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HER2 Positive Breast Cancer Updates

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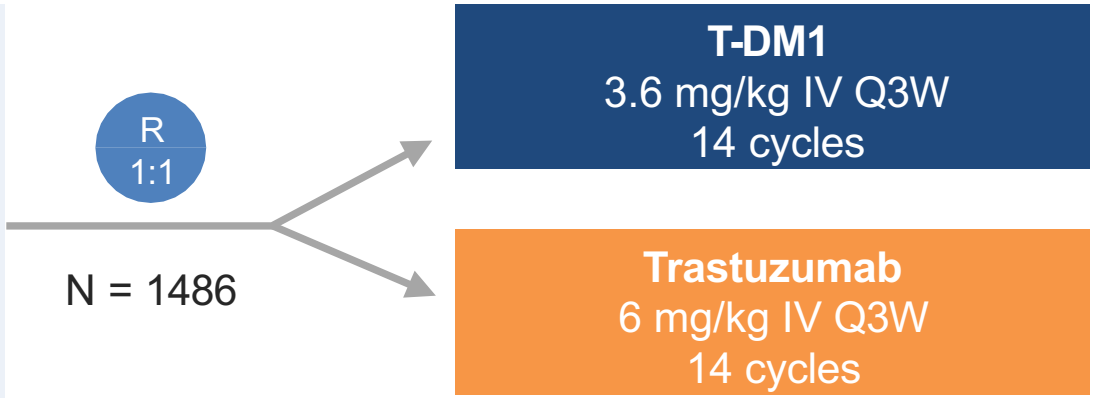
KATHERINE study design

- Prior neoadjuvant therapy consisting of:
  - Minimum 6 cycles of chemotherapy
  - Minimum 9 weeks of trastuzumab
    - Second HER2-targeted agent allowed
- Residual invasive tumor in breast or axillary nodes
- Randomization within 12 weeks of surgery



- Radiation and endocrine therapy per protocol and local guidelines
- Switch to trastuzumab permitted if T-DM1 discontinued due to AEs

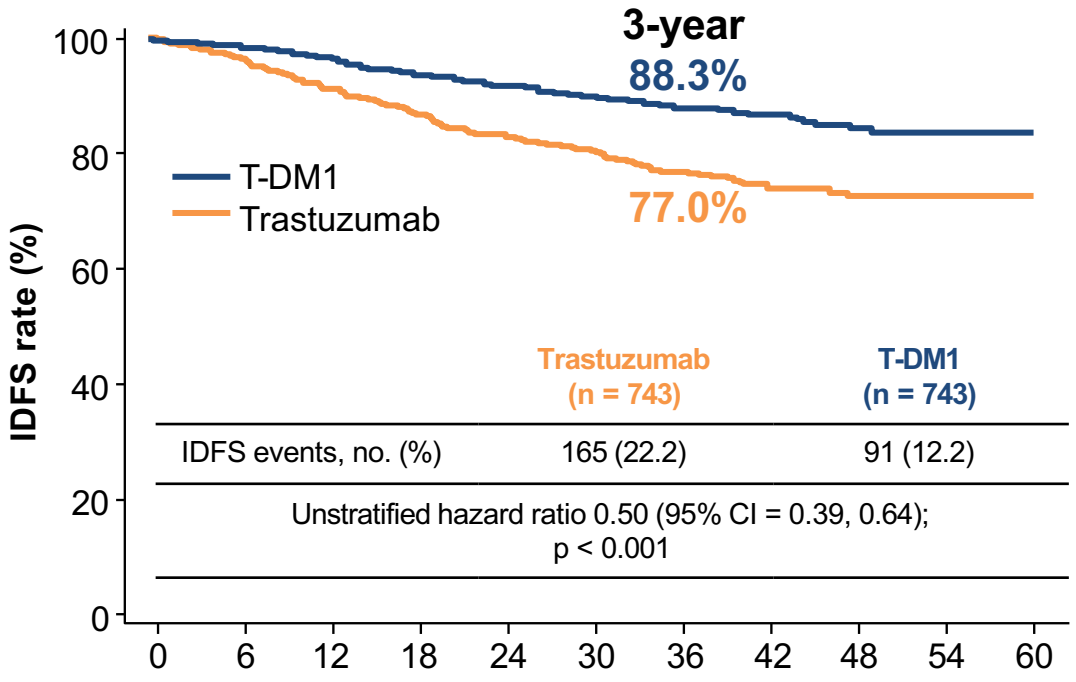
- **Primary endpoint:** IDFS
- **Secondary endpoints:** IDFS with second primary non-breast cancers included, DFS, OS, DRFI, safety, and QoL
- **Stratification factors:** Clinical stage at presentation (inoperable vs operable), HR status, preoperative HER2-directed therapy, pathologic nodal status after preoperative therapy

AE, adverse event; DFS, disease-free survival; DRFI, distant recurrence-free interval; HR, hormone receptor; IDFS, invasive disease-free survival; IV, intravenous; OS, overall survival; Q3W, every 3 weeks; QoL, quality of life; R, randomized; T-DM1, ado-trastuzumab emtansine.

Adapted from *N Engl J Med*, von Minckwitz *et al*., Trastuzumab emtansine for residual invasive HER2-positive breast cancer, Vol. 380, Pages 617–628.

KATHERINE primary analysis (2018)

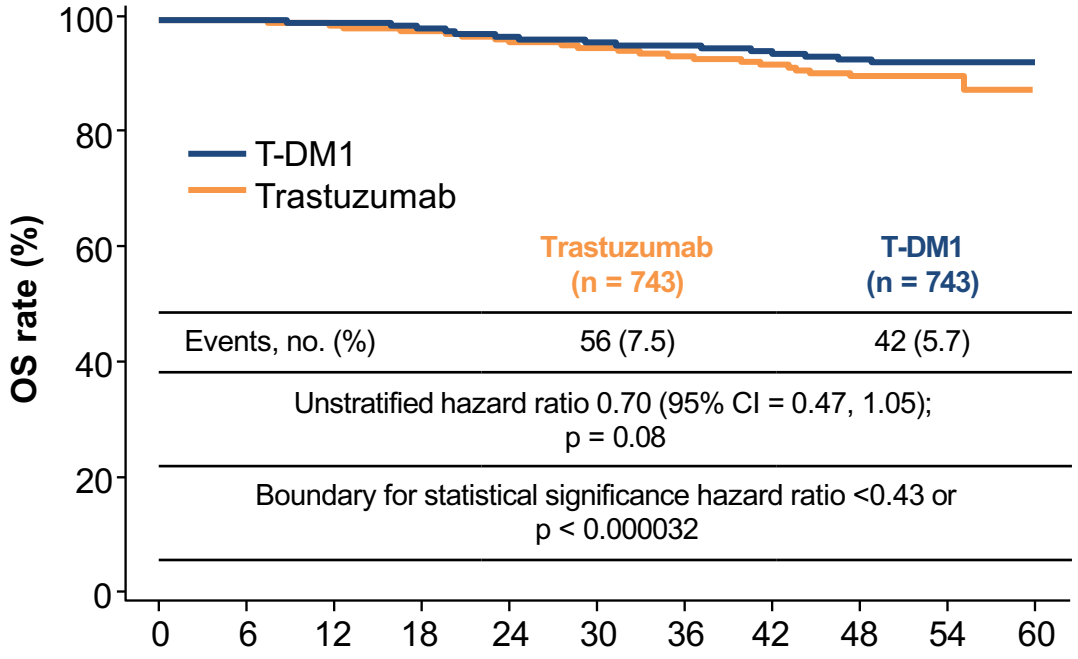
IDFS



	Trastuzumab (n = 743)	T-DM1 (n = 743)
IDFS events, no. (%)	165 (22.2)	91 (12.2)
Unstratified hazard ratio 0.50 (95% CI = 0.39, 0.64); p < 0.001		

No. at risk											
Trastuzumab	743	676	635	594	555	501	342	220	119	38	4
T-DM1	743	707	681	658	633	561	409	255	142	44	4

OS



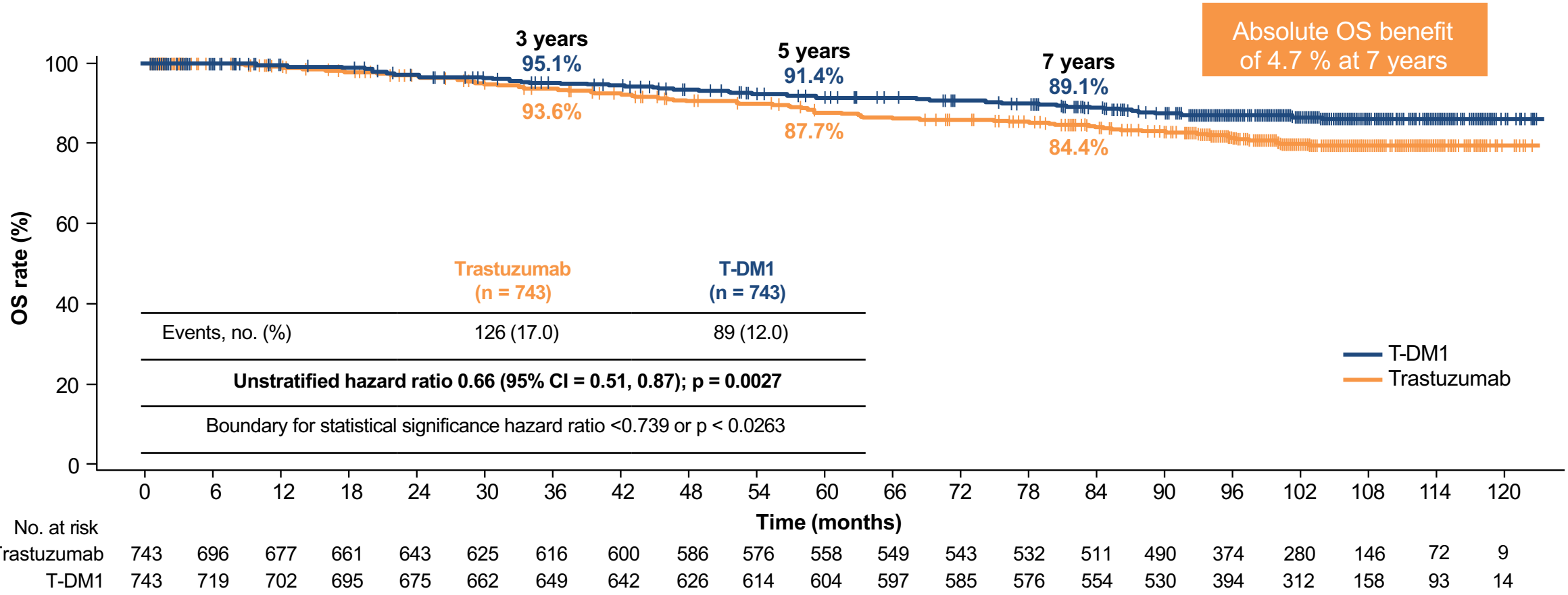
	Trastuzumab (n = 743)	T-DM1 (n = 743)
Events, no. (%)	56 (7.5)	42 (5.7)
Unstratified hazard ratio 0.70 (95% CI = 0.47, 1.05); p = 0.08		
Boundary for statistical significance hazard ratio <0.43 or p < 0.000032		

No. at risk											
Trastuzumab	743	695	677	657	635608	471	312	175		71	8
T-DM1	743	719	702	693	668648	508	345	195		76	12

CCOD: July 25, 2018; median follow-up: 41.4 months (T-DM1) and 40.9 months (trastuzumab).
CCOD, clinical cutoff date; CI, confidence interval; IDFS, invasive disease-free survival; OS, overall survival; T-DM1, ado-trastuzumab emtansine.

Adapted from *N Engl J Med*, von Minckwitz *et al*., Trastuzumab emtansine for residual invasive HER2-positive breast cancer, Vol. 380, Pages 617–628.

KATHERINE 2nd OS interim analysis; median follow-up 8.4 years (101 months)

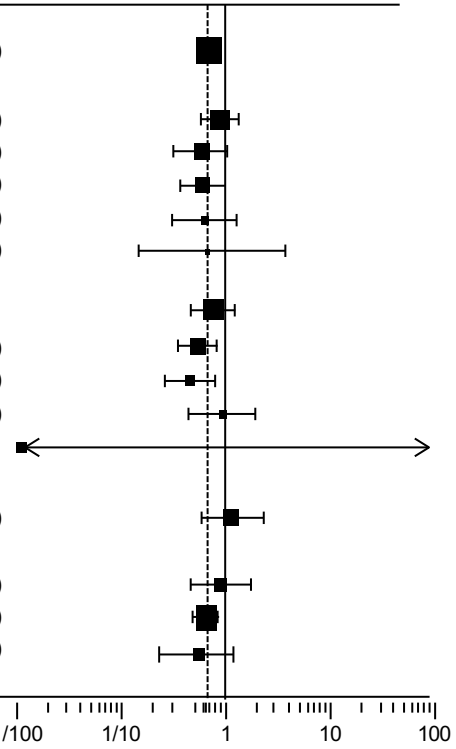


Significant reduction in risk of death by 34% with T-DM1

CI, confidence interval; OS, overall survival; T-DM1, ado-trastuzumab emtansine.

2nd OS interim analysis: Subgroups (2/2)

Baseline risk factors	Total n	Trastuzumab (n = 743) Patients per group	Trastuzumab (n = 743) n events	Trastuzumab (n = 743) 7-year OS	T-DM1 (n = 743) Patients per group	T-DM1 (n = 743) n events	T-DM1 (n = 743) 7-year OS	Hazard ratio	95% CI
All	1486	743	126	84.4	743	89	89.1	0.66	(0.51, 0.87)
Primary tumor stage (at definitive surgery)									
ypT0, ypT1a, ypT1b, ypT1mic, ypTis	637	306	41	89.4	331	38	89.5	0.86	(0.55, 1.34)
ypT1, ypT1c	359	184	27	84.6	175	15	91.1	0.55	(0.29, 1.03)
ypT2	359	185	38	79.9	174	23	89.8	0.57	(0.34, 0.95)
ypT3	108	57	17	74.1	51	10	78.2	0.59	(0.27, 1.29)
ypT4*	23	11	3	63.5	12	3	80.0	0.72	(0.14, 3.58)
Regional lymph node stage (at definitive surgery)									
ypN0	673	332	32	90.7	341	27	92.8	0.82	(0.49,1.37)
ypN1	432	212	46	80.9	220	30	86.6	0.57	(0.36, 0.90)
ypN2	189	103	33	70.0	86	16	87.1	0.48	(0.26, 0.87)
ypN3	67	30	11	53.8	37	16	54.2	0.93	(0.43, 2.00)
ypNX	125	66	4	94.8	59	0	100.0	<0.01	(0.00, NE)
Residual disease ≤1 cm with negative axillary lymph nodes									
ypT1a, ypT1b or ypT1mic and ypN0	328	160	13	93.1	168	16	92.3	1.18	(0.57, 2.45)
Age group (years)									
<40	296	153	16	89.2	143	15	88.4	0.93	(0.46, 1.88)
40–64	1064	522	92	83.9	542	66	89.3	0.65	(0.47, 0.89)
≥65	126	68	18	77.6	58	8	88.8	0.50	(0.22, 1.14)



* Includes all ypT4 and one patient with ypTX. CI, confidence interval; NE, not evaluable; OS, overall survival; T-DM1, ado-trastuzumab emtansine.

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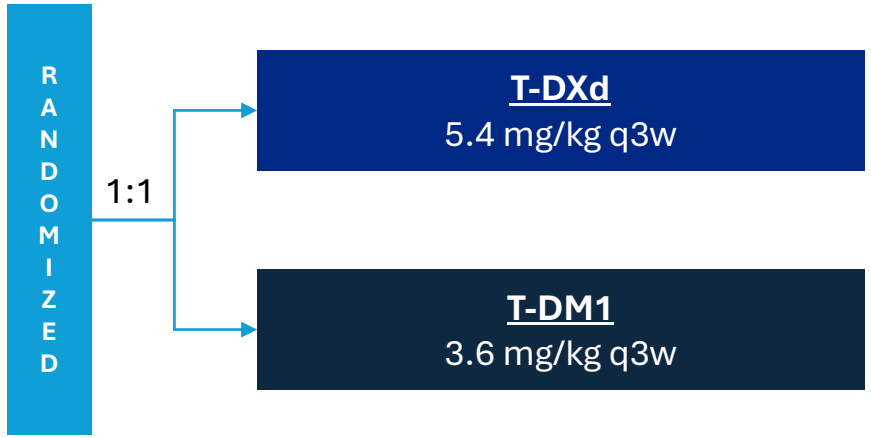
T-DXd vs T-DM1 in HER2+ MBC: DESTINY-Breast03 Study

Key Eligibility Criteria

- HER2+ unresectable or MBC[a]
- Previous treatment with trastuzumab and taxane in the advanced/metastatic setting[b]
- Clinically stable, treated brain metastases allowed



Primary endpoint: PFS by BICR
Secondary endpoints: OS, ORR (BICR and investigator),
DOR (BICR), PFS (investigator), safety

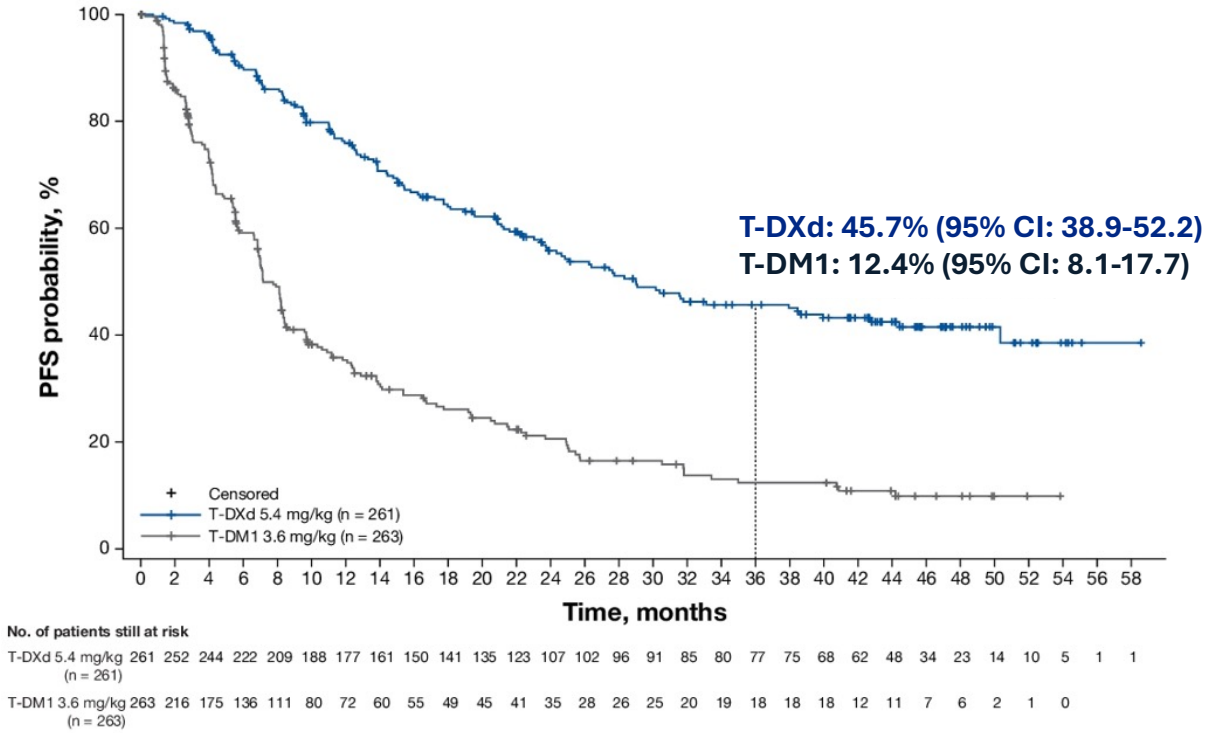
Patient Characteristics		T-DXd (n=261)	T-DM1 (n=263)
Median age (range), years		54.3 (27.9-83.1)	54.2 (20.2-83.0)
Region, Asia		57.1	60.8
HER2 status (IHC,[c] %)	3+	89.7	88.2
	2+ (ISH amplified)	9.6	11.4
	1+/NE/not examined	0.4/0.4/0	0/0.4/0
ECOG PS, %	0/1/missing	59.0/40.6/0.4	66.5/33.1/0.4
Brain metastases, %	Yes/no	23.8/76.2	19.8/80.2
Visceral disease, %	Yes/no	70.5/29.5	70.3/29.7
Prior lines of therapy in the metastatic setting (includes rapid progressors as 1 line of treatment), n (%)	0	2 (0.8)	3 (1.1)
	1	130 (49.8)	123 (46.8)
	2	56 (21.5)	65 (24.7)
	3	35 (13.4)	35 (13.3)
	4	15 (5.7)	19 (7.2)
	≥5	23 (8.8)	18 (6.8)
Prior trastuzumab, %		99.6	99.6
Prior pertuzumab, %		62.1	60.1

[a] HER2+ is defined as IHC 3+ or IHC 2+/ISH+ based on central confirmation. [b] Progression during or <6 months after completing adjuvant therapy involving trastuzumab and taxane. [c] HER2 status as evaluated by central lab.

Cortes J, et al. ESMO 2021. Abstract LBA1.

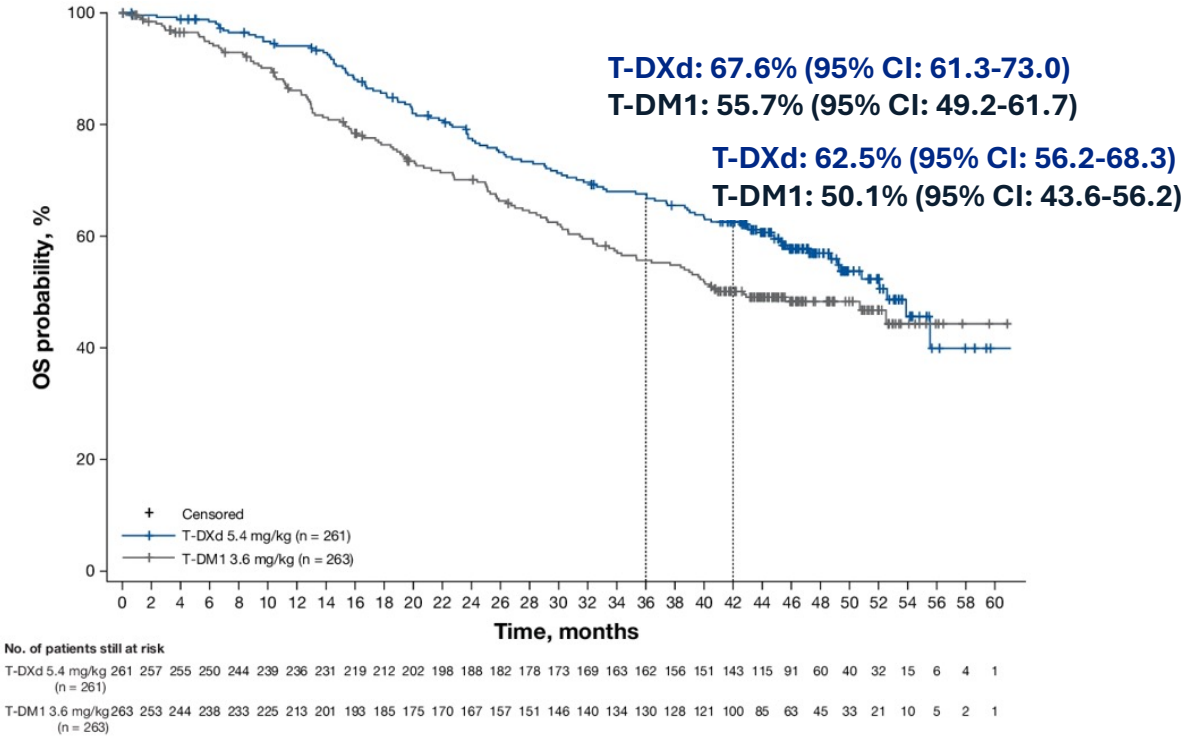
DESTINY-Breast03 Study-Median Follow-Up: 43.0 mo for T-DXd and 35.4 mo for T-DM1

PFS Assessed by INV



	T-DXd (n=261)	T-DM1 (n=263)
Median PFS, mo (95% CI)	29.0 (23.7-40.0)	7.2 (6.8-8.3)
HR (95% CI)	0.30 (0.24-0.38)	

OS



	T-DXd (n=261)	T-DM1 (n=263)
Median OS, mo (95% CI)	52.6 (48.7-NE)	42.7 (35.4-NE)
HR (95% CI)	0.73 (0.56-0.94)	

[a] The *P* value for OS crossed the prespecified boundary (*P*=0.013) and was statistically significant.
[b] Two-sided from stratified log-rank test.

Hamilton EP, et al. ASCO 2024. Abstract 1025.

T-DXd vs T-DM1 : Updated Safety Results DESTINY-Breast03

Median Follow-Up: 28.4 mo for T-DXd and 26.5 mo for T-DM1

Drug-Related TEAEs (≥35% Patients in Either Arm)				
TEAEs, n (%)	T-DXd (n=257)		T-DM1 (n=261)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Nausea	198 (77.0)	18 (7.0)	79 (30.3)	1 (0.4)
Vomiting	133 (51.8)	4 (1.6)	28 (10.7)	2 (0.8)
Alopecia	102 (39.7)	1 (0.4)	9 (3.4)	0
Constipation	96 (37.4)	0	51 (19.5)	0
Thrombocytopenia	64 (24.9)	20 (7.8)	114 (43.7)	52 (19.9)
AST increased	72 (28.0)	2 (0.8)	108 (41.4)	14 (5.4)

Adjudicated as Drug-Related ILD/Pneumonitis						
n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
T-DXd (n=257)	11 (4.3)	26 (10.1)	2 (0.8)	0	0	39 (15.2)
T-DM1 (n=261)	4 (1.5)	3 (1.1)	1 (0.4)	0	0	8 (3.1)

Safety

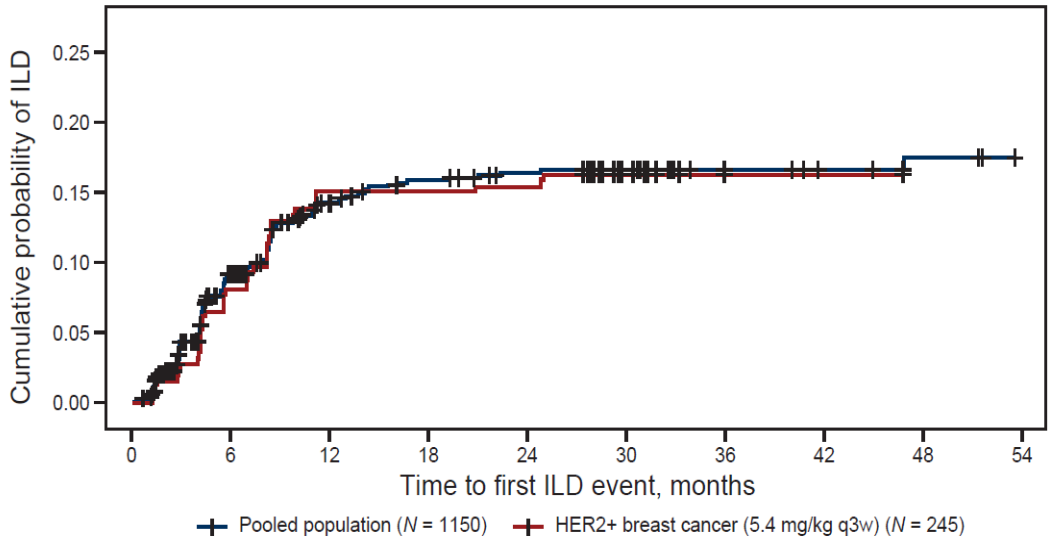
- The most common TEAE associated with treatment discontinuation for T-DXd was ILD/pneumonitis (10.9%) and for T-DM1 was thrombocytopenia (2.6%)
- The median treatment duration was 18.2 mo (range, 0.7-44.0) for T-DXd and 6.9 mo (range, 0.7-39.3) for T-DM1

Relationship to study drug was determined by the treating investigator.

Hurvitz SA, et al. *Lancet*. 2023;401(10371):105-117.

ILD Risk Factors: Pooled Analysis From 9 Phase 1 and Phase 2 T-DXd Monotherapy Studies

Time to First Adjudicated Drug-Related ILD Event



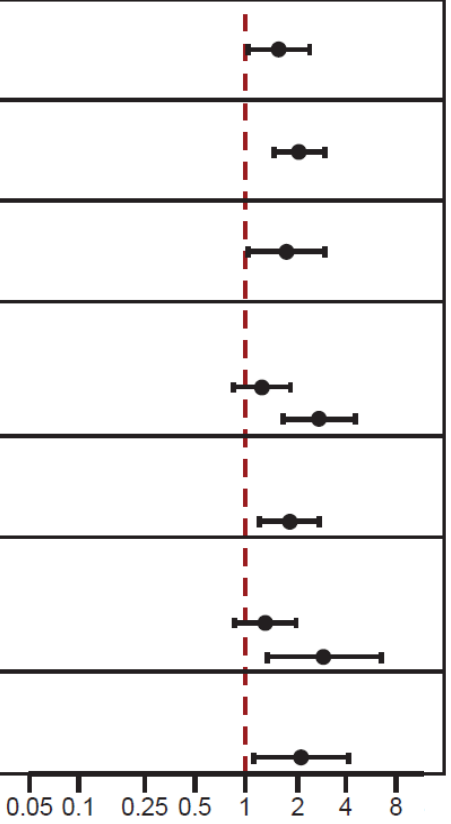
No. at risk (events)										
Pooled population	1150 (0)	547 (101)	262 (154)	142 (170)	84 (174)	35 (176)	13 (176)	7 (176)	4 (177)	0 (177)
HER2+ breast cancer	245 (0)	170 (20)	95 (37)	66 (37)	45 (38)	11 (40)	2 (40)	1 (40)	0 (40)	0 (40)
ILD rate										
Pooled population	0	9.2%	14.3%	16.0%	16.4%	16.6%	16.6%	16.6%	17.5%	17.5%
HER2+ breast cancer	0	8.2%	15.1%	15.1%	15.5%	16.3%	16.3%	16.3%	16.3%	16.3%

This was a retrospective review of investigator-assessed ILD/pneumonitis events across 9 phase 1 and phase 2 studies and multiple tumor types.

[a] Hazard ratios are presented relative to the reference categories indicated. [b] Includes asthma, chronic obstructive pulmonary disease, prior ILD/pneumonitis, pulmonary fibrosis, pulmonary emphysema, and radiation pneumonitis. [c] Due to differences in data collection among the studies, some data were not collected for all patients; thus, the number of patients may not add up to the total population. [d] Determined by Cockcroft-Gault formula.

Hazard Ratios[a]

Potential risk factor	Patients, *n* (*N* = 1150)	Hazard ratio[a] (95% CI)
Age group		
<65 years	754	1.56 (1.02-2.38)
≥65 years	396	Ref
Country		
Japan	506	2.08 (1.45-2.98)
Non-Japan	644	Ref
Lung comorbidities[b]		
Yes	81	1.75 (1.03-2.98)
No	1069	Ref
Baseline renal function[c,d]		
Normal	470	Ref
Mild decrease	458	1.24 (0.83-1.84)
Moderate/severe decrease	196	2.73 (1.65-4.52)
Time since disease diagnosis[c]		
0 to ≤4 years	624	Ref
>4 years	403	1.82 (1.20-2.75)
Dose		
5.4 mg/kg q3w	315	Ref
6.4 mg/kg q3w	808	1.30 (0.85-1.99)
>6.4 mg/kg q3w	27	2.92 (1.32-6.42)
Baseline SpO_2[c]		
≥95%	1080	Ref
<95%	57	2.14 (1.11-4.13)



Powell CA, et al. *ESMO Open*. 2022;7(4):100554.

T-DXd in Patients With HER2+ MBC and Active BMs: The Single-Arm Phase 2 TUXEDO-1 Trial

Key Eligibility Criteria

- HER2+ (IHC 3+) MBC
- Brain metastases either recently diagnosed or recently progressed after local therapy

T-DXd: 5.4 mg/kg q3w
Until progression or unacceptable toxicity

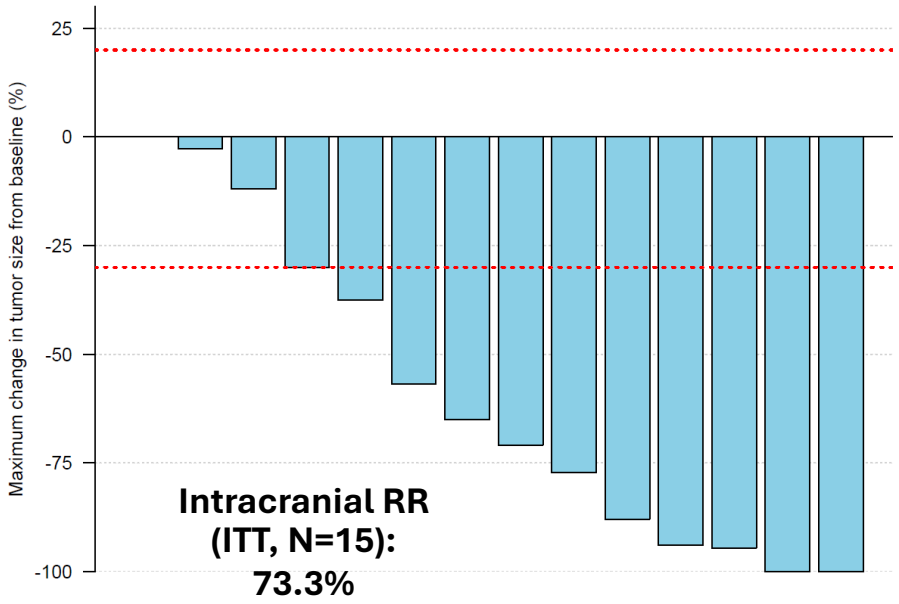
Primary Endpoint

- ORR (CNS) by RANO-BM criteria

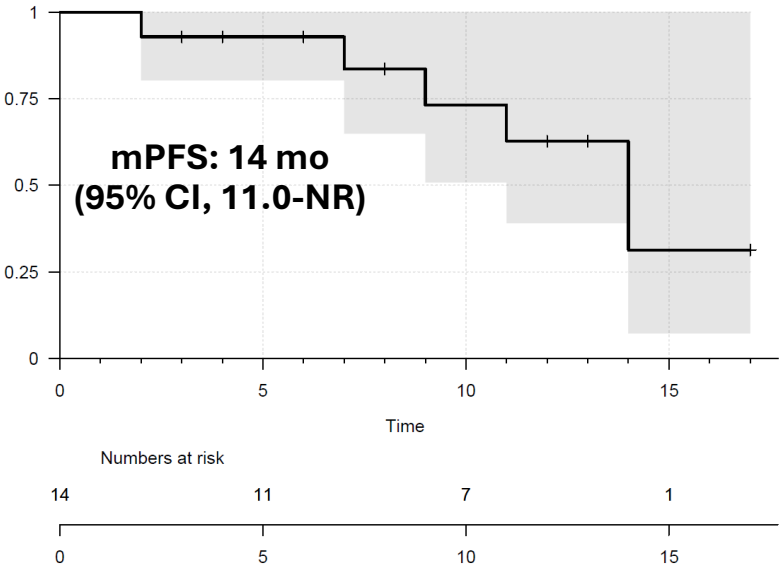
Secondary Endpoints

- CBR, extracranial response rate, PFS, OS, safety, QoL

Primary Endpoint: Intracranial ORR



Secondary Endpoint: PFS

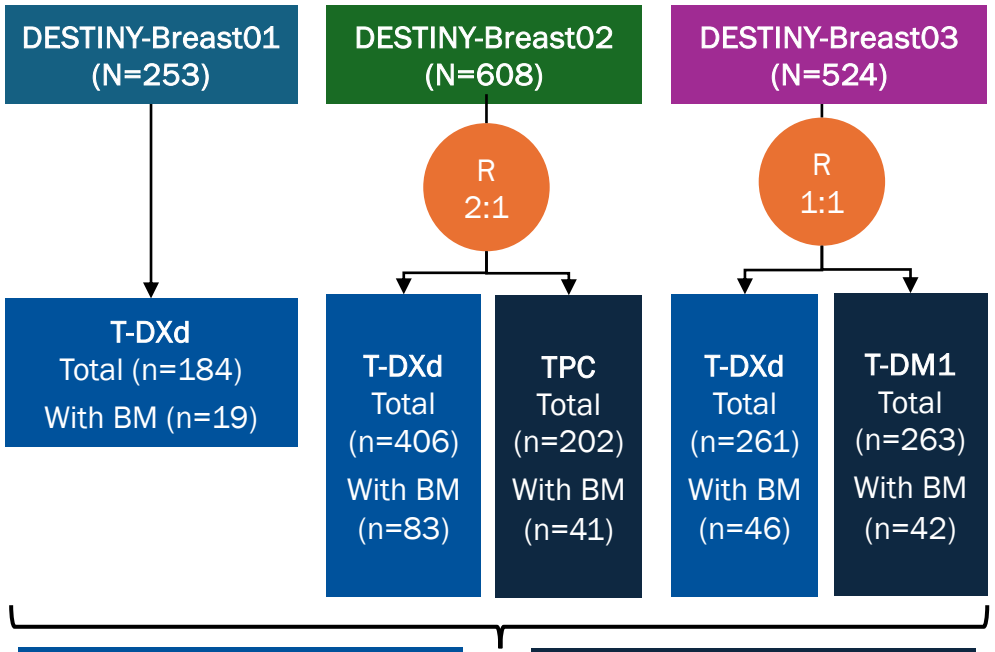


Safety: AEs of Special Interest

- Ejection fraction decrease in 1 patient (grade 3)
- ILD in 1 patient (grade 2)
- Grade 5 urosepsis in 1 patient (deemed unrelated)

Bartsch R, et al. *Nat Med*. 2022;28(9):1840-1847.

DESTINY-Breast01, -02, and -03 Pooled Analysis in Brain Metastases:



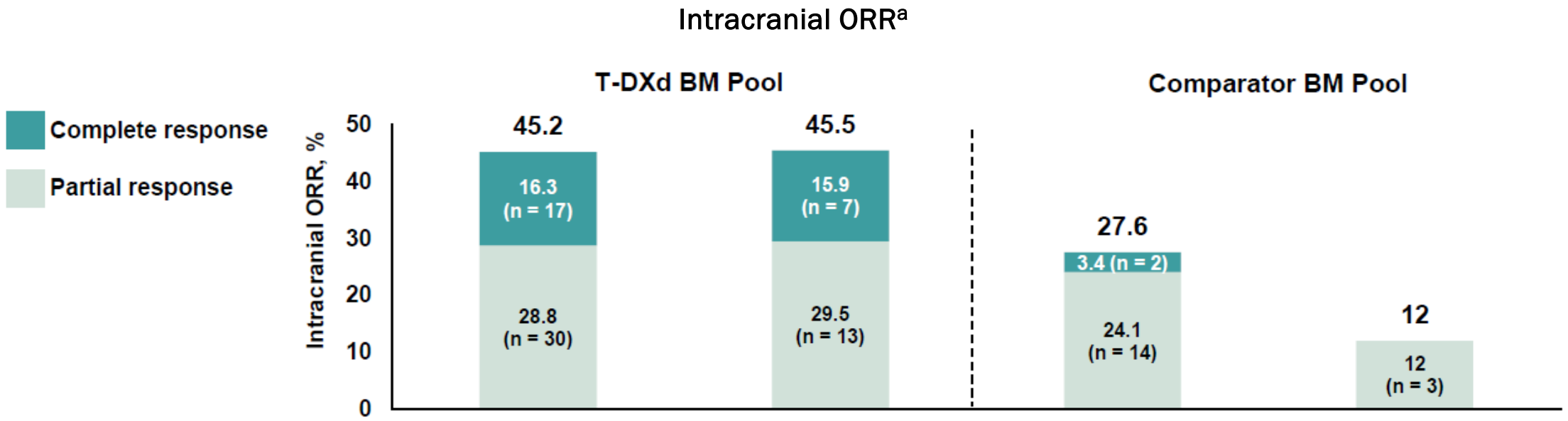
Endpoints: IC-ORR (CR + PR in brain) per BICR, IC-DoR per BICR, CNS-PFS per BICR, safety

Patient Characteristics		T-DXd Pool (n=851)		Comparator Pool (n=465)	
		BM (n=148)	Non-BM[a] (n=703)	BM (n=83)	Non-BM[a] (n=382)
Median age (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)
Median time from diagnosis of BC to randomization (range), mo		55.9 (8.3-271.6)	50.9 (1.5-431.4)	53.0 (6.7-303.2)	47.3 (5.1-326.0)
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)
Visceral disease, n (%)		143 (96.6)	537 (76.4)	78 (94.0)	271 (70.9)
Prior regimens in the metastatic setting, median (range)		3 (1-14)	3 (0-27)	3 (1-15)	2 (0-12)
Prior treatment for BM, n (%)	None (untreated/active)	44 (29.7)	642 (91.3)	25 (30.1)	359 (94.0)
	Any prior treatment for BM (treated/stable)	104 (70.3)	61 (8.7)	58 (69.9)	23 (6.0)
	RT alone	80 (54.1)	45 (6.4)	44 (53.0)	15 (3.9)
	Surgery alone	5 (3.4)	6 (0.9)	5 (6.0)	5 (1.3)
	RT and surgery	19 (12.8)	10 (1.4)	9 (10.8)	3 (0.8)

[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.

Hurvitz SA, et al. ESMO 2023. Abstract 377O.

DESTINY-Breast01, -02, and -03 Pooled Analysis in Brain Metastases: Intracranial ORR



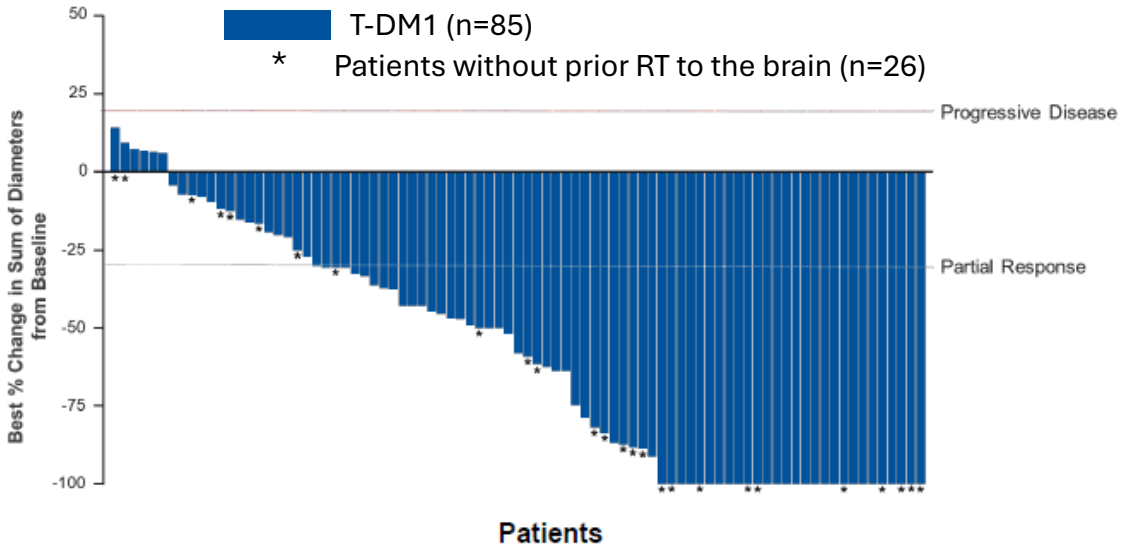
	Treated/Stable BM (n=104)	Untreated/Active BM (n=44)	Treated/Stable BM (n=58)	Untreated/Active BM (n=25)
Best overall IC response, n (%)				
SD	48 (46.2)	15 (34.1)	28 (48.3)	15 (60.0)
PD	3 (2.9)	1 (2.3)	7 (12.1)	5 (20.0)
NE/missing	6 (5.8)	8 (18.2)	7 (12.1)	2 (8.0)
Median IC-DoR, months (95% CI)	12.3 (9.1, 17.9)	17.5 (13.6, 31.6)	11.0 (5.6, 16.0)	NA[b]

[a] IC-ORR was assessed per RECIST v1.1. [b] IC-DoR NA due to small number of responders (n<10).

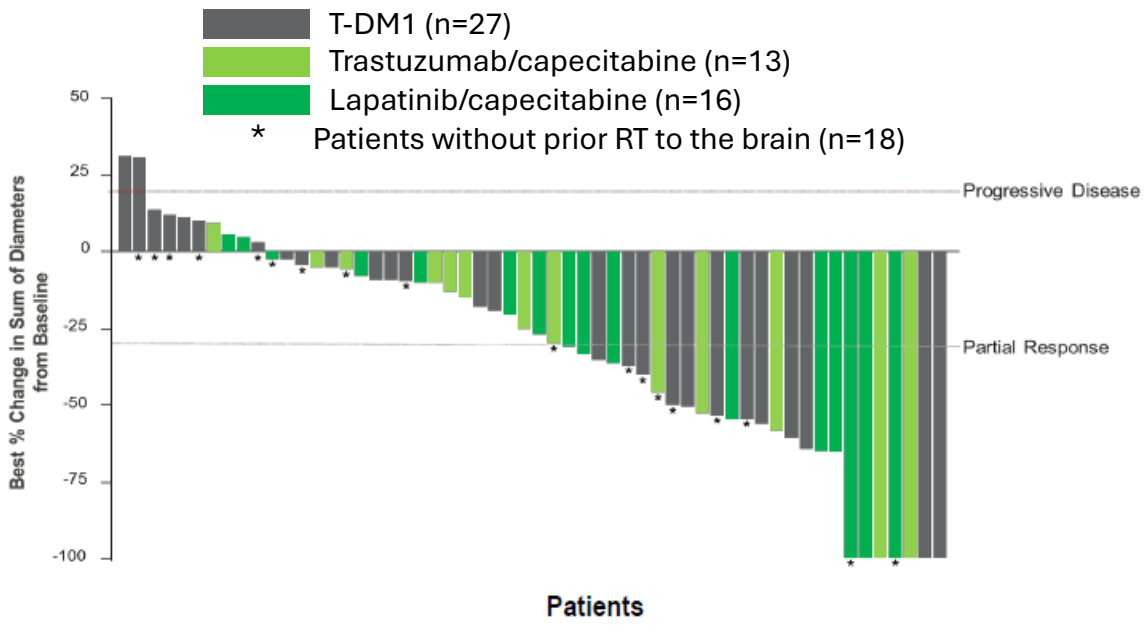
Hurvitz SA, et al. ESMO 2023. Abstract 377O.

DESTINY-Breast01, -02, and -03 Pooled Analysis in Brain Metastases: Best Percentage Change From Baseline in Sum of Diameters of Brain Tumors

T-DXd



Comparator

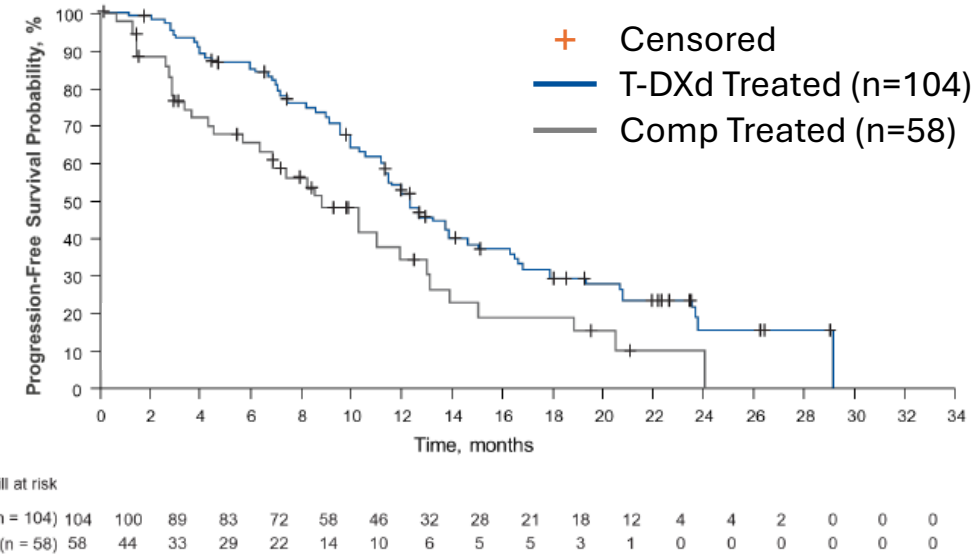


For patients with measurable brain lesion(s) at baseline and at least 1 postbaseline assessment.

Hurvitz SA, et al. ESMO 2023. Abstract 377O.

DESTINY-Breast01, -02, and -03 Pooled Analysis in Brain Metastases: Exploratory CNS-PFS by BICR

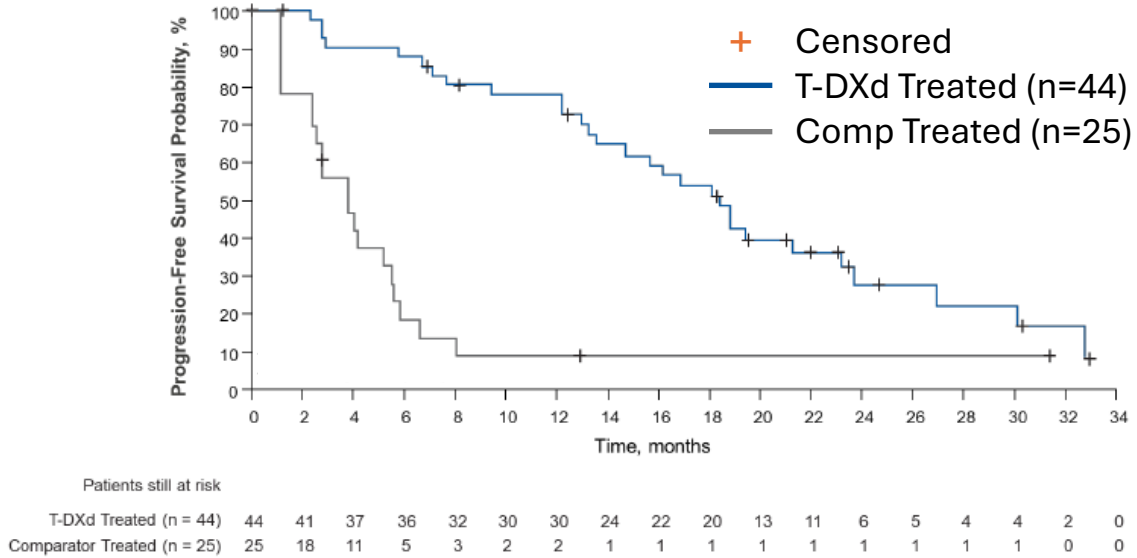
CNS-PFS in Treated/Stable BMs



Treated/Stable BMs	T-DXd (n=104)	Comparator (n=58)
Median CNS-PFS, mo (95% CI)	12.3 (11.1-13.8)	8.7 (6.3-11.8)
HR (95% CI)	0.59 (0.39-0.89)	

Treated/stable BMs: Patients have received prior CNS-directed therapy for their BMs, and their CNS disease is stable

CNS-PFS in Untreated/Active BMs



Untreated/Active BMs	T-DXd (n=44)	Comparator (n=25)
Median CNS-PFS, mo (95% CI)	18.5 (13.6-23.3)	4.0 (2.7-5.7)
HR (95% CI)	0.19 (0.11-0.35)	

Untreated/active BMs: Patients have new BMs or progressive BMs that have not been subjected to CNS-directed therapy since documented progression

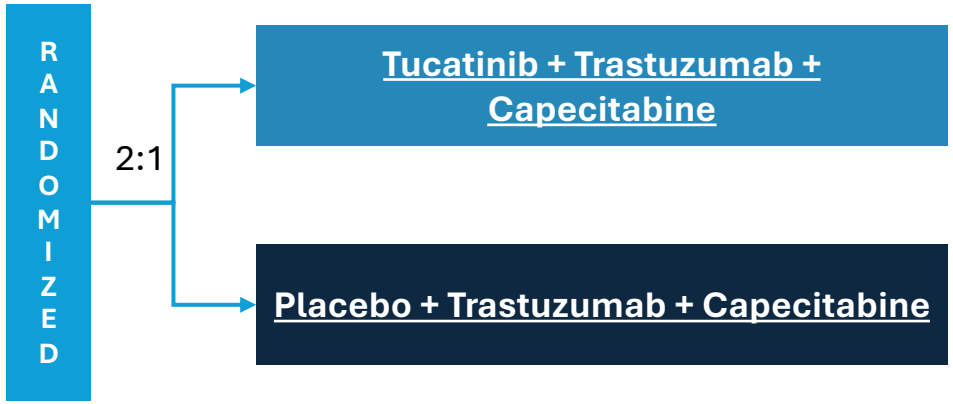
CNS-PFS was defined by BICR as only radiological progression.

Hurvitz SA, et al. ESMO 2023. Abstract 377O.

Randomized Phase 3 HER2CLIMB Study: Study Design and Patients

Key Eligibility Criteria

- Metastatic HER2+ breast cancer with progression after pertuzumab, trastuzumab, and T-DM1
- Patients with and without brain metastases



Primary endpoint: PFS by in all patients
Secondary endpoints: PFS in patients with brain metastases, OS in all patients, ORR, safety

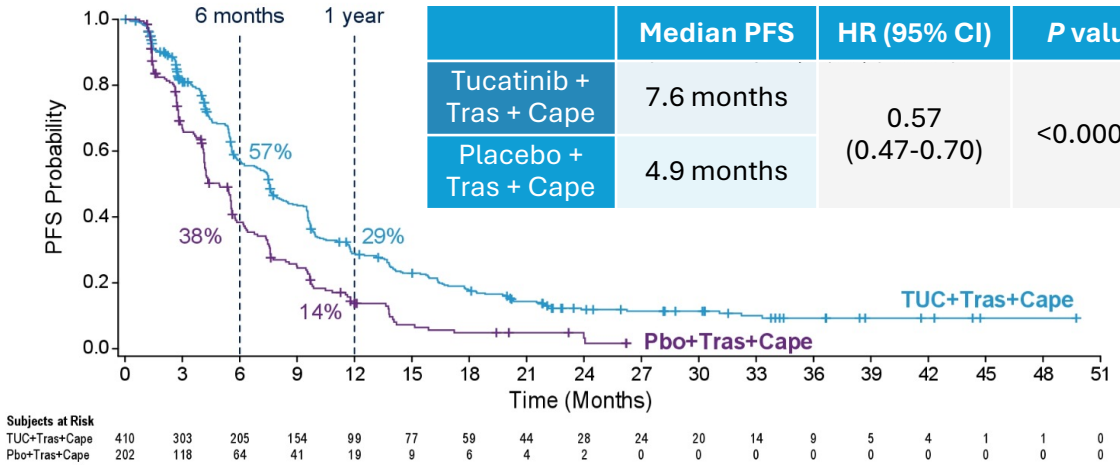
Patient Characteristics		Tucatinib (n=410)	Placebo (n=202)
Median age, years		55	54
ECOG PS, %	0	49.8	46.5
	1	50.2	53.5
Presence or history of brain metastases, %		48.3	46.0
Previous lines of therapy, median no. (range)		4 (2-14)	4 (2-17)
Previous lines of therapy in MBC, median no. (range)		3 (1-14)	3 (1-13)
Prior trastuzumab, %		100	100
Prior pertuzumab, %		99.8	99.5
Prior T-DM1, %		100	100

Murthy RK, et al. *New Engl. J. Med.* 2020;382(7):597-609.

Phase 3 HER2CLIMB Study: PFS and OS Median Follow-Up: 29.6 months

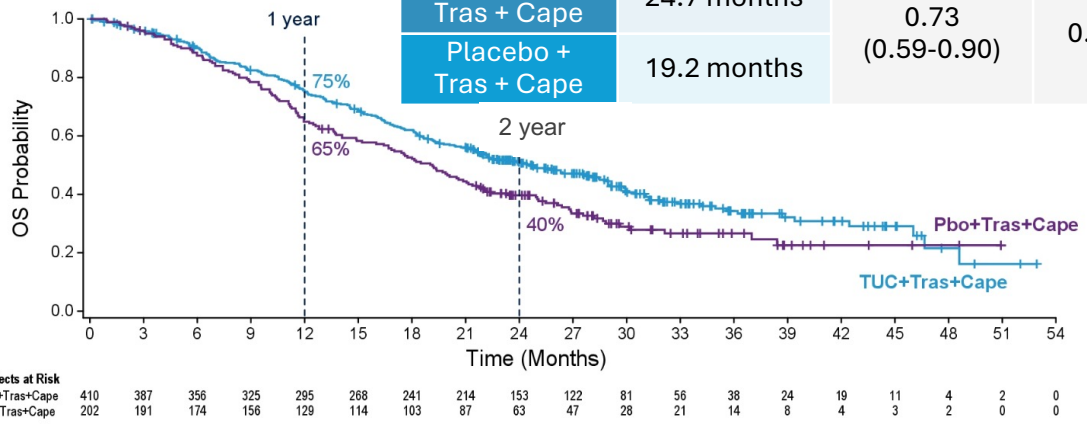
Progression-Free Survival

	Median PFS	HR (95% CI)	*P* value
Tucatinib + Tras + Cape	7.6 months	0.57 (0.47-0.70)	<0.00001
Placebo + Tras + Cape	4.9 months		



Overall Survival

	Median OS	HR (95% CI)	*P* value
Tucatinib + Tras + Cape	24.7 months	0.73 (0.59-0.90)	0.004
Placebo + Tras + Cape	19.2 months		



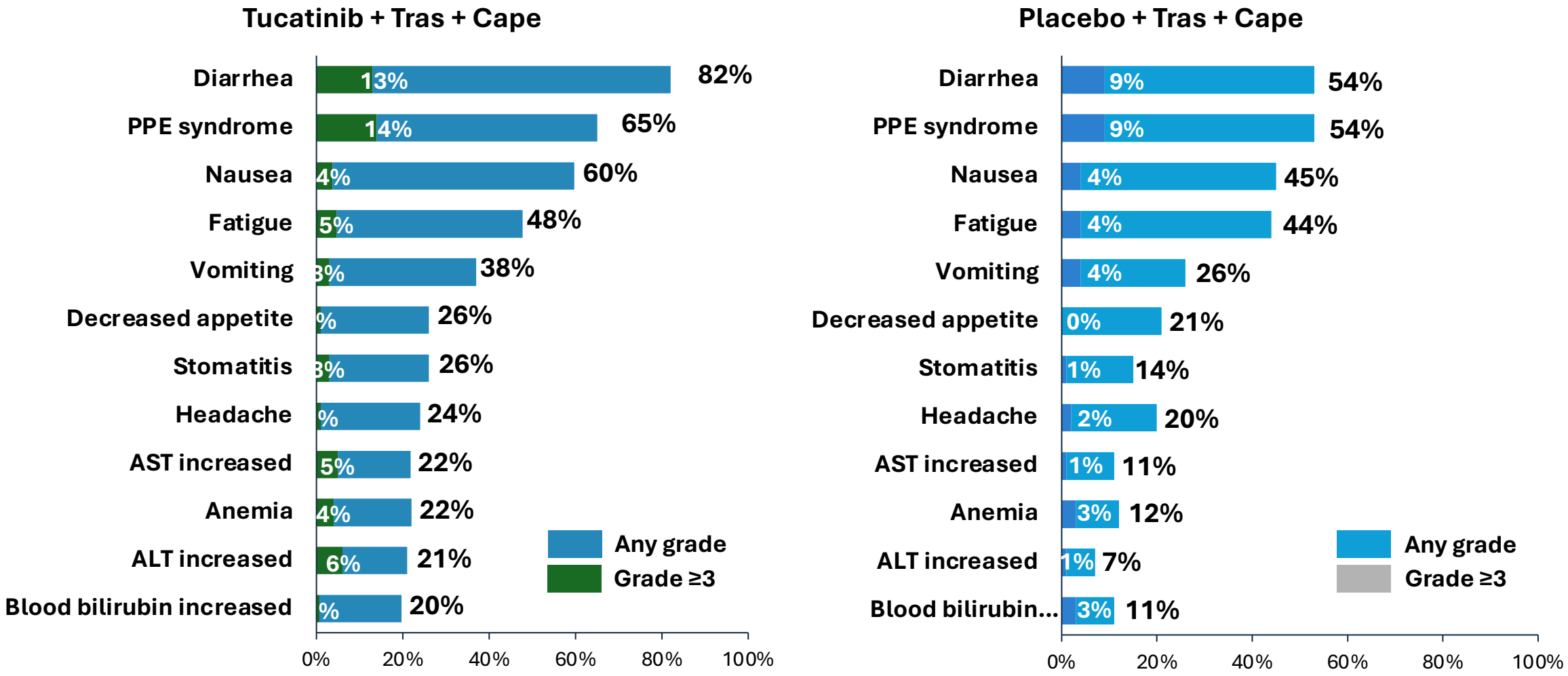
Overall Survival in an Exploratory Analysis in Patients With and Without Visceral Metastases

	Patients With Visceral Metastases (n=455)			Patients Without Visceral Metastases (n=157)		
	HR (95% CI)	*P* value	Median OS	HR (95% CI)	*P* value	Median OS
Tucatinib + Tras + Cape	0.70 (0.55-0.89)	0.004	21.6 months	0.80 (0.48-1.3)	0.36	32.9 months
Placebo + Tras + Cape			16.9 months			26.9 months

Curigliano G, et al. *Ann Oncol*. 2022;33(3):321-329.

Phase 3 HER2CLIMB Study: Safety

Median Follow-Up: 29.6 months



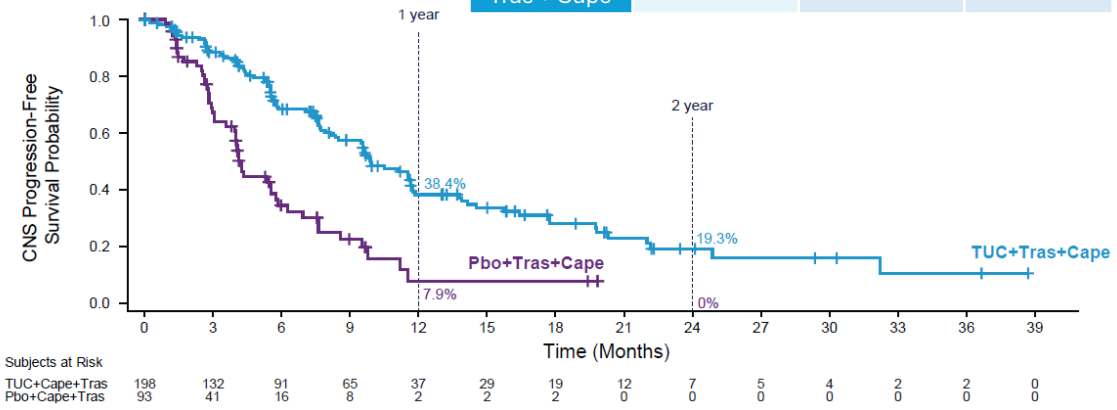
Curigliano G, et al. *Ann Oncol*. 2022;33(3):321-329.

Brain Metastases: Subgroup Analyses From HER2CLIMB

Median Follow-Up: 29.6 months

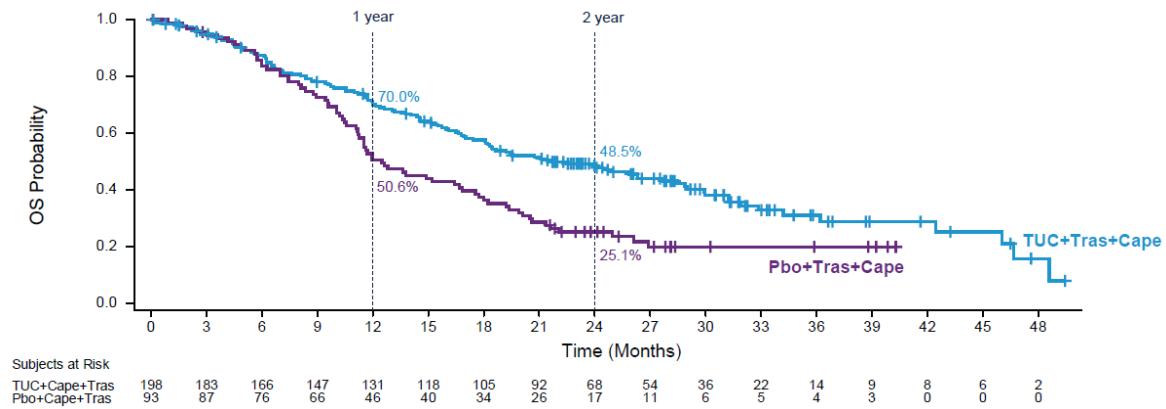
CNS PFS for All Patients With Brain Metastases

	Median PFS	HR (95% CI)	*P* value
Tucatinib + Tras + Cape	9.9 months	0.39 (0.27-0.56)	<0.00001
Placebo + Tras + Cape	4.2 months		



OS for All Patients With Brain Metastases

	Median OS	HR (95% CI)	*P* value
Tucatinib + Tras + Cape	21.6 months	0.60 (0.44-0.81)	0.00078
Placebo + Tras + Cape	12.5 months		



OS for Patients With Active Brain Metastases

	Median OS	HR (95% CI)	*P* value
Tucatinib + Tras + Cape	21.4 months	0.52 (0.36-0.77)	0.00087
Placebo + Tras + Cape	11.8 months		

OS for Patients With Treated Stable Brain Metastases

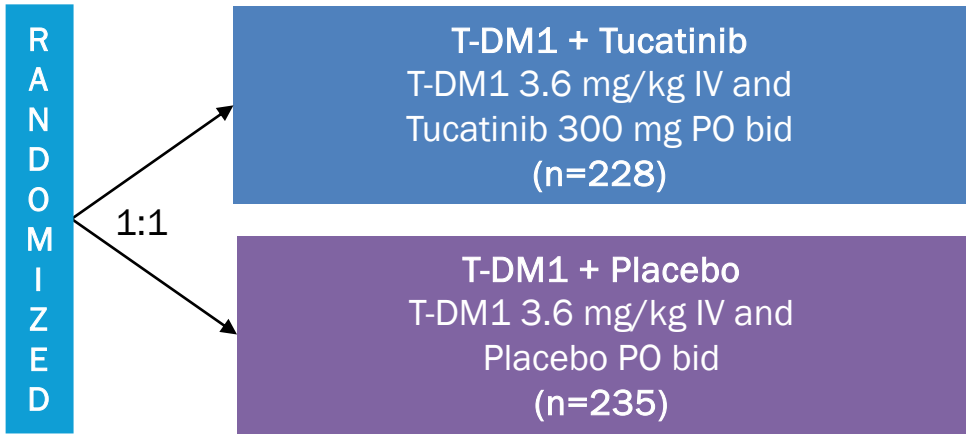
	Median OS	HR (95% CI)	*P* value
Tucatinib + Tras + Cape	21.6 months	0.70 (0.42-1.16)	0.162
Placebo + Tras + Cape	16.4 months		

Lin NU, et al. *JAMA Oncol*. 2023;9(2):197-205.

HER2CLIMB-02 Trial of Tucatinib + T-DM1

Key Eligibility Criteria 2+ LA/MBC with progression after trastuzumab and taxane in any setting

- ECOG PS ≤1
- Previously treated stable, progressing, or untreated brain metastases not requiring immediate local therapy



N≈460

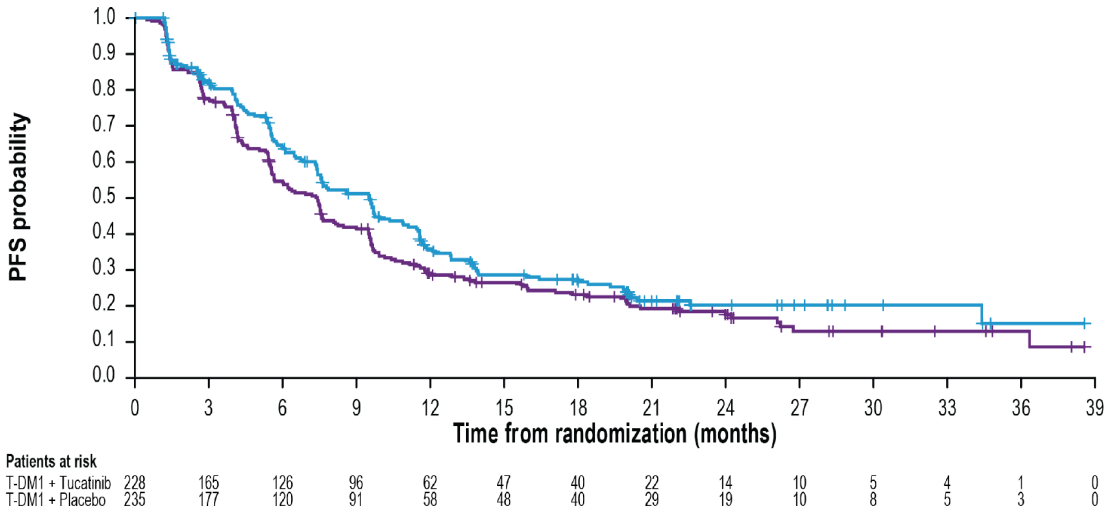
Primary endpoint: PFS
Key secondary endpoints: OS, PFS in patients with brain metastases, cORR, OS in patients with brain metastases

Patient Characteristics, n (%)		T-DM1 + Tucatinib (n=228)	T-DM1 + Placebo (n=235)
Median age (range), years		55.0 (26-83)	53.0 (27-82)
HR+		137 (60.1)	140 (59.6)
ECOG PS	0	137 (60.1)	141 (60.0)
	1	91 (39.9)	94 (40.0)
Stage at initial diagnosis	0-III	120 (52.6)	130 (55.3)
	IV	103 (45.2)	98 (41.7)
Presence/history of brain metastases	Yes	99 (43.4)	105 (44.7)
	Active	50 (21.9)	57 (24.3)
	Stable/treated	49 (21.5)	48 (20.4)
Number of Prior LOT in metastatic setting	Median (range)	1 (0-8)	1 (0-6)
	0	29 (12.7)	33 (14.0)
	1	146 (64.0)	150 (63.8)
	2	36 (15.8)	31 (13.2)
	≥3	17 (7.5)	21 (8.9)
Prior pertuzumab		202 (88.6)	214 (91.1)
Prior anti-HER2 TKIs		3 (1.3)	5 (2.1)

Hurvitz S, et al. SABCS 2023. Abstract GS01-10.

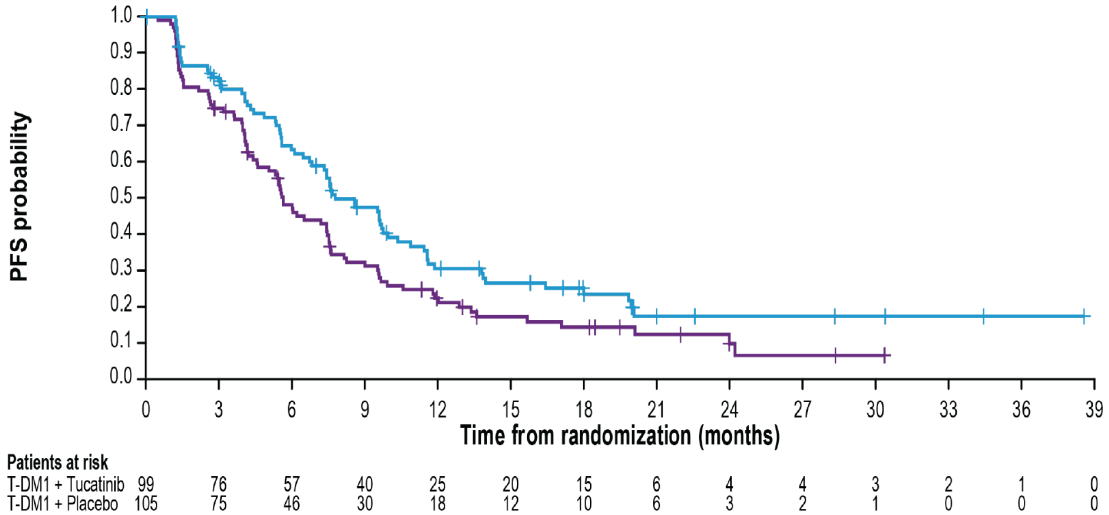
Phase 3 HER2CLIMB-02 Trial of Tucatinib + T-DM1 in Previously Treated HER2+ MBC: PFS

PFS



PFS	T-DM1 + Tucatinib (n=228)	T-DM1 + Placebo (n=235)
# of events	151	182
Median PFS, mo (95% CI)	9.5 (7.4-10.9)	7.4 (5.6-8.1)
HR (95% CI); *P* value	0.76 (0.61-0.95); *P*=0.0163	

PFS in Patients With BMs



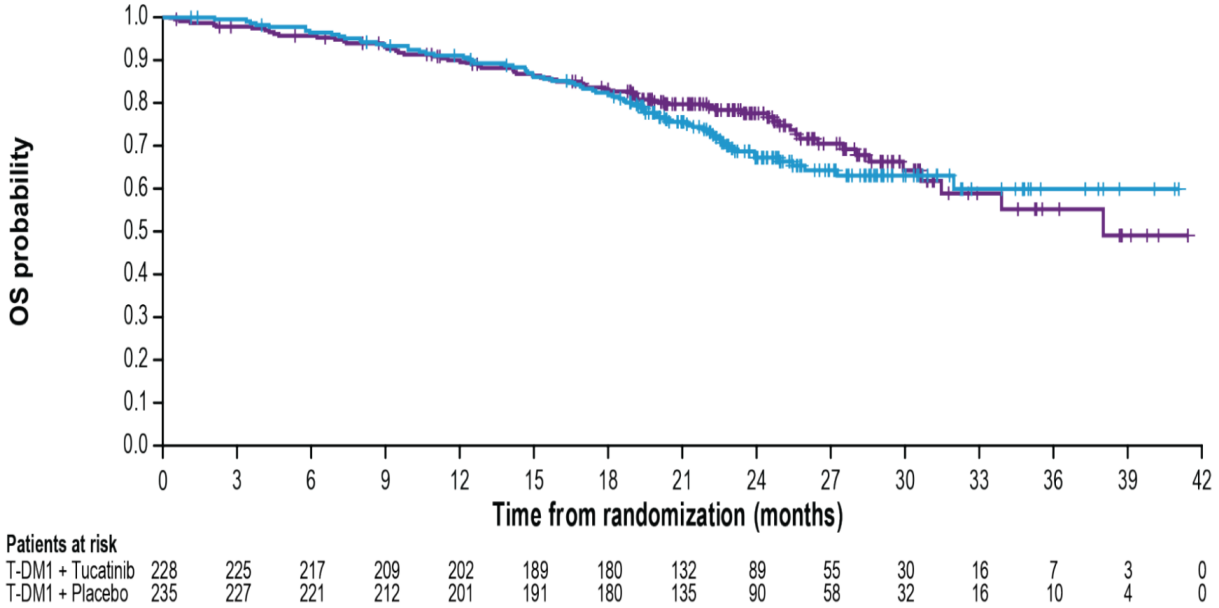
PFS in Patients With BMs	T-DM1 + Tucatinib (n=228)	T-DM1 + Placebo (n=235)
# of events	70	85
Median PFS, mo (95% CI)	7.8 (6.7-10.0)	5.7 (4.6-7.5)
HR (95% CI)	0.64 (0.46-0.89)	

- PFS benefit was consistent across prespecified subgroups

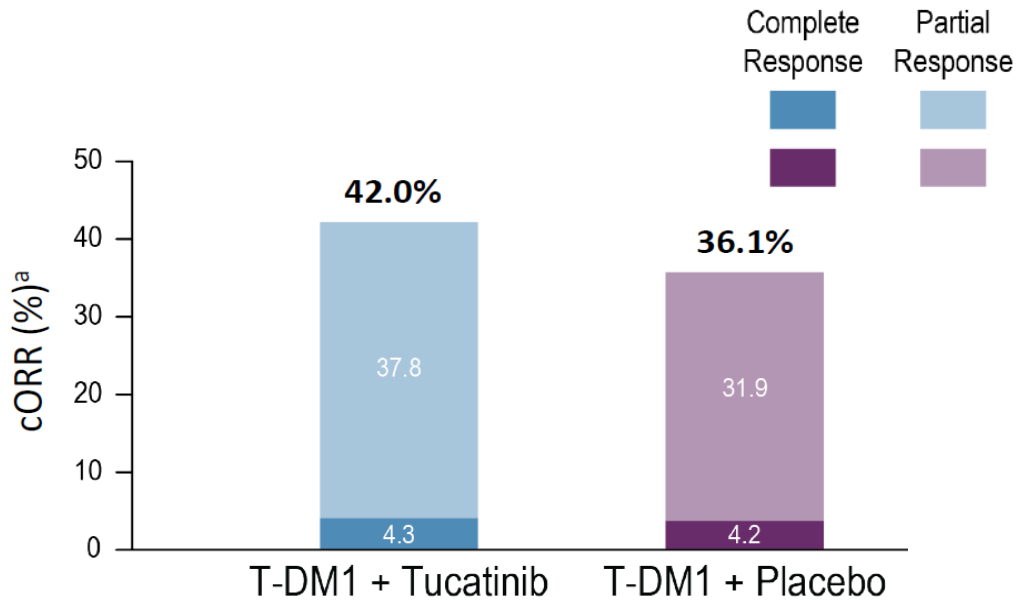
Hurvitz S, et al. SABCS 2023. Abstract GS01-10.

HER2CLIMB-02 Trial of Tucatinib + T-DM1 in Previously Treated HER2+ MBC: OS and ORR

OS



Confirmed ORR[a]



OS	T-DM1 + Tucatinib (n=228)	T-DM1 + Placebo (n=235)
# of events	71	63
Median OS, mo (95% CI)	NR (NR-NR)	38.0 (31.5-NR)
HR (95% CI)	1.23 (0.87-1.74)	

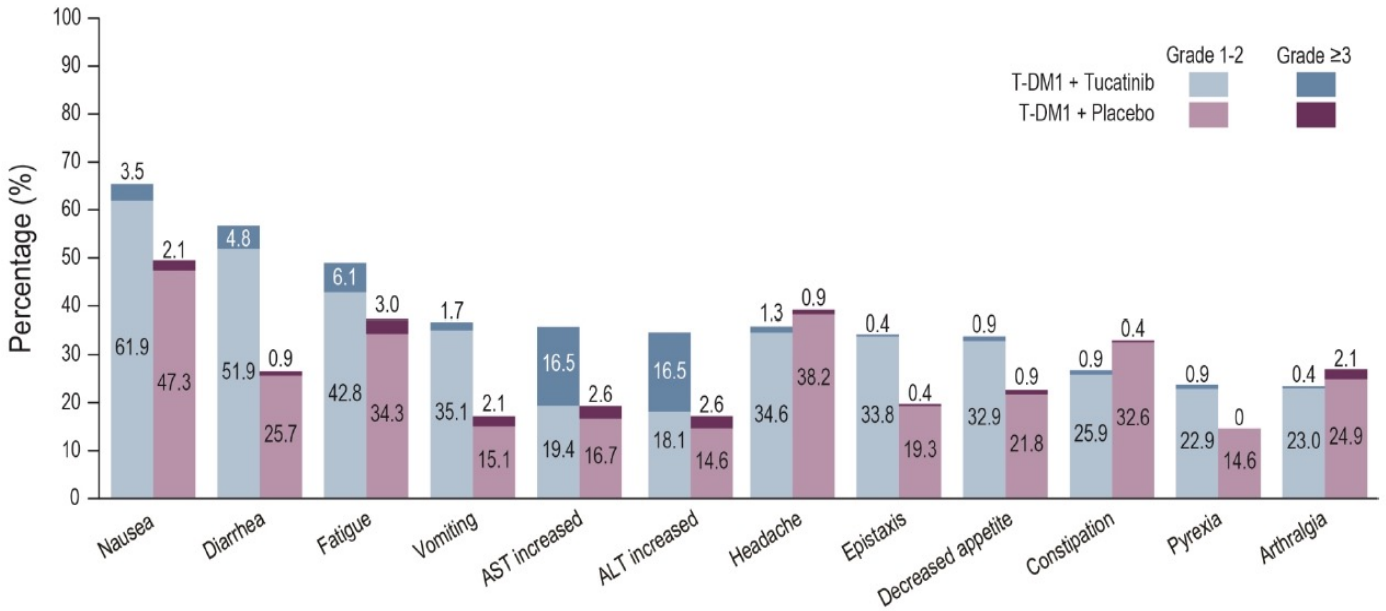
- Median follow-up was 24.4 months
- 134 of 253 (53%) prespecified events for the OS final analysis were observed (as of data cutoff)
- Interim OS results did not meet the prespecified crossing boundary of $P \leq 0.0041$

a Only patients with measurable disease were included in the cORR analysis (n=188 for T-DM1 + tucatinib arm; n=191 for T-DM1 + placebo arm).

Hurvitz S, et al. SABCS 2023. Abstract GS01-10.

HER2CLIMB-02 Trial of Tucatinib + T-DM1 in Previously Treated HER2+ MBC: Safety and Summary

Most Common TEAEs (≥20%)



Overall Safety Summary

	T-DM1 + Tucatinib (n=231)	T-DM1 + Placebo (n=233)
Any TEAE	230 (99.6)	233 (100)
Grade ≥3 TEAE	159 (68.8)	96 (41.2)
Any TE Serious AE	70 (30.3)	52 (22.3)
TEAE leading to death	3 (1.3)	2 (0.9)
Discontinued due to TEAE	40 (17.3)	16 (6.9)
Discont. T-DM1 due to TEAE	47 (20.3)	26 (11.2)

Dose Modifications Due to AEs of Interest

- Treatment-emergent hepatic AEs led to discontinuation of tucatinib and/or T-DM1 in 6.9% and 7.8% of patients, respectively, in patients receiving T-DM1 + tucatinib, compared with 2.1% of patients receiving T-DM1 + placebo
- Diarrhea led to discontinuation of tucatinib in 0.4% of patients in the T-DM1 + tucatinib arm, compared with 0% in the T-DM1 + placebo arm

Hurvitz S, et al. SABCS 2023. Abstract GS01-10.

NCCN Guidelines® Update: HER2+ MBC

Setting	Regimen	NCCN Category of Preference (Category of Evidence)
First line	Pertuzumab + trastuzumab + docetaxel	Preferred regimen (1)
	Pertuzumab + trastuzumab + paclitaxel	Preferred regimen (2A)
Second line	Fam-trastuzumab deruxtecan-nxki (T-DXd)	Preferred regimen (1) (May be considered in the first-line setting as an option for select patients, ie, those with rapid progression within 6 months of neoadjuvant or adjuvant therapy [12 months for pertuzumab-containing regimens])
Third line	Tucatinib + trastuzumab + capecitabine	Preferred regimen (1) (Preferred in patients with both systemic and CNS progression in the third-line setting or beyond; may be given in the second-line setting)
	Ado-trastuzumab emtansine (T-DM1)	Other recommended regimen (2A) (If not a candidate for T-DXd, could be considered in second line)
Fourth line and beyond (optimal sequence is not known)	Trastuzumab + docetaxel or vinorelbine	Other recommended regimen (2A)
	Trastuzumab + paclitaxel ± carboplatin	Other recommended regimen (2A)
	Capecitabine + trastuzumab or lapatinib	Other recommended regimen (2A)
	Trastuzumab + lapatinib (without cytotoxic therapy)	Other recommended regimen (2A)
	Trastuzumab + other chemotherapy agents	Other recommended regimen (2A)
	Neratinib + capecitabine	Other recommended regimen (2A)
	Margetuximab-cmkb + chemotherapy (Capecitabine, eribulin, gemcitabine, or vinorelbine)	Other recommended regimen (2A)

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer. V.2.2024. Accessed March 14, 2024.

Thank You

- The West Cancer Center and Research Institute