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A Pooled Analysis of Trastuzumab Deruxtecan in Patients With HER2-Positive Metastatic Breast Cancer With Brain Metastases (BMs) from DESTINY-Breast01, -02, and -03

Presentation 3770

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On behalf of the DESTINY-Breast01, -02, and -03 pooled investigators

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Declaration of Interests

Sara A. Hurvitz:

Contracted research paid to institution +/- editorial support for authorship: Ambrx, Arvinas, Astra Zeneca, Bayer, Celcuity, Cytomx, Daiichi-Sankyo, Dantari, Dignitana, Genentech/Roche, G1-Therapeutics, Gilead, Greenwich Life Sciences Inc, GSK, Immunomedics, Eli Lilly, Loxo, Macrogenics, Novartis, OBI Pharma, Orinove, Orum, Pfizer, Phoenix Molecular Designs, Ltd., Pieris, PUMA, Radius, Sanofi, Seattle Genetics/Seagen, Zymeworks

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Member (uncompensated) National Comprehensive Cancer Center Guidelines (end 7/31/23), ESMO Breast Cancer Guidelines

Integration Panel Member, Department of Defense Congressionally Directed Medical Research Program, Breast Cancer Research Program

Certified Medical Education Speaker: axis medical, cancer expert now, Clinical Care Options, Curio, ICHE, MJH Associates, Peer Education, PER, PrecisCA, Primo, Projects in Knowledge, Prova Education, Research to Practice, Ultimate Medical Academy, Vaniam, Invited Speaker, WebMD

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DSMB: Alliance Foundation, Atossa, Quantum Leap (I-SPY)

Background and Objectives

- T-DXd is approved for the treatment of patients with HER2-positive unresectable or mBC who have received ≥1 prior anti-HER2-based regimens, including patients with BMs, based on the randomized phase 3 DB-03 study[1-3]
- The efficacy of T-DXd in patients with BMs has not been fully established, as inclusion of these patients is often limited in clinical trials
- The objective of this exploratory pooled analysis is to describe the population of patients enrolled in DB-01, DB-02, and DB-03 with baseline BM, to analyze exploratory pooled efficacy of T-DXd by BICR, and to assess safety versus a comparator
- BM status was according to the following definitions by the US FDA Clinical Trial Eligibility Criteria[4]:
  - **Treated/stable BMs:** Patients have received prior CNS-directed therapy for their BMs, and their CNS disease is stable
  - **Untreated/active BMs:** Patients have new BMs or progressive BMs that have not been subjected to CNS-directed therapy since documented progression

BM, brain metastasis; DB, DESTINY-Breast; BICR, blinded independent central review; CNS, central nervous system; FDA, Food and Drug Administration; HER2, human epidermal growth factor receptor 2; mBC, metastatic breast cancer; T-DXd, trastuzumab deruxtecan.

1. Enhertu [package insert]. Daiichi Sankyo; 2022. 2. Cortes J et al. *N Engl J Med*. 2022; 368(12):1143-1154 3. Zimmer A et al. *Cancer Reports*. 2022;5:e1274. 4.U.S. Department of Health and Human Services – Food and Drug Administration. Cancer Clinical Trial Eligibility Criteria: Brain Metastases. 2020.

BM Eligibility Criteria Evolution in Each Trial

Inclusion Criteria	
DESTINY-Breast01[1]	**DESTINY-Breast02 and DESTINY-Breast03[2-4]**
• Patients with asymptomatic, previously locally treated, and stable BMs	• Initially, patients with previously untreated and asymptomatic BM were eligible • After protocol amendments, only patients with treated, asymptomatic BMs were allowed

- Per FDA criteria, patients with untreated BMs from DESTINY-Breast02 and -03 would be considered to have active BMs[5]
  - The population of patients with baseline BMs from DESTINY-Breast02 and -03 therefore consists of a mix of treated/stable and untreated/active metastases

BM, brain metastasis; FDA, Food and Drug Administration.

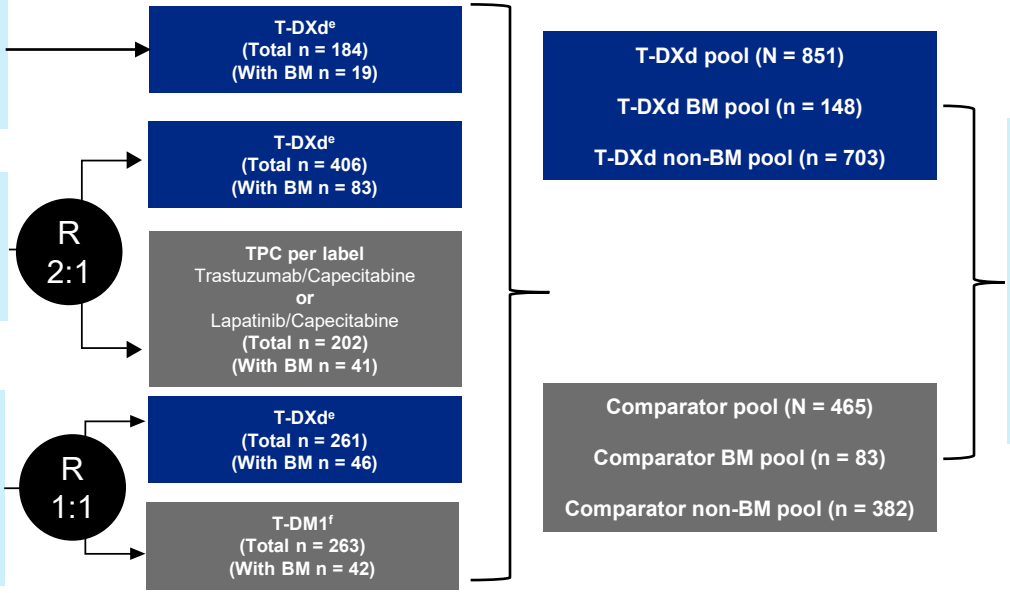
1. Modi S et al. *N Engl J Med*. 2020; 382:610-621. 2. Cortes J et al. *N Engl J Med*. 2022; 368(12):1143-1154. 3. André F et al. *The Lancet*. 2023. https://doi.org/10.1016/S0140-6736(23)00725-0. 4. Hurvitz SA et al. *Lancet*. 2023;401(10371):105-117. 5. U.S. Department of Health and Human Services – Food and Drug Administration. Cancer Clinical Trial Eligibility Criteria: Brain Metastases. 2020.

Retrospective Exploratory Pooled Analysis Plan[1-3]

DESTINY-Breast01 (N = 253)[a,b]
- Phase II study
- Patients previously treated with T-DM1
- Patients with asymptomatic and previously locally treated BM eligible
- Prior BM therapy within 60 days prohibited

DESTINY-Breast02 (N = 608)[a,c]
- Phase III study
- Patients previously treated with T-DM1
- Patients with asymptomatic and previously treated/untreated BM eligible
- Prior BM therapy within 14 days of randomization prohibited

DESTINY-Breast03 (N = 524)[a,d]
- Phase III study
- Patients previously treated with trastuzumab and a taxane in metastatic or (neo)adjuvant setting with recurrence within 6 months of therapy
- Patients with asymptomatic and previously treated/untreated BM eligible
- Prior BM therapy within 14 days of randomization prohibited



Endpoints:
- IC-ORR (CR+PR in brain) per BICR per RECIST v1.1
- IC-DoR per BICR
- CNS-PFS per BICR
- Safety and tolerability

- **The BM and non-BM pools were determined by BICR at baseline among all patients based on mandatory brain CT/MRI screening**

BICR, blinded independent central response; BM, brain metastasis; CNS, central nervous system; CR, complete response; CT, computed tomography; DB, DESTINY-Breast; DoR, duration of response; HER2, human epidermal growth factor receptor 2; IC, intracranial; mBC, metastatic breast cancer; MRI, magnetic resonance imaging; ORR, objective response rate; PFS, progression-free survival; PR, partial response; R, randomization; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice (trastuzumab/capecitabine or lapatinib/capecitabine).
Data for patients in the 5.4 mg/kg T-DXd arms were pooled from the DB-01, DB-02, and DB-03 trials. Comparator data were pooled from the DB-02 and DB-03 trials. All three studies were conducted in unresectable/mBC; HER2 status was confirmed centrally; and a documented radiographic progression after most recent treatment was required.
[a]The presence of BMs was not a stratification factor. [b]Data Cutoff: March 26, 2021. [c]Data Cutoff: June 30, 2022. [d]Data Cutoff: May 21, 2021. [e]5.4 mg/kg Q3W. [f]3.6 mg/kg Q3W.
1. Modi S et al. *N Engl J Med.* 2020; 382:610-621 [article and supplementary appendix]. 2. André F et al. *The Lancet.* 2023. https://doi.org/10.1016/S0140-6736(23)00725-0 [article and supplementary appendix]. 3. Cortes J et al. *N Engl J Med.* 2022; 368(12):1143-1154 [article and supplementary appendix].

Demographics and Baseline Characteristics

	T-DXd Pool (N = 851)		Comparator Pool (N = 465)	
	BM Pool (n = 148)	Non-BM Pool[a] (n = 703)	BM Pool (n = 83)	Non-BM Pool[a] (n = 382)
Patients randomized from each clinical study, n (%)				
DESTINY-Breast01	19 (12.8)	165 (23.5)	0	0
DESTINY-Breast02	83 (56.1)	323 (45.9)	41 (49.4)	161 (42.1)
DESTINY-Breast03	46 (31.1)	215 (30.6)	42 (50.6)	221 (57.9)
Region, n (%)				
Europe	42 (28.4)	232 (33.0)	16 (19.3)	112 (29.3)
Asia	54 (36.5)	270 (38.4)	40 (48.2)	172 (45.0)
North America	19 (12.8)	92 (13.1)	6 (7.2)	34 (8.9)
Rest of World	33 (22.3)	109 (15.5)	21 (25.3)	64 (16.8)
Age, median (range), years	53.4 (22.4-81.6)	54.7 (27.9-96.0)	52.6 (26.0-78.2)	55.1 (20.2-86.5)
Sex, n (%)				
Female	148 (100)	699 (99.4)	82 (98.8)	380 (99.5)
Male	0	4 (0.6)	1 (1.2)	2 (0.5)
Time from initial diagnosis of BC to randomization, median (range), months	55.9 (8.3-271.6)	50.9 (1.5-431.4)	53.0 (6.7-303.2)	47.3 (5.1-326.0)

- **Demographic characteristics were well balanced across subgroups**
- **Patients in the BM pools tended to have a longer time from initial diagnosis to randomization compared with the non-BM pools**

BC, breast cancer; BICR, blinded independent central response; BM, brain metastasis; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
[a]Patients with a reported history of BMs who did not have BMs at baseline by BICR were not included in the BM pools.

Demographics and Baseline Characteristics (cont.)

	T-DXd Pool (N = 851)		Comparator Pool (N = 465)	
	BM Pool (n = 148)	Non-BM Pool[a] (n = 703)	BM Pool (n = 83)	Non-BM Pool[a] (n = 382)
Disease history, n (%)				
De novo mBC	44 (29.7)	188 (26.7)	32 (38.6)	121 (31.7)
Recurrent BC	85 (57.4)	347 (49.4)	51 (61.4)	260 (68.1)
Missing[b]	19 (12.8)	168 (23.9)	0	1 (0.3)
HER2 status (IHC), n (%)				
3+	131 (88.5)	583 (82.9)	73 (88.0)	318 (83.2)
2+	17 (11.5)	116 (16.5)	9 (10.8)	63 (16.5)
1+	0	3 (0.4)	0	1 (0.3)
Not evaluable	0	1 (0.1)	1 (1.2)	0
Hormone receptor, n (%)				
Positive	84 (56.8)	384 (54.6)	43 (51.8)	214 (56.0)
Negative	63 (42.6)	311 (44.2)	40 (48.2)	165 (43.2)
Indeterminate/Unknown/Missing	1 (0.7)	8 (1.1)	0	3 (0.8)
Visceral disease, n (%)				
Yes	143 (96.6)	537 (76.4)	78 (94.0)	271 (70.9)
No	5 (3.4)	166 (23.6)	5 (6.0)	111 (29.1)

- **Patients with recurrent mBC represent the majority of the population in T-DXd and comparator pools**

BC, breast cancer; BICR, blinded independent central review; BM, brain metastasis; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; mBC, metastatic breast cancer; T-DXd, trastuzumab deruxtecan.
[a]Patients with a reported history of BMs who did not have BMs at baseline by BICR were not included in the BM pools. [b]The missing data are due to the single arm, non-randomized DESTINY-Breast01 trial.

Prior Systemic and Local BM Therapies

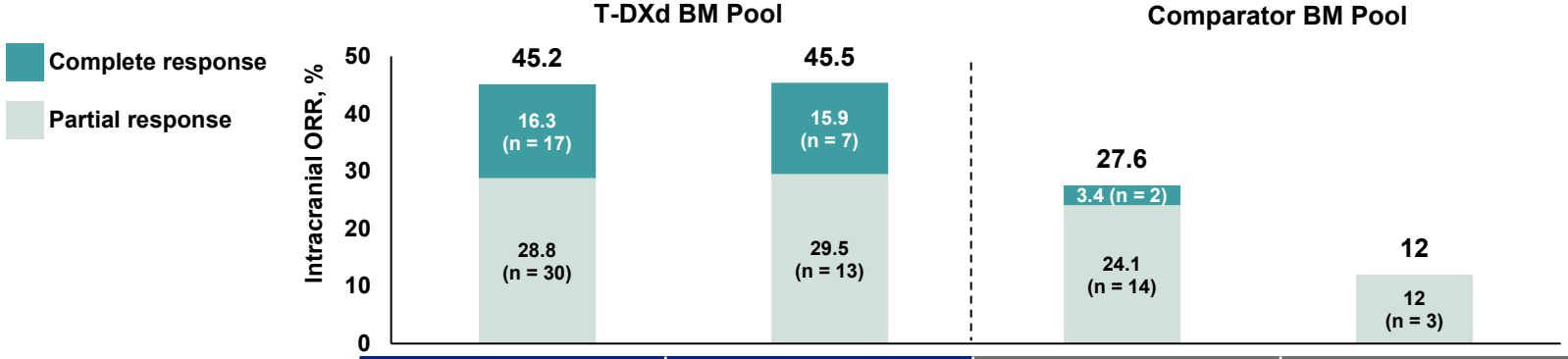
	T-DXd Pool (N = 851)		Comparator Pool (N = 465)	
	BM Pool (n = 148)	Non-BM Pool (n = 703)	BM Pool (n = 83)	Non-BM Pool (n = 382)
Prior regimens in the metastatic setting, Median, (range), n (%)	**3.0 (1.0-14.0)**	**3.0 (0-27.0)**	**3.0 (1.0-15.0)**	**2.0 (0-12.0)**
0	0	2 (0.3)	0	1 (0.3)
1	16 (10.8)	108 (15.4)	14 (16.9)	99 (25.9)
2	41 (27.7)	192 (27.3)	27 (32.5)	110 (28.8)
3	35 (23.6)	156 (22.2)	22 (26.5)	89 (23.3)
4	18 (12.2)	71 (10.1)	9 (10.8)	39 (10.2)
≥5	38 (25.7)	174 (24.8)	11 (13.3)	44 (11.5)
Prior anti-HER2 therapy, n (%)				
Trastuzumab	142 (95.9)	643 (91.5)	83 (100)	381 (99.7)
Pertuzumab	104 (70.3)	497 (70.7)	59 (71.1)	255 (66.8)
T-DM1	102 (68.9)	487 (69.3)	41 (49.4)	161 (42.1)
HER2 TKI	17 (11.5)	51 (7.3)	14 (16.9)	39 (10.2)
Prior treatment for brain metastasis, n (%)				
None (untreated/active)	**44 (29.7)**	642 (91.3)	**25 (30.1)**	359 (94.0)
Any prior treatment for BMs (treated/stable)	**104 (70.3)**	61 (8.7)[a]	**58 (69.9)**	23 (6.0)[a]
RT alone	80 (54.1)	45 (6.4)[a]	44 (53.0)	15 (3.9)[a]
Surgery alone	5 (3.4)	6 (0.9)[a]	5 (6.0)	5 (1.3)[a]
RT and surgery	19 (12.8)	10 (1.4)[a]	9 (10.8)	3 (0.8)[a]

- **Overall, patients with BM were heavily pretreated with a median of 3 prior systemic regimens in the metastatic setting**
- **In both T-DXd and comparator pools, of the patients with BMs at baseline, ~70% had treated/stable BMs and ~30% had untreated/active BMs**
  - **This was balanced between T-DXd and comparator**

BM, brain metastasis; HER2, human epidermal growth factor receptor 2; RT, radiation therapy; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TKI, tyrosine kinase inhibitor.
RT includes whole-brain RT, brain-directed stereotactic RT, and brain-directed radiosurgery. Surgery includes any brain-directed surgery (craniotomy, metastasectomy in brain, resection, or removal of brain lesion).
[a]Patients with a reported history of BMs who did not have BMs at baseline.

Exploratory Best IC Response, ORR, and DoR per BICR

Intracranial ORR[a]

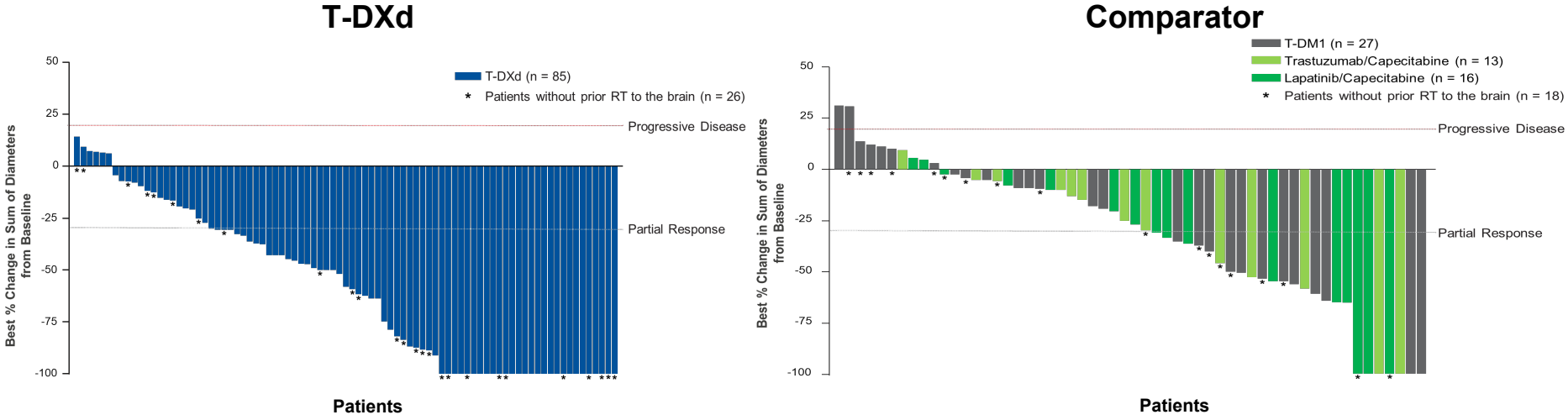


	Treated/stable BMs (n = 104)	Untreated/active BMs (n = 44)	Treated/stable BMs (n = 58)	Untreated/active BMs (n = 25)
Best overall IC response, n (%)				
Stable disease	48 (46.2)	15 (34.1)	28 (48.3)	15 (60.0)
Progressive disease	3 (2.9)	1 (2.3)	7 (12.1)	5 (20.0)
Not evaluable/Missing	6 (5.8)	8 (18.2)	7 (12.1)	2 (8.0)
IC-DoR, median, months (95% CI)	12.3 (9.1-17.9)	17.5 (13.6-31.6)	11.0 (5.6-16.0)	NA[b]

- **T-DXd consistently demonstrated superior rates of IC responses over comparator in patients with treated/stable and untreated/active BMs**
- **A trend in prolonged median IC-DoR was most pronounced in the untreated/active BMs subgroup**

BM, brain metastasis; BICR, blinded independent central review; DoR, duration of response; IC, intracranial; NA, not available; ORR, objective response rate; T-DXd, trastuzumab deruxtecan.
This table considers both target and non-target lesions at baseline. Lesions in previously irradiated areas were not considered measurable target lesions unless there was demonstrated progression in the lesion.
[a]IC-ORR was assessed per RESIST v1.1. [b]IC-DoR NA due to small number of responders (n < 10).

Best Percentage Change from Baseline in Sum of Diameters of Brain Tumors

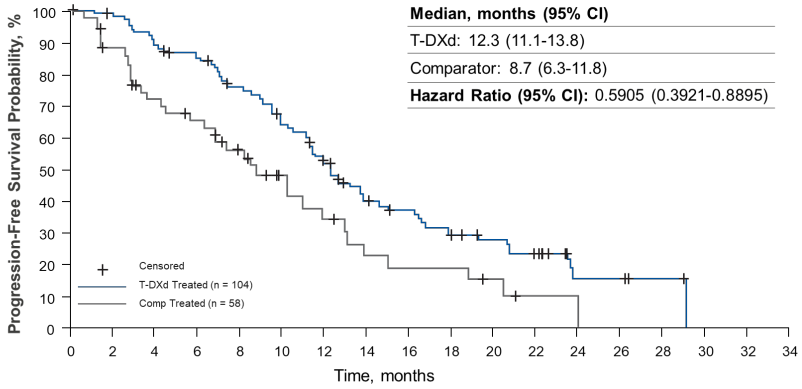


- **The shrinkage of BMs in response to T-DXd was more prominent, whereas in the comparator pool, BMs showed less of a response**

BM, brain metastases; RT, radiotherapy; T-DXd, trastuzumab deruxtecan.
For patients with measurable brain lesion(s) at baseline and at least one post-baseline assessment.

Exploratory CNS-PFS per BICR

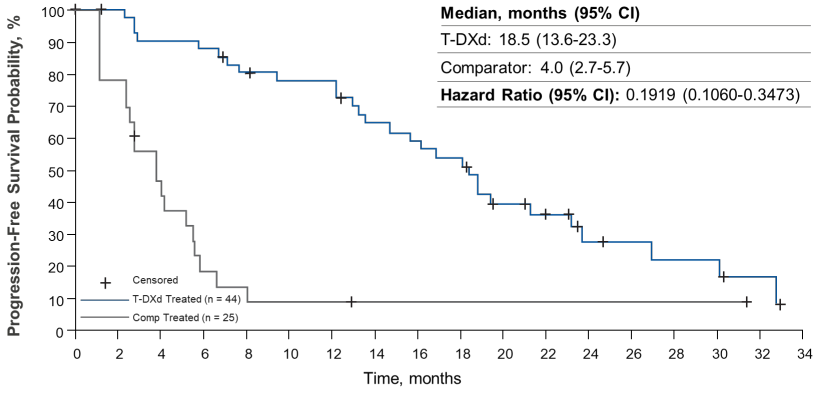
Treated/Stable BMs



Patients still at risk

T-DXd Treated (n = 104)	104	100	89	83	72	58	46	32	28	21	18	12	4	4	2	0	0	0
Comparator Treated (n = 58)	58	44	33	29	22	14	10	6	5	5	3	1	0	0	0	0	0	0

Untreated/Active BMs



Patients still at risk

T-DXd Treated (n = 44)	44	41	37	36	32	30	30	24	22	20	13	11	6	5	4	4	2	0
Comparator Treated (n = 25)	25	18	11	5	3	2	2	1	1	1	1	1	1	1	1	1	0	0

- **T-DXd demonstrated a trend towards prolonged CNS-PFS over comparator, with a noticeably greater advantage for patients with untreated/active BMs**

BICR, blinded independent central review; BM, brain metastasis; CNS, central-nervous system; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan.
CNS-PFS was defined by BICR as only radiological progression.

Site of First Progression per BICR

	T-DXd Pool (N = 851)		Comparator Pool (N = 465)	
	BM Pool (n = 148)	Non-BM Pool (n = 703)	BM Pool (n = 83)	Non-BM Pool (n = 382)
Patients with PD, n (%)	88 (59.5)	291 (41.4)	49 (59.0)	244 (63.9)
Site of first progression				
Intracranial only	38 (25.7)	16 (2.3)	13 (15.7)	6 (1.6)
Extracranial only	47 (31.8)	270 (38.4)	31 (37.3)	237 (62.0)
Both	3 (2.0)	2 (0.3)	5 (6.0)	0
Missing	0	3 (0.4)	0	1 (0.3)

- **Rates of any PD were comparable in patients in both BM pool populations**

BICR, blinded independent central review; BM, brain metastasis; PD, progressive disease; T-DXd, trastuzumab.
This table is a description of the first site of progression and does not capture all locations of progression. Progressive disease is defined as a ≥20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (including the baseline sum), and must demonstrate an absolute increase of at least 5mm (Note: the appearance of ≥1 new lesions is also considered progression).

Overall Drug-Related Safety Summary

n, (%)	T-DXd Pool (N = 845)		Comparator Pool (N = 456)	
	BM Pool (n = 146)	Non-BM Pool (n = 699)	BM Pool (n = 83)	Non-BM Pool (n = 373)
Any drug-related TEAE	138 (94.5)	691 (98.9)	78 (94.0)	330 (88.5)
Drug-related TEAEs grade ≥3	63 (43.2)	324 (46.4)	30 (36.1)	140 (37.5)
Drug-related serious TEAEs	19 (13.0)	87 (12.4)	6 (7.2)	29 (7.8)
Drug-related TEAEs associated with discontinuation	21 (14.4)	121 (17.3)	6 (7.2)	21 (5.6)
Drug-related TEAEs associated with dose reduction	31 (21.2)	172 (24.6)	22 (26.5)	105 (28.2)
Drug-related TEAEs associated with an outcome of death	0	7 (1.0)	0	0

- The median treatment duration was 12.7 months (range, 0.7-45.1 months) with T-DXd and 5.6 months (range, 0.1-43.0 months) with comparator
- Rates of any drug-related TEAEs and grade ≥3 TEAEs were generally similar across all patient subgroups
- Rates of TEAEs associated with discontinuations and dose reductions were similar in patients with and without BMs

BM, brain metastasis; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event.

Conclusions

- T-DXd demonstrated robust IC responses in patients with treated/stable and active BMs vs comparator
  - Stable BMs:
    - IC-ORR: 45.2% (17 CR; 30 PR) vs 27.6% (2 CR; 14 PR)
    - Median IC-DoR: 12.3 vs 11.0 months
  - Active BMs:
    - IC-ORR: 45.5% (7 CR; 13 PR) vs 12.0% (0 CR; 3 PR)
    - Median IC-DoR: 17.5 months vs NA[a]
- Numerically longer median CNS-PFS was observed in patients with treated/stable and active BMs randomized to T-DXd vs comparator
  - Stable BMs: 12.3 vs 8.7 months
  - Active BMs: 18.5 vs 4.0 months
- The safety profile of T-DXd in patients with BMs was acceptable, generally manageable, and similar to the safety profile in the overall patient population[1-3]

T-DXd is an effective treatment option for patients with HER2-positive mBC with treated/stable and active BMs with an acceptable and manageable safety profile

BM, brain metastasis; CNS, central nervous system; CR, complete response; DoR, duration of response; HER2, human epidermal growth factor receptor 2; IC, intracranial; mBC, metastatic breast cancer; NA, not available; ORR, objective response rate; PFS, progression-free survival; PR, partial response; T-DXd, trastuzumab deruxtecan.

[a]IC-DoR NA due to small number of responders (n < 10).

1. Cortes J et al. *N Engl J Med*. 2022; 368(12):1143-1154. 2. Modi S et al. *N Engl J Med*. 2020; 382:610-621. 3. André F et al. *The Lancet*. 2023. https://doi.org/10.1016/S0140-6736(23)00725-0.

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Supplementary content, including a plain-language summary, available:

Most Common TEAEs Leading to Treatment Discontinuation or Dose Reduction

	T-DXd Pool (N = 845)		Comparator Pool (N = 456)	
	BM Pool (n = 146)	Non-BM Pool (n = 699)	BM Pool (n = 83)	Non-BM Pool (n = 373)
TEAE associated with discontinuation, n (%)	**27 (18.5)**	**143 (20.5)**	**9 (10.8)**	**34 (9.1)**
Pneumonitis	11 (7.5)	43 (6.2)	0	4 (1.1)
Pneumonia	2 (1.4)	7 (1.0)	0	1 (0.3)
Asthenia	2 (1.4)	1 (0.1)	0	0
Interstitial lung disease	1 (0.7)	33 (4.7)	0	2 (0.5)
Platelet count decreased	1 (0.7)	4 (0.6)	2 (2.4)	3 (0.8)
Thrombocytopenia	1 (0.7)	1 (0.1)	0	3 (0.8)
Diarrhea	0	1 (0.1)	2 (2.4)	0
Blood bilirubin increased	0	0	0	3 (0.8)
TEAEs associated with dose reduction, n (%)	**33 (22.6)**	**181 (25.9)**	**22 (26.5)**	**105 (28.2)**
Fatigue	10 (6.8)	23 (3.3)	2 (2.4)	5 (1.3)
Nausea	4 (2.7)	43 (6.2)	2 (2.4)	7 (1.9)
Vomiting	4 (2.7)	12 (1.7)	5 (6.0)	1 (0.3)
Asthenia	3 (2.1)	9 (1.3)	1 (1.2)	2 (0.5)
Diarrhea	2 (1.4)	7 (1.0)	2 (2.4)	17 (4.6)
Palmar-plantar erythrodysesthesia syndrome	1 (0.7)	0	8 (9.6)	38 (10.2)
Neutrophil count decreased	1 (0.7)	22 (3.1)	0	3 (0.8)
Platelet count decreased	2 (1.4)	10 (1.4)	3 (3.6)	9 (2.4)

- **Overall rates of TEAEs related to dose reduction were lower with T-DXd**

BMs, brain metastasis; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event.
Most common TEAEs by preferred term in each treatment group, sorted in descending order of frequency in the T-DXd BM pooled arm.

Plain Language Summary

Why did we perform this research?

Breast cancer is the most common type of cancer in women and can be categorized based on whether the tumor expresses a protein called human epidermal growth factor receptor 2 (HER2+).[1,2] Trastuzumab deruxtecan (T-DXd) is a HER2-directed anticancer therapy designed to target and kill HER2-expressing cancer cells.[3] It is being studied for the treatment of HER2+ metastatic breast cancer. Currently, there is limited efficacy data of T-DXd in patients with untreated/active brain metastases (BMs), which could stop doctors from treating these patients with T-DXd. The objective of this study was to provide additional, in-depth efficacy and safety data for T-DXd or comparator treatment in HER2+ metastatic breast cancer patients with BMs at baseline.

How did we perform this research?

In the DESTINY-Breast01, DESTINY-Breast02, and DESTINY-Breast03 trials, we assessed the efficacy and safety of T-DXd (5.4 mg/kg every 3 weeks) in patients with HER2+ metastatic breast cancer that have disease progression on or after previous therapy.[4-6] In the DESTINY-Breast02 trial, T-DXd was compared with treatments of physicians' choice, which included trastuzumab plus capecitabine or lapatinib plus capecitabine.[5] In the DESTINY-Breast03 trial, T-DXd was compared with trastuzumab emtansine.[6] Results of the 3 studies (DESTINY-Breast01, -02, and -03) were pooled to evaluate the efficacy and safety of T-DXd and comparator in patients with treated/clinically stable (treated) and untreated/active (untreated) BMs at baseline, as defined by the US Food and Drug Administration Clinical Trial Eligibility Criteria.[7]

What were the findings of this research and what are the implications?

This analysis showed T-DXd to be an effective treatment option across patients with both treated and, notably, for the first time, untreated BMs compared to comparator. Complete and partial responses in the brain were similar and greater in both BM subgroups compared to comparator. A numerically longer median time until a patient's intracranial cancer got worse or caused death (known as central nervous system-progression-free survival) and duration of response within the brain were observed with T-DXd in patients with untreated BMs. Rates of adverse events associated with treatment were similar across all patient subgroups. The overall safety profile of T-DXd was acceptable and generally manageable.

Where can I access more information?

DESTINY-Breast01: ClinicalTrials.gov. A study of T-DXd in metastatic breast cancer previously treated with trastuzumab emtansine (T-DM1). https://clinicaltrials.gov/ct2/show/NCT03248492
DESTINY-Breast02: ClinicalTrials.gov. T-DXd in pre-treated HER2 breast cancer that cannot be surgically removed or has spread. https://clinicaltrials.gov/ct2/show/NCT03523585
DESTINY-Breast03: ClinicalTrials.gov. T-DXd versus T-DM1 for human epidermal growth factor receptor 2 (HER2)-positive, unresectable and/or metastatic breast cancer previously treated with trastuzumab and taxane. https://clinicaltrials.gov/ct2/show/NCT03529110

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1. International Agency for Research on Cancer. GLOBOCAN 2020. Published 2021. Accessed March 21, 2022. http://gco.iarc.fr/today/home. 2. Female Breast Cancer Subtypes - Cancer Stats. Accessed May 2 2023. https://seer.cancer.gov.statfacts. 3. Nakada T, et al. *Chem Pharm Bull (Tokyo).* 2019;67(3):173-185. 4. Modi S. et al. *N Engl J Med*. 2020; 382(7):610-621. 5. André et al. *The Lancet.* 2023. https://doi.org/10.1016/S0140-6736(23)00725-0. 6. Cortés et al. *N Engl J Med*. 2022; 368(12):1143-1154. 7. FDA. Cancer Clinical Trial Eligibility Criteria: Brain Metastases. 2020.