trastuzumab, and pertuzumab given as first-line therapy in patients with HER2-positive metastatic breast cancer was associated with high response rates and prolonged PFS, but also with higher rates of grade 3/4 adverse effects (44.0% of patients) than those observed in this trial. Similar findings were reported in another trial conducted in a Japanese population of untreated advanced or metastatic HER2-positive breast cancer patients.[22] In another trial in patients with metastatic breast cancer who previously received ≥2 chemotherapy regimens in the metastatic setting,[23] the administration of a median of 10 cycles of eribulin plus a median of 11 cycles of trastuzumab led to an overall response rate of 71.2%, with better efficacy outcomes in trastuzumab-naïve patients compared with those who had received prior trastuzumab, and less incidence of neutropenia and febrile neutropenia.

In a recently published Italian observational retrospective study in 24 heavily pre-treated HER2-positive advanced breast cancer patients,[24] treatment with eribulin plus standard dose of trastuzumab for a median number of 11.5 cycles was associated with an overall response rate of 41.7%, a median PFS of 5.4 months, a median PPS of 5.4 months, a median OS of 8 months and a safety comparable to that observed in this study. These findings are in line with those reported in a similar retrospective analysis conducted in Turkey[16] on the effects of the eribulin-trastuzumab combination in 36 aggressively pre-treated metastatic HER2-positive breast cancer patients. The results of our survey are in line with those reported in these previous surveys, but with a prolonged OS compared to the standard eribulin-trastuzumab fixed regimen used in these two observational studies.

Although this exploratory observational study has provided evidence of acceptable safety and satisfactory efficacy of treatment with eribulin as single agent in patients with HER2-positive, locally advanced or metastatic breast cancer previously treated with multiple lines of anti-HER2 drugs, some limitations should be underlined, in particular the retrospective nature and the small number of patients. On the other hand, the application in daily practice of the results obtained in randomized clinical study is generally difficult, since many patients do not fit the profile of clinical studies participants. The “real-life” and retrospective studies aim to evaluate effectiveness and safety in populations with broad eligibility criteria, bridging the gap from the highly controlled setting of the experimental conditions and the clinical practice.

CONCLUSIONS

The results of this observational Italian study have provided insight on the role of eribulin as single agent in patients with HER2-positive, locally advanced or metastatic breast cancer previously treated with multiple lines of anti-HER2 treatments. The findings from this trial should be confirmed in further randomised controlled studies including large and adequate sample of patients, in order to better elucidate the role and the timing of administration of eribulin in the management of HER2-positive advanced or metastatic breast cancer.

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