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Eribulin plus carboplatin combination for HER2-negative metastatic breast cancer: a multicenter, real-world cohort study

Mengqian Ni[1†], Lijia Zhou[1†], Yongkui Lu[2†], Dachuan Guo[3], Xiuyue Li[4], Lixia Li[5], Lidong Zhang[6], Meiting Chen[1], Lulu Zhang[1], Fei Xu[1], Zhongyu Yuan[1], Shusen Wang[1], Yanxia Shi[1*], Anli Yang[7*] and Xin An[1*]

Abstract

Background Pre-clinical data suggests a potential synergistic effect of eribulin and platinum. However, clinical data on the combination for metastatic breast cancer (mBC) is lacking. We evaluated the efficacy and safety of eribulin plus carboplatin (ErCb) in patients with mBC.

Patients and methods This multicenter, real-world cohort study included patients with pre-treated metastatic triple negative breast cancer (TNBC) or endocrine-refractory hormone receptor (HR) positive, HER2-negative mBC who received ErCb. Eribulin (1.4 mg/m2) and carboplatin (target AUC = 2) were administered intravenously on day 1 and 8 of 21-day cycle. Objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), overall survival (OS), and adverse events (AEs) were evaluated.

Results From March 2022 to December 2023, a cohort of 37 patients were recruited to the study. Among them, 22 patients have TNBC and 15 have HR + HER2 – mBC. Of the 22 patients with TNBC, 8 had an initial diagnosis of the HR + HER2 – subtype. The median treatment was 6 cycles (range, 2 – 8 cycles). In the full cohort, TNBC, and HR + HER2 – subgroup, the ORR were 51.4%, 54.5% and 46.7%, the DCR were 81.1%, 81.8% and 80%, and the median PFS were 5 months, 5 months, and 5.2 months, respectively. The median OS was 12.7 months in the entire cohort and 12.8 months in TNBC subgroup. The most common grade 3/4 hematological AEs were neutropenia (37.8%), leukopenia (35.1%), febrile neutropenia (10.8%), thrombocytopenia (5.4%), and anemia (2.7%). No grade 3/4 non-hematological AEs were observed.

†Mengqian Ni, Lijia Zhou and Yongkui Lu contributed equally to this work.

*Correspondence:
Yanxia Shi
shiyx@sysucc.org.cn
Anli Yang
yangal@sysucc.org.cn
Xin An
anxin@sysucc.org.cn

Full list of author information is available at the end of the article

Conclusion ErCb demonstrated favorable efficacy and tolerability in patients with heavily pre-treated mBC, especially TNBC. The findings of the current study warrant further investigation of the application of this combination in earlier lines of mBC treatment.

Keywords Metastatic breast cancer, Eribulin, Carboplatin, Efficacy, Safety

Introduction

Breast cancer (BC) is one of the most common cancers worldwide, and metastatic breast cancer (mBC) is the leading cause of cancer-related death among females worldwide [1]. Over the past decades, significant advances have been made in the treatment of mBC, with several novel targeted agents have been approved, including CDK4/6 inhibitors, immune check point inhibitors (ICIs), and antibody-drug conjugates (ADCs). Even though, chemotherapy remains a mainstay of treatment, especially for triple-negative (TN) and endocrine-refractory hormone receptor positive (HR+), human epidermal growth factor receptor 2-negative (HER2–) diseases [2, 3]. Moreover, the optimal chemotherapeutic regimen remains unclear, particularly for patients pre-treated with anthracycline and/or taxanes.

Eribulin is a non-taxane microtubule dynamic targeting agent that inhibits microtubule polymerization to induce cancer cell death [4, 5]. Eribulin also elicits anticancer effect by modulating tumor microenvironment and anti-angiogenetic mechanism [6, 7]. The phase III EMBRCAE (305) trial demonstrated that eribulin monotherapy improved overall survival (OS) by 2.7 months compared with treatment of physician's choice (TPC) in heavily pre-treated mBC patients [8]. Subsequent studies suggested eribulin was particularly active in HER2-negetive subgroup including TNBC [9–11]. Even though, eribulin monotherapy showed unsatisfactory efficacy, with an overall response rate (ORR) of only 12%, and median progression free survival (PFS) of 3.7 months [8], indicating the needs to further investigate optimal combinational strategies to enhance treatment efficacy.

Platinum drugs exert anti-tumor effect through producing cross-linking of DNA, leading to inhibition of DNA replication and DNA damage [12–14]. A series of studies have established the efficacy of carboplatin and cisplatin in BC, especially for TNBC [15–17]. Different mechanism of action and toxicity profiles make eribulin and platinum a potentially perfect combination. Indeed, synergistic anti-tumor effect has been suggested by preclinical and phase I studies [18, 19]. A phase II clinical study demonstrated promising efficacy and tolerability of carboplatin and eribulin (ErCb) combination as neoadjuvant therapy for TNBC, with an ORR and pathological complete response (pCR) rate of 80% and 43.3%, respectively [20]. However, there is limited data on the efficacy of eribulin combined with platinum drugs in patients with mBC.

Herein, we performed a multicenter, real-world cohort study to assess the efficacy and safety of this combination therapy in HER2-negative mBC.

Patients and methods

This retrospective, multicenter, real-world cohort study recruited patients with HER2-negative mBC who received ErCb regimen at the Sun Yat-sen University Cancer Center (SYSUCC), the Affiliated Cancer Hospital of Guangxi Medical University, the Central Hospital of Pan-Yu, the Cancer Hospital, Affiliated Hospital of Guangdong Medical University, and the Puning People's Hospital between March 2022 to December 2023. The inclusion criteria were (1) histopathologically confirmed as BC; (2) HER2-nagetive disease, defined as HER2 IHC 0, 1+, and 2+but FISH non-amplification. The cut-off for ER and PR positivity was ≥1%; (3) received ErCb treatment; (4) measurable disease metastatic disease and available response assessments; and (5) adequate cardiac, bone marrow, and hepatic functions apart from organ function affected by their disease. We extracted data from medical charts within the hospital information system (HIS) and included the demographics, tumor characteristics, treatment plan, standard laboratory tests detail and test results, and imaging results of patients. This study was approved by the ethical committee of the SYSUCC (B2023-570-01).

Treatment

Eribulin was administered at a dose of 1.4mg/m^2, and carboplatin was given at a dose of AUC=2, both on day 1 and day 8 of 21-day cycle. Patients received continuous treatment cycle as described above, until disease progression, or intolerable toxicity, or any other reasons that required treatment discontinuation. The investigators evaluated patients' response to treatment every two cycles using computed tomography (CT) or magnetic resonance imaging (MRI) according to the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. ORR was defined as the proportion of evaluable patients who achieved complete response (CR) or partial response (PR) as their best objective tumor response. DCR was defined as the proportion of patients who had CR, PR, and stable disease (SD). PFS was defined as the period from the start of ErCb treatment until either clinical or objective disease progression or death by any cause. OS was defined as the period from the first ErCb treatment until death by any cause or the last follow-up.

AEs were graded according to the National Cancer Institute-Common Terminology Criteria (NCI-CTCAE) version 5.0.

Statistics analysis

All statistical analyses were conducted using R 4.3.1 (The R Project for Statistical Computing, www.r-project.org) and Prism 5.01 (GraphPad Software Inc., San Diego, CA, USA). Clinicopathologic characteristics, effectiveness and safety data were analyzed with descriptive statistics. The median PFS and OS and the corresponding 95% confidence intervals (CIs) were calculated through Kaplan–Meier plots. A two-sided *P* value < 0.05 was considered statistically significant.

Results

Patient characteristics

A total of 37 women treated with ErCb regimen across five medical institutions between March 2022 and December 2023 participated in the study. Baseline characteristics of enrolled patients were presented in Table 1. The median age was 46 (range, 31–61) years. Twenty-two patients had mTNBC including 8 patients who were initially diagnosed as HR+HER2−subtype, and 15 had HR+HER2−mBC. Seventeen (45.9%) patients showed HER2-low status, and 20 (54.1%) were HER2-zero. Visceral metastases were presented in 27 (73.0%) patients, with 22 (59.5%) patients had ≥3 metastatic organ sites, and 4 (10.8%) had brain metastases (BrM). The median number of prior therapies for metastatic disease was 2 (range, 1–6). All patients had received taxanes and anthracyclines in adjuvant and/or metastasis settings. All patients in the HR+HER2−cohort progressed on prior endocrine therapies (ET) and CDK 4/6 inhibitors. Twelve de novo and one converted TNBC (35.1%) patients received ICIs, 3 (8.1%) germline BRCA mutated patients received poly ADP-ribose polymerase (PARP) inhibitors, and 4 (10.8%) received ADC treatments.

Treatment

The median treatment cycles were 6 (range, 2–8), with 28 (75.7%) patients completed at least 4 cycles, and 10 (27.0%) patients received eribulin monotherapy as maintenance treatment after 6 cycles of ErCb combination. Two (5.4%) patients received subsequent surgical resection due to a good response to ErCb treatment (Table S1).

Efficacy outcomes

Up to July 31, 2024, the median follow-up duration was 11.9 months (95% confidence interval [CI]: 9.7–15.1 months).All patients experienced disease progression (Fig. 1a), and 20 (54.1%) patients died of disease progression (Fig. 1b). Among the overall cohort, nineteen (51.4%) patients achieved PR, 11 (29.7%) had SD, and 7 (18.9%) showed PD, with an ORR of 51.4% and DCR of 81.1%. The ORR and DCR were 54.5% and 81.8% for TNBC subgroup, compared with 46.7% and 80% for HR+HER2−subgroup. The ORR and DCR were 55% and 85% in HER2-zero patients, compared with 47.1% and 76.5% in HER2-low disease (Table 2 and Figure S1a). Among four TNBC patients with BrM, 2 achieved PR, and another 2 showed SD (Figure S1b). Response was also observed in patients who were pre-treated with ADC (2 out of 4), platinum-base chemotherapy (6 out of 9), and TNBC patients converted from HR+HER2−mBC (7 out of 8) (Table 3). The maximum change of tumor size from baseline was illustrated using waterfall plots in Fig. 2.

The median PFS for the whole cohort was 5 (95% CI: 3.8–6.2) months (Fig. 3a). Median PFS were 5 (95% CI: 3.2–6.7) months versus 5.2 (95% CI: 3.3–7.1) months for TNBC and HR+HER2−subgroups, respectively (hazard ratio [HR]: 0.83, 95% CI: 0.42–1.63, $p=0.57$) (Fig. 3b), and 5.3 (95% CI: 3.4–6.6) months versus 5 (95% CI: 2.4–7.6) months for HER2-zero and HER2-low subgroups, respectively (HR: 1.22, 95% CI: 0.64–2.32, $p=0.53$) (Fig. 3c). The median OS was 12.7 (95% CI: 9.3–16.0) months for the entire cohort (Fig. 3d). The median OS was 12.8 (95% CI: 10.0–15.6) months and not reached for TNBC and HR+HER2−subgroups, respectively (HR: 1.15, 95% CI: 0.47–2.83, $p=0.77$) (Fig. 3e), and 11.1 (95% CI: 8.4–13.1) months versus not reached for HER2-zero and HER2-low subgroups, respectively (HR: 2.44, 95% CI: 1.02–5.87, $p=0.054$) (Fig. 3f).

Safety

Toxicity profiles were assessed for the entire cohort (Table 4). The most common hematological AEs were neutropenia (70.3%), leukopenia (70.3%), and anemia (54.1%). The most common non-hematological AEs were anorexia (64.7%), nausea (62.2%), and fatigue (54.1%). The most reported grade 3/4 AEs were hematological AEs, including neutropenia (37.8%), leukopenia (35.1%), febrile neutropenia (FN) (10.8%), thrombocytopenia (5.4%), and anemia (2.7%). No grade 3/4 non-hematological AEs were observed. Dose reduction occurred in 5 (13.5%) patients, due to neutropenia (2 patients), thrombocytopenia (1 patients), and both (2 patients). Dose delay occurred in 11 (29.7%) patients (Table S1).

Discussion

The current multicenter, real-world cohort study showed a remarkable efficacy and tolerability of ErCb combination in patients with heavily pre-treated HER2−mBC. The overall ORR was 51.4% and PFS was 5 months, which appeared to be better than the 11% and 4.1 months of eribulin monotherapy in 301 study, where eribulin was used almost in ≤3 lines treatment [9].

Table 1 Clinical characteristics of the patients at baseline

Characteristics	Patients (*n* = 37)	TNBC* (*n* = 22)	HR + HER2- (*n* = 15)
Age, years			
Median (range)	46 (31–61)	46 (35–60)	46 (31–61)
Gender			
Female	37 (100)	22 (100)	15 (100)
ECOG			
0	4 (10.8)	4 (18.2)	0 (0)
1	31 (83.8)	17 (77.3)	14 (93.3)
2	2 (5.4)	1 (4.5)	1 (6.7)
Genetic testing			
Somatic PIK3CA	4 (10.8)	3 (13.6)	1 (6.7)
Germline BRCA1/2	3 (8.1)	1 (4.5)	2 (13.3)
Wild type	7 (18.9)	5 (13.5)	2 (13.3)
Untested	23 (62.2)	13 (59.1)	10 (66.7)
HER2 status			
Low	17 (45.9)	8 (36.4)	9 (60.0)
Zero	20 (54.1)	14 (63.6)	6 (40.0)
PD-L1			
CPS < 10	11 (29.7)	10 (45.5)	1 (6.7)
CPS≥ 10	3 (8.1)	3 (13.6)	0 (0)
Untested	23 (62.2)	9 (40.9)	14 (93.3)
Stage			
De novo stage IV cancer	9 (24.3)	5 (22.7)	4 (26.7)
Recurrent disease	28 (75.7)	17 (77.3)	11 (73.3)
Number of metastatic sites			
Median (range)	3 (1–6)	3 (1–6)	3 (1–5)
1	5 (13.5)	4 (18.2)	1 (6.7)
2	10 (27.0)	7 (31.8)	3 (20.0)
≥ 3	22 (59.5)	11 (50.0)	11 (73.3)
Metastatic sites			
Visceral metastasis	27 (73.0)	15 (68.2)	12 (80.0)
Liver	18 (48.6)	9 (40.9)	9 (60.0)
Lung	15 (40.5)	10 (45.5)	5 (33.3)
Brain	4 (10.8)	4 (18.2)	0 (0)
Bone	24 (70.3)	13 (59.1)	11 (73.3)
Lymph nodes	27 (73.0)	16 (72.7)	11 (73.3)
Prior therapies for metastatic disease			
Median (range)	2 (1–6)	2 (1–5)	3 (1–6)
1st	12 (32.4)	10 (45.5)	2 (13.3)
2nd	10 (27.0)	5 (22.7)	5 (33.3)
3rd	7 (18.9)	4 (18.2)	3 (20.0)
≥ 4th	8 (21.6)	3 (13.6)	5 (33.3)
Chemotherapy			
Anthracyclines	37 (100)	22 (100)	15 (100)
Taxanes	37 (100)	22 (100)	15 (100)
Capecitabine	22 (59.5)	12 (54.5)	10 (66.7)
Vinorelbine	17 (45.9)	9 (40.9)	8 (53.3)
Platinum	9 (24.3)	4 (18.2)	5 (33.3)
Gemcitabine	5 (13.5)	3 (13.6)	2 (13.3)
Endocrine therapy			
AI	18 (48.6)	3 (22.7)	15 (100)
SERM	5 (13.5)	0 (0)	5 (33.3)
SERD	16 (43.2)	1 (4.5)	15 (100)

Table 1 (continued)

Characteristics	Patients (*n* = 37)	TNBC* (*n* = 22)	HR + HER2- (*n* = 15)
CDK4/6 inhibitor	17 (45.9)	2 (9.1)	15 (100)
Other			
Bevacizumab	7 (18.9)	7 (31.8)	0 (0)
ICIs	13 (35.1)	12 (54.5)	1 (6.7)
PARP inhibitor	3 (8.1)	1 (4.5)	2 (13.3)
ADC	4 (10.8)	4 (18.2)	0 (0)

Abbreviations TNBC, triple-negative breast cancer; HR, hormone receptor; HER2, human epidermal growth factor receptor-2; ECOG, Eastern Cooperative Oncology Group; PV, pathogenic variant; AI, aromatase inhibitor; SERM, selective estrogen receptor modulator; SERD, selective estrogen receptor degrader; ICIs, immune checkpoint inhibitors; PARP, poly ADP-ribose polymerase; ADC, antibody-drug conjugates

*: Fourteen patients were primary TNBC and 8 were converted by HR + HER2−

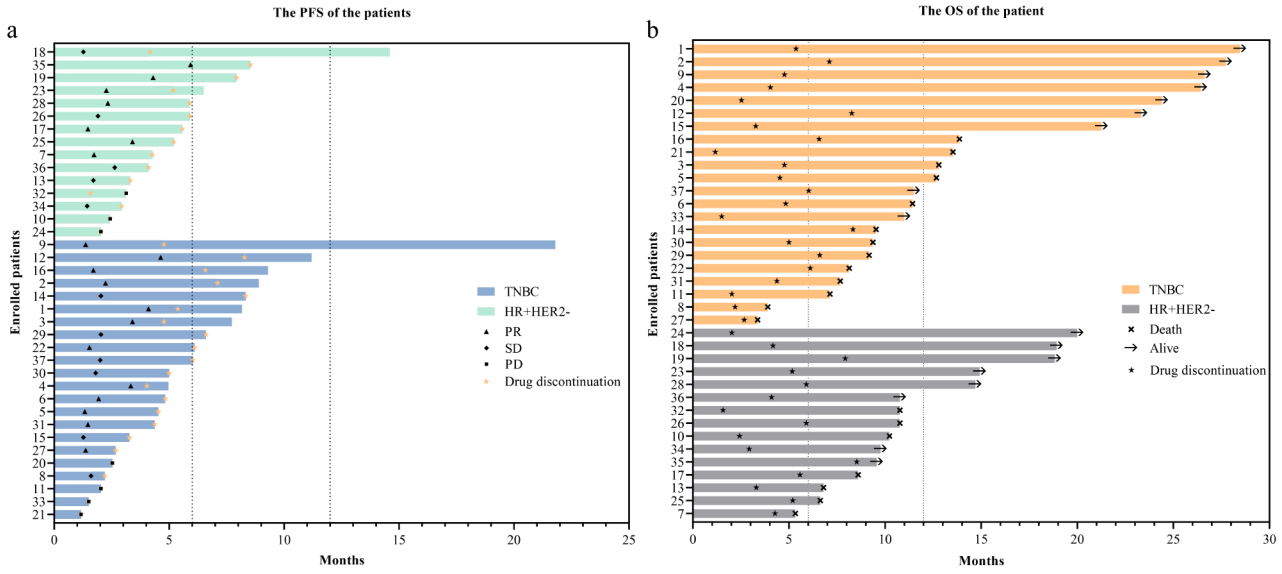

Fig. 1 Swimmer plot of treatment outcomes (**a**). Swimmer plot of survival outcomes (**b**)

Table 2 Evaluation of efficacy

Response	No. Patients, *n* (%)				
	All patients (*N* = 37)	TNBC group (*N* = 22)	HR + HER2- group (*N* = 15)	HER2-zero (*N* = 20)	HER2-low (*N* = 17)
CR	0	0	0	0	0
PR	19 (51.4)	12 (54.5)	7 (46.7)	11 (55.0)	8 (47.1)
SD	11 (29.7)	6 (27.3)	5 (33.3)	6 (30.0)	5 (29.4)
PD	7 (18.9)	4 (18.2)	3 (20.0)	3 (15.0)	4 (23.5)
ORR	19 (51.4)	12 (54.5)	7 (46.7)	11 (55.0)	8 (47.1)
DCR	30 (81.1)	18 (81.8)	12 (80.0)	17 (85.0)	13 (76.5)
Median PFS (95% CI)	5.0 (3.8–6.2)	5.0 (3.2–6.7)	5.2 (3.3–7.1)	5.3 (3.4–6.6)	5.0 (2.4–7.6)
Median OS (95% CI)	12.7(9.3–16.0)	12.8 (10.0–15.6)	Not reached	11.1 (8.4–13.1)	Not reached

Abbreviations TNBC, triple-negative breast cancer; HR, hormone receptor; HER2, human epidermal growth factor receptor-2; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; NE, not evaluable; ORR, objective response rate; DCR, disease control rate; PFS, progression-free survival; OS, overall survival; NE, not evaluable

Generally, single-agent chemotherapy used in sequence is a preferred treatment choice for mBC. While combination chemotherapy is only reserved for patients with rapid progression disease burden, life-threatening visceral metastases, or rapid symptom and/or disease control [21]. However, this recommendation was based on results of older trials, which enrolled a mixture of different subtypes of mBC, and showed no OS benefit but increased toxicities of combination chemotherapy compared with sequential single-agent therapy [2, 22,

Table 3 Evaluation of efficacy in special cases

Patients	Response PR/SD/PD	PFS (months) Range
BrM ($n=4$)	2/2/0	2.7–9.3
Prior therapy of ADC ($n=4$)	2/0/2	1.2–8.5
Prior therapy of platinum ($n=9$)	6/0/3	1.2–9.3
TNBC converted by HR+HER2− ($n=8$)	7/1/0	2.2–11.2

Abbreviations PR, partial response; SD, stable disease; PD, progressive disease; PFS, progression-free survival; BrM, brain metastasis; ADC, antibody-drug conjugate; TNBC, triple-negative breast cancer; HR, hormone receptor; HER2, human epidermal growth factor receptor-2

23]. While the contemporary studies focus on mTNBC showed particularly unsatisfactory efficacy of single-agent chemotherapy (taxane, eribulin, vinorelbine, gemcitabine, or capecitabine) [24]. The median PFS generally varies 5–6 months, and ORR approximately 46-47% in first-line setting [25–27], but decrease to less than 2 months and 5-10% in second-line or later mTNBC setting [24, 28]. On the other hand, several studies suggested the importance of combination chemotherapy for TNBC [21–23], probably due to its aggressive clinical behavior, and higher tendencies of heavy tumor burden and visceral metastases. In our current study, all mTNBC patients enrolled were pre-treated with anthracycline and taxane and received a median 2 lines of prior treatment for metastatic disease. In this setting, ErCb still yielded an ORR of 54.5% and a PFS of 5 months, which was significantly better than the aforementioned single-agent chemotherapy, as well as the reported ORR of 18.2% and PFS of 3.5 months of second-line eribulin monotherapy [29]. Moreover, ErCb also appeared to be more promising than another combination of eribulin plus gemcitabine, which reported an ORR of 37.3%, and PFS of 5.1 months with 80% of patients as first-line treatment [21]. Notably, among the four patients diagnosed with TNBC combined with BrM, two showed intracranial response, with the PFS of 2.7 and 9.3 months, suggesting the potential effectiveness of ErCb for TNBC BrM.

Treatment of endocrine resistant HR+HER2−mBC has long been a challenge for clinicians, especially for patients progressed after CDK4/6 inhibitor. Some patients develop resistance due to the loss of HR expression. As shown in our current study, 8 patients converted to TNBC subtype, and were sensitive to chemotherapy. While for other mechanisms of ET resistance, treatment options include novel selective estrogen receptor degrader (SERD), PI3K/AKT/mTOR inhibitors, and ADCs [30–33]. Nonetheless, chemotherapy is still a reasonable choice for patients who have no chance to use target drugs, or experienced disease progression after these target drugs. The literature showed single-agent chemotherapy usually yields an ORR of 15–20%, and PFS of 4.0-5.4 month in second or third-line treatment [32–34]. In our current study enrolled similar population with HR+HER2−mBC, and ErCb showed an ORR of 46.7% and PFS of 5.2 months, suggesting the potential benefit of

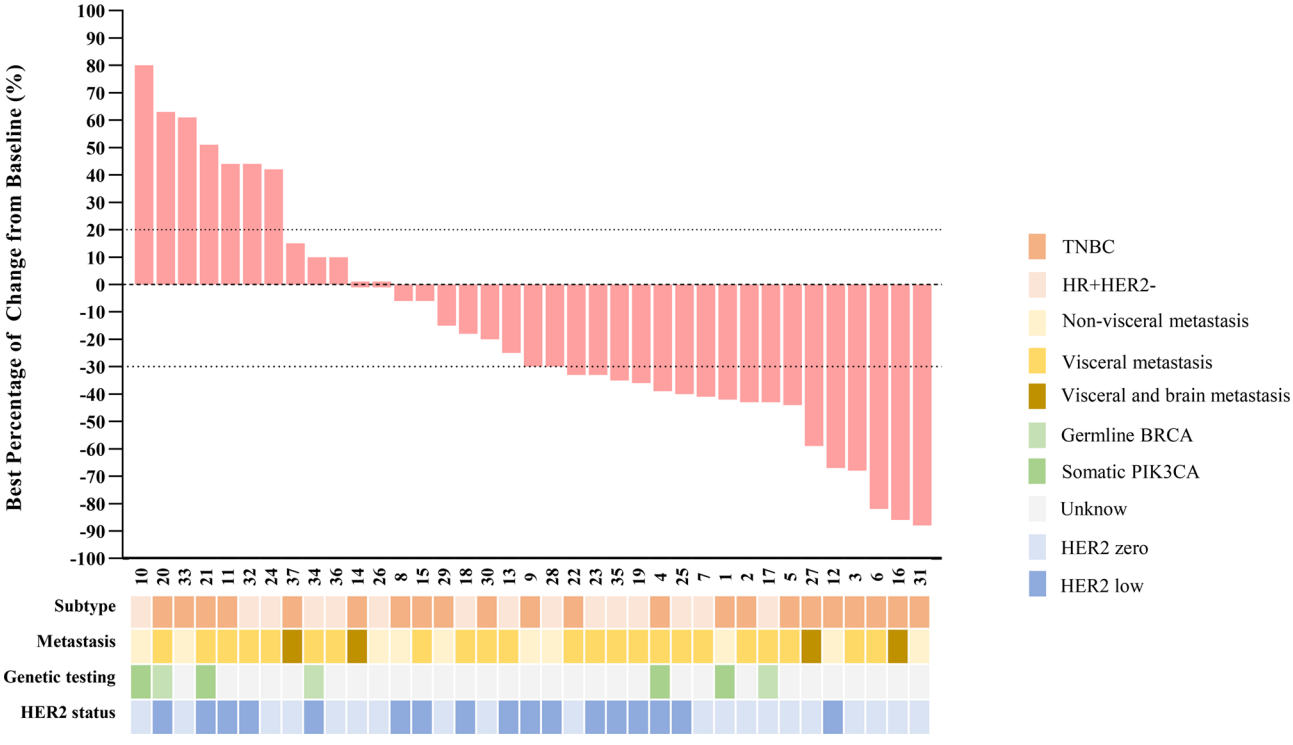

Fig. 2 Waterfall plot of response for ErCb

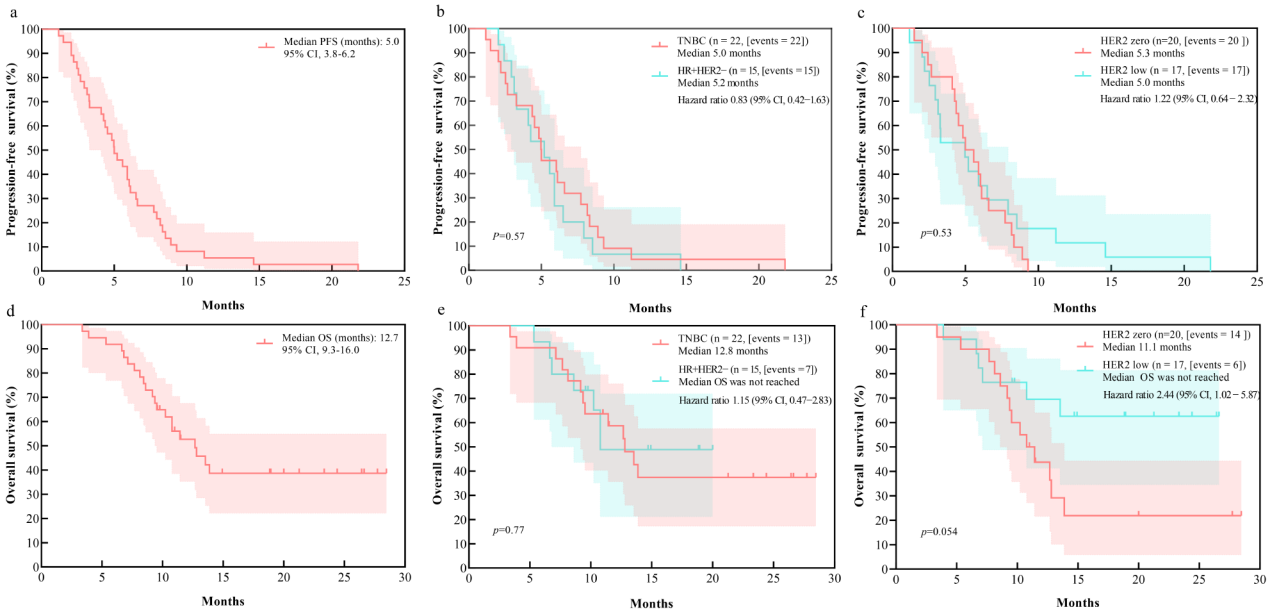

Fig. 3 Kaplan-Meier curve for progression-free survival of entire cohort (**a**), TNBC and HR + HER2 − subgroups (**b**), and HER2-zero and HER2-low subgroups (**c**). Kaplan-Meier curve for overall survival of entire cohort (**d**), TNBC and HR + HER2 − subgroups (**e**), and HER2-zero and HER2-low subgroups (**f**)

Table 4 Adverse events (AEs)

Adverse event, *n* (%)	All grades (%)	Grade 3–4 (%)
Hematological AE		
Neutropenia	26 (70.3)	14 (37.8)
Leukopenia	26 (70.3)	13 (35.1)
Anemia	20 (54.1)	1 (2.7)
Thrombocytopenia	10 (27.0)	2 (5.4)
Febrile neutropenia	4 (10.8)	4 (10.8)
Non-hematological AE		
Anorexia	24 (64.7)	0 (0.0)
Nausea	23 (62.2)	0 (0.0)
Fatigue	20 (54.1)	0 (0.0)
Alopecia	18 (46.6)	0 (0.0)
Constipation	13 (35.1)	0 (0.0)
Hyperpigmentation	13 (35.1)	0 (0.0)
Stomatitis	10 (27.0)	0 (0.0)
Peripheral sensory neuropathy	9 (24.3)	0 (0.0)
Skin pruritus and/or rash	8 (21.6)	0 (0.0)
Vomiting	8 (21.6)	0 (0.0)
AST elevation	5 (13.5)	0 (0.0)
ALT elevation	5 (13.5)	0 (0.0)
Headache	4 (10.8)	0 (0.0)
Myalgia	3 (8.1)	0 (0.0)
Diarrhea	3 (8.1)	0 (0.0)

Abbreviations ALT, alanine transaminase; AST, aspartate aminotransferase

combination versus single-agent chemotherapy, but the efficacy gain appeared less in HR+/HER2 − subgroup than in the TNBC subgroup.

We found HER2 low expression didn't affect ErCb efficacy. Interestingly, we observed 4 patients progressed on ADCs (one was pretreated with trastuzumab deruxtecan, and 3 were pretreated with sacituzumab govitecan) achieved PR on ErCb treatment, suggesting its potential use as a salvage treatment beyond ADCs progression. In addition, more patients received subsequent ADCs treatment in HER2-low subgroup than that in HER2-zero group, which might be an explanation of the prolonging survival trend in this subgroup of patients.

Overall, ErCb was well-tolerated. No patients died due to AEs. The most common AEs were hematological toxicities. Grade 3/4 neutropenia occurred in 37.8% of the study population, and FN occurred in 10.8% of the cohort, which suggesting that prophylactic use of granulocyte colony-stimulating factor (G-CSF) following day 8 of chemotherapy might be appropriate. The main common non-hematological toxicities were grade 1/2 anorexia, nausea, and fatigue. Incidence of other patient-perceived toxicity incidence including peripheral sensory neuropathy, myalgia, and hand-foot syndrome was very low, indicating the potential benefits of ErCb in maintaining patients' quality of life.

Currently, eribulin was approved for the treatment of mBC in patients who have received at least two prior chemotherapy regimens including an anthracycline and a taxane. While several studies have shown the potential benefit of first-line treatment of eribulin. For example, eribulin plus gemcitabine for HER2-negative mBC, and eribulin plus trastuzumab and pertuzumab for HER2-positive mBC [35–37]. In light of the efficacy and safety profiles of ErCb in mTNBC observed in our current study, we speculate this combination might be challenge first-line albumin-paclitaxel and cisplatin (AP) or

gemcitabine and cisplatin (GP) in mTNBC. Moreover, based on the synergistic efficacy between eribulin and immunotherapy, we are conducting a prospective phase II study of ErCb in combination with ICI for mTNBC.

This study is limited by the nature of retrospective research, as well as the small sample size, hence the findings should be interpreted with caution.

Conclusion

ErCb shows promising efficacy and tolerability in patients with heavily pre-treated HER2-negative mBC, especially for TNBC subgroup. Prospective studies are warranted to further validate this combination, particular as early-line therapy for mTNBC.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12885-024-12953-9.

Supplementary Material 1: Specific treatment

Supplementary Material 2: Swimmer plot of the patients with different HER2 expressions (a). Swimmer plot of the patients with different metastatic sites (b)

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Not applicable.

Author contributions
MQN, LJZ and YKL contribute equally to this work. XA, ALY and YXS: Study concept and experimental design; MQN, LJZ, YKL, XYL, LXL, LDZ, MTC, LLZ and FX collected the samples and medical history. ZYY and SSW: Analysis and interpretation of data; MQN, LJZ and DCG: Writing of the manuscript, preparation of figures and statistical analysis. The authors read and approved this manuscript.

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Data availability
The original data presented in the study are included in the article/supplementary materials. Further inquiries can be directed to the corresponding authors.

Declarations

Ethics approval and consent to participate
This study was performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and received approval from the ethics committee of the Sun Yat-sen University Cancer Center (file number: B2023-570-01). All patients had approved for the use of clinical samples and data for research purposes and signed informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Medical Oncology, State Key Laboratory of Oncology in South China, Guangdong Provincial Clinical Research Center for Cancer, Sun Yat-sen University Cancer Center, No. 651, Dongfeng Road East, Yuexiu District, Guangzhou 510060, China
[2]Affiliated Cancer Hospital of Guangxi Medical University, Nanning 530021, China
[3]Department of Minimally Invasive Interventional Therapy, State Key Laboratory of Oncology in South China, Guangdong Provincial Clinical Research Center for Cancer, Sun Yat-sen University Cancer Center, Guangzhou 510060, P. R. China
[4]Central Hospital of Pan-Yu, Guangzhou 511486, China
[5]Cancer Hospital, Affiliated Hospital of Guangdong Medical University, Zhanjiang 524000, China
[6]Puning People's Hospital, Jieyang, Guangdong 515300, China
[7]Department of Breast Oncology, State Key Laboratory of Oncology in South China, Guangdong Provincial Clinical Research Center for Cancer, Sun Yat-sen University Cancer Center, No. 651, Dongfeng Road East, Yuexiu District, Guangzhou 510060, China

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