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PANKU-Breast01: Randomized phase III study of izalontamab brengitecan (iza-bren) in previously treated unresectable locally advanced or metastatic (LA/M) hormone receptor-positive/HER2-negative (HR+/HER2-) breast cancer (BC)

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Background

Although first-line endocrine therapy plus CDK4/6 inhibitors has improved clinical outcome of HR+/HER2- BC, patients (pts) inevitably develop resistance and survival outcomes remain poor with subsequent therapy. Iza-bren is a first-in-class bispecific antibody-drug conjugate (ADC) against EGFR and HER3, containing a potent topoisomerase I inhibitor payload (Ed-04).

Methods

Eligible pts had unresectable LA/M HR+/HER2- BC (HR+, ER≥1% and/or PR≥1%; HER2-, IHC 0, 1+, or 2+/ISH-), progressed after at least 1L of endocrine therapy and 1 or 2L prior chemotherapy, and had previously received CDK4/6 inhibitors and taxanes. Pts were randomized 1:1 to receive iza-bren (2.5 mg/kg D1D8 Q3W) or TPC (eribulin, capecitabine, gemcitabine, or vinorelbine). The primary endpoint was PFS by blinded independent central review (BICR). Secondary endpoint included OS. The pre-planned final analysis for PFS serves as the interim analysis for OS.

Results

As of Jul 21, 2026, a total of 383 pts were randomized and treated (iza-bren/TPC, 190/193). Median follow-up for PFS was 15.24 vs 13.63 mo (iza-bren/TPC). Iza-bren significantly improved PFS by BICR vs TPC; mPFS was 8.18 mo (95% CI, 6.93-8.58) vs 4.01 mo (95% CI, 2.92-4.30) (HR, 0.41; 95% CI, 0.33-0.53; P<0.0001). OS was immature at the interim analysis, and no detrimental effect was observed. The cORR by BICR was 40.5% with iza-bren vs 20.2% with TPC, and mDOR was 6.93 vs 4.21 mo, respectively. Grade ≥3 TRAEs were predominantly hematologic in nature. TRAEs were manageable with standard supportive care, and only 1.6% of pts discontinued iza-bren treatment due to TRAEs. Adjudicated ILD occurred in 2 (1.1%) pts with iza-bren (grade 1 or 2). No new safety signals were identified.

Conclusions

The study met its primary endpoint at the prespecified analysis. Iza-bren demonstrated a statistically significant and clinically meaningful improvement in PFS vs TPC in previously treated HR+/HER2- BC. The safety profile was manageable and consistent with previous studies. The results support iza-bren as a new standard of care option in this population in China.

Clinical trial identification

NCT06343948.

Legal entity responsible for the study

Baili-Bio (Chengdu) Pharmaceutical Co, Ltd.

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Disclosure

S. Xiao: Financial Interests, Personal, Full or part-time Employment: Baili-Bio (Chengdu) Pharmaceutical Co., Ltd. H. Zhu: Financial Interests, Personal, Full or part-time Employment: SystImmune Inc; Financial Interests, Personal, Stocks/Shares: SystImmune Inc. Y. Zhu: Financial Interests, Personal, Full or part-time Employment: SystImmune Inc; Financial Interests, Personal, Ownership Interest: SystImmune Inc, Baili Pharmaceutical. All other authors have declared no conflicts of interest.

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