Efficacy and Safety Analysis of Pyrotinib in Lapatinib Resistant HER2-Positive Metastatic Breast Cancer: A Retrospective Study

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ABSTRACT

66 (86.8%) patients received pyrotinib immediately after lapatinib and 10 (13.2%) received pyrotinib following one or more other therapies. The median PFS of pyrotinib was 8.0 months (95%CI 5.1-10.9) and OS has not reached. Objective response rate (ORR) was 17.1%, and clinical benefit rate (CBR) was 60.5%. Patients who benefited from lapatinib ≥6.0 months were found to have a longer PFS (P=0.034; stratified hazard ratio [HR] 0.534, 95%CI 0.293-0.975). In patients who had received lapatinib in 3 or later line therapy (35, 46.1%), the median PFS of pyrotinib was 9.9 months (95%CI 6.97-12.83) and was relevant to whether lapatinib PFS had reached 6.0 months (P=0.044; HR 0.412, 95%CI 0.167-1.013). No relations were detected between pyrotinib PFS and estrogen receptor (ER) status, trastuzumab resistance, brain metastasis or the sequential use of pyrotinib. In patients who had received lapatinib earlier (41,53.9%), the median PFS of pyrotinib was 6.4 months (95%CI 3.57-9.23). No relevant factors were observed. There was no difference in PFS between these two groups with different lapatinib lines. Toxicity profiles were similar in both groups. The most common adverse effects were diarrhea (34, 44.7%) and hand-foot syndrome (10, 13.2%).

OBJECTIVES

Lapatinib has shown effectiveness in treating HER2-positive metastatic breast cancer, but therapies after lapatinib resistance are still controversial. In this retrospective study, we assessed the efficacy and safety of pyrotinib in lapatinib resistant HER2-positive metastatic breast cancer .

METHODS

From August 2018 to March 2020, 76 HER2-positive metastatic breast cancer patients who previously failed by lapatinib received pyrotinib in four hospitals. The primary endpoint was investigator-assessed progression-free survival (PFS) per Respond Evaluation Criteria in Solid Tumors (RECIST) version 1.1. The secondary endpoint was the overall survival (OS) and safety of pyrotinib.

RESULTS

Table 1. **Baseline characteristics of 76 lapatinib-resistant HER2 positive metastatic breast cancer patients.**

Characteristic	No. (%) (n=76)
Age	
Median (interquartile range)	55(46-60)
HR status	
HR positive	34 (44.7%)
HR negative	29 (38.2%)
Unknown	13 (17.1%)
Visceral metastases	
Yes	49 (64.5%)
No	27 (35.5%)
Metastatic sites	
Lymph nodes	16 (21.1%)
Lung	35 (46.1%)
Liver	17 (22.4%)
Bone	14 (18.4%)
Brain	14 (18.4%)
Chest wall	4 (5.3%)
Lines of pyrotinib therapy	
2	13 (17.1%)
3	23 (30.3%)
⩾4	40 (52.6%)
Pyrotinib Regimens	
pyrotinib	7 (9.2%)
pyrotinib+capetabine	38 (50.0%)
pyrotinib+vinorelbine	12 (15.8%)
pyrotinib+trastuzumab	6 (7.9%)
other	13 (17.1%)

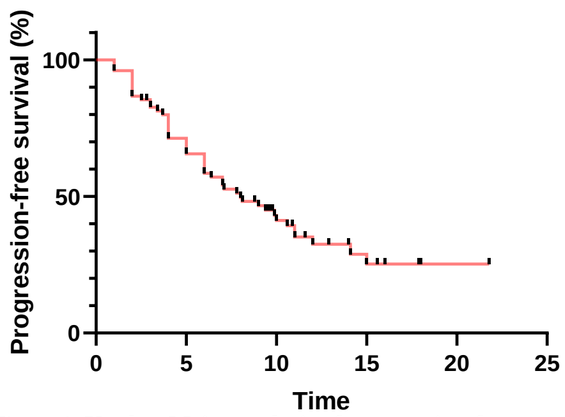

Figure 1. **Kaplan-Meier analysis of progression-free survival in patients who received pyrotinib.**

Response	No. (%) (n=76)
Complete response	0
Partial response	13 (17.1%)
Stable disease	59 (77.6%)
Progressive disease	4 (5.3%)
ORR	17.10%
CBR	60.50%

Table 2. **Overall response of patients who received pyrotinib.**

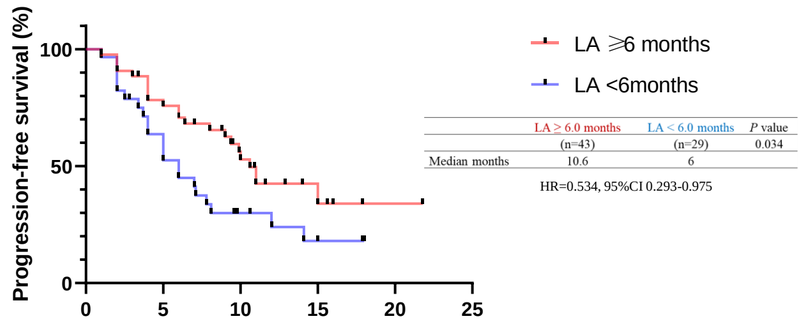

Figure 2 . **Kaplan-Meier analysis of progression-free survival of pyrotinib in patients who benefited from lapatinib ≥6.0 months and <6.0 months.**

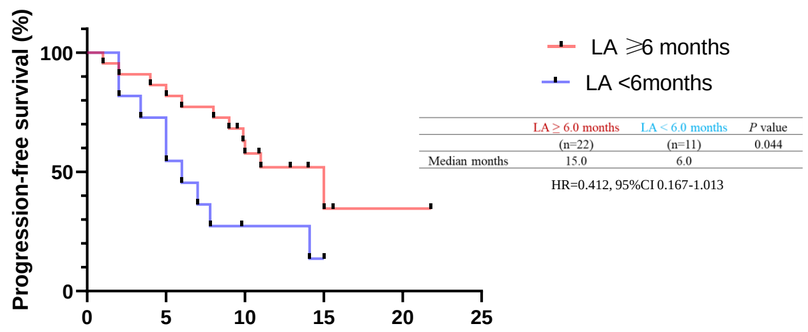

Figure 3 . **Kaplan-Meier analysis of progression-free survival of pyrotinib in patients who received lapatinib in 3 or later lines.**

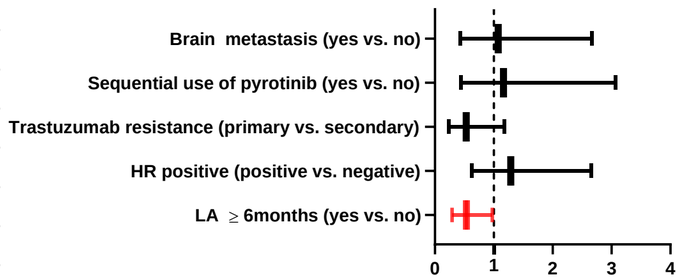

Figure 4**. Multivariate analysis for progression-free survival of patients who received pyrotinib.**

Aadverse events (grade 1-5)	No. (%) (n=76)
Diarrhea	34 (44.7%)
Hand-foot sydrome	10 (13.2%)
Nausea	4 (5.2%)
Neutropenia	2 (2.6%)
Anemia	2 (2.6%)
Vomiting	2 (2.6%)
Increased ALT and /or AST	2 (2.6%)
Dizziness	2 (2.6%)
Rash	1 (1.3%)
Cardiac dysfunction	1 (1.3%)
Nipple ulceration	1 (1.3%)

Table 3. **Adverse events of 76 lapatinib-resistant HER2 positive metastatic breast cancer patients who received pyrotinib.**

CONCLUSIONS

Pyrotinib could improve the survival of HER2-positive metastatic breast cancer patients after the failure of lapatinib. For patients who benefited from lapatinib ≥ 6.0 months in 3 or later line therapy, pyrotinib could provide a clinically meaningful longer PFS.

* The authors have declared no conflicts of interest.

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