Pyrotinib plus capecitabine with or without radiotherapy in patients with HER2-positive metastatic breast cancer and brain metastases: A multicenter, retrospective-prospective, real-world study in China (Post-PERMEATE)

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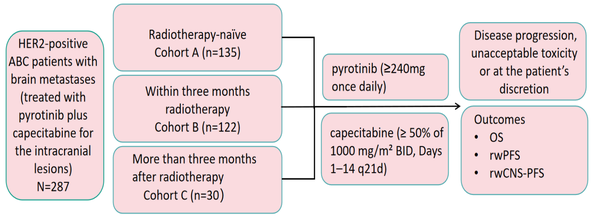
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Background

The combination of pyrotinib and capecitabine has shown promising efficacy in patients with HER2-positive metastatic breast cancer and brain metastases (BMs)[1-3]. However, it remains uncertain whether the timing of local radiotherapy affect overall survival (OS) on the basis of this systemic regimen. The purpose of our study is to investigate the impact on OS of the addition of brain radiotherapy to the treatment with pyrotinib and capecitabine in patients with HER2-positive breast cancer BMs in a real-world clinical practice setting.

Methods

This is a multicenter, retrospective-prospective, real-world study conducted across 41 centers in China (NCT05359120). Patients diagnosed with HER2-positive breast cancer and BMs, with complete diagnostic and treatment records available in hospital electronic medical record systems were eligible for this study. Enrolled patients were categorized into three cohorts based on the radiotherapy status while undergoing systemic treatment: those who were radiotherapy-naïve (Cohort A), those who received whole-brain radiotherapy (WBRT) and/or stereotactic radiosurgery (SRS) within three months of initiating systemic treatment (Cohort B), and those who received systemic treatment more than three months after radiotherapy (Cohort C). Systemic treatment was defined as pyrotinib (no less than 240 mg once daily) combined with capecitabine (no less than 50% of 1000 mg/m² twice daily on days 1–14 of each 21-day cycle) until disease progression, unacceptable toxicity or at the patient's discretion. The endpoints included OS and progression-free survival(PFS). Here we present the results of Cohort A and B.



Results

From September 2018 to January 2024, a total of 287 female patients were enrolled in the study. In Cohort A, 27.4% (37/135) of patients presented with symptomatic BMs, while 52.5% (64/122) in Cohort B. Additionally, a greater percentage of patients in Cohort A (88.9%) had active BMs compared to those in Cohort B (61.5%).

As of May 6, 2025, the median follow-up duration was 35.9 months (95% CI: 34.3-37.5) in Cohort A and 45.3 months (95% CI: 41.9-48.6) in Cohort B. The median OS was 35.4 months (95% CI: 31.4-39.4) in Cohort A and 37.3 months (95% CI: 27.4-47.2) in Cohort B, with no statistically significant difference between the two groups (p = 0.793). Similarly, the median progression-free survival (PFS) was comparable between Cohort A and Cohort B, at 15.0 months (95% CI: 11.7–18.3) and 15.5 months (95% CI: 12.1–18.9), respectively (p = 0.073). However, CNS-PFS was significantly longer in Cohort B (20.7 vs. 15.5 months, p = 0.007).

Table 1. Patient characteristics for each cohort

	Cohort A(n=135) No. ,%	Cohort B(n=122) No. ,%
Age, years	52 (26-77)	52 (27-70)
Eastern Cooperative Oncology Group performance status		
0-1	119 (88.1%)	107 (87.0%)
≧2	16 (11.9%)	15 (13.0%)
Unknown	0	0
Brain metastasis-free survival (BMFS): median (range)		
BMFS from diagnosis of metastatic disease (months)	7.9 (0-162.5)	5.6 (0-147.7)
Symptomatic brain metastases		
Yes	37 (27.4%)	64 (52.5%)
No	98 (72.6%)	58 (47.5%)
Unknown	0	0
Number of previous therapy lines		
0	45 (33.3%)	49 (40.2%)
1	64 (47.4%)	61 (50.0%)
≧2	26 (19.3%)	12 (9.8%)
No. of brain metastases		
≤3	93 (68.9%)	65 (53.3%)
4-10	27 (20.0%)	35 (28.7%)
＞10	12 (8.9%)	15 (12.3%)
Unknown	3 (2.2%)	7 (5.7%)
Size of the largest brain lesion, cm		
≦2	91 (67.4%)	66 (54.1%)
＞2	36 (26.7%)	41 (33.6%)
Unknown	8 (5.9%)	15 (12.3%)
State of brain lesion		
Active/radiotherapy-naïve	120 (88.9%)	72 (59.0%)
Stable/radiotherapy-naïve#	15 (11.1%)	7 (5.7%)
Active/progress after radiotherapy	0	3 (2.5%)
Stable/treated after radiotherapy	0	40 (32.8%)
Measurable disease status		
Yes	89 (65.9%)	83 (68.0%)
No	41 (30.4%)	29 (23.8%)
Unknown	5 (3.7%)	10 (8.2%)
Previous CNS local therapy		
Surgery	16 (11.9%)	17 (13.9%)
Stereotactic radiotherapy	0	18 (14.8%)
Whole-brain radiotherapy	0	25 (20.5%)
None	119 (88.1%)	68 (55.7%)
Site of metastases (not mutually exclusive)		
Visceral metastasis	85 (63.0%)	71 (58.2%)
Meningeal metastasis	10 (7.4%)	12 (9.8%)
Non-visceral metastasis	15 (11.1%)	18 (14.8%)
None	35 (25.9%)	33 (27.0%)

#: In Cohort A, among the 16 patients who received CNS surgical therapy, 15 had stable brain lesions at enrollment; 7 cases received CNS surgical therapy in Cohort B

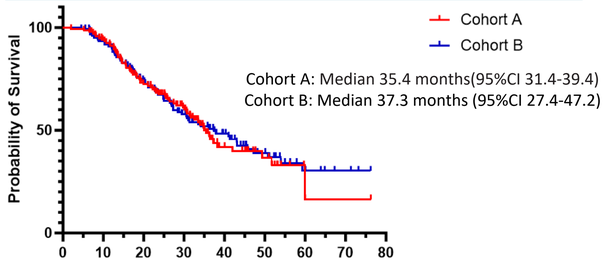


Figure 2. Overall Survival

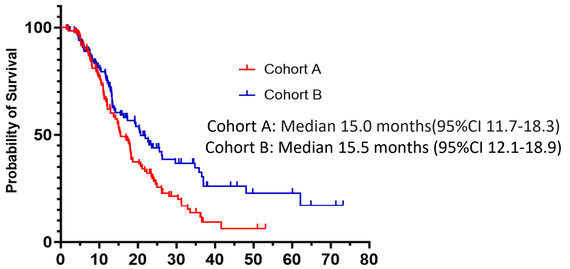


Figure 3. Progression-free Survival

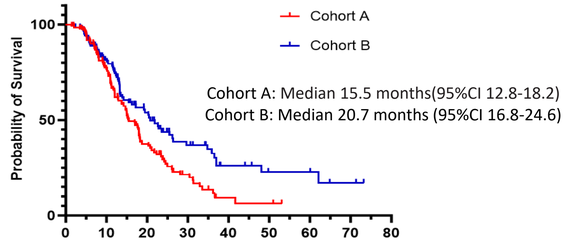


Figure 4. Progression-free Survival(central nervous system)

Conclusion

To our knowledge, this is the largest study of pyrotinib plus capecitabine in HER2-positive breast cancer patients with BMs. No significant difference was observed in OS or PFS between the two groups: priority systemic therapy with pyrotinib plus capecitabine until disease progression or unacceptable toxicity, or systemic therapy concurrently with radiotherapy. Therefore, future studies should further elucidate the characteristics of patients most likely to benefit from specific systemic-local treatment combinations and enabling personalized therapeutic strategies for HER2-positive breast cancer patients with BMs. These findings warrant prospective clinical investigation.

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