

LBA1

Trastuzumab deruxtecan (T-DXd) vs trastuzumab emtansine (T-DM1) in patients (pts) with high-risk human epidermal growth factor receptor 2–positive (HER2+) primary breast cancer (BC) with residual invasive disease after neoadjuvant therapy (tx): Interim analysis of DESTINY-Breast05

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Background

Pts with HER2+ early BC with residual invasive disease after neoadjuvant tx are at high risk of recurrence highlighting a significant unmet need. We present interim analysis results of DESTINY-Breast05 (NCT04622319), an open-label, phase 3 trial of post-neoadjuvant T-DXd vs standard of care (SOC) T-DM1 in HER2+ early BC.

Methods

Pts with residual invasive HER2+ BC after neoadjuvant tx consisting of taxane-based chemotherapy and anti-HER2 tx and at high risk for recurrence* were randomized 1:1 to T-DXd 5.4 mg/kg or T-DM1 3.6 mg/kg once every 3 weeks for 14 cycles. Primary endpoint was IDFS. Key secondary endpoint was DFS; others were overall survival, distant recurrence-free interval, brain metastasis-free interval (BMFI), and safety.

Results

At data cutoff (July 2, 2025), 1635 pts were randomized to T-DXd (n = 818) or T-DM1 (n = 817). Median study duration was 29.9 months with T-DXd and 29.7 months with T-DM1. IDFS and DFS benefit with T-DXd vs T-DM1 was statistically significant (HR, 0.47 each; Table); BMFI improvement with T-DXd was clinically meaningful (HR, 0.64; 95% CI, 0.35-1.17). Grade ≥3 treatment-emergent adverse events (TEAEs) occurred in 50.6% of pts with T-DXd and 51.9% of pts with T-DM1; adjudicated drug-related interstitial lung disease occurred in 9.6% (n = 2 grade 5) and 1.6% of pts (0 grade 5) and were mostly grade 1 or 2. TEAEs associated with death occurred in 0.4% (n = 3) and 0.6% (n = 5) of pts, respectively. Table: LBA1

Efficacy summary at interim analysis (data cutoff, July 2, 2025)

Efficacy	T-DXd n = 818	T-DM1 n = 817	HR (95% CI)
IDFS Patients with events, n (%)	51 (6.2)	102 (12.5)	0.47 (0.34-0.66); $P^{\dagger} = <0.0001$
DFS Patients with events, n (%)	52 (6.4)	103 (12.6)	0.47 (0.34-0.66); $P^{\dagger} = <0.0001$

DFS, disease-free survival; HR, hazard ratio; IDFS, invasive disease-free survival. *Defined as clinical stages T4, N0-3, M0 or T1-3, N2-3, M0 at presentation (prior to neoadjuvant therapy) or clinical stages T1-3, N0-1, M0, with axillary node-positive disease (ypN1-3) following neoadjuvant therapy. [†]Stratified log rank.

Conclusions

T-DXd showed a statistically significant and clinically meaningful IDFS and DFS benefit vs T-DM1, extending its superiority to post-neoadjuvant residual disease in pts with HER2+ early BC, and representing a potential new SOC. Safety of T-DXd was generally manageable with no new safety signals.

Clinical trial identification

NCT04622319.

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Legal entity responsible for the study

Daiichi Sankyo, Inc.

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Disclosure

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