The addition of pyrotinib in early or locally advanced HER2-positive breast cancer patients with no response to 2 cycles of neoadjuvant therapy: A prospective, multicenter study

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Abstract #155P

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Background

- Early assessment of clinical response to treatment would facilitate individualized therapy, and response-guided neoadjuvant chemotherapy improves cancer outcomes.
- The anti-HER2 monoclonal antibody trastuzumab and tyrosine kinase inhibitor pyrotinib have complementary mechanisms of action and synergistic antitumour activity in models of HER2-overexpressing breast cancer.
- In this preliminary analysis, we explored the efficacy and safety of neoadjuvant pyrotinib in combination with docetaxel, carboplatin and trastuzumab (TCH) in patients with early or locally advanced HER2-positive breast cancer who did not respond after two cycles of neoadjuvant TCH.

Methods

- This was a prospective, open-label, multicenter phase II study (NCT03847818).
- All patients received two 3-week cycles of TCH first, those with complete or partial response (RECIST 1.1) continued four cycles of TCH (cohort A). Non-responder after two cycles of TCH received four cycles of TCH (cohort B) or pyrotinib (400 mg orally once per day) + TCH (cohort C) (Figure 1).
- The primary endpoint was total pathological complete response (tpCR) rate, defined as ypT0/Tis ypN0.

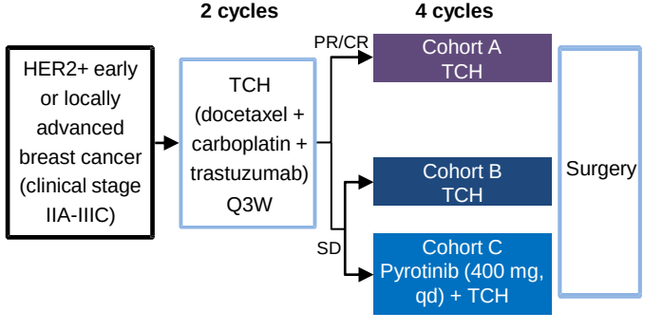

Figure 1. Study design.

PR, partial response; CR, complete response; SD, stable disease.

Results

Patients

- A total of 85 patients received six cycles of neoadjuvant therapy and completed surgery between December 2018 and August 2021 (Table 1).

Table 1. Clinical and pathological characteristics of patients at baseline

Characteristics	Cohort A (n=33)	Cohort B (n=21)	Cohort C (n=31)
Median age (range), years	49 (29-64)	53 (32-67)	50 (31-59)
Menopausal status, n (%)			
Postmenopausal	16 (48.5)	14 (66.7)	13 (41.9)
Premenopausal	17 (51.5)	7 (33.3)	18 (58.1)
Clinical tumour stage, n (%)			
T1	2 (6.1)	2 (9.5)	3 (9.7)
T2	29 (87.9)	16 (76.2)	24 (77.4)
T3	1 (3.0)	2 (9.5)	2 (6.5)
T4	1 (3.0)	1 (4.8)	2 (6.5)
Clinical lymph node status, n (%)			
N0	15 (45.5)	10 (47.6)	12 (38.7)
N1	12 (36.4)	4 (19.0)	11 (35.5)
N2	5 (15.2)	6 (28.6)	8 (25.8)
N3	1 (3.0)	1 (4.8)	0
Clinical stage, n (%)			
II	25 (75.8)	12 (57.1)	21 (67.7)
III	8 (24.2)	9 (42.9)	10 (32.3)
Hormone receptor status, n (%)			
ER+ and/or PR+	20 (60.6)	16 (76.2)	20 (64.5)
ER- and PR-	13 (39.4)	5 (23.8)	11 (35.5)
Ki67 level, n (%)			
<20%	4 (12.1)	0	2 (6.5)
≥20%	29 (87.9)	21 (100)	29 (93.5)

ER, estrogen receptor; PR, progestogen receptor.

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The authors have no conflicts of interest to declare.

Safety

- The adverse event profile is shown in Table 2. Grade ≥3 treatment-related adverse events were observed in 29.0% (9/31) of cohort C patients. Among them, the most frequent events were decreased neutrophil count in 6 patients (19.4%), diarrhea in 6 patients (19.4%), decreased white blood cell count in 5 patients (16.1%), and vomiting in 2 patients (6.5%).

Table 2. Adverse events occurring in ≥20% of patients who received neoadjuvant therapy

	Cohort A (n=33)		Cohort B (n=21)		Cohort C (n=31)	
Adverse events	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
Diarrhea	15 (45.5)	0	11 (52.4)	0	23 (74.2)	6 (19.4)
Vomiting	15 (45.5)	0	12 (57.1)	0	21 (67.7)	1 (3.2)
Elevated Alanine aminotransferase	15 (45.5)	0	11 (52.4)	0	9 (29.0)	0
Neutropenia	11 (33.3)	5 (15.2)	8 (38.1)	3 (14.3)	12 (38.7)	6 (19.4)
Nausea	10 (30.3)	0	7 (33.3)	0	11 (35.5)	0
Rash	8 (24.2)	0	6 (28.6)	0	12 (38.7)	0
Anemia	8 (24.2)	0	5 (23.8)	0	8 (25.8)	0
Elevated Aspartate aminotransferase	7 (21.2)	0	7 (33.3)	0	9 (29.0)	0
Hand-foot syndrome	6 (18.2)	0	6 (28.6)	0	6 (19.4)	0
Oral mucositis	5 (15.2)	0	5 (23.8)	0	9 (29.0)	0
Cardiac events	3 (9.1)	0	3 (14.3)	0	4 (12.9)	0

Efficacy

- The tpCR rate was the highest in cohort A (33.3%; 11/33), followed by 29.0% (9/31) in cohort C and 14.3% (3/21) in cohort B (Figure 2).

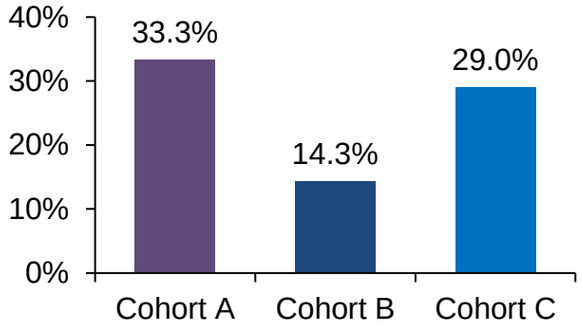

Figure 2. Total pathological complete response rate.

Conclusions

This preliminary analysis strongly suggested the efficacy and tolerable toxicity of pyrotinib + TCH in patients with early or locally advanced HER2-positive breast cancer who did not respond after two cycles of TCH in the neoadjuvant setting, and also confirmed the importance of early efficacy assessment during neoadjuvant therapy.