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First-line (1L) datopotamab deruxtecan (Dato-DXd) vs chemotherapy in patients (pts) with locally recurrent inoperable or metastatic triple-negative breast cancer (mTNBC) for whom immunotherapy was not an option: Exploratory analysis of pts with brain metastases in TROPION-Breast02

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Background

Brain metastases (BMs) occur at a high rate in TNBC and are associated with poor prognosis. In TROPION-Breast02 (NCT05374512), 1L Dato-DXd showed statistically significant and clinically meaningful improvements in OS (HR 0.79 [95.01% CI 0.64–0.98]) and PFS by BICR (HR 0.57 [99% CI 0.44–0.73]), and improved confirmed ORR (63% vs 29%), vs investigator's choice of chemotherapy (ICC) in pts with locally recurrent inoperable or mTNBC for whom immunotherapy was not an option. We report efficacy outcomes in pts with BMs.

Methods

Pts were randomised 1:1 to Dato-DXd (6 mg/kg IV Q3W) or ICC ([nab]-paclitaxel/capecitabine/eribulin mesylate/carboplatin). Pts with asymptomatic, stable BMs at baseline with/without prior central nervous system (CNS)-directed therapy were eligible; for pts with prior whole brain radiation or corticosteroids, a 14-day and 3-day washout period, respectively, was required before Cycle 1 Day 1. Brain MRI or CT was mandated at baseline, Q6W for 48 weeks, then Q9W until RECIST v1.1 progression. Analyses of PFS by BICR, OS, confirmed ORR and intracranial response per mRECIST v1.1 in pts with previously treated/untreated BMs were exploratory.

Results

Of 644 pts enrolled, 61 had baseline BMs (31 previously treated vs 30 untreated). Extracranial efficacy results are shown in the table. In a preliminary analysis of intracranial efficacy, Dato-DXd demonstrated intracranial objective responses, including one complete response. Further intracranial data will be presented.Table: LBA96

	Pts with baseline BMs		Treated BMs n=31		Untreated BMs n=30		Pts without baseline BMs	
	All n=61 Dato-DXd n=35	ICC n=26	Dato-DXd n=16	ICC n=15	Dato-DXd n=19	ICC n=11	Dato-DXd n=288	ICC n=295
Median PFS by BICR, months	7.7	3.5	6.8	3.5	7.7	2.6	11.1	5.6
HR (95% CI)	0.37 (0.20–0.72)	0.43 (0.17–1.11)	0.29 (0.12–0.76)	0.56 (0.46–0.69)				

	Pts with baseline BMs				Pts without baseline BMs			
	All n=61 Dato-DXd n=35	ICC n=26	Treated BMs n=31 Dato-DXd n=16	ICC n=15	Untreated BMs n=30 Dato-DXd n=19	ICC n=11	Dato-DXd n=288	ICC n=295
Median OS, months	13.5	10.7	19.3	12.8	11.6	9.1	23.7	19.3
HR (95% CI)	0.55 (0.29–1.05)	0.77 (0.28–2.08)	0.35 (0.14–0.84)	0.80 (0.64–1.00)				
Extracranial confirmed ORR, %	62.9	19.2	62.5	33.3	63.2	0	62.5	30.2

BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

Conclusions

In TROPION-Breast02, 1L Dato-DXd showed efficacy benefit vs ICC in pts with or without asymptomatic, stable BMs at baseline, including in pts with/without prior CNS-directed therapy. Preliminary findings indicate intracranial activity with Dato-DXd.

Clinical trial identification

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Legal entity responsible for the study

AstraZeneca.

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Disclosure

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