

LBA49

A DESTINY-Breast09 (DB-)09 analysis of trastuzumab deruxtecan (T-DXd) + pertuzumab (P) vs taxane + trastuzumab + pertuzumab (THP) for patients (pts) with HER2+ advanced/metastatic breast cancer (a/mBC) and baseline (BL) brain metastases (BMs)

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Background

BMs are associated with poor prognosis and occur in 30–50% of pts with HER2+ mBC. Management relies on locoregional intervention, but systemic treatments with intracranial (IC) activity remain needed. T-DXd, recommended for pts with HER2+ a/mBC and BMs, showed substantial IC activity in previously treated pts in DB-12. First-line (1L) T-DXd + P is approved in the US and EU for HER2+ a/mBC, based on interim results from DB-09 (NCT04784715; median progression-free survival [PFS]: 40.7 [T-DXd + P] vs 26.9 [THP] months [mo]; HR 0.56). We report results of an exploratory central nervous system (CNS) efficacy analysis from DB-09.

Methods

Pts had no prior systemic therapy for a/mBC (1 line of endocrine therapy allowed). Pts with clinically inactive or treated and stable BL BMs, with ≥2 weeks from end of radiotherapy to randomization, were permitted. MRI/CT scans, done at BL and end of treatment, were assessed by blinded independent central review (BICR) and/or the investigator (INV). Pts with INV-assessed BL BMs had follow-up brain scans, per protocol and RECIST 1.1. Efficacy outcomes, assessed in pts with BL BMs by BICR who had ≥1 post-BL brain scan, included PFS, CNS-PFS, CNS confirmed objective response rate (CNS-cORR; complete + partial response in brain), and CNS duration of response (CNS-DOR), all BICR assessed per RECIST 1.1.

Results

In the 61 pts with BL BMs by BICR and ≥1 post-BL brain scan, at interim data cutoff (Feb 26, 2025), median PFS was 36.5 mo with T-DXd + P vs 11.1 mo with THP; median CNS-PFS was not estimable (NE) with T-DXd + P vs 9.7 mo with THP. CNS-cORR was 51.6% with T-DXd + P vs 26.7% with THP (Table).Table: LBA49

	Pts with BL BMs	
	T-DXd + P (n=31)	THP (n=30)
Median follow-up, mo (range)	23.6 (2.8, 41.4)	
	Events, n (%)	9 (29.0)17 (56.7)
CNS-PFS	Median, mo(95% CI)*	NE (19.1, NE)9.7 (4.2, 19.2)
	HR(95% CI)†	0.26 (0.11, 0.57)
CNS-cORR, % (95% CI)‡	51.6 (33.1, 69.8)26.7 (12.3, 45.9)	
Best overall CNS response, n (%)		

	Pts with BL BMs	
	T-DXd + P (n=31)	THP (n=30)
Complete response	11 (35.5)	7 (23.3)
Partial response	5 (16.1)	1 (3.3)
Stable disease	12 (38.7)	13 (43.3)
Progressive disease	3 (9.7)	6 (20.0)
Not evaluable	0	3 (10.0)
Median CNS-DOR, mo (95% CI)*	NE (14.3, NE)	18.5 (8.3, NE)

Outcomes by BICR.* Medians + CIs calculated by Kaplan–Meier method; †HR + CIs calculated by unstratified Cox proportional hazard model; ‡CIs calculated by Clopper–Pearson method.

Conclusions

In DB-09, T-DXd + P elicited robust CNS responses and prolonged CNS disease control in pts with BMs, consistent with the second-line efficacy observed in DB-12 and supporting its use in 1L HER2+ mBC.

Clinical trial identification

NCT04784715.

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Legal entity responsible for the study

AstraZeneca.

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Disclosure

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