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First-line (1L) datopotamab deruxtecan (Dato-DXd) vs chemotherapy in patients with locally recurrent inoperable or metastatic triple-negative breast cancer (mTNBC) for whom immunotherapy was not an option: Primary results from the randomised, phase 3 TROPION-Breast02 trial

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Background

Treatment (tx) options are limited and prognosis is poor for the ~70% of patients (pts) with locally recurrent inoperable or mTNBC for whom immunotherapy is not an option; moreover, approximately half of pts with mTNBC do not receive tx beyond 1L. Here, we report the primary analysis from the TROPION-Breast02 study (NCT05374512).

Methods

Adult pts with previously untreated locally recurrent inoperable or mTNBC, for whom immunotherapy was not an option, were randomised 1:1 to Dato-DXd (6 mg/kg IV Q3W) or investigator's choice of chemotherapy (ICC; [nab]-paclitaxel/ capecitabine/ eribulin mesylate/ carboplatin). Randomisation was stratified by geographic location, PD-L1 status and disease-free interval history (*de novo* vs DFI 0–12 months vs DFI >12 months; DFI defined as time from completion of tx with curative intent to first documented local/distant disease recurrence). Dual primary endpoints were OS and PFS by BICR per RECIST 1.1.

Results

644 pts were randomised (Dato-DXd: 323; ICC: 321). At data cutoff (25 Aug 2025), median study follow-up was 27.5 months. Results are shown in the Table. There was a statistically significant, ≥5 mo improvement in both median OS and PFS by BICR with Dato-DXd compared with ICC; OS HR 0.79 [95% CI 0.64–0.98]; p=0.0291, and PFS HR 0.57 [95% CI 0.47–0.69]; p<0.0001. Despite more than double the duration of tx in the Dato-DXd arm, rates of grade ≥3 TRAEs were similar and discontinuations were lower vs ICC.

	Dato-DXd	ICC
Efficacy	N=323	N=321
OS		
Median OS, mo (95% CI)	23.7 (19.8–25.6)	18.7 (16.0–21.8)
HR (95% CI)	0.79 (0.64–0.98); p=0.0291	
PFS (BICR)		
Median PFS, mo (95% CI)	10.8 (8.6–13.0)	5.6 (5.0–7.0)
HR (95% CI)	0.57 (0.47–0.69); p<0.0001	
Response		
Confirmed objective response rate (BICR), n (%)	202 (62.5)	94 (29.3)
Median duration of response, mo (95% CI)	12.3 (9.1–15.9)	7.1 (5.6–8.9)
Safety	N=319	N=309
Median duration of tx, mo (range)	8.5 (0.7–38.0)	4.1 (0.1–32.0)
TRAEs, %		
Any grade	92.8	83.2
Grade ≥3	32.9	28.8
Leading to discontinuation	4.4	7.4
Leading to death	0	0

BICR, blinded independent central review; OS, overall survival; PFS, progression-free survival; TRAEs, tx-related adverse events.

Conclusions

TROPION-Breast02 met both dual primary endpoints; 1L Dato-DXd demonstrated statistically significant and clinically meaningful OS and PFS improvement over chemotherapy in pts with locally recurrent inoperable or mTNBC for whom immunotherapy was not an option. The Dato-DXd safety profile was manageable. Results support Dato-DXd as the new 1L standard of care.

Clinical trial identification

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Legal entity responsible for the study

AstraZeneca.

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Disclosure

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