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DESTINY-Breast11: MRI-assessed objective responses during neoadjuvant treatment (NAT) with trastuzumab deruxtecan (T-DXd) followed by paclitaxel + trastuzumab + pertuzumab (THP) vs dose-dense doxorubicin + cyclophosphamide followed by THP (ddAC-THP) in HER2+ early breast cancer (eBC)

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Background

In the Phase 3 DESTINY-Breast11 study (NCT05113251), NAT with T-DXd-THP showed a statistically significant, clinically meaningful improvement in pathologic complete response (pCR) rate and improved safety profile vs ddAC-THP in high-risk, HER2+ eBC. We report analyses of radiological assessments conducted by breast MRI and association with pCR.

Methods

Patients (pts) were randomized to one of three arms, including T-DXd-THP (4+4 cycles) and ddAC-THP (4+4 cycles). Breast MRI scans were taken at screening, mid-NAT (after Cycle 4), and end of treatment (EOT). Objective response rate (ORR; per RECIST 1.1 per investigator; prespecified exploratory endpoint) was analyzed in pts with baseline scans, and association of response with pCR (ypT0/Tis ypN0) was assessed *post hoc*.

Results

Mid-NAT ORR and complete response [CR] rate were higher with T-DXd-THP (N=309) vs ddAC-THP (N=313) overall (ΔORR: 26.5%; ΔCR: 10.7%; Table), and across hormone receptor (HR) status (ORR: HR–, 80.0% [64/80] vs 57.3% [47/82]; HR+, 76.2% [173/227] vs 48.5% [112/231]). At EOT, ORRs were higher vs mid-NAT. Median best % change in target lesion size was greater with T-DXd-THP vs ddAC-THP at mid-NAT (–59% vs –35%) and further increased through EOT (–81% vs –74%). The positive predictive value of mid-NAT CR for pCR was 90.2% (T-DXd-THP) and 87.5% (ddAC-THP), but negative predictive value was lower at 36.6% and 43.6%, respectively. Table: 543R0

T-DXd-THP N=309	Overall pCR		Non-pCR			
	n	%	n	%*	n	%*
Mid-NAT objective response	239	77.3	133	169	70.7	90.2
CR	41	64.1	22	37	66.7	54.3
PR	198		132		66	33.3
					45	7

T-DXd-THP N=309	Overall pCR		Non-pCR			
	n	%	n	% *	n	% *
NR	70		38		32	
EOT objective response	287	92.9	27.8	202	70.4	83.7
CR	86	65.0	72	64.7	22.7	14
PR	201	7.1	130		71	
NR	22		5		17	
ddAC-THP N=313	Overall pCR		Non-pCR			
	n	%	n	% *	n	% *
Mid-NAT objective response	159	50.8	115	72.3	87.5	44
CR	8	2.6	7	71.5	41.6	1
PR	151	48.2	49.2	108		43
NR	154		64		90	
EOT objective response	273	87.2	24.6	172	63.0	75.3
CR	77	62.6	12.8	58	58.2	17.5
PR	196		114		82	
NR	40		7		33	

*Percentages based on the overall number of pts in the response categoryNR, non-response; PR, partial response

Conclusions

T-DXd showed rapid antitumor activity, and responses deepened through EOT with T-DXd-THP, highlighting the importance of completing the full regimen to maximize tumor shrinkage. Consistent with prior studies, MRI responses, while informative, did not reliably predict pCR. Data complement previously reported pCR outcomes and support T-DXd-THP as an effective NAT for pts with HER2+ eBC.

Clinical trial identification

NCT05113251.

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Legal entity responsible for the study

AstraZeneca.

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Disclosure

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