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LBA1

Trastuzumab deruxtecan (T-DXd) vs trastuzumab emtansine (T-DM1) in patients (Pts) with HER2+ metastatic breast cancer (mBC): Results of the randomized phase III DESTINY-Breast03 study

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Background

T-DXd is a HER2-targeting antibody–drug conjugate approved for pts with advanced HER2+ mBC based on the results from DESTINY-Breast01 (NCT03248492). This is the first report of DESTINY-Breast03 (NCT03529110), a multicenter, open-label, randomized phase 3 study comparing the efficacy and safety of T-DXd vs T-DM1 in pts with HER2+ mBC previously treated with trastuzumab and taxane. This is the first reported randomized study of T-DXd in BC.

Methods

Pts were randomized 1:1. The primary endpoint was progression-free survival (PFS) by blinded independent central review (BICR). Secondary endpoints include overall survival (OS), objective response rate (ORR), duration of response, PFS by investigator, and safety.

Results

As of May 21, 2021, 524 pts were randomized. Median age was 54 years (range, 20-83). The hazard ratio (HR) for PFS was 0.2840 ($P = 7.8 \times 10^{-22}$); median PFS not reached for T-DXd vs 6.8 mo for T-DM1. The estimated 12-month OS event rates were 94.1% (95% CI, 90.3-96.4) for T-DXd and 85.9% (95% CI, 80.9-89.7) for T-DM1; HR: 0.5546 (95% CI, 0.3587-0.8576; $P =$ 0.007172 did not cross pre-specified boundary for significance). Median treatment duration was 14.3 mo (range, 0.7-29.8) with T-DXd vs 6.9 mo (range, 0.7-25.1) with T-DM1; similar rates of TEAEs were observed. No drug-related deaths occurred in either arm. Adjudicated drug-related interstitial lung disease (ILD) occurred in 10.5% of pts with T-DXd (most [9.7%] grade 1/2; 0 grade 4/5) vs 1.9% with T-DM1 (all grade 1/2).Table: LBA1

Summary of results

	T-DXd N = 261	T-DM1 N = 263
PFS by BICR	HR 0.2840 (95% CI, 0.2165-0.3727); $P = 7.8X10^{-22}$,[a]	
Median PFS, mo (95% CI)	Not reached (18.5-NE)	6.8 (5.6-8.2)
PFS by Investigator	HR 0.2649 (95% CI, 0.2011-0.3489); $P = 6.5X10^{-24}$,[a]	
Median PFS, mo (95% CI)	25.1 (22.1-NE)	7.2 (6.8-8.3)
Confirmed ORR, % (95% CI)[b]	79.1 (74.3-84.4)	34.2 (28.5-40.3)
	$P < 0.0001$[a]	
Safety, n (%)	T-DXd N = 257[c]	T-DM1 N = 261[c]
Any grade TEAEs	256 (99.6)	249 (95.4)

	T-DXd N = 261	T-DM1 N = 263
Grade ≥3	134 (52.1)	126 (48.3)
Serious TEAEs	49 (19.1)	47 (18.0)

[a]Two-sided. [b]By BICR. [c]Of 524 pts, 257 and 261 received [3]1 dose of T-DXd and T-DM1, respectively.

Conclusions

T-DXd demonstrated a highly statistically significant and clinically meaningful improvement in PFS vs T-DM1 in pts previously treated with trastuzumab and taxane for HER2+ mBC. These data confirm that T-DXd is tolerable with manageable toxicity and a significant improvement in ILD profile vs studies performed in more heavily pretreated pts. This study will lead to a paradigm shift in the treatment of HER2+ mBC.

Clinical trial identification

NCT03529110.

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