RESEARCH ARTICLE

Editorial Process: Submission:12/19/2024 Acceptance:05/14/2025

The Effectiveness and Adverse Events of Eribulin Monotherapy in Indonesian Metastatic Breast Cancer (MBC) Patients

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Abstract

Objective: Metastatic breast cancer (MBC) remains a major cause of cancer-related mortality, with limited treatment options in advanced stages. Eribulin is now recommended for MBC and covered by the Indonesian National Health Insurance Policy as monotherapy for 6 cycles. However, data on its effectiveness and safety in Indonesian patients remain scarce. This study aimed to evaluate the disease control rate, overall survival (OS), and adverse events of eribulin monotherapy after 6 treatment cycles in Indonesian MBC patients. **Methods:** This multi-center bidirectional longitudinal study was conducted in Indonesia (November 2023 – December 2024). Patients with stage IV MBC receiving eribulin were included. Demographic data, tumor response, OS, and adverse events were extracted from medical records. Kaplan-Meier analysis and the log-rank test were used to assess OS, while Cox regression evaluated potential prognostic factors. Adverse events were analyzed using descriptive statistics. **Result:** A total of 53 patients were included, with 54.7% aged >50 years and 56.6% classified as luminal subtype. The majority (51.0%) received eribulin as a third-line or later treatment, and 56.6% had lung metastases. Disease control was achieved in 43.4% of patients after 6 cycles. The median OS was 10 months (95% CI: 6.81 – 13.18 months). Eribulin was well tolerated, with nausea (32.1%) being the most common adverse event. **Conclusion:** This study suggests that eribulin monotherapy is associated with disease control and survival benefits in Indonesian MBC patients while maintaining a manageable safety profile. However, further prospective studies are needed to confirm its long-term efficacy, impact beyond 6 cycles, and comparative effectiveness relative to other chemotherapy regimens.

Keywords: Adverse event- breast cancer- effectiveness- eribulin- metastatic

Asian Pac J Cancer Prev, **26 (5)**, 1773-1780

Introduction

Breast cancer is a global health burden. Based on GLOBOCAN data, breast cancer is responsible for 11.6% of total cancer cases in 2022. In Indonesia, breast cancer ranks first as the most common cancer in Indonesia and is the first contributor to deaths due to malignancy. Based on GLOBOCAN data in 2022, the number of new cases of breast cancer reached 66,271 cases (16.2%) of the total 408,661 new cases of cancer in Indonesia [1]. Based on Indonesian Health Survey, the prevalence of breast cancer is 18 per 100,000 woman, comprise over 61,682 cases a year [2]. According to the Indonesian Ministry of Health, the average death rate from breast cancer in Indonesia reaches 17 people per 100 thousand population [2].

Breast cancer is a serious health problem in Indonesia. As one of low and middle-income countries (LMICs), Indonesia is still struggle in developing nation-wide prevention, early detection, and comprehensive treatment program [3]. Indonesia breast cancer patients tend to present at later stages and younger ages compared to other regional countries [4]. Furthermore, more than 50% of breast cancer patients in Indonesia come at an advanced stage [5]. Advanced stage breast cancer includes inoperable tumor and evidence of spreading to distant organ or metastasis [6].

The life expectancy of breast cancer patients tends to decrease along with the discovery of metastasis [7, 8]. Based on previous research, it was found that 30% of breast cancer patients diagnosed at earlier stage will experience metastasis. As much as 10% of patients also have metastasis breast cancer at a time of diagnosis [9,

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10]. A study by Tenggara et al showed that luminal B was the most common subtype having metastasis (55.8%) in Jakarta, Indonesia [11]. The high mortality burden of MBC is due to metastatic cells being able to invade several different organs, with complex tumor heterogeneity, plasticity, and different tumor microenvironments requiring specific therapeutic approaches [9, 10].

Systemic therapy is the main choice in MBC cases combined with locoregional treatment based on the patient's condition. The selection of the type of therapy to be given to the patient depends on age, comorbidities, and tumor characteristics with the main goal being to improve the quality of life and prolong patient survival [12, 13]. Anthracycline and/or taxane chemotherapy is the most common chemotherapy option used as a first-line neoadjuvant in HER2-negative MBC cases [14].

Unfortunately, many patients do not respond or become refractory to treatments such as anthracyclines and taxanes. This cause limited option of effective treatment for MBC patients [15].

The resistance occurred through alterations of β-tubulin or modification of membrane transporter like P-glycoprotein [15]. Tubulin or micro-tubulin targeting agent is effective for metastatic breast cancer because it can disrupt spindle formation, cell shape, and micro-vesicle transportation of the cell which can lead to cell death, even in metastatic cancer cells [16]. Eribulin mesylate is a nontaxane microtubule inhibitor from the halichodrin group of antineoplastic drugs. Structurally, eribulin is a modified synthetic analog of halichodrin B, a natural product isolated from Halichondria okadai.

Eribulin acts differently from other tubulin-targeting agents, inhibiting the growth phase of microtubules without affecting the shortening phase, and causing tubulin sequestration into non-productive aggregates. In preclinical trials, eribulin caused less neuropathy than paclitaxel and retained activity in paclitaxel-resistant cells through β-tubulin mutations. Therefore, Eribulin may be effective in patients with diseases resistant to other tubulin-targeting agents [17, 18]. In Indonesia, since 2023, eribulin mesylate is covered by the Indonesian National Health Insurance Policy for 6 cycles as monotherapy for MBC patients who previously had received anthracycline or taxane.

However, there is still no study that evaluate the effectiveness and side effects of eribulin use in metastatic breast cancer patients in Indonesia, especially in the frame of 6 cycles covered by the Indonesian National Health Insurance Policy. Therefore, this study aims to assess the efficacy and side effects of eribulin monotherapy in metastatic breast cancer patients after 6 cycles in several cancer treatment centers in Indonesia.

Materials and Methods

Patients Selection

This is a multi-center bidirectional longitudinal study in several hospitals in Indonesia, including RSPAD Gatot Soebroto-Jakarta, RSUP Prof. I G.N.G. Ngoerah-Denpasar, RSUP Moh. Hoesin-Palembang, RS Materna-Medan, RS Pantai Indah Kapuk-Jakarta and RS Pondok Indah-Jakarta Indonesia from November 2023 – December 2024. The inclusion criteria in this study were all patients with stage IV metastatic breast cancer confirmed by pathologic assessment receiving eribulin therapy. Patients with incomplete data were excluded from this study.

Eribulin Treatment

Eribulin therapy is given as monotherapy or combined therapy with palliative intention. Eribulin administration was regulated by the Indonesian Ministry of Health regulation with a dose of 1.4 mg/m^2 on days 1 and 8 of each 21-day cycle intravenously for 6 cycles. The disease progression and adverse events were monitored during the course of the therapy.

Measurement

The age, histologic type, estrogen status, progesterone status, HER2 status, Ki67 status, subtype, number of the metastasis, site of metastasis, line of treatment, overall survival, and treatment response were collected from the medical record. The hormonal status (ER and PR) is positive when the expression is ≥1% in metastatic or primary lesions. The HER2 is positive when IHC staining shows 3+ or 2+. The Ki67 is positive when the expression is ≥20%. The subtype was then categorized into triple negative breast cancer (TNBC) (HR-/HER2-), HER2 type (HR-/HER2+) and luminal type (HR+/HER2+ or HER2-). The line of treatment is divided into first line, second line, and third or later line. Patient who received eribulin as the third line of treatment is the patients who covered by National Health Policy. Meanwhile, the patient who received eribulin as the first-or-second line treatment pay independently.

The primary endpoint in this study is treatment response. The treatment response was evaluated based on clinical and radiological evaluation of the patient after 6 cycles of eribulin treatment. This procedure was done by two surgical oncologists in each cancer center. The treatment response was categorized into disease control and progression. The patients categorized as disease control if meet these criteria: 1) the tumor size decreases or remains the same after 6 cycles of eribulin and 2) no sign of new metastasis based on clinical or radiological (x-ray, CT-scan, or MRI) evaluation. The criteria of progression included: 1) increase tumor size during or after 6 cycles of eribulin 2) evidence of new metastasis based on clinical or radiological (x-ray, CT-scan, or MRI) evaluation; and 3) patient died during or after 6 cycles of eribulin. The secondary endpoint of this study is overall survival (OS). The OS defined as the time of first eribulin cycle to death. Some of the data was followed-up every 3 weeks (each cycle), while the rest was collected from medical record to assess the progression of the cancer. Patients with missing data for either the treatment start date and date of death were excluded from the analysis to ensure completeness and accuracy in survival outcome estimation.

Adverse event was collected through medical record after eribulin administration. The definition of each adverse event observed in this study as follows: 1) neutropenia: total neutrophil count less than 1000/mm3 accompanied with fever above 38.3°C; 2) peripheral

neuropathy: physical symptoms characterized with dysfunction or damage of peripheral motor or sensory nerves; 3) alopecia: reduced hair density compared to the normal population; 4) fatigue: general weakness and unable to do daily activity; 5) nausea: physical symptoms characterized with decreased of appetite and urge to vomit; 5) elevated transaminase: increase level of blood alanine aminotransferase (ALT) more than 3 times upper limit normal (ULN) if the baseline level is normal, or 1.5 – 3 times baseline, if the baseline level is abnormal.

Statistical Analysis

The collected data were then analyzed using SPSS ver. 26. The univariate data were presented as numbers and percentages. We using chi-square for the bivariate analysis of the treatment response. The survival analysis was performed using the Kaplan-Meier method and differences between groups were evaluated using the log-rank test. The Cox regression analysis was used to evaluate the independent factor affecting overall survival. The differences in adverse events in both groups were analyzed using the chi-square test. A p-value <0.05 was considered statistically significant.

Results

Patients Characteristics

This study successfully collected 53 patients with metastatic breast cancer. The mean age of patients included in this study is 50.85±9.48 years old, and 54.7% of them is above 50 years old during the diagnosis. The most common histologic type is invasive carcinoma no special type (NST) (77.3%). The hormonal status of the patients is 50% ER (+), 53.7% PR (+), 20.4% HER2 (+), and 92.6% Ki67 (+). Eventually, in this study, there were no HER2 type (HR-/HER2+) patients, which makes luminal type (55.6%) is the most common subtype, and the rest (44.4%) is TNBC. Most of the patients (51.0%) received eribulin as the third line or later line of treatment. Thirty (56.6%) patients had lung metastasis, and 47.2% of patients at least had 1 site metastasis (shown in Table 1). As much as 62.3% of the patients complete the cycle (6 cycle) and the rest is unable to complete the cycle due to disease progression (50%), death (35%), or side effects of eribulin (15%). This showed that 62.3% of patients remained alive after completing 6 cycles of eribulin (approximately 18 weeks).

Treatment Response

We evaluated the treatment response of the patients after receiving 6 cycles of eribulin, either in complete or uncomplete cycle. We found 43.4% of the patients experienced disease control to the treatment, while 56.6% is having progression or death. These results show that despite receiving eribulin therapy, more than half of the samples experienced cancer progression. Based on age, patient <50 years old had better disease control rate to eribulin (56.5%), and less progression (36.7%) of the disease. Similarly, patient with luminal subtype had better disease control rate to eribulin (6-.9%), even though more progression was observed in the luminal subtype

Table 1. Baseline Characteristics

Variables	N (%)
Age (mean±SD)	50.85±9.48
Age	
<50 years old	24 (45.3%)
≥ 50 years old	29 (54.7%)
Histologic type	
Invasive lobular carcinoma	11 (20.8%)
Invasive carcinoma of no special type (NST)	41 (77.3%)
Mucinous carcinoma	1 (1.9%)
Estrogen status	
ER +	27 (50.9%)
ER -	26 (49.1%)
Progesteron status	
PR +	29 (54.7%)
PR -	24 (45.3%)
HER2 status	
HER2 +	10 (18.9%)
HER2 -	43 (81.1%)
Ki67 status	
Ki67 +	49 (92.5%)
Ki67 -	4 (7.5%)
Subtype	
TNBC	23 (43.4%)
Luminal	30 (56.6%)
Line of treatment	
1	6 (11.3%)
2	20 (37.7%)
≥3	27 (51.0%)
Metastatic sites	
Liver	18 (34.0%)
Bone	22 (41.5%)
Ovary	2 (3.8%)
Lung	30 (56.6%)
Brain	7 (13.2%)
Contralateral breast	9 (17.0%)
Number of metastatic sites	
1	25 (47.2%)
2	21 (39.6%)
≥3	7 (13.2%)
Cycle	
Complete cycle	33 (62.3%)
Uncomplete cycle	20 (37.7%)
Reason for uncomplete cycle	
Disease progression	10 (50%)
Death	7 (35%)
Side effect (s)	5 (15%)

ER, estrogen receptor; PR, progesterone receptor; *HER2*, human epidermal growth factor receptor 2; TNBC, triple negative breast cancer

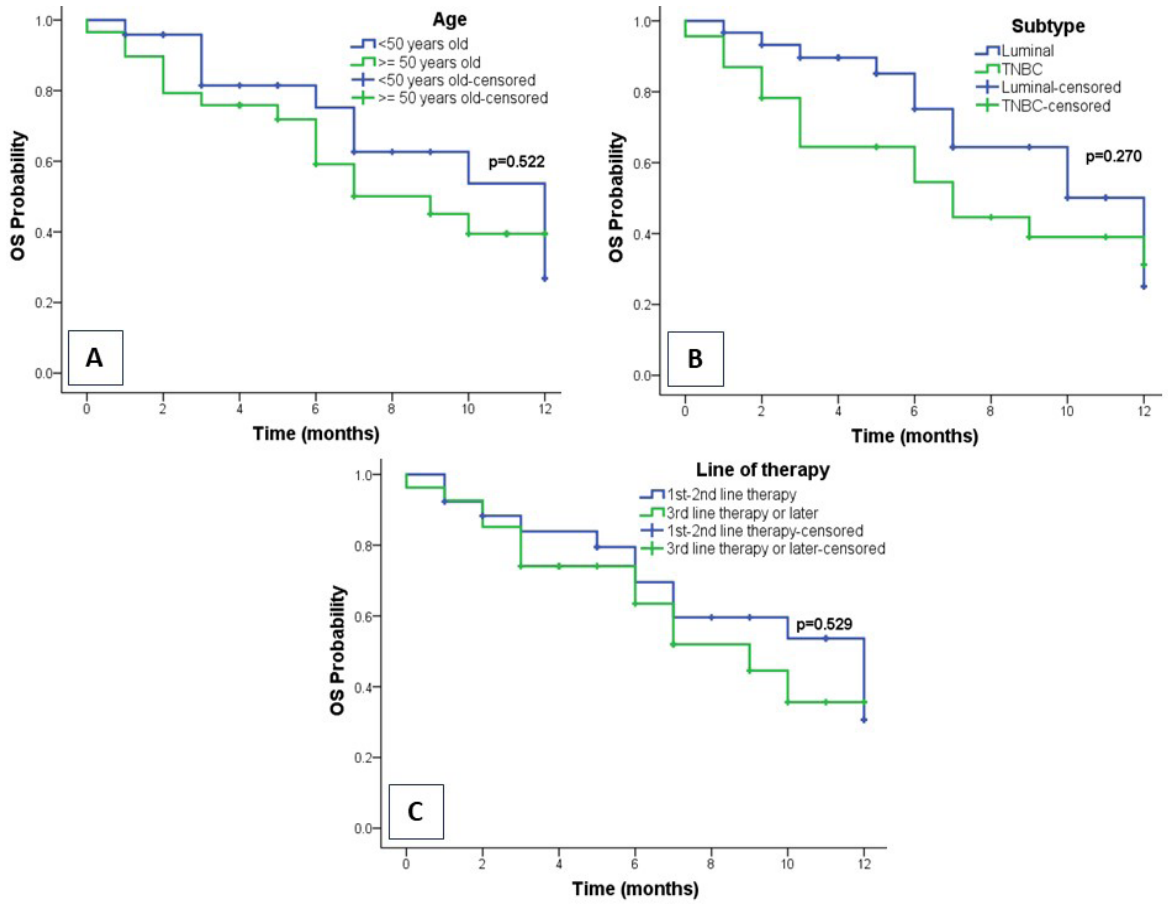

Figure 1. Overall Survival Curves of Eribulin on MBC Patients based on A) age, B) subtypes, C) line of therapy. TNBC, triple negative breast cancer; PFS, progression-free survival

(53.3%) after eribulin administration. Lastly, patient who received eribulin as the 1st or 2nd line of treatment have better disease control rate (60.9%) and less progression (40%). However, all differences found is not statistically significant (p>0.05) (shown in Table 2). These results indicate that patients aged <50 years and luminal subtype who received eribulin as first or second line responded to therapy better, although not statistically significantly different. This insignificant finding needs to be further elaborated through further research with larger samples and longer observation periods, to see a broader picture of the effects.

Survival

The median overall survival (OS) of the patients is 10 months (95%CI: 6.81 – 13.18). The median OS patients

Table 2. Effectiveness of Eribulin in Indonesian Metastatic Breast Cancer Patients

Variables	Treatment Response		p-value
	Disease Control n (%)	Progression n (%)	
All patients	23 (43.4%)	30 (56.6%)	-
Age			
<50 years old	13 (56.5%)	11 (36.7%)	0.15
≥50 years old	10 (43.5%)	19 (63.3%)	
Subtypes			
TNBC	14 (60.9%)	16 (53.3%)	0.583
Luminal	9 (39.1%)	14 (46.7%)	
Line of treatment			
1st – 2nd line	14 (60.9%)	12 (40.0%)	0.132
3rd line or later	9 (39.1%)	18 (60.0%)	

TNBC, triple negative breast cancer

Table 3. Median Overall Survival of Indonesian Metastatic Breast Cancer Patients Receiving Eribulin Treatment

Variables	Median OS (months)	Standard Error	95%CI	p-value
Overall	10	1.62	6.81 – 13.18	-
Age				
<50 years old	12	1.77	8.52 – 15.48	0.522
≥50 years old	9	2.07	4.93 – 13.06	
Subtypes				
TNBC	12	1.76	8.53 – 15.46	0.27
Luminal	7	2.18	2.72 – 11.28	
Line of treatment				
1st – 2nd line	12	2.04	7.98 – 16.01	0.529
3rd line or later	9	1.84	5.37 – 12.62	

OS, Overall Survival; TNBC, triple negative breast cancer; CI, confidence interval

Table 4. The Predictive Factor of Overall Survival in MBC Patients who Received Eribulin

Variables	HR	95%CI	p-value
Age (<50 years old)	1.17	0.53 – 2.58	0.694
Subtype (Luminal)	1.75	0.75 – 4.10	0.193
Line of therapy (1st – 2nd line)	1.57	0.66 – 3.75	0.303

below 50 years old are longer than patients above 50 years old (12.0 vs. 9.0 months) but not statistically different (p=0.522). Patients with luminal type also had longer median OS compared to TNBC patients (12.0 vs. 7.0) although not statistically significant (p=0.270). Patients who received eribulin as first-line and second-line therapy had longer median OS compared to patients who received eribulin as the third-line or later therapy (12.0 vs. 9.0) but were not statistically different (p=0.529) (shown in Figure 1) as summarized in Table 3. Cox regression analysis showed that neither age (HR: 1.17; 95%CI: 0.53 – 2.58; p: 0.694), subtype (HR: 1.75; 95%CI: 0.75 – 4.10; p: 0.193) or line of therapy (HR: 1.57; 95%CI: 0.66 – 3.75; p: 0.303) significantly affected the progression-free survival of MBC patients treated with eribulin (shown in Table 4). Although a trend was observed, this difference was not statistically significant and should be interpreted with caution

Adverse Event

Eribulin is generally well tolerated with low adverse events as summarized in Figure 2. The most common adverse event is nausea (32.1%), followed by neutropenia (28.3%) and fatigue (13.2%). Based on the line of therapy, there is no difference in adverse events between patients who received the first and second line or the third line or later therapy (p>0,05). These results show that the safety profile of eribulin is relatively similar whether given as first line or third line. Patients who experienced nausea are mostly patients who received eribulin as the third line or later therapy. Meanwhile, patients who experienced fatigue are mostly patients who received eribulin as the first and second-line therapy. The differences in the patterns of side effects experienced by these patients need to be further evaluated in studies with larger samples and longer observation periods. The proportion of patients who experienced neutropenia is equal in both groups (50%) (shown in Table 5).

Table 5. Adverse Event of Eribulin based on Line of Therapy

Adverse event	Line of therapy		p-value
	1st – 2nd line	3rd line or later	
Neutropenia, n (%)			
Yes	6 (40.0%)	9 (60.0%)	0.407
No	20 (52.6%)	18 (47.4%)	
Peripheral neuropathy, n (%)			
Yes	3 (50.0%)	3 (50.0%)	1.000
No	23 (58.9%)	24 (51.1%)	
Fatigue			
Yes	4 (57.1%)	3 (42.9%)	0.704
No	22 (47.8%)	24 (52.2%)	
Alopecia, n (%)			
Yes	2 (66.7%)	1 (33.3%)	0.61
No	24 (48.0%)	26 (52.0%)	
Nausea, n (%)			
Yes	7 (41.2%)	10 (58.8%)	0.43
No	19 (52.8%)	17 (47.2%)	
Elevated transaminase, n (%)			
Yes	1 (100.0%)	0 (0.0%)	0.491
No	25 (48.1%)	27 (51.9%)	

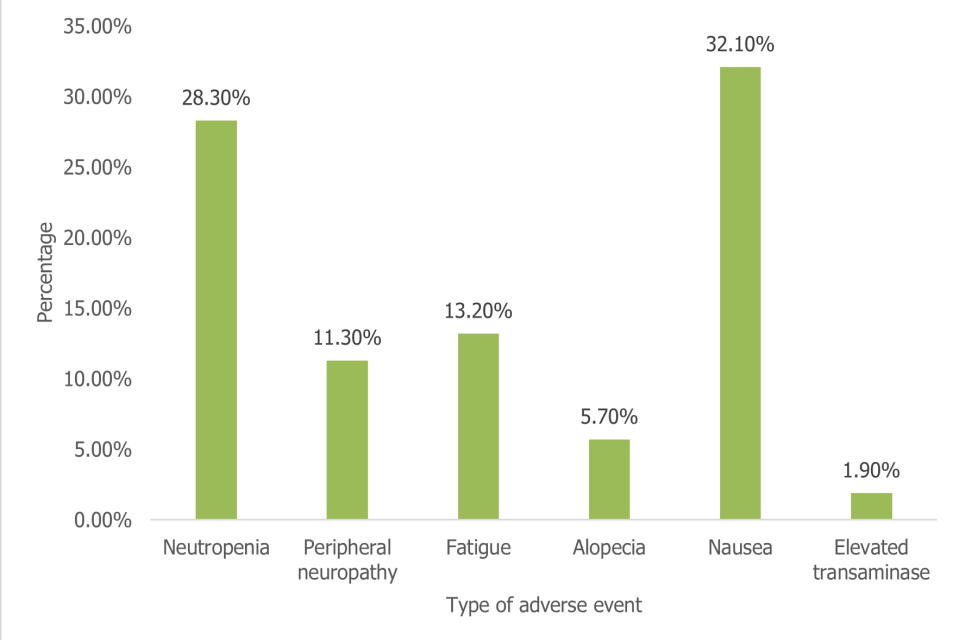

Figure 2. Adverse Event of Eribulin in Indonesian Metastatic Breast Cancer Patients

Discussion

Metastatic breast cancer is a terminal condition with low survival rates. Several previous studies have shown that the median survival rate of MBC patients is limited to only 3 years. Current therapeutic regimens are also still limited in improving the survival of MBC patients. Eribulin is one of the chemotherapies that is currently being evaluated as a chemotherapy option in heavily pre-treated MBC patients. Eribulin is a synthetic analog of halichondrin B which is a polyether macrolide, a derivative of a very potent mitotic tubule inhibitor. Eribulin works by inhibiting microtubule dynamics. Eribulin can bind to one of the positive ends of microtubules and suppress microtubule growth in the interphase which causes shortening of the phase and sequestration of tubulin into unproductive aggregates. This condition causes cell cycle block in the G2/M phase which triggers apoptosis due to prolonged mitotic blockade [17, 18].

This study found that in MBC patients who received eribulin, the majority experienced lung metastasis (56.6%), followed by bone (41.5%), and liver (34.0%). This finding is slightly different from several previous studies which showed that bone metastasis was the most common type of metastasis found (75%), followed by lung and liver.[9] This study also found that the majority of MBC patients received eribulin as 3rd line therapy or later (51.0%), and only 11.3% received eribulin as the first line. This finding is in line with the study by Gui et al which found that MBC patients who received eribulin were mostly in 3rd line (24.6%) or fourth line and later (52.4%) [19].

In terms of treatment response, this study found that 43.4% of MBC patients who received eribulin had disease control. This study also found that patients aged < 50 years old, luminal subtype, and 1st-2nd line treatment had better disease control. The findings of this study are in line with the Gui et al study which found that MBC patients who received eribulin as the second line had a better ORR (15.4%) compared to patients who received eribulin as the third or fourth line. However, this study found slightly different with a study by Orditura that found MBC patients who received eribulin as the third and fourth line had the best DCR rates (65.4% and 70.4%) [14]. The differences between this study and previous studies because genetic, racial, and ethnic differences of the study population. This study also used real-world settings that often include patients with worse ECOG status or more comorbidities, which could negatively impact response rates.

The median overall survival of MBC patients receiving eribulin in this study is 10 months (95%CI: 6.81 – 13.18). This study found that patients <50 years old, luminal subtype, and 1st - 2nd line of therapy had a longer median overall survival. However, the Cox regression analysis showed that neither age, subtype, and line of therapy significantly affected the progression-free survival of MBC patients treated with eribulin (p>0.05). The median OS found in this study was longer than in several previous studies. A study by Takahashi et al found that the median OS of HER2+ breast cancer patients receiving eribulin was 34.7 months [20]. Another study by O'Shaughnessy et al showed that the median OS of MBC patients receiving eribulin was 14.9 months [21]. These differences suggest that patient responses to eribulin vary widely, which may be influenced by race, prior therapy, and other factors that need to be evaluated in further studies. However, this Cox-regression analysis only included age, subtype, and line of therapy, while ECOG status and prior therapies were missing. This shows that the OS findings in this study cannot be concluded to be entirely caused by eribulin because it was only given for 6 cycles and there were several factors that were not controlled.

This study found that eribulin is relatively safe for MBC patients. This study found that the most common adverse event was nausea (32.1%), and no major adverse events were found. This study also found that there was no significant difference in the incidence of adverse events between MBC patients who received eribulin as 1st – 2nd line therapy or 3rd line or later therapy. A study by Chen et al found that neutropenia (33.5%) was the most common adverse event found in MBC patients with eribulin therapy [22]. Another study by Martin-Babau also found that eribulin administration in elderly MBC patients was relatively safe, with the most common adverse events found being neutropenia, fatigue, and neurotoxicity [23]. The findings of chemotherapy-induced neutropenia (CIN) in this study and previous studies may be due to a direct effect of the cytotoxic activity of this drug [24]. The different trend between the most common adverse event for patient who received eribulin as first or second-line treatment with patient who received eribulin as third line treatment can be caused by the effect of previous chemotherapy agent that potentially strengthen or weaken the side effect reaction. But, this hypothesis needs to be confirm in the future studies.

However, this study has several limitations. First, this study has not succeeded in comparing the effectiveness and side effects of eribulin based on the patient's previous treatment history or the combination of eribulin treatment with other types of chemotherapies. Second, this study time frame is limited, so it did not observe the effect and adverse event of eribulin after more than 1 year. Third, this study has not been able to evaluate progression-free survival due to the limited observation time as a preliminary study. We acknowledge that PFS is an important endpoint for assessing treatment efficacy. However, due to limitations in the availability of disease progression data in our medical records, we focused on OS as the primary outcome. OS remains the gold standard in clinical oncology trials and provides meaningful insight into the overall treatment benefit of eribulin. Forth, we agree that additional covariates such as ECOG performance status and prior therapies may impact OS. Unfortunately, these data were not consistently available across all centers.

In the future, further research is needed on a larger scale to provide the differences of eribulin effectivity and adverse event based on race or other demographic background in Indonesian setting. Further research also needs to be done in longer observation periods to see a broader picture of the effects. A prospective comparative studies comparing eribulin versus other chemotherapy

regimens (e.g., capecitabine, vinorelbine) to establish its optimal placement in the Indonesian treatment landscape. Further studies also need to address the real-world data on PFS and post-eribulin treatment outcomes

In conclusion, this study found that 43.4% of metastatic breast cancer patients who received 6 cycles of eribulin achieved disease control, with a median overall survival of 10 months. These findings suggest that eribulin may be associated with survival benefits in this population; however, further prospective studies are needed to confirm its efficacy beyond 6 cycles and relative to other treatment options. Future research should also explore the potential role of eribulin as a first- or second-line therapy in the Indonesian setting, along with its long-term safety and cost-effectiveness before considering broader policy recommendations.

Author Contribution Statement

PATA and WG: project development, data collection, data analysis, manuscript writing and editing. KMS, DH, NQ, DH: data collection, manuscript writing and editing..

Acknowledgements

General

The authors would like to thanks Indonesian Society of Surgical Oncology (ISSO) that fully supported this study.

Ethical Declaration

This study protocol was reviewed and approved by The Research Ethics Committee Faculty of Medicine Udayana University. Written informed consent was obtained from all patients or their legal representatives before study enrollment.

Data Availability

The data of this study is available upon request to the authors.

Statement

This study was not approved by any scientific Body and was not part of an approved student thesis

Conflict of Interest

The authors have no conflicts of interest to declare.

References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229–63. https://doi.org/10.3322/caac.21834
2. Ministry of Health of the Republic of Indonesia. Riskesdas Report 2018. National Riskesdas Report 2018. 2018: 154–165.
3. Setyawan IB, Kurnia D, Setiaji K, Anwar SL, Purwanto DJ, Azhar Y, et al. Sociodemographic disparities associated with advanced stages and distant metastatic breast cancers at diagnosis in indonesia: A cross-sectional study. Ann Med Surg (Lond). 2023;85(9):4211-7. https://doi.org/10.1097/ms9.0000000000001030.
4. Ng CH, Pathy NB, Taib NA, Teh YC, Mun KS, Amiruddin A, et al. Comparison of breast cancer in indonesia and malaysia--a clinico-pathological study between dharmais cancer centre jakarta and university malaya medical centre, kuala lumpur. Asian Pac J Cancer Prev. 2011;12(11):2943-6.
5. Soediro R, Jayalie VF, Djoerban Z, Siregar N, Poetiray E. Multicenter management of breast cancer in indonesia: Ten years of experience. eJournal Kedokteran Indonesia. 2020;8. https://doi.org/10.23886/ejki.8.11020.
6. Carson E, Dear R. Advanced breast cancer: An update to systemic therapy. Aust J Gen Pract. 2019;48(5):278-83. https://doi.org/10.31128/ajgp-10-18-4729.
7. Valachis A, Carlqvist P, Ma Y, Szilcz M, Freilich J, Vertuani S, et al. Overall survival of patients with metastatic breast cancer in sweden: A nationwide study. Br J Cancer. 2022;127(4):720-5. https://doi.org/10.1038/s41416-022-01845-z.
8. Kesireddy M, Elsayed L, Shostrom VK, Agarwal P, Asif S, Yellala A, et al. Overall survival and prognostic factors in metastatic triple-negative breast cancer: A national cancer database analysis. Cancers (Basel). 2024;16(10). https://doi.org/10.3390/cancers16101791.
9. Dissanayake R, Towner R, Ahmed M. Metastatic Breast Cancer: Review of Emerging Nanotherapeutics. Cancers (Basel). 2023;15(11):2906. https://doi.org/10.3390/cancers15112906
10. Park M, Kim D, Ko S, Kim A, Mo K, Yoon H. Breast Cancer Metastasis: Mechanisms and Therapeutic Implications. Int J Mol Sci. 2022;23(12):6806. https://doi.org/10.3390/ijms23126806
11. Tenggara JB, Steven R, Rachman A. P67-1 Metastatic patterns based on breast cancer subtypes: A study in a private Indonesian cancer hospital. Ann Oncol. 2023;34:S1465. https://doi.org/10.1016/j.annonc.2023.09.3097
12. Gennari A, André F, Barrios CH, Cortés J, de Azambuja E, DeMichele A, et al. Esmo clinical practice guideline for the diagnosis, staging and treatment of patients with metastatic breast cancer. Ann Oncol. 2021;32(12):1475-95. https://doi.org/10.1016/j.annonc.2021.09.019.
13. Al Sukhun S, Temin S, Barrios CH, Antone NZ, Guerra YC, Chavez-MacGregor M, et al. Systemic treatment of patients with metastatic breast cancer: Asco resource-stratified guideline. JCO Glob Oncol. 2024;10:e2300285. https://doi.org/10.1200/go.23.00285.
14. Orditura M, Gravina A, Riccardi F, Diana A, Mocerino C, Leopaldi L, et al. Eribulin for metastatic breast cancer (mbc) treatment: A retrospective, multicenter study based in campania, south italy (eri-001 trial). ESMO Open. 2017;2(2):e000176. https://doi.org/10.1136/esmoopen-2017-000176.
15. Rivera E. Implications of anthracycline-resistant and taxane-resistant metastatic breast cancer and new therapeutic options. Breast J. 2010;16(3):252-63. https://doi.org/10.1111/j.1524-4741.2009.00896.x.
16. Tang SC. Predictive markers of tubulin-targeting agents in breast cancer. Clin Breast Cancer. 2008;8 Suppl 2:S79-84. https://doi.org/10.3816/cbc.2008.s.004.
17. Swami U, Chaudhary I, Ghalib MH, Goel S. Eribulin -- a review of preclinical and clinical studies. Crit Rev Oncol Hematol. 2012;81(2):163-184. https://doi.org/10.1016/j.critrevonc.2011.03.002
18. Shetty N, Gupta S. Eribulin drug review. South Asian J Cancer. 2014;3(1):57-59. https://doi.org/10.4103/2278-330X.126527
19. Gui X, Liang X, Li H. Effectiveness, safety, and impact on quality of life of eribulin-based therapy in heavily pretreated

patients with metastatic breast cancer: A real-world analysis. Cancer Med. 2023;12(16):16793–804. https://doi.org/10.1002/cam4.6301
20. Takahashi M, Kikawa Y, Kashiwabara K, Taira N, Iwatani T, Shimozuma K, et al. Eribulin versus s-1 as first or second-line chemotherapy to assess health-related quality of life and overall survival in her2-negative metastatic breast cancer (resq study): A non-inferiority, randomised, controlled, open-label, phase 3 trial. EClinicalMedicine. 2024;74:102715. https://doi.org/10.1016/j.eclinm.2024.102715.
21. O'Shaughnessy J, Cortes J, Twelves C, Goldstein LJ, Alexis K, Xie R, et al. Efficacy of eribulin for metastatic breast cancer based on localization of specific secondary metastases: A post hoc analysis. Sci Rep. 2020;10(1):11203. https://doi.org/10.1038/s41598-020-66980-0.
22. Chen L, Yan X, Luo T, Tian T, He P, Zhong X. Efficacy and safety of eribulin mesylate in patients with locally advanced or metastatic breast cancer previously treated with anthracycline/taxanes. Cancer Med. 2024;13(10):e7295. https://doi.org/10.1002/cam4.7295.
23. Martin-Babau J, Robert M, Seegers V, Paillard MJ, Pivot X, Gourmelon C, et al. 299peribulin is safe and efficient in metastatic breast cancer in elderly patients. Results from the reproline multicentric retro-prospective cohort. Ann Oncol. 2017;28. https://doi.org/10.1093/annonc/mdx365.062.
24. Tanni KA, Truong CB, Johnson BS, Qian J. Comparative effectiveness and safety of eribulin in advanced or metastatic breast cancer: A systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;163:103375. https://doi.org/10.1016/j.critrevonc.2021.103375.