Safety and Effectiveness of eribulin in Thai metastatic breast cancer patients: a post-marketing observational retrospective study.

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Introduction

Non-taxane microtubule inhibitor Eribulin is approved as the later line chemotherapy for metastatic breast cancer (MBC). Several phase III studies revealed its efficacy similar to other single agent treatment option. However, data of effectiveness and safety profile in real practice is still limit.

Objective

To evaluate the effectiveness and safety of eribulin in Thai metastatic breast cancer patients.

Material and Methods

The retrospective chart review was performed in 55 MBC patients who received eribulin at King Chulalongkorn Memorial Hospital during 2013 to 2018. From 126 cases who received eribulin, 55 cases (43.65%) were MBC patients with complete and evaluable medical records. Adverse events during treatment were recorded to assess safety of this drug. Time to progression (TTP) and median survival were used as effectiveness outcomes.

Results

The patients' average age was 56.85 ± 14.4 years old (range: 23-85) and average body surface area was 1.52 ± 0.2 m^2. Most of patients were in good performance status before starting eribulin. Other disease-related characteristics were presented in Table 1. The most common grade 3-4 hematologic adverse events were found in this study was neutropenia at 38.2%. Grade 1-2 peripheral neuropathy was also commonly found at 52.7%. The median TTF was 2.6 months (77 days : range 7-237). Twenty-five patients died which resulted in 45.5% of overall survival rate. The median survival was 6.9 months (208 days : range 74-953).

Table 1 : Patients Characteristics

Diseases related characteristicsa	N	%
ER/PgR positive	24	43.64
HER2 positive	11	20
Triple negetive	19	34.55
Number of prior chemotherapy for advanced disease		
0	2	3.64
1	19	34.55
2	15	27.27
3	12	21.82
4	5	9.09
5	2	3.64
Metastatic lesions		
Lung	39	70.90
Lymph node	13	23.64
Liver	24	43.64
Bone	30	54.55
Brain	8	14.55
Skin	6	10.90
others	10	18.18
Previous chemotherapy for advanced disease		
Anthracyclines	2	3.64
Taxanes	42	76.36
Capecitabine	39	70.91
Hormonal therapy	15	27.27

Table 2 : Treatment profile

Eribulin exposure and treatment outcome	N	%
Starting dose (mg/m2)		
0.7	2	3.64
1.1	11	20
1.4	41	74.55
Other (1.25)	1	1.82
No of cycles administered		
1-4	31	56.36
5-8	21	38.18
9-10	2	3.64
Median (range)	4 (1-10)	
Events of treatment delay or dose reduction		
Delay treatment due to AEs	22	40
Dosage reduction	19	34.55
Reasons of treatment discontinuation		
Disease Progression	42	76.36
Chemotherapy intolerance	6	10.91
Dead	2	3.64
N/A	5	9.10

Table 3 : Adverse events (according to CTCAE version 5.0)

Toxicity	Any grade (%)	Grade ≥3 (event)
overall		24
Hematologic events		
Neutropenia	21 (38.18)	21
anemia	2 (3.64)	1
infection	1 (1.81)	
Non-hematologic events		
Peripheral neuropathy	29 (52.73)	1
Alopecia	16 (29.09)	
Anorexia	10 (18.18)	
Fatigue	7 (12.73)	
Nausea/vomiting	7 (12.73)	
Myalgia	6 (10.91)	
Constipation	4 (7.27)	
Weight loss	3 (5.45)	
Diarrhea	3 (5.45)	
Rash	3 (5.45)	
Mucositis	3 (5.45)	
Dizziness	2 (3.63)	
Itching	2 (3.63)	
HFS	1 (1.81)	
Insomnia	1 (1.81)	
cramping	1 (1.81)	

Discussion [1,2,3]

Summary of major clinical trials, median OS of patients was 15.2 months, while PFS were reported at 4.0 months which markedly different from our findings. Grade 3/4 AE neutropenia (52.4%) and peripheral neuropathy (6.6%) were reported which also higher than our results. However, previous report from real-world pooled analysis data presented that peripheral neuropathy and grade 3/4 neutropenia were seen in 31% and 28.1% respectively which lower than reported in our study.

Conclusions

Effectiveness of eribulin treatment in Thai patients was relatively less half than reported in clinical trials. The incidence of grade 3-4 neutropenia was lower while the rate of grade 1-2 peripheral neuropathy was higher.

References
1. Twelves et al. Efficacy of eribulin in women with metastatic breast cancer: a pooled analysis of two phase 3 studies. Breast Cancer Res Treat (2014) 148:553–561
2. Goodin S et al. Safety and tolerability of eribulin mesylate in patients with pretreated metastatic breast cancer. Am J Health Syst Pharm. 2015;72:2150–2156.
3. Voutsadakis IA. A systematic review and pooled analysis of retrospective series of eribulin in metastatic breast cancer. Anticancer Drugs. 2017;28:557–564.