

LBA13

Trastuzumab rezetecan (SHR-A1811) in HER2-low advanced breast cancer (BC): A randomized, phase 3 study (HORIZON-Breast06)

Y. Fan¹, Y. Liu², Y. Wang³, Q. Ouyang⁴, Q.Y. Zhang⁵, J. Cui⁶, J. Li⁷, Q. Ding⁸, X. Wu⁹, X. Wang¹⁰, Z. Tong¹¹, Y. Zeng¹², W. Wang¹³, M. Yan¹⁴, Y. Wang¹⁵, Y. Li¹⁶, S. Cui¹⁷, X. Zhang¹⁷, X. Zhu¹⁷, B. Xu¹

¹ Department of Medical Oncology, Beijing Key Laboratory of Innovative Drug Research and Translational Study for Breast Cancer, State Key Laboratory of Advanced Medical Materials and Devices, Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China, ² Breast Surgery Department, The Fourth Hospital of Hebei Medical University, Shijiazhuang, China, ³ Department of Breast Surgery, Shandong Cancer Hospital and Institute, Shandong First Medical University and Shandong Academy of Medical Sciences, Jinan, China, ⁴ Department of Breast Medicine, Hunan Cancer Hospital & The Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, China, ⁵ Ward One of the Department of Breast Medicine, Harbin Medical University Cancer Hospital, Harbin, China, ⁶ Tumor Center Oncology Department, The First Hospital of Jilin University, Changchun, China, ⁷ Department of Breast Surgery, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China, ⁸ Breast Center, The First Affiliated Hospital with Nanjing Medical University, Nanjing, China, ⁹ Breast Center, Hubei Cancer Hospital, Wuhan, China, ¹⁰ Internal Medicine of Breast Tumors, Zhejiang Cancer Hospital, Hangzhou, China, ¹¹ Breast Medical Oncology, Tianjin Medical University Cancer Institute and Hospital, Tianjin, China, ¹² Breast Tumour Centre, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China, ¹³ Department of Breast Diseases, Weifang People's Hospital, Weifang, China, ¹⁴ Breast Department, The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital, Zhengzhou, China, ¹⁵ Fifth Department of Breast Surgery, Nanchang People's Hospital, Nanchang, China, ¹⁶ Biometrics Department, Jiangsu Hengrui Pharmaceuticals Co., Ltd., Shanghai, China¹⁷ Clinical Development-Oncology, Jiangsu Hengrui Pharmaceuticals Co., Ltd., Shanghai, China

Background

HORIZON-Breast06 is a pivotal, randomized, multicenter, open-label, phase 3 study comparing trastuzumab rezetecan (a HER2 ADC) with physician’s choice of chemotherapy in patients (pts) with HER2-low advanced BC who had received ≤1 prior line of chemotherapy for metastatic disease, with prior endocrine therapy required for hormone receptor (HR)-positive disease.

Methods

Pts were randomized (1:1) to receive trastuzumab rezetecan (6.4 mg/kg IV, Q3W) or physician’s choice of chemotherapy (taxanes, eribulin, capecitabine, or gemcitabine). The co-primary endpoints were PFS by blinded independent central review (BICR) in chemo-naïve (0 prior line of chemotherapy for metastatic disease) and overall pts.

Results

As of Mar 20, 2026, 551 pts were randomized (trastuzumab rezetecan, n=277; chemotherapy, n=274; chemo-naïve: 81.5%; HR-positive: 73.0%; prior CDK4/6 inhibitor: 64.8%). Median follow-up was 18.0 months (95% CI 16.8–19.3) for all patients. Trastuzumab rezetecan significantly prolonged PFS by BICR in both chemo-naïve (median 16.6 vs. 6.8 months; HR 0.25, 95% CI 0.19–0.33; P<0.0001; table) and overall pts (median 16.4 vs. 6.8 months; HR 0.27, 95% CI 0.21–0.34; P<0.0001). The PFS benefit was consistent across all prespecified subgroups, including HR-negative disease (16.5 vs. 6.8 months; HR 0.34) and HR-positive disease (16.4 vs. 6.7 months; HR 0.24). OS data remain immature, with a trend favoring trastuzumab rezetecan. Grade ≥3 treatment-related adverse events occurred in 84.1% (trastuzumab rezetecan) and 67.9% (chemotherapy) of patients, respectively. Interstitial lung disease (ILD) was reported in only 7 pts (2.5%) with trastuzumab rezetecan.Table: LBA13

	Chemo-naïve patients Trastuzumab rezetecan (N=225)	Chemotherapy (N=224)	Overall patients Trastuzumab rezetecan (N=277)	Chemotherapy (N=274)
PFS				
Events, n (%)	91 (40.4)	146 (65.2)	130 (46.9)	185 (67.5)
Median (95% CI), months	16.6 (14.0–19.4)	6.8 (5.7–7.0)	16.4 (14.0–16.8)	6.8 (5.7–6.9)
12–mo rate, % (95% CI)	65.2 (57.6–71.8)	18.9 (12.8–25.8)	63.1 (56.4–69.1)	18.0 (12.7–24.1)

	Chemo-naïve patients Trastuzumab rezetecan (N=225)	Chemotherapy (N=224)	Overall patients Trastuzumab rezetecan (N=277)	Chemotherapy (N=274)
HR (95% CI); 1-sided P	0.25 (0.19–0.33); P<0.0001	0.27 (0.21–0.34); P<0.0001		
OS				
Events, n (%)	43 (19.1)	55 (24.6)	66 (23.8)	77 (28.1)
12-mo rate, % (95% CI)	92.0 (87.3–95.1)	83.0 (76.9–87.6)	90.6 (86.2–93.6)	81.4 (75.9–85.8)
ORR, % (95% CI)	76.0 (69.9–81.4)	43.3 (36.7–50.1)	75.5 (69.9–80.4)	41.2 (35.4–47.3)

Conclusions

Trastuzumab rezetecan significantly improved PFS over physician’s choice of chemotherapy in pts with HER2-low advanced BC regardless of prior lines of chemotherapy or HR status, with a trend toward OS benefit and a favorable safety profile including a low incidence of ILD.

Clinical trial identification

NCT05814354.

Legal entity responsible for the study

Jiangsu Hengrui Pharmaceuticals Co., Ltd.

Funding

Jiangsu Hengrui Pharmaceuticals Co., Ltd.

Disclosure

Y. Li: Financial Interests, Personal and Institutional, Full or part-time Employment: Jiangsu Hengrui Pharmaceuticals Co Ltd. S. Cui: Financial Interests, Personal and Institutional, Full or part-time Employment: Jiangsu Hengrui Pharmaceuticals Co Ltd. X. Zhang: Financial Interests, Personal and Institutional, Full or part-time Employment: Jiangsu Hengrui Pharmaceuticals Co Ltd. X. Zhu: Financial Interests, Personal and Institutional, Full or part-time Employment: Jiangsu Hengrui Pharmaceuticals Co Ltd. All other authors have declared no conflicts of interest.

© European Society for Medical Oncology