SAN ANTONIO BREAST CANCER SYMPOSIUM®

PS5-01-02

Pyrotinib or placebo in combination with trastuzumab and docetaxel for untreated HER2-positive metastatic breast cancer: long-term survival results from the phase 3 PHILA study

Binghe Xu[1], Fei Ma[1], Min Yan[2], Wei Li[3], Quchang Ouyang[4], Zhongsheng Tong[5], Yuee Teng[6], Yongsheng Wang[7], Shusen Wang[8], Cuizhi Geng[9], Ting Luo[10], Jincai Zhong[11], Qingyuan Zhang[12], Qiang Liu[13], Xiaohua Zeng[14], Tao Sun[15], Qinguo Mo[16], Shoubing Zhou[17], Ying Cheng[18], Jing Cheng[19], Xiaojia Wang[20], Jianyun Nie[21], Jin Yang[22], Xinhong Wu[23], Xinshuai Wang[24], Huiping Li[25], Guangyu Yao[26], Yang Fan[27], Jiaman Lin[27], Xiaoyu Zhu[27]

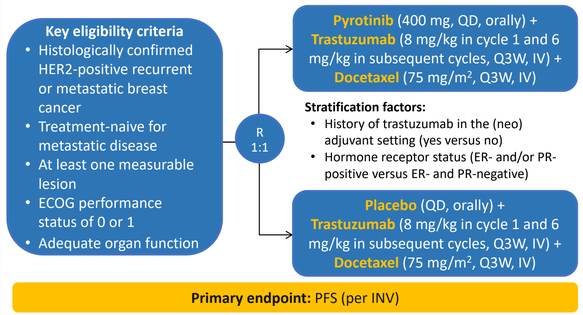
1Department of Medical Oncology, Cancer Hospital Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; 2Department of Breast Disease, Henan Breast Cancer Center, The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital, Zhengzhou, China; 3Department of Oncology, The First Hospital of Jilin University, Changchun, China; 4Breast Internal Medicine Department, Hunan Cancer Hospital, The Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, China; 5Department of Breast Oncology, Tianjin Medical University Cancer Institute & Hospital, Tianjin, China; 6Department of Breast Internal Medicine, The First Hospital of China Medical University, Shenyang, China; 7Breast Surgery, Shandong Cancer Hospital and Institute, Jinan, China; 8Department of Internal Medicine, Sun Yat-sen University Cancer Center, Guangzhou, China; 9Breast Center, The Fourth Hospital of Hebei Medical University and Hebei Tumor Hospital, Shijiazhuang, China; 10Department of Medical Oncology of Cancer Center, West China Hospital, Sichuan University, Chengdu, China; 11Medical Oncology, The First Affiliated Hospital of Guangxi Medical University, Nanning, China; 12Ward One of Mammary Department, Harbin Medical University Cancer Hospital, Harbin, China; 13Breast Tumor Center, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China; 14Breast Cancer Center, Affiliated Cancer Hospital of Chongqing University, Chongqing, China; 15Breast Internal Medicine Department, Liaoning Cancer Hospital & Institute, Shenyang, China; 16Breast Surgery, Guangxi Medical University Affiliated Tumor Hospital, Nanning, China; 17Department of Breast Oncology, The First Affiliated Hospital of USTC West District, Hefei, China; 18Department of Thoracic Oncology, Jilin Cancer Hospital, Changchun, China; 19Oncology Center Breast Department, Union Hospital, Tongji Medical College, Huazhong University of Science & Technology, Wuhan, China; 20Breast Medicine, Zhejiang Cancer Hospital, Hangzhou, China; 21Breast Surgery, Yunnan Cancer Hospital, Kunming, China; 22Department of Medical Oncology, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China; 23Department of Breast Oncology, Hubei Cancer Hospital, Wuhan, China; 24Department of Medical Oncology, Henan Key Laboratory of Cancer Epigenetics, Cancer Hospital, The First Affiliated Hospital, College of Clinical Medicine, Medical College of Henan University of Science and Technology, Luoyang, China; 25Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Department of Breast Oncology, Peking University Cancer Hospital and Institute, Beijing, China; 26Department of Breast, Southern Medical University Nanfang Hospital, Guangzhou, China; 27Jiangsu Hengrui Pharmaceuticals Co, Ltd, Shanghai, China

Introduction

- Approximately 20 % of breast cancers over-express human epidermal growth factor receptor 2 (HER2), a phenotype historically associated with aggressive disease and poor prognosis. The current first-line standard is dual HER2 blockade using pertuzumab and trastuzumab plus chemotherapy.
- Pyrotinib is an irreversible pan-ErbB inhibitor targeting EGFR/HER1, HER2, and HER4.
- The interim analysis of the phase 3 PHILA trial demonstrated that pyrotinib, trastuzumab, and docetaxel (PyroHT) significantly improved progression-free survival compared to placebo, trastuzumab, and docetaxel (HT) in patients with untreated HER2-positive metastatic breast cancer.[1, 2]
- Here, we report updated long-term survival results of this study.

Methods and Materials

- PHILA, a randomized, double-blind, placebo-controlled phase 3 trial (NCT03863223), assessed the efficacy and safety of pyrotinib plus trastuzumab and docetaxel as first-line therapy in HER2-positive metastatic breast cancer.



ECOG, Eastern Cooperative Oncology Group; ER, estrogen receptor; INV, investigator; PFS, progression-free survival; PR, progesterone receptor; QD, once a day; Q3W, once every three weeks; IV, intravenous.

Figure 1. Study design

Results

Patients

- From May 2019 to January 2022, 590 patients were randomized and received treatment (PyroHT n=297; HT n=293).

Results

- Detailed baseline characteristics were previously reported.[1]
- As of May 30, 2025, the median follow-up was 46.5 months (IQR 36–55) for PyroHT and 44.6 months (IQR 31–53) for HT.
- In the PyroHT group, 75 patients (25.3%) were still receiving study treatment, compared with 19 (6.5%) in the HT group.

Efficacy

- At data cutoff, 85 deaths (28.6%) occurred in the PyroHT group and 108 (36.9%) in the HT group.
- The median overall survival (OS) was not reached in either group (**Figure 2**).

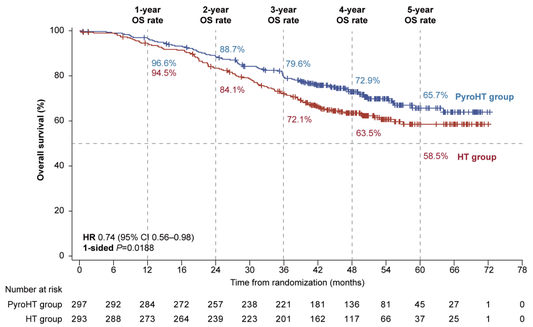


Figure 2. Kaplan-Meier curve of overall survival

- OS was superior in the PyroHT group compared to the HT group (HR 0.74, 95% CI 0.56–0.98; nominal 1-sided P=0.0188).
- As reported previously, consistent and prolonged benefit of investigator-assessed progression-free survival (PFS) in the PyroHT group was observed (HR 0.44, 95% CI 0.36–0.54; nominal 1-sided P<0.0001) (**Figure 3**).
- Although cross-over was not allowed, the proportions of patients receiving pyrotinib, trastuzumab, pertuzumab, or anti-HER2 antibody–drug conjugate (incl. T-DM1, T-DXd, SHR-A1811) after study treatment discontinuation in each group were 18.5% vs. 51.9%, 26.3% vs. 25.6%, 15.5% vs. 14.0%, and 22.6% vs. 28.0%, respectively.
- For patients with prior (neo)adjuvant trastuzumab, median PFS was 62.8 months (95% CI 19.2–not reached) in the PyroHT group (n=46) vs 10.4 months (95% CI 6.4–13.2) in the HT group (n=42) (**Figure 4**).

Results

- Among patients who developed brain metastases, the median time to onset was 16.6 months (IQR 13–28) with PyroHT (n=34) compared to 9.1 months (IQR 8–14) with HT (n=30).

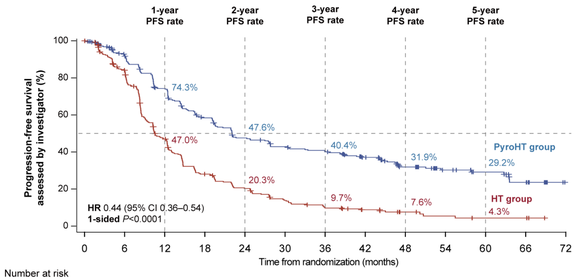


Figure 3. Kaplan-Meier curve of progression-free survival

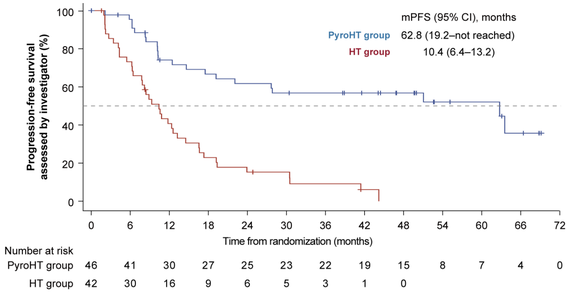


Figure 4. Kaplan-Meier curve of progression-free survival in patients who had received prior (neo)adjuvant trastuzumab

Safety

- Safety data cutoff was April 30, 2024.
- The incidence of all adverse events decreased considerably after docetaxel discontinuation (**Table 1**).
- In the PyroHT group, the incidence of any grade diarrhea decreased from 98.4% (245/249) to 79.9% (199/249), and grade 3 diarrhea incidence declined from 46.2% (115/249) to 16.1% (40/249).

Results

- No grade 4 or 5 diarrhea was reported.

Table 1. Treatment-related adverse events

	PyroHT group		HT group	
	Overall (n=297)	Post docetaxel (n=249)	Overall (n=293)	Post docetaxel (n=226)
Diarrhea	293 (98.7)	199 (79.9)	158 (53.9)	31 (13.7)
WBC count decreased	251 (84.5)	70 (28.1)	250 (85.3)	41 (18.1)
Anemia	236 (79.5)	178 (71.5)	142 (48.5)	63 (27.9)
Neutrophil count decreased	236 (79.5)	65 (26.1)	246 (84.0)	41 (18.1)
Vomiting	188 (63.3)	34 (13.7)	46 (15.7)	4 (1.8)
Weight decreased	181 (60.9)	155 (62.2)	31 (10.6)	20 (8.8)
Hypokalemia	134 (45.1)	79 (31.7)	34 (11.6)	18 (8.0)
Blood creatinine increased	132 (44.4)	111 (44.6)	21 (7.2)	15 (6.6)
ALT increased	131 (44.1)	71 (28.5)	123 (42.0)	52 (23.0)
Nausea	129 (43.4)	31 (12.4)	57 (19.5)	4 (1.8)
AST increased	127 (42.8)	71 (28.5)	115 (39.2)	57 (25.2)
Alopecia	115 (38.7)	88 (35.3)	141 (48.1)	97 (42.9)
Asthenia	99 (33.3)	29 (11.6)	73 (24.9)	15 (6.6)
Decreased appetite	98 (33.0)	35 (14.1)	36 (12.3)	3 (1.3)
Hypertriglyceridemia	84 (28.3)	64 (25.7)	93 (31.7)	63 (27.9)
Hypoalbuminemia	82 (27.6)	49 (19.7)	62 (21.2)	36 (15.9)
Rash	60 (20.2)	30 (12.0)	30 (10.2)	11 (4.9)

Data are n (%). Treatment-related adverse events occurring in 20% or more of patients in PyroHT group are listed. WBC, white blood cell; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Conclusions

- The long-term analysis confirms that the previously observed improvements in OS and PFS with PyroHT compared to HT in the first-line treatment of HER2-positive metastatic breast cancer were maintained.
- Notably, with PyroHT, 5-year OS rate remained at 66% and nearly 30% of patients remained progression-free at 5 years. PyroHT treatment delayed time to onset of brain metastasis.
- It reinforces dual anti-HER2 regimen (pyrotinib plus trastuzumab) as an established therapeutic strategy for this patient population.

Acknowledgements: We thank all patients and their families, all investigators, research personnel, and staff who conducted this trial.

Funding: Sponsored by Jiangsu Hengrui Pharmaceuticals Co., Ltd.

Contact: Prof. Binghe Xu MD (xubinghe@medmail.com.cn)

References: 1. Xu et al., BMJ 2023 2. Xu et al., SABCS 2024

This presentation is the intellectual property of the author/presenter. Contact them at xubinghe@medmail.com.cn for permission to reprint and/or distribute.

© Poster Template by Genigraphics® 1.800.790.4001 www.genigraphics.com