The Oncologist®

Breast Cancer

Eribulin Mesylate as Third or Subsequent Line Chemotherapy for Elderly Patients with Locally Recurrent or Metastatic Breast Cancer: A Multicentric Observational Study of GIOGer (Italian Group of Geriatric Oncology)-ERIBE

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Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Eribulin mesylate • Metastatic breast cancer • Elderly • Health-related quality of life • Comprehensive geriatric assessment

Abstract

Background. Metastatic breast cancer (MBC) is highly prevalent in middle-aged or elderly patients. Eribulin is a nontaxane microtubule inhibitor, approved for the treatment of pretreated MBC. This multicentric study (sponsored by GIOGer, Italian Group for Geriatric Oncology) was designed to assess the efficacy and tolerability of eribulin, according to parameters usually used in geriatric oncology.

Subjects, Materials, and Methods. An observational study was conducted on 50 consecutive elderly patients with MBC. The primary endpoint was to evaluate the change in items score of comprehensive geriatric assessment (CGA) and health-related quality of life (HRQL). Italian versions of the CGA and HRQL questionnaires were administered at baseline, before the third and fifth cycles, and then every three cycles until treatment discontinuation. Secondary endpoints were efficacy and safety.

Results. Overall, both EQ-5D scores and EQ-5D-3 L visual analogic scale did not significantly change from baseline; the percentage of subjects without problems doing usual activities tended to decrease during treatment (p for linear trend .018), and the percentage of patients with minor problems performing usual activities tended to increase (p for linear trend.012). Among CGA items, Instrumental Activities of Daily Living tended to decrease during treatment and Geriatric Depression Scale tended to increase. After 12 months follow-up, 24 patients (out of 47) showed clinical benefits; median progression-free survival was 4.49 months (2.10–10.33) and median OS was 7.31 months (3.70–14.03). The treatment was associated with mild toxicity.

Conclusion. Eribulin treatment preserved quality of life and geriatric parameters included in the CGA, except for instrumental functioning and geriatric depression, in elderly patients with MBC. ***The Oncologist*** 2019;24:e232–e240

Implications for Practice: A collaboration between oncologist and geriatric specialists is essential in the management of patients with metastatic breast cancer, who are frequently elderly or frail. The assessment of geriatric parameters in the decision-making process can contribute to direct toward the most appropriate therapeutic plan and preserve the quality of life of patients. Eribulin does not seem to affect quality of life or worsen the overall geriatric status; therefore, it can be considered a suitable option for elderly patients with metastatic breast cancer.

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Introduction

Over the past few years, breast cancer has become the most prevalent type of cancer among women in many countries. In Italy, breast cancer (BC) represents 28% of all female cancers; it is the most frequent tumor in women, with approximately 50,000 new cases a year [1]. The 5-year survival rate of patients with breast cancer is relatively high compared with other malignant tumors, but it drastically falls in the presence of distant metastases [2]. A recent review of data from the Surveillance, Epidemiology, and End Results database has shown that metastatic breast cancer (MBC) is highly prevalent in middle-aged or elderly patients, as 63.7% of MBC occurs at 50–69 years and 31.2% over 70 years [3]. No cure for MBC yet exists; the main aims of treatment are to alleviate symptoms and prolong survival, while minimizing toxicity and preserving the quality of life. These aspects are central in MBC management in elderly women who may present concomitant conditions and tend to tolerate toxic medical treatments less than their younger counterparts. When chemotherapy is required, a sequential single-agent approach is the most appropriate therapeutic plan to preserve the quality of life and reduce the risk of toxicity, whereas it has been shown that a combination of therapies is often too toxic and does not impact on overall survival [4]. As initial lines of therapy in MBC, anthracyclines and taxanes are routinely used; however, when they are used as adjuvant or neoadjuvant treatment and with disease recurrence within 6 months, other drugs, including capecitabine, ixabepilone, and eribulin, should be considered [5].

Eribulin, a nontaxane microtubule inhibitor, has been approved in the U.S. and Europe for treatment of pretreated MBC, based on the results of a single randomized, open-label, multicenter trial (EMBRACE study) [6]. In this trial, eribulin improved the overall survival compared with any single agent of the physician's choice (13.1 vs. 10.6 months, hazard ratio 0.81; 95% confidence interval [CI] 0.66–0.99; p = .041), even if with a higher rate of all grades and grades 3 and 4 neutropenia, febrile neutropenia, and neuropathy [6]. A subgroup analysis did not indicate age as a potential factor of increased toxicity or decreased efficacy of eribulin; therefore, age alone should not preclude the consideration of eribulin for patients over 65 [7]. In real-world studies, no significant differences in toxicity were observed according to age, and even in patients aged >70 years, treatment was well tolerated [8]. Eribulin obtained a stable disease in 40.9% of elderly patients and a partial response in 31.8%, with mild drug toxicity, mainly represented by G3–G4 hematological (neutropenia and thrombocytopenia in 8.2% and 4.5% of patients, respectively) [9].

The European Society of Breast Cancer Specialists (EUSOMA) and International Society of Geriatric Oncology (SIOG) multidisciplinary task force identified physiological age, life expectancy, risk-to-benefit ratio, treatment tolerance, patient preference, and potential barriers to treatment as factors that should be evaluated in the breast cancer management in elderly patients [10]. In this setting, a collaborative effort between geriatric and oncology specialists and multidomain geriatric assessment are invaluable to successfully manage patients [11, 12]. Currently, there are no standard methods for geriatric assessment; however, use of the comprehensive geriatric assessment (CGA), which evaluates physical function, comorbidity, cognitive function nutrition, medication, socioeconomic issues, and geriatric syndromes, may help to direct toward the most appropriate approach and best personalized treatment for older patients with cancer [12]. Some evidence in the cancer population indicates that CGA can positively contribute to patient management [13–15]; in elderly patients with metastatic breast cancer, the results of the OMEGA study indicated that the number of geriatric conditions correlated with grade 3–4 chemo-therapy-related toxicity of pegylated liposomal doxorubicin or capecitabine treatment [16].

This multicentric study was designed to assess the efficacy and tolerability of eribulin, according to parameters usually used in geriatric oncology. The research was focused on health-related quality of life (HRQL) and on CGA in a consecutive series of elderly patients (over 65) with metastatic breast cancer.

Subjects, Materials, and Methods

Study Design

This prospective, observational study was conducted on consecutive elderly patients with metastatic breast cancer, treated with eribulin in 14 Italian centers. All patients provided written informed consent, and the study protocol was approved by all relevant institutional ethics committees. The study was conducted in accordance with the provisions of the Declaration of Helsinki (2013) and local laws.

Patients were eligible for enrollment if they were diagnosed with locally recurrent or metastatic breast cancer, previously treated with at least two lines of chemotherapy for advanced disease (including anthracycline and taxanes); the disease should be measurable or evaluable per RECIST criteria version 1.1. Patients must be 65 years of age or older and must have a good performance status, life expectancy >3 months, and adequate bone marrow, liver, renal, and cardiac function.

Two- to five-minute intravenous infusions of eribulin mesylate were performed on day 1 and 8 in a 21-day cycle, at 1.23 mg/m^2. The treatment was continued until disease progression, unacceptable toxicity, or consent withdrawal.

Endpoints and Assessments

The primary endpoint was to evaluate the change in the score of each item of the CGA and HRQL. The CGA included the following geriatric conditions: Activities of Daily Living (ADL) essential elements of self-care (score 0–6; 6 = patients independent) [16]; functional status per the Lawton & Brody scale for Instrumental Activities of Daily Living (IADL; cutoffs for partial dependence 14–27, full functional dependence ≤13) [17]; Geriatric Depression Scale (GDS; cutoff for severe depressive symptoms >10, moderate depressive symptoms 5–9) [18]; Mini Mental State Examination (MMSE; cutoff for cognitive impairment <23) [19];

Mini Nutritional Assessment (MNA) [20]; Charlson Comorbidity Index (cutoff score ≥ 2) [21]; and Eastern Cooperative Oncology Group (ECOG) Performance Status [22]. Quality of life (QoL) was evaluated by the EQ-5D questionnaire, a standardized measure of health status developed by the Euro QoL Group to provide a simple, generic measure of health for clinical appraisal [23]. Italian-translated versions of the CGA and HRQL questionnaires in paper form were administered in the hospital at baseline, before the third and fifth cycles, and then every three cycles until treatment discontinuation.

Secondary endpoints were response rate, disease control rate, progression-free survival (PFS), and overall survival (OS). The response rate was assessed according to RECIST criteria [24] for target and nontarget lesions; radiograms were not centrally reviewed. Disease control rate was defined as the sum of RECIST responses, with a stable disease lasting at least 4 months. PFS and OS were measured from the first dose of eribulin to disease progression or death and to death for any cause, respectively. Adverse events were collected and graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0.

Sample Size Calculation

Because of the multiplicity of outcomes, power study was based on the well-recognized Cohen effect size [25]. A sample size of 50 patients could achieve 80% power to detect a Cohen effect size for paired data of 0.4 with a significance level (alpha) of 0.05.

Statistical Analysis

Descriptive analyses were reported as mean ± standard deviation or median and interquartile range (IQR; i.e., first to third quartiles) and range (minimum to maximum), or absolute and relative frequencies (percentages), for continuous and categorical variables, respectively.

Mortality and disease progression rates were calculated as number of events per 100 person-years. OS and PFS were calculated by Kaplan–Meier method and compared with the log-rank test. For subjects who did not experience the endpoint, the survival time was censored at the last available follow-up evaluation.

Changes in EQ-5D questionnaire health states, CGA scores, and ECOG performance status were statistically assessed from baseline until the third revaluation using hierarchical generalized linear model (HGLM) for longitudinal data, for each domain at issue. In this framework, Poisson distribution was assumed to model scores of CGA (ADL, IADL, GDS, MNA, and MMSE), whereas logistic distribution was used to model each domain of EQ-5D questionnaire and ECOG performance status, which had multiple grades. The Italian utility index was computed combining each EQ-5D questionnaire health state, therefore deriving an EQ-5D score, following the formula proposed in the study by Scalone et al. [26], and a normal distribution was assumed to model such score. The first-order autoregressive covariance structure was used to correlate repeated measurements and evaluations. Estimated means (or percentages for categorical variables) resulted from HGLMs and were reported with their 95% CI, including the follow-up time variable (i.e., the time to evaluation), as a categorical covariate. If no patients had the condition defined by the categorical item within a specific time category, the 95% CI from HGLM (around 0%) was unreliable, because of an extremely high estimated error variance. Therefore, such 95% CI was replaced by the exact 95% CI obtained from a binomial distribution.

Pairwise comparisons were performed (involving contrasts within HGLMs) with respect to the first evaluation and were adjusted with the Dunnett's procedure. The presence of a linear trend for the estimated means (or percentages) over time was assessed by looking at the significance of the regression coefficient of the follow-up time variable, included into the model as continuous covariate into HGLMs (p for trend). For each continuous outcome at issue, longitudinal plots of the estimated means over time were further reported, whereas histograms of the estimated percentages were reported for each categorical outcome. Error bars represented 95% CI around the point estimate.

Two-sided p values <.05 were considered statistically significant. All analyses were performed using SAS Software, Release 9.4 (SAS Institute, Cary, NC), and plots were

Table 1. Clinical and demographic characteristics

Variable	Category	All patients (n = 50)
Age at first eribulin treatment, years	Mean ± SD	72.17 ± 4.84
Histology, n (%)	Carcinoma	5 (10.0)
	Ductal	43 (86.0)
	Lobular	2 (4.0)
Hormone receptor status, n (%)	Negative (ER and PgR)	7 (14.0)
	Positive (ER and/or PgR)	43 (86.0)
Initial grading, n (%)	Missing data	3
	Grade 1	1 (2.1)
	Grade 2	21 (44.7)
	Grade 3	22 (46.8)
	Unknown	3 (6.4)
Ki-67 in the original tumor, n (%)	Missing data	6
	<20%	24 (54.6)
	≥20%	20 (45.5)
Pre-eribulin disease sites, n (%)	Bone	25 (50.0)
	Liver	17 (34.0)
	Lung	18 (36.0)
	Lymph nodes	14 (28.0)
	Soft tissue	6 (12.0)
	Skin	6 (12.0)
	Other	3 (6.0)
Number of involved organs, n (%)	Mean ± SD	1.78 ± 0.95
	1	25 (50.0)
	>1	25 (50.0)

n (%): Absolute and relative (percentage) frequencies.
Abbreviations: ER, estrogen receptor; PgR, progesterone receptor; SD, standard deviation.

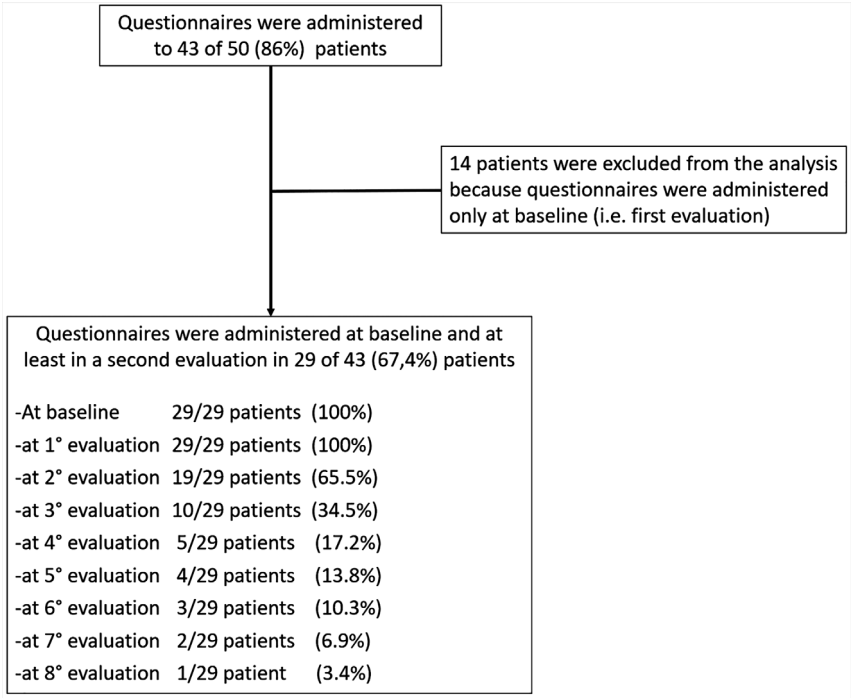

Figure 1. Flow chart of the patients' disposition, according to the compliance with questionnaire.

performed using R version 3.4.1 (http://www.r-project.org - packages: survival, ggplot2, gridExtra).

Results

From April 2013 to June 2016, 50 patients were enrolled: 10 patients in Lecce, 6 in Bergamo and Sanremo, 5 in Brindisi and Prato, 4 in Monza and Bari, 3 in Castellana Grotte, 2 in Taranto and Castellaneta, and 1 in Manduria, Roma, Pontedera, and Aviano. Median age was 71 years (65–84), and 70% of patients had visceral disease. Twenty-five (50%) patients had multiple metastatic lesions, with bone as the most frequent metastatic site (50%), followed by lung (36%), liver (34%), lymph nodes (28.0%), and skin (12%). Seven (14%) patients were triple-negative for estrogen receptor, progesterone receptor, and Erb2. In the metastatic setting, the median number of previous chemotherapies was two (IQR 1–3), received by 86% of patients; 72% of patients received a median of one hormonal therapy for advanced disease (IQR 0–3). Table 1 summarizes demographic and clinical baseline characteristics.

As shown in Figure 1, among the 43 patients who responded to the questionnaire at baseline, only 29 had at least two revaluations and were included in the analysis. Among patients who did not have two revaluations, seven received only one (four patients) or two (three patients) cycles of eribulin and stopped the treatment before the third revaluation; one patient refused to perform revaluations for personal reasons; in one center, there was a mistake during questionnaire administration—six patients had only the baseline questionnaires and were excluded from the final analysis. The changes of the item scores were statistically assessed from baseline until the third revaluation, because after that time the sample size was inadequate. Indeed, a sample size of 10 patients was just enough to achieve the 80% of statistical power to detect a standardized paired mean difference of 0.9 only (i.e., a very large Cohen effect size), using a two-sided paired z-test and a significance level of 5% (type I error). This effect size referred to the difference of the estimated means of any continuous item's score of the questionnaire for the same paired group of patients observed until the third evaluation versus baseline.

Baseline geriatric assessment is described in Table 2. Most common geriatric conditions were partial IADL dependency (40.7%) and mild-to severe depressive symptoms (35.7%). Nutritional status was normal in 72.7% of patients and comorbidity was limited, with 24 women (92.3%) having Charlson Comorbidity Index of 0–1. Performance status was 0–1 in 87.5% of patients. In the health-related quality of life questionnaires, mean baseline EQ-5D score was 0.69 (95% CI 0.58–0.81), and in the EQ-5D-3 L visual analogic scale (VAS), mean score was 65.9 (95% CI 60.0–71.6).

Overall, both EQ-5D scores and EQ-5D-3 L VAS did not significantly change from baseline to the third revaluation (Fig. 2). However, when specific items were considered (Fig. 3), the proportion of subjects who did not have problems doing usual activities tended to decrease during the treatment (p for linear trend .018), and the proportion of patients who had moderate problems performing usual activities tended to increase (p for linear trend .012). Among CGA items, IADL tended to decrease during the treatment and GDS tended to increase, especially at the first and second revaluation (Fig. 4). The percentage of patients with ECOG performance status 0 tended to decrease during treatment (p for linear trend .027), from 62.5% at baseline to 55.6% at the third revaluation; the

Table 2. Baseline scores of comprehensive geriatric assessment

Score	Category	*n* (%)
ADL	<6 (Dependent)	5 (17.24)
	=6 (Independent)	24 (82.76)
IADL	Info not available	2
	<8 (Dependent)	11 (40.74)
	=8 (Independent)	16 (59.26)
GDS	Info not available	1
	0–5 (No depressive symptoms)	18 (64.29)
	6–10 (Mild depressive symptoms)	8 (28.57)
	>10 (Severe depressive symtoms)	2 (7.14)
Total MMSE	Info not available	3
	24–30: No cognitive impairment	25 (96.15)
	18–23: Mild to moderate cognitive impairment	1 (3.85)
	0–17: Severe cognitive impairment	0 (0.00)
Total MNA	Info not available	7
	12–14: Normal nutritional status	16 (72.73)
	8–11: At risk of malnutrition	6 (27.27)
	0–7: Malnourished	0 (0.00)
Charlson Comorbidity Index	Info not available	3
	0–1	24 (92.31)
	2+	2 (7.69)
ECOG Performance Status	Info not available	5
	Grade 0	15 (62.50)
	Grade 1	6 (25.00)
	Grade 2	3 (12.50)

Abbreviations: ADL, Activities of Daily Living; ECOG, Eastern Cooperative Oncology Group; GDS: Geriatric Depression Scale; IADL, Instrumental Activities of Daily Living; MMSE, Mini Mental State Examination; MNA, Mini Nutritional Assessment.

percentages of patients with ECOG performance status 1 and 2 did not significantly change.

Patients were exposed to a median of four cycles (IQR 2–8; range 1–21) of therapy, with a median dose of 1.76 mg (IQR 1.4–1.99; range 0–2,5). After a median follow-up of 12 months, 24 patients showed clinical benefit (9 had a partial response and 15 had stable disease), 23 had progressive disease, 3 were not evaluable, and no patients showed a complete response. Among triple-negative patients (n = 7), three had a partial response, one had stable disease, two had progressive disease, and one was not evaluable. Overall, the median PFS was 4.49 months (range 2.10–10.33) and the median OS was 7.31 months (range 3.70–14.03). All patients were included in the safety analysis and showed at least one adverse event of any grade (Table 3). Eribulin was associated with mild toxicity (grade 1 or 2); fatigue (35%) and mucositis (15%) were the most common nonhematological adverse events of grade 3–4. Anemia was accounted in 11 patients (one of grade 3). Treatment-related toxicities led to dose reduction in 16 patients (32%), mainly due to neutropenia (22.7%) or hematological toxicity (34.1%); dose was delayed in 20 patients (40%) for logistic reason (31.4%) or hematological toxicity (19.6%).

Discussion

This is the first prospective study in which elderly women with MBC were evaluated with a comprehensive geriatric assessment during eribulin treatment and, for the first time, the efficacy of chemotherapy treatment on the items of CGA was evaluated. In this trial, eribulin treatment did not significantly change the scores of EQ-5D and CGA items from baseline in elderly patients with metastatic breast cancer, thus demonstrating a limited impact on quality of life. During treatment, a decreased tendency in having problems doing usual activities was observed, although other aspects such as mobility, self-care, pain/discomfort, and anxiety/depression were not impaired. In the specific comprehensive geriatric scale, only the instrumental activities of daily living and the geriatric depression significantly changed during treatment. We furthermore confirmed that eribulin was well tolerated, with toxicities only of grade 1 and 2, and effective in disease control.

Previous real-world studies supported the use of eribulin in elderly women and did not report higher toxicities or lower effectiveness than those observed in younger counterparts [8, 9, 27]. Nevertheless, even if chronologic age alone should not be the sole reason for not offering an older patient with cancer treatment, the effects of aging on function, physiology, and the availability of social supports are important and need to be considered during the treatment decision-making process [28]. The physical function of elderly patients with cancer can be evaluated by assessing ADL or IADL [29]. In our population, most patients could independently perform ADL and maintained this ability through the study; dependency in IADL was reported in a higher proportion of patients (40.9% were dependent in IADL) and worsened during eribulin treatment. In patients with MBC, IADL had not been associated with an increased rated of toxicities of grade 3–4 [16], whereas in those with advanced lung cancer, it was an independent prognostic factor of overall survival [30]. Monitoring IADL throughout the treatment may provide useful indications for patient management and eventually lead to modifications of the therapeutic plan, according to an increasing dependency.

Decline in physical performance and loss of independence have been associated with depressive symptoms in elderly subjects [31, 32]. Even though elderly patients were psychologically less affected by cancer compared with younger ones, with an incidence of clinically significant depression of 3%–25% in this population [31], identifying patients who required psychological support may facilitate their independence and improve outcomes [32]. Especially in MBC, it would critical to determine the depressive status, because depressed patients tend to refuse and withdraw from antitumor chemotherapy [33]. In our study, 35.7% of patients had mild or severe depression symptoms, and the geriatric depression scores tended to decrease during the study.

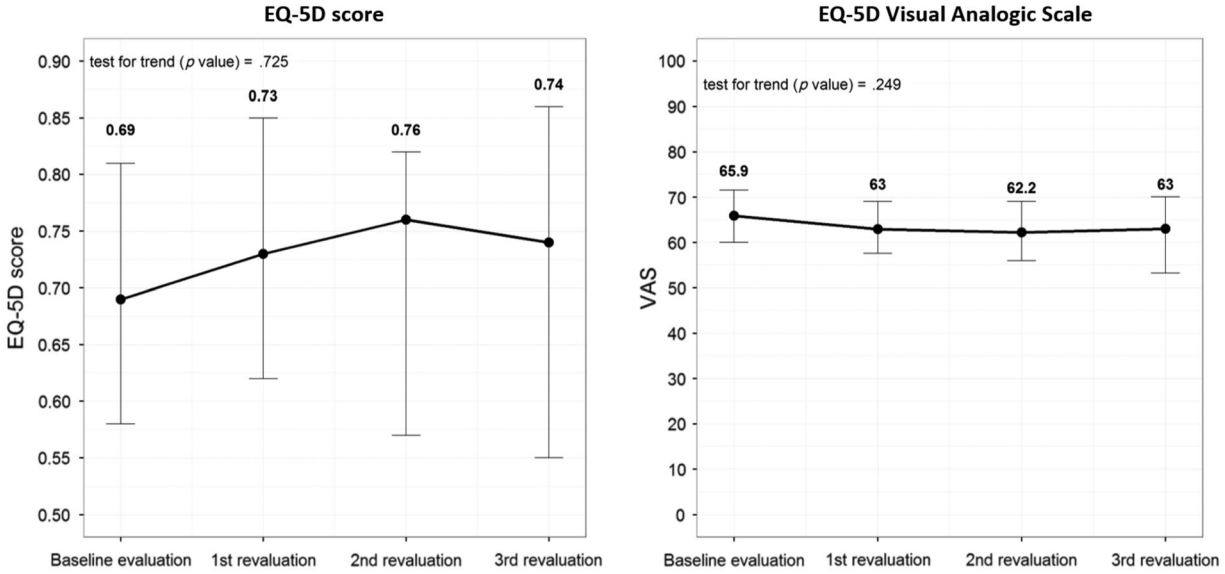

Figure 2. Estimated scores at baseline and after each revaluation of EQ-5D Italian utility index and the VAS. Error bars represent the 95% confidence interval around the point estimate.
Abbreviation: VAS, visual analogic scale.

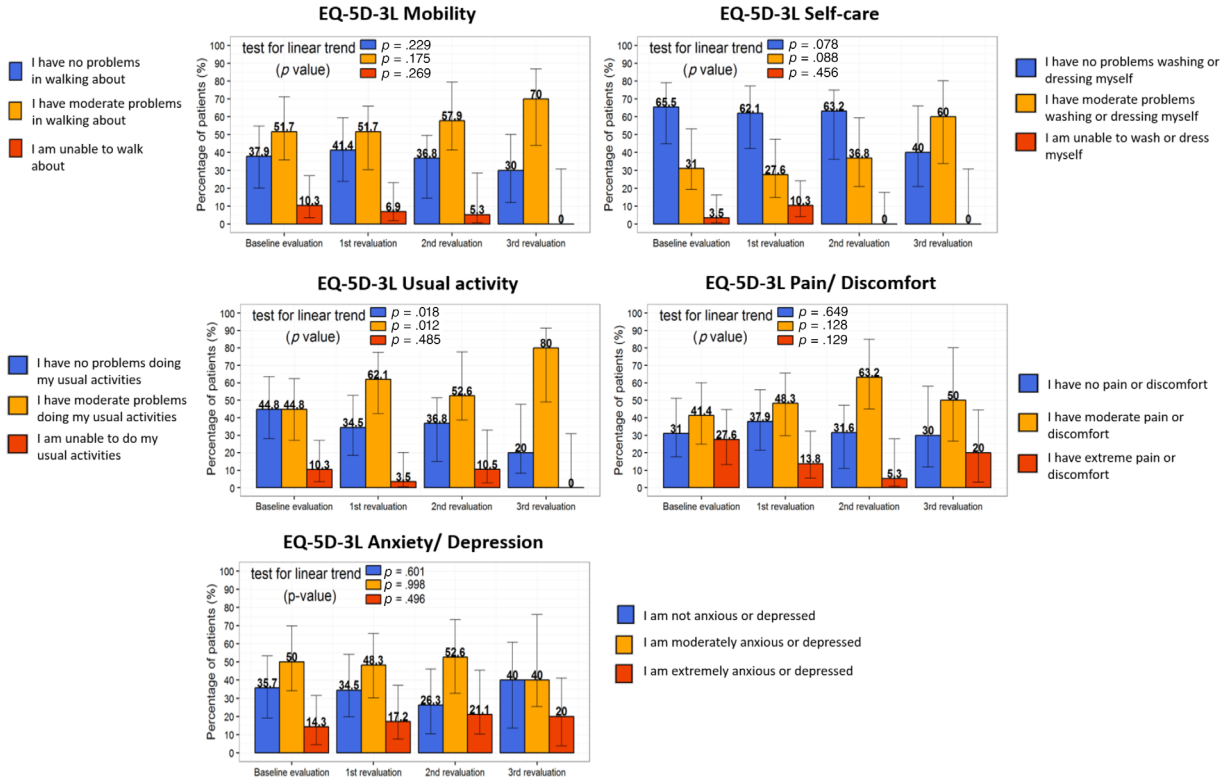

Figure 3. Estimated proportions at baseline and after each revaluation of EQ-5D questionnaire health states. Error bars represent the 95% confidence interval around the point estimate.

Other parameters that were considered in the CGA were in the normal range at baseline and did not significantly change during the study.

Baseline HRQL parameters of physical functioning, pain, and appetite loss provided significant prognostic information, in addition to the parameters of age, sex, and distant metastases [34], and recent clinical trials of newer agents, including eribulin, incorporated quality-of-life analyses among prespecified clinical endpoints [6, 35]. To preserve quality of life in the case of an incurable disease such as MBC, beneficial therapies should reduce tumor burden and tumor-related symptoms and have an easily manageable toxicity profile [36, 36, 37]. When eribulin or capecitabine were administered in patients with locally advanced MBC or with MBC previously treated with an anthracycline and taxane, they maintained or improved patients' functioning and quality of life and showed favorable safety results compared with baseline [35]. However, significant differences were described in the timing

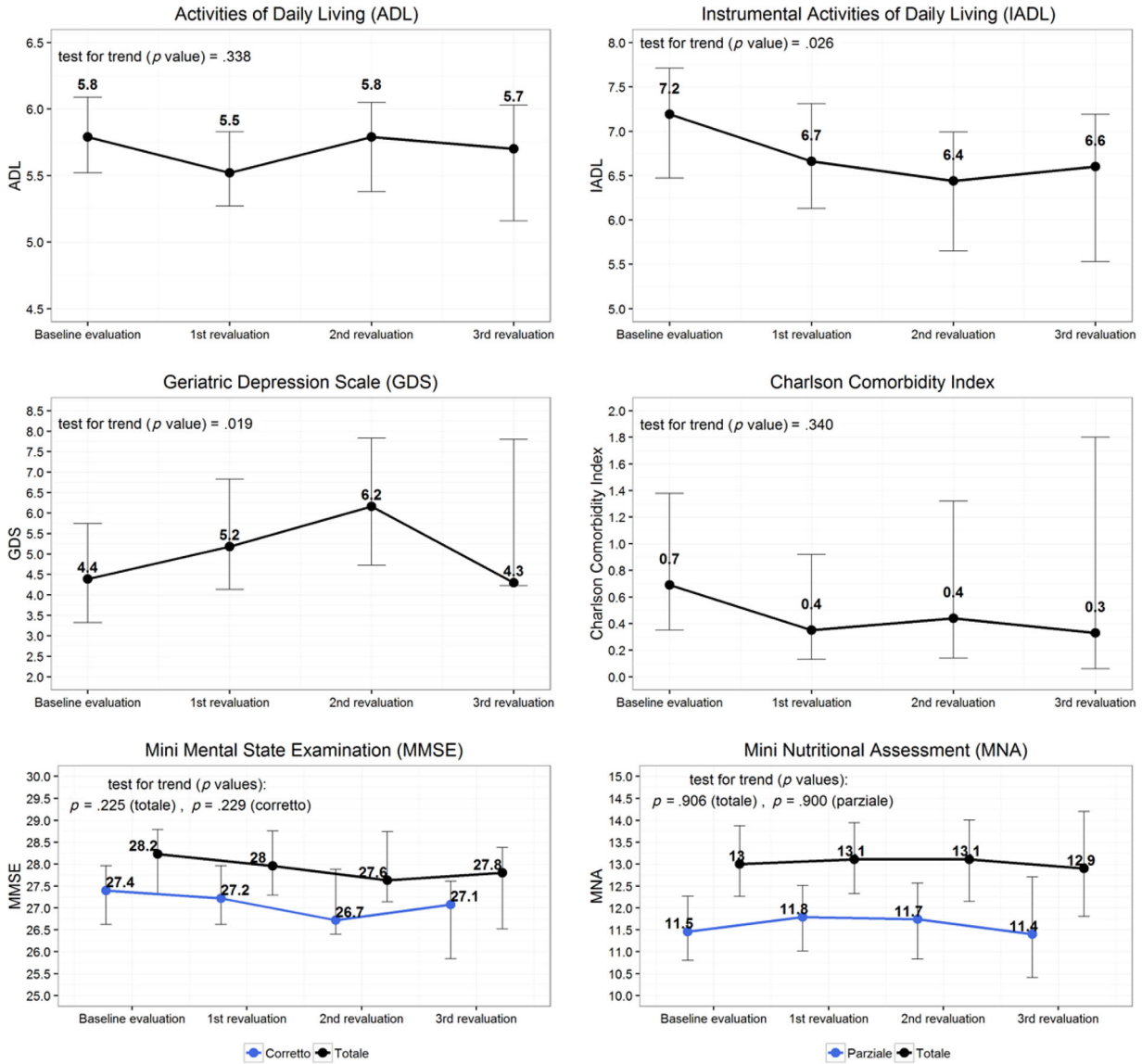

Figure 4. Estimated scores at baseline and after each revaluation of comprehensive geriatric assessment items. Error bars represent the 95% confidence interval around the point estimate.

and type of side effects, mirroring a peculiar toxicity profile for each drug: Patients treated with capecitabine had worse scores, and more rapid time to symptom worsening for gastrointestinal symptoms, whereas patients treated with eribulin had worse scores for systemic therapy side effects; all differences were greatest at 6 weeks, and tended to decline thereafter [35]. In our study, we reported mild side effects during treatment; the most common effect of grade 3–4 was asthenia, as expected from previous studies [8, 27] and from the recent results of the REPROLINE study, which was specifically focused on elderly patients with MBC [38]; we did not report any case of neutropenia or neurotoxicity of grade 3–4.

Clinical outcomes in terms of PFS and clinical benefit rate were similar to those reported in the EMBRACE study (overall PFS 4.0 months, clinical benefit rate [CBR] 30.6%) [6] and in other real-world studies [8, 9], whereas OS was shorter (7.3 months vs 15.2 months) [6, 8], because physical deterioration and general health status were worse.

The study has some limitations. The sample size was limited, and almost one third of patients did not respond to questionnaires after baseline evaluation, thus restricting the analysis within three revaluations. Geriatric assessment was performed at baseline, after second and fourth cycles, and, subsequently, every three cycles of chemotherapy. So a third assessment was scheduled before the eighth cycle. Most patients discontinued treatment because of toxicity or progression of disease before this time and CGA was not performed, and this partially explains the consistent number of patients who did not have at least two revaluations. In addition, we found that some clinicians had difficulties in administering the questionnaires: lack of time, lack of support by geriatric specialists, and underestimation of the relevance of geriatric assessment are potential reasons for these results. Finally, we enrolled patients with good performance status (as per clinical practice) who may not be completely representative of the majority of patients with MBC in the community. Because the lack of significant differences in many items might be related to the limited population and to the high number of patients

Table 3. Adverse events (overall and according to their grades)

Category	Adverse events	All events (*n* = 130)	Grade 1 (*n* = 58)	Grade 2 (*n* = 52)	Grade 3 (*n* = 15)	Grade 4 (*n* = 5)
Hematological, *n* (%)	Neutropenia	2 (1.54)	0 (0)	2 (3.85)	0 (0)	0 (0)
	Leucopenia	3 (2.31)	3 (5.17)	0 (0)	0 (0)	0 (0)
	Anemia	11 (8.46)	4 (6.9)	6 (11.54)	1 (6.67)	0 (0)
Nonhematological, *n* (%)	AST/ALT transaminases	4 (3.08)	4 (6.9)	0 (0)	0 (0)	0 (0)
	Alopecia	3 (2.31)	1 (1.72)	2 (3.85)	0 (0)	0 (0)
	Anorexia	2 (1.54)	2 (3.45)	0 (0)	0 (0)	0 (0)
	Arthralgia/myalgia	5 (3.85)	4 (6.9)	1 (1.92)	0 (0)	0 (0)
	Asthenia/fatigue	26 (20)	6 (10.34)	13 (25)	6 (40)	1 (20)
	Constipation	11 (8.46)	6 (10.34)	5 (9.62)	0 (0)	0 (0)
	Cough	3 (2.31)	1 (1.72)	2 (3.85)	0 (0)	0 (0)
	Diarrhea	2 (1.54)	1 (1.72)	1 (1.92)	0 (0)	0 (0)
	Abdominal pain	5 (3.85)	4 (6.9)	1 (1.92)	0 (0)	0 (0)
	Dyspnea	3 (2.31)	0 (0)	1 (1.92)	0 (0)	2 (40)
	Fever	3 (2.31)	2 (3.45)	1 (1.92)	0 (0)	0 (0)
	Mucositis	12 (9.23)	3 (5.17)	6 (11.54)	3 (20)	0 (0)
	Nausea	5 (3.85)	3 (5.17)	2 (3.85)	0 (0)	0 (0)
	Peripheral neuropathy	2 (1.54)	2 (3.45)	0 (0)	0 (0)	0 (0)
	Rash	11 (8.46)	5 (8.62)	5 (9.62)	1 (6.67)	0 (0)
	Cerebral infarction	2 (1.54)	2 (3.45)	0 (0)	0 (0)	0 (0)
	Cerebral vascular event	1 (0.77)	0 (0)	0 (0)	0 (0)	1 (20)
	Hyporexia	1 (0.77)	0 (0)	0 (0)	0 (0)	1 (20)
	Ocular toxicity	1 (0.77)	0 (0)	1 (1.92)	0 (0)	0 (0)
	Hepatotoxicity	1 (0.77)	0 (0)	1 (1.92)	0 (0)	0 (0)
	Urine infection	1 (0.77)	1 (1.72)	0 (0)	0 (0)	0 (0)

Abbreviation: AST/ALT, aspartate aminotransferase/alanine aminotransferase.

lost to follow-up, further larger studies are recommended to implement and validate the use of CGA and HRQL questionnaires in the management of elderly patients with MBC. SIOG and EUSOMA recommended geriatric assessment in trials with elderly patients with BC.

In addition, educational activities should be advisable to train clinicians about the importance of geriatric assessment in elderly patients.

Conclusion

Eribulin treatment preserved the health-related quality of life and geriatric parameters included in the comprehensive geriatric assessment, except for instrumental functioning and geriatric depression, in elderly patients with metastatic breast cancer. Clinical outcomes and tolerability were favorable and consistent with previous data reported for younger women.

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Disclosures

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