2025 ASCO ANNUAL MEETING

DESTINY Breast09

Trastuzumab deruxtecan (T-DXd) + pertuzumab vs taxane + trastuzumab + pertuzumab (THP) for first-line treatment of patients with human epidermal growth factor receptor 2–positive (HER2+) advanced/metastatic breast cancer: interim results from DESTINY-Breast09

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Monday, June 2, 2025

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On behalf of the DESTINY-Breast09 investigators

Key takeaways

44%
Reduction in risk of disease progression or death with T-DXd + P vs THP (by BICR)

- **T-DXd + P** demonstrated a **PFS improvement** vs the established first-line standard of care (THP) in HER2+ a/mBC
- Safety of T-DXd + P was **consistent with known profiles of individual treatments**

T-DXd + P demonstrated a statistically significant and clinically meaningful PFS benefit vs THP that was consistently observed across subgroups and may represent a new first-line standard of care for patients with HER2+ a/mBC

a/mBC, advanced/metastatic breast cancer; BICR, blinded independent central review; HER2+, human epidermal growth factor receptor 2–positive; P, pertuzumab; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

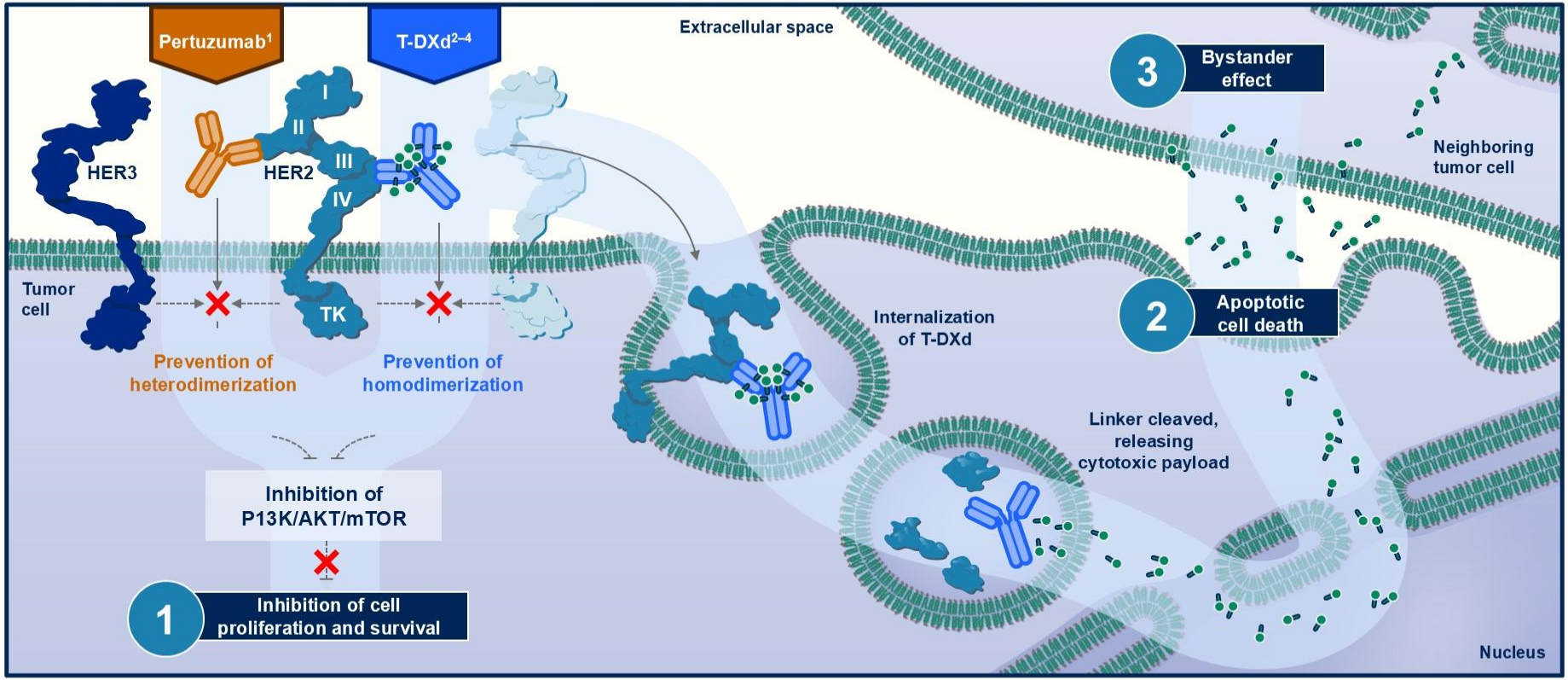
Evolution of T-DXd in HER2+ a/mBC

Observed mPFS*

*Comparisons are hypothesis-generating only as it is not possible to directly compare the studies due to differences in trial population and design; †capecitabine plus trastuzumab or lapatinib
1L, first line; 2L, second line; 3L, third line; a/mBC, advanced/metastatic breast cancer; CTx, chemotherapy; HER2+, human epidermal growth factor receptor 2–positive; mo, months; mPFS, median progression-free survival; P, pertuzumab; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice; THP, taxane + trastuzumab + pertuzumab

1. Baselga J, et al. *N Engl J Med.* 2012;366:109–119; 2. Cottu P, et al. *Breast Cancer Res Treat.* 2024;209:419–430; 3. Hurvitz SA, et al. *Lancet.* 2023;401:105–117; 4. André F, et al. *Lancet.* 2023;401:1773–1785; 5. Modi S, et al. *N Engl J Med.* 2020;382:610–621

Rationale for combining pertuzumab with T-DXd



AKT, protein kinase B; HER2/3, human epidermal growth factor receptor 2/3; mTOR, mammalian target of rapamycin; P13K, phosphoinositide 3-kinase; T-DXd, trastuzumab deruxtecan; TK, tyrosine kinase

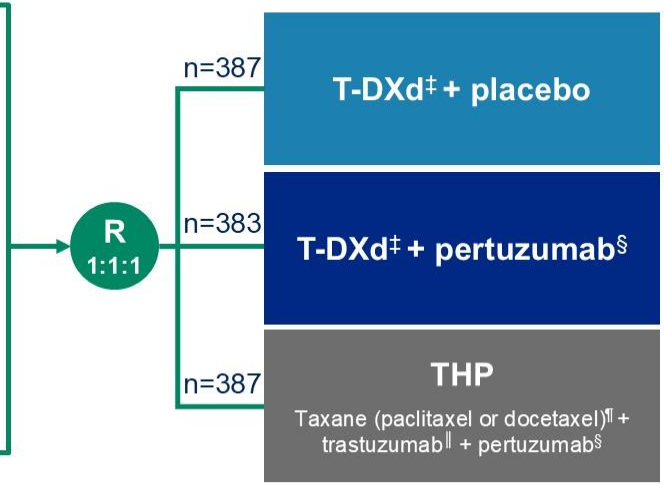
1. Nami B, et al. *Cancers (Basel).* 2018;10:342; 2. Nakada T, et al. *Chem Pharm Bull (Tokyo).* 2019;67:173-185; 3. Ogitani Y, et al. *Clin Cancer Res.* 2016;22:5097–5108; 4. Geng W, et al. *Eur J Pharmacol.* 2024:977:176725

DESTINY-Breast09 study design

A randomized, multicenter, open-label,* Phase 3 study (NCT04784715)

Eligibility criteria

- HER2+ a/mBC
- Asymptomatic/inactive brain mets allowed
- DFI >6 mo from last chemotherapy or HER2-targeted therapy in neoadjuvant/adjuvant setting
- One prior line of ET for mBC permitted
- **No other prior systemic treatment for mBC†**



Endpoints

Primary

- PFS (BICR)

Key secondary

- OS

Secondary

- PFS (INV)
- ORR (BICR/INV)
- DOR (BICR/INV)
- PFS2 (INV)
- Safety and tolerability

Stratification factors

- De-novo vs recurrent mBC
- HR+ or HR−
- *PIK3CA*m (detected vs non-detected)

- If T-DXd was discontinued due to AEs (except Grade >2 ILD), patients could switch to trastuzumab**
- Concurrent use of ET (AI or tamoxifen) was allowed for those with HR+ disease after six cycles of T-DXd or discontinuation of taxane in THP arm

*Open label for THP arm. Double blinded for pertuzumab in experimental arms; †HER2-targeted therapy or chemotherapy; ‡5.4 mg/kg Q3W; §840 mg loading dose, then 420 mg Q3W; ¶paclitaxel 80 mg/m^2 QW or 175 mg/m^2 Q3W, or docetaxel 75 mg/m^2 Q3W for a minimum of six cycles or until intolerable toxicity; ‖8 mg/kg loading dose, then 6 mg/kg Q3W; **without loading dose

AE, adverse event; AI, aromatase inhibitor; a/mBC, advanced/metastatic breast cancer; BICR, blinded independent central review; DFI, disease-free interval; DOR, duration of response; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HER2+, HER2-positive; HR+/−, hormone receptor–positive/–negative; ILD, interstitial lung disease; INV, investigator; mets, metastases; mo, months; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PFS2, second progression-free survival; *PIK3CA*m, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha mutation; Q3W, every 3 weeks; QW, once every week; R, randomization; T-DXd, trastuzumab deruxtecan

NCT04784715. Updated. May 6, 2025. Available from: https://clinicaltrials.gov/study/NCT04784715 (Accessed May 29, 2025)

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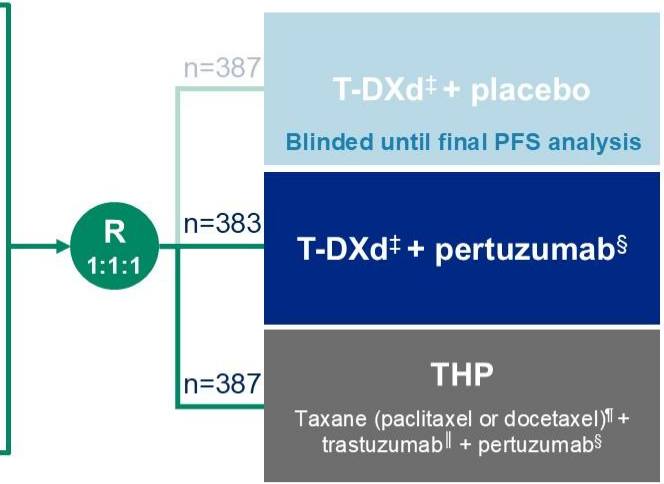


Endpoints

Primary

- PFS (BICR)

Key secondary

- OS

Secondary

- PFS (INV)
- ORR (BICR/INV)
- DOR (BICR/INV)
- PFS2 (INV)
- Safety and tolerability

At this planned interim analysis (DCO Feb 26, 2025), results are reported for the T-DXd + P and THP arms

*Open label for THP arm. Double blinded for pertuzumab in experimental arms; †HER2-targeted therapy or chemotherapy; ‡5.4 mg/kg Q3W; §840 mg loading dose, then 420 mg Q3W; ¶paclitaxel 80 mg/m^2 QW or 175 mg/m^2 Q3W, or docetaxel 75 mg/m^2 Q3W for a minimum of six cycles or until intolerable toxicity; ‖8 mg/kg loading dose, then 6 mg/kg Q3W

a/mBC, advanced/metastatic breast cancer; BICR, blinded independent central review; DCO, data cutoff; DFI, disease-free interval; DOR, duration of response; HER2, human epidermal growth factor receptor 2; HER2+, HER2-positive; HR+/−, hormone receptor–positive/–negative; INV, investigator; mBC, metastatic breast cancer; mets, metastases; mo, months; ORR, objective response rate; OS, overall survival; P, pertuzumab; PFS, progression-free survival; PFS2, second progression-free survival; *PIK3CA*m, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha mutation; Q3W, every 3 weeks; QW, once every week; R, randomization; T-DXd, trastuzumab deruxtecan

NCT04784715. Updated. May 6, 2025. Available from: https://clinicaltrials.gov/study/NCT04784715 (Accessed May 29, 2025)

Statistical analysis

Interim analysis for PFS by BICR

(planned after approximately 399 events across three arms, and at least 277 events per comparison)

- At this DCO (Feb 26, 2025), interim analysis criterion for superiority (P-value <0.00043) was already met for T-DXd + P vs THP (**maturity: ~38% of total N**)
- T-DXd + placebo remains blinded until final PFS analysis per protocol

First interim OS analysis

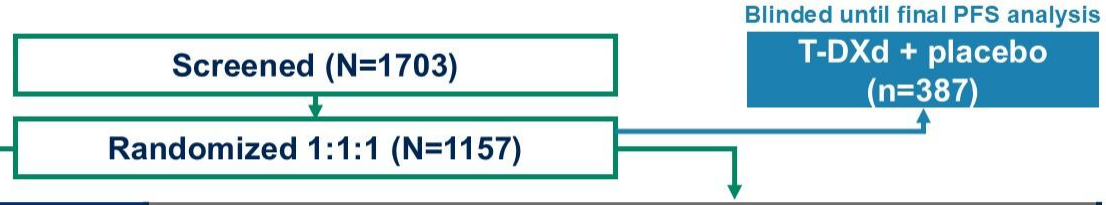
(prespecified)

- At DCO, 126 events had occurred (**maturity: ~16% of total N**)
- Final OS analysis will be conducted per protocol

BICR, blinded independent central review; DCO, data cutoff; OS, overall survival; P, pertuzumab; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

PRESENTED BY: Sara M Tolaney, MD, MPH

Patient disposition



Discontinuation reasons, %*	T-DXd + P (n=383) Treated (n=380; 99.2%)	THP (n=387) Treated (n=383; 99.0%)‡	
	Discontinued **T-DXd** (59.7%)*†	Discontinued **taxane** (96.3%)*	Discontinued **trastuzumab** (66.6%)*
PD	21.3	18.8	52.5
AE	20.8	25.8	3.4
Patient decision	11.1	7.3	5.7
Protocol deviation	0.3	0.3	0.3
Lost to follow up	–	0.5	0.5
Other	2.4	43.6§	3.7
Death	3.9	–	0.5

- In the T-DXd + P arm, **8.7% (n=33/380)** of patients switched to trastuzumab (+ P) after discontinuation of T-DXd for reasons other than PD
- Concurrent ET use was **13.5% (T-DXd + P)** vs **38.3% (THP)** among patients with HR+ disease¶

At DCO, 39.6% (n=302) of patients remained on **any treatment**: 45.8% (n=174) T-DXd + P vs 33.4% (n=128) THP*

Median duration of follow up: 29.2 months

Pertuzumab could not be continued as a single agent without T-DXd or trastuzumab. THP was administered as per institutional standards

*Percentages are based on the patients who started treatment; †54.2% of patients discontinued all treatments; ‡64.6% (n=250) of patients were assigned to docetaxel, and 34.4% (n=133) were assigned to paclitaxel; §>50% of patients completed the minimum of six cycles of taxane per protocol; ¶patients with HR+ disease could receive ET after six cycles of T-DXd or discontinuation of taxane

AE, adverse event; DCO, data cutoff; ET, endocrine therapy; HR+, hormone receptor–positive; P, pertuzumab; PD, progressive disease; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

Patient demographics and key baseline characteristics

	T-DXd + P (n=383)	THP (n=387)
Age, median (range), years	54 (27–85)	54 (20–81)
Female, n (%)	383 (100)	387 (100)
Geographical region, n (%)		
Asia	188 (49.1)	191 (49.4)
Western Europe and North America	87 (22.7)	78 (20.2)
Rest of World	108 (28.2)	118 (30.5)
ECOG performance status, n (%)		
0 (normal activity)	256 (66.8)	246 (63.6)
1 (restricted activity)	127 (33.2)	141 (36.4)
HER2 score by central test, n (%)		
IHC 3+	318 (83.0)	315 (81.4)
IHC <3 / ISH+	62 (16.2)	71 (18.3)
IHC NR / ISH+	3 (0.8)	1 (0.3)
HR status, n (%)		
Positive*	207 (54.0)	209 (54.0)
Negative	176 (46.0)	178 (46.0)
De-novo disease at diagnosis, n (%)	200 (52.2)	200 (51.7)
***PIK3CA* mutations detected, n (%)**	116 (30.3)	121 (31.3)
Brain metastases, n (%)†	25 (6.5)	22 (5.7)
Visceral metastases, n (%)	281 (73.4)	268 (69.3)

*Defined as estrogen receptor–positive and/or progesterone receptor–positive (≥1%); †participants were eligible if they had brain metastases that were clinically inactive or treated/asymptomatic
ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IHC, immunohistochemistry; ISH, in situ hybridization; NR, not recorded; P, pertuzumab; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

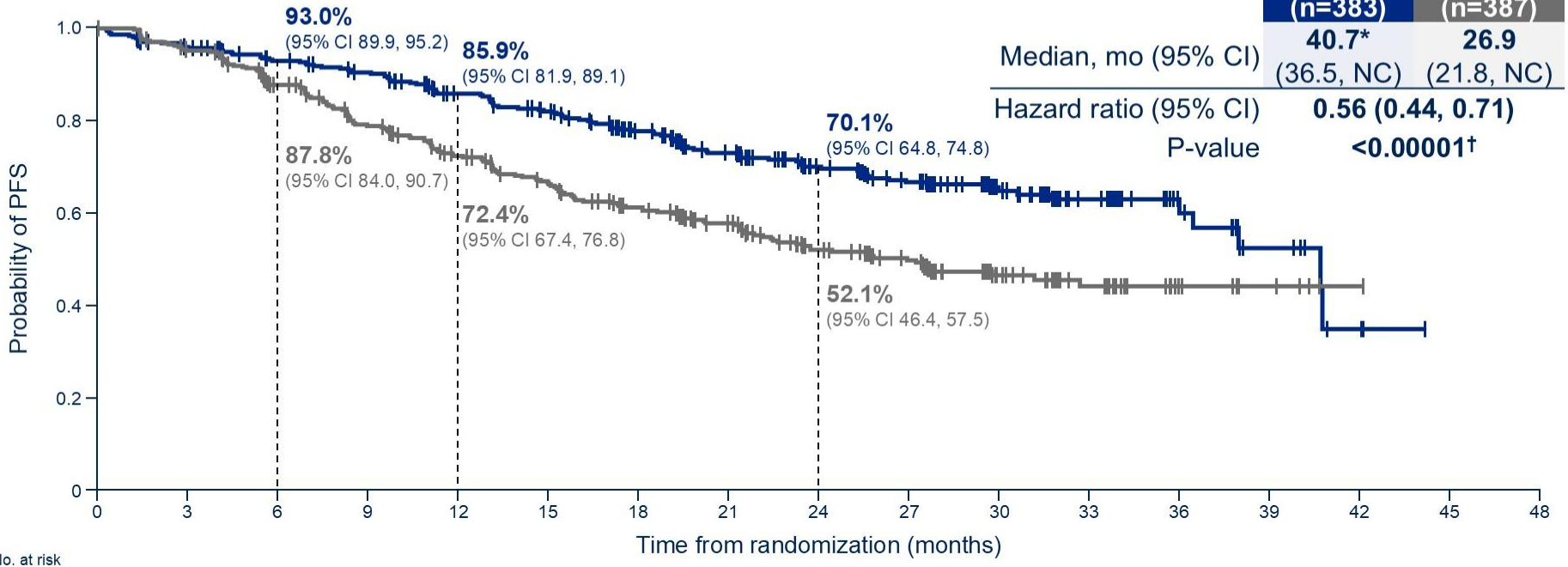
Prior therapies

	T-DXd + P (n=383)	THP (n=387)
(Neo)adjuvant setting, n (%)		
Any (neo)adjuvant treatment	166 (43.3)	169 (43.7)
Chemotherapy	159 (41.5)	152 (39.3)
Endocrine therapy	74 (19.3)	85 (22.0)
Targeted therapy	112 (29.2)	108 (27.9)
Trastuzumab	110 (28.7)	108 (27.9)
Pertuzumab	31 (8.1)	24 (6.2)
T-DM1	3 (0.8)	4 (1.0)
Pyrotinib	1 (0.3)	1 (0.3)
CDK4/6 inhibitor	0	1 (0.3)
First-line a/mBC setting, n (%)		
Endocrine therapy	5 (1.3)	5 (1.3)

a/mBC, advanced/metastatic breast cancer; CDK4/6, cyclin-dependent kinase 4/6; HER2, human epidermal growth factor receptor 2; P, pertuzumab; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

PFS (BICR): primary endpoint

	T-DXd + P (n=383)	THP (n=387)
Median, mo (95% CI)	40.7* (36.5, NC)	26.9 (21.8, NC)
Hazard ratio (95% CI)	0.56 (0.44, 0.71)	
P-value	<0.00001†	



No. at risk

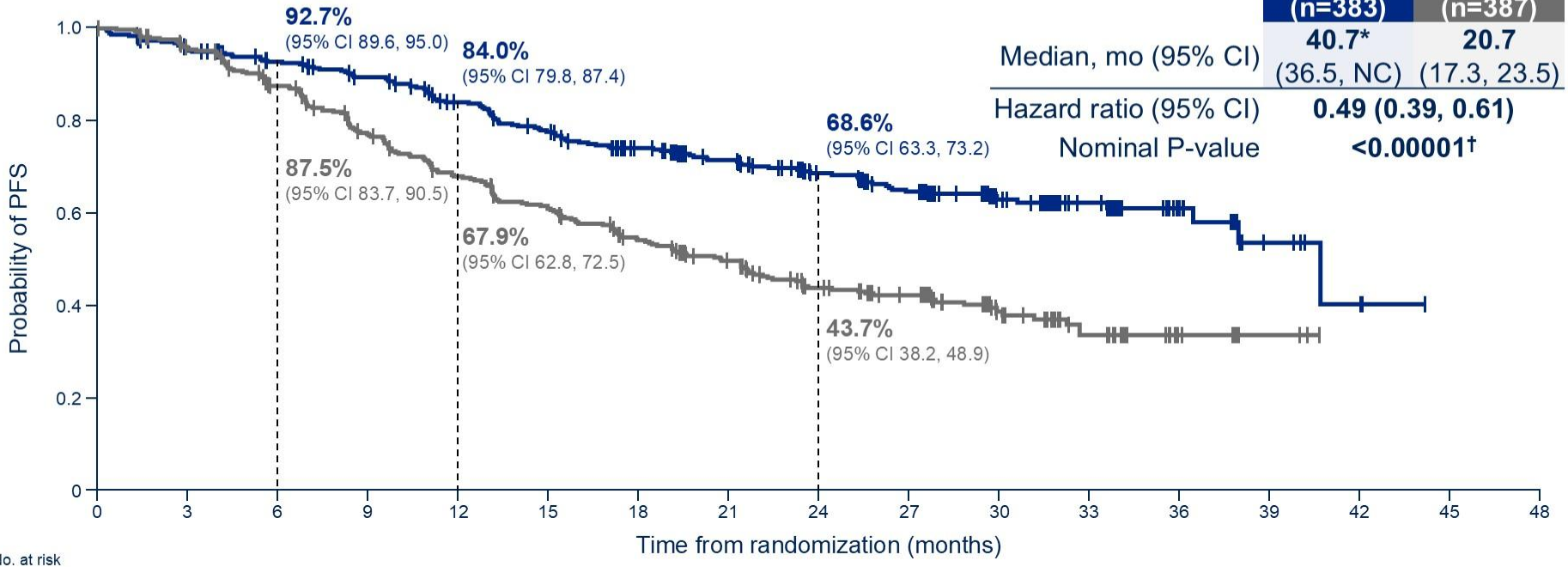
T-DXd + P	383	358	355	321	293	275	242	208	175	153	82	49	21	10	3	0
THP	387	353	312	273	241	215	187	160	124	106	51	32	12	5	1	0

Statistically significant and clinically meaningful PFS benefit with T-DXd + P (median Δ 13.8 mo)

*Median PFS estimate for T-DXd + P is likely to change at updated analysis; †stratified log-rank test. A P-value of <0.00043 was required for interim analysis superiority
BICR, blinded independent central review; CI, confidence interval; mo, months; (m)PFS, (median) progression-free survival; NC, not calculable; P, pertuzumab; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

PFS (investigator assessment)

	T-DXd + P (n=383)	THP (n=387)
Median, mo (95% CI)	40.7* (36.5, NC)	20.7 (17.3, 23.5)
Hazard ratio (95% CI)	0.49 (0.39, 0.61)	
Nominal P-value	<0.00001†	



No. at risk

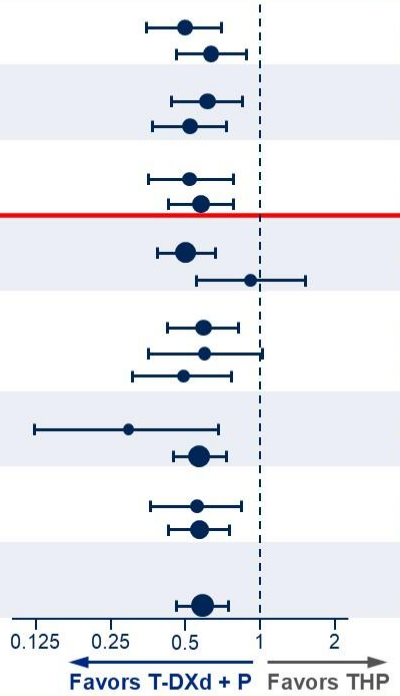
T-DXd + P	383	357	336	317	289	265	239	211	179	156	89	54	24	8	3	0
THP	387	352	315	270	235	208	176	148	115	100	47	29	10	3	0	0

Clinically meaningful improvement in PFS with T-DXd + P over THP (median Δ 20.0 mo)

*Median PFS estimate for T-DXd + P is likely to change at updated analysis; †stratified log-rank test
CI, confidence interval; mo, months; (m)PFS, (median) progression-free survival; NC, not calculable; P, pertuzumab; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

PFS (BICR): subgroup analyses

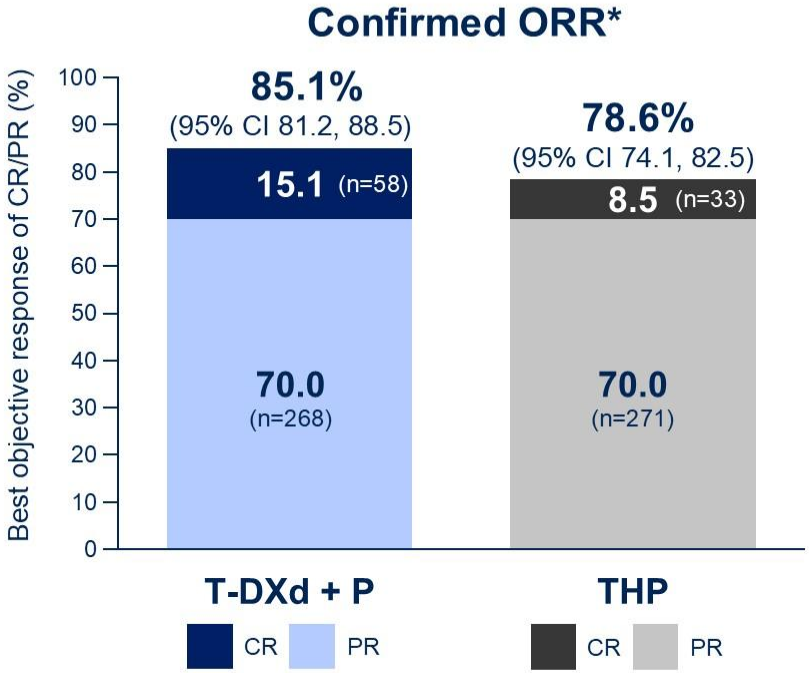
	No. of events / no. of patients		mPFS, months (95% CI)		Hazard ratio (95% CI)
	T-DXd + P	THP	T-DXd + P	THP	
Prior treatment status					
De novo	52/200	85/200	NC (36.5, NC)	31.2 (23.5, NC)	0.49 (0.35, 0.70)
Recurrent	66/183	87/187	38.0 (26.9, NC)	22.5 (18.1, NC)	0.63 (0.46, 0.87)
HR status					
Positive	65/207	87/209	38.0 (36.0, NC)	27.7 (22.4, NC)	0.61 (0.44, 0.84)
Negative	53/176	85/178	40.7 (40.7, NC)	22.6 (17.3, 32.7)	0.52 (0.37, 0.73)
***PIK3CA* mutation status**					
Detected	41/116	64/121	36.0 (29.7, NC)	18.1 (15.1, 25.6)	0.52 (0.35, 0.77)
Not detected	76/266	108/266	40.7 (38.0, NC)	32.7 (24.4, NC)	0.57 (0.43, 0.77)
Age at randomization					
<65 years	90/315	139/315	40.7 (36.5, NC)	27.4 (22.4, NC)	0.50 (0.38, 0.65)
≥65 years	28/68	33/72	27.6 (14.9, NC)	21.5 (13.9, NC)	0.92 (0.55, 1.51)
Geographical region					
Asia	62/188	87/191	40.7 (36.5, NC)	27.2 (21.5, NC)	0.60 (0.43, 0.83)
Western Europe and North America	27/87	31/78	36.0 (30.6, NC)	31.2 (15.8, NC)	0.60 (0.35, 1.01)
Rest of World	29/108	54/118	NC (38.0, NC)	24.4 (14.8, NC)	0.48 (0.30, 0.76)
Brain metastases at baseline					
Present	10/25	15/22	31.8 (18.5, NC)	9.5 (5.6, 13.3)	0.30 (0.12, 0.68)
Not present	108/358	157/365	40.7 (36.5, NC)	27.6 (22.6, NC)	0.58 (0.45, 0.74)
Prior exposure to anti-HER2 therapies					
Yes	39/115	51/112	38.0 (26.9, NC)	21.5 (15.3, NC)	0.55 (0.36, 0.83)
No	79/268	121/275	40.7 (36.5, NC)	27.6 (22.5, NC)	0.56 (0.42, 0.74)
Prior exposure to pertuzumab					
Yes	5/31	12/26	40.8 (25.4, NC)	19.8 (7.5, NC)	NC
No	113/352	160/361	40.7 (36.0, NC)	27.4 (22.4, NC)	0.61 (0.48, 0.77)



Size of circle is proportional to the number of events
BICR, blinded independent central review;
CI, confidence interval; HER2, human epidermal growth factor receptor 2; HR, hormone receptor;
NC, not calculable; P, pertuzumab;
(m)PFS, (median) progression-free survival;
T-DXd, trastuzumab deruxtecan;
THP, taxane + trastuzumab + pertuzumab

PFS benefit with T-DXd + P vs THP was consistently observed across prespecified subgroups, including stratification factors

ORR and DOR (BICR)

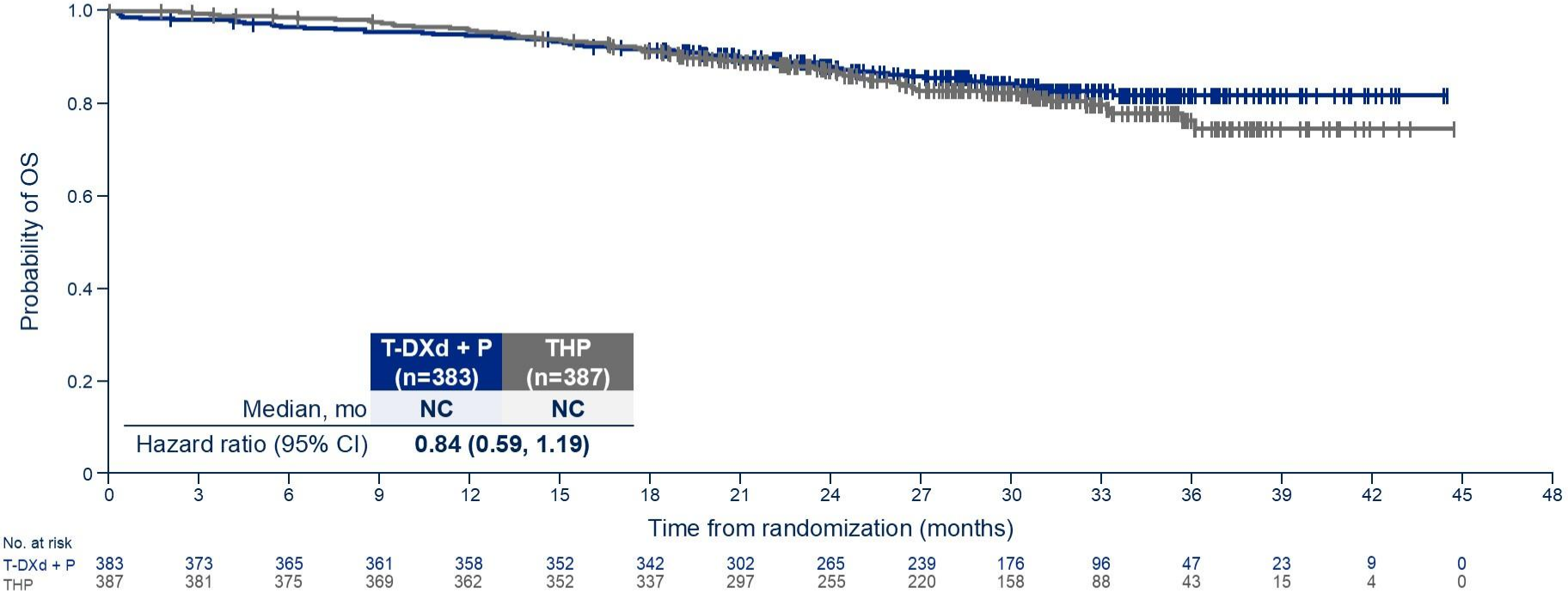


	T-DXd + P (n=383)	THP (n=387)
Median DOR, mo (95% CI)	39.2 (35.1, NC)	26.4 (22.3, NC)
Remaining in response at 24 mo (%)	73.3	54.9
Stable disease, n (%)	38 (9.9)	56 (14.5)

Response rates were greater with T-DXd + P vs THP and were durable

*Based on RECIST v1.1; response required confirmation after 4 weeks
BICR, blinded independent central review; CI, confidence interval; CR, complete response; DOR, duration of response; mo, months; NC, not calculable; ORR, objective response rate; P, pertuzumab; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

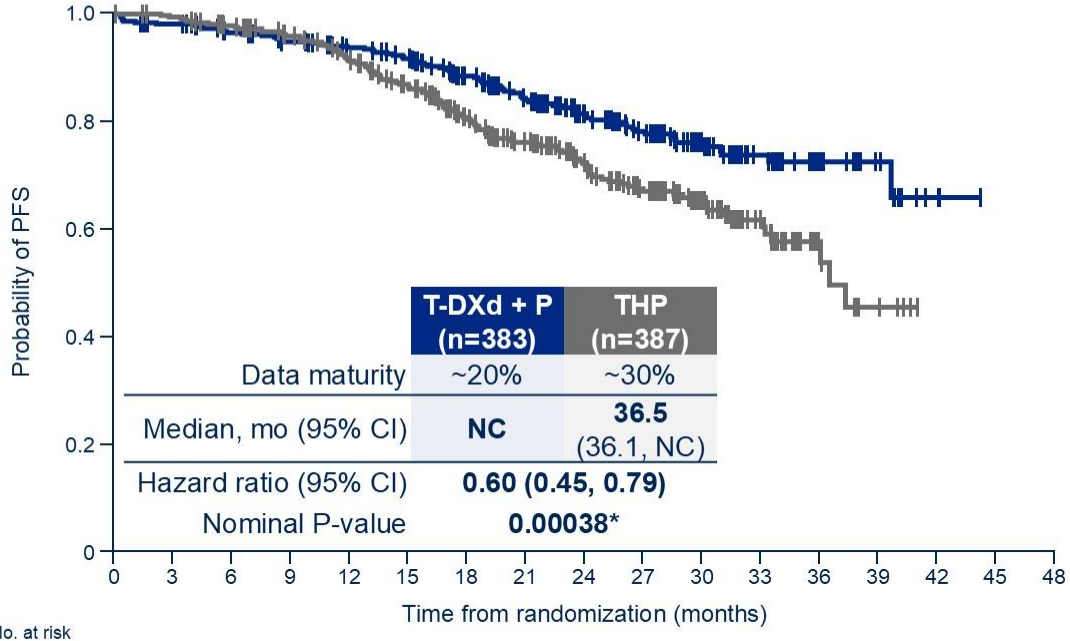
Overall survival (~16% maturity)



Early OS data suggest a positive trend favoring T-DXd + P over THP

CI, confidence interval; OS, overall survival; NC, not calculable; P, pertuzumab; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

PFS2 (investigator assessment) and post-trial treatments



	T-DXd + P (n=383)	THP (n=387)
Data maturity	~20%	~30%
Median, mo (95% CI)	**NC**	**36.5** (36.1, NC)
Hazard ratio (95% CI)	**0.60 (0.45, 0.79)**	
Nominal P-value	**0.00038***	

No. at risk

T-DXd + P	383	370	356	343	331	320	290	254	209	180	101	59	28	12	3	0
THP	387	373	358	341	319	292	252	212	174	143	80	48	15	5	0	0

	T-DXd + P (n=383)	THP (n=387)
Received post-discontinuation therapy in second line, n (%)†	124 (32.4)	181 (46.8)
Targeted therapy, n (%)†	111 (29.0)	166 (42.9)
T-DXd	6 (1.6)	39 (10.1)
T-DM1	7 (1.8)	47 (12.1)
Trastuzumab-containing regimen‡	78 (20.4)	51 (13.2)
Pertuzumab-containing regimen‡	53 (13.8)	34 (8.8)
Chemotherapy, n (%)†	68 (17.8)	57 (14.7)
Docetaxel	24 (6.3)	8 (2.1)
Paclitaxel	18 (4.7)	4 (1.0)
Capecitabine	24 (6.3)	35 (9.0)
Endocrine therapy, n (%)†	19 (5.0)	13 (3.4)

Clinically meaningful improvement in PFS2 with T-DXd + P vs THP

PFS2 was defined by investigators according to local standard clinical practice as the time from randomization to second progression (earliest progression event following first subsequent therapy) or death
*Stratified log-rank test; †percentages are based on the overall population. Therapies listed are not exhaustive. Patients may have received more than one type of therapy; ‡patients may have received trastuzumab and pertuzumab concurrently
CI, confidence interval; NC, not calculable; P, pertuzumab; PFS2, second progression-free survival; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

Overall safety summary

	Safety analysis set*	
	T-DXd + P (n=381)	THP (n=382)
Total exposure, patient years	659.7	564.0
Any TEAE, n (%)	380 (99.7)	378 (99.0)
Possibly treatment-related TEAEs (investigator assessed), n (%)	373 (97.9)	369 (96.6)
Grade ≥3	209 (54.9)	200 (52.4)
Serious TEAEs, n (%)	103 (27.0)	96 (25.1)
TEAEs associated with any treatment discontinuation,† n (%)	79 (20.7)	108 (28.3)
TEAEs associated with any dose interruptions,† n (%)	262 (68.8)	187 (49.0)
TEAEs associated with any dose reductions,† n (%)	175 (45.9)	76 (19.9)
TEAEs with outcome of death, n (%)	13 (3.4)	3 (0.8)
Possibly treatment related (investigator assessed)‡	5 (1.3)	1 (0.3)

Median total treatment duration:

- **T-DXd + P: 21.7 mo (range 0.3–44.5)**
  - T-DXd: 20.0 mo§
- **THP: 16.9 mo (range 0.7–41.7)**

Median treatment duration for taxanes:

- Docetaxel: 5.5 mo (range 0.7–37.4)
- Paclitaxel: 4.4 mo (range 0.2–30.7)

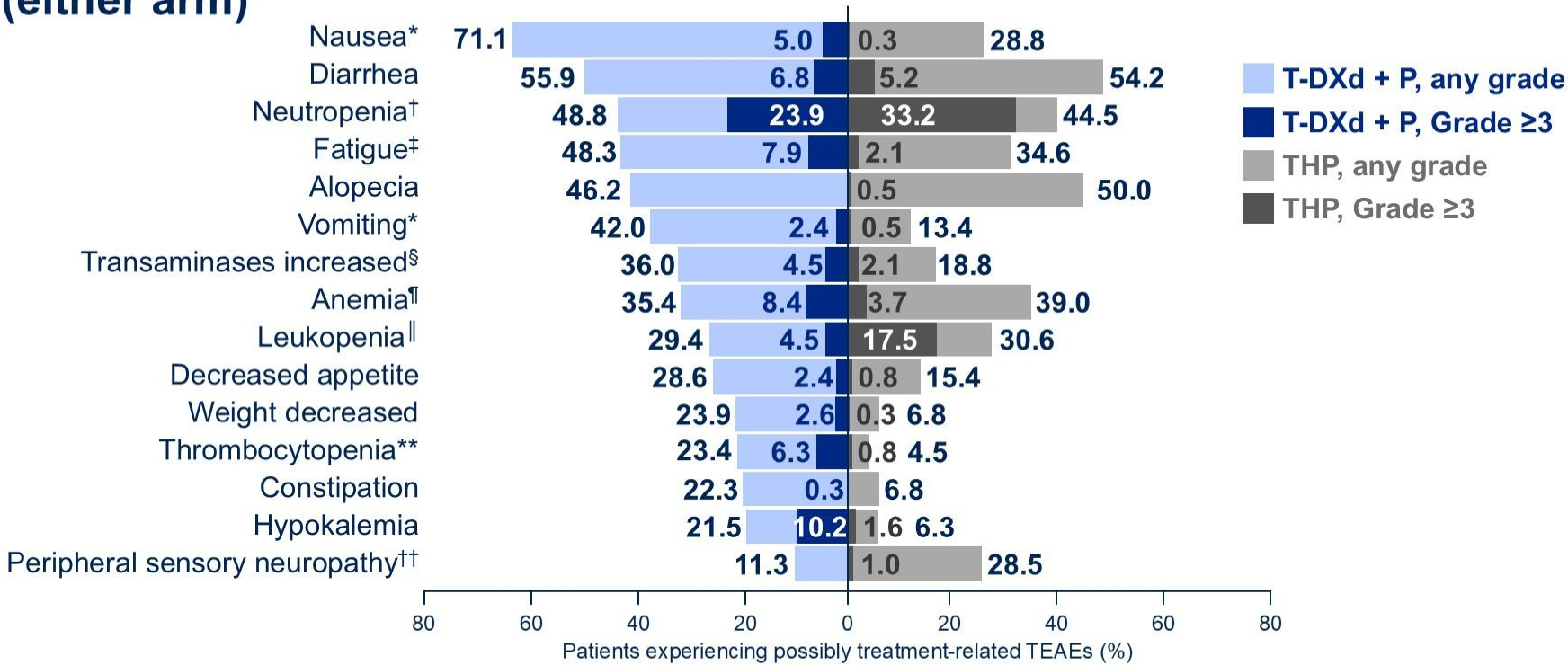
Median number of cycles for taxanes:

- Docetaxel: 8 (range 1–51)
- Paclitaxel: 6 (range 1–42)

*Safety analyses included all patients who received at least one dose of study treatment (at least one study drug); †dose modifications or discontinuations relate to any component of each arm; ‡treatment-related TEAEs with outcome of death were pneumonitis (n=1), sepsis (n=1), septic shock (n=1), febrile neutropenia (n=1), and dyspnea (n=1) in the T-DXd + P arm, and anemia (n=1) in the THP arm; §excludes data from the 8.7% (33/380) of treated patients who received trastuzumab after discontinuing T-DXd due to TEAEs

mo, months; P, pertuzumab; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event; THP, taxane + trastuzumab + pertuzumab

Possibly treatment-related (investigator assessed) TEAEs in ≥20% of patients (either arm)



*Antiemetic prophylaxis was recommended but not mandated by protocol; †neutropenia (grouped term) includes: neutropenia and neutrophil count decreased; ‡fatigue (grouped term) includes: fatigue, asthenia, malaise, and lethargy; §transaminases increased (grouped term) includes: transaminases increased, aspartate aminotransferase increased, alanine aminotransferase increased, gamma-glutamyltransferase increased, liver function test abnormal, hepatic function abnormal, and liver function test increase; ¶anemia (grouped term) includes: anemia, hemoglobin decreased, hematocrit decreased, and red blood cell count decreased; ‖leukopenia (grouped term) includes: leukopenia and white blood cell count decreased; **thrombocytopenia (grouped term) includes: platelet count decreased and thrombocytopenia; ††peripheral sensory neuropathy (grouped term) includes: neuropathy peripheral, peripheral sensory neuropathy, and polyneuropathy
P, pertuzumab; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event; THP, taxane + trastuzumab + pertuzumab

Adverse events of special interest

Adjudicated drug-related ILD/pneumonitis*

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
T-DXd + P (n=381)	17 (4.5)	27 (7.1)	0	0	2 (0.5)	46 (12.1)
THP (n=382)	2 (0.5)	2 (0.5)	0	0	0	4 (1.0)

Left ventricular dysfunction†

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
T-DXd + P (n=381)	4 (1.0)	30 (7.9)	7 (1.8)	1 (0.3)	0	42 (11.0)
THP (n=382)	1 (0.3)	19 (5.0)	7 (1.8)	0	0	27 (7.1)

Safety analysis set
*Adjudicated drug-related ILD/pneumonitis (grouped term) includes: chronic obstructive pulmonary disease, interstitial lung disease, organizing pneumonia, pneumonia, and pneumonitis, †left ventricular dysfunction (grouped term) includes: potential heart failure, cardiac failure, cardiac failure chronic, ejection fraction decreased, left ventricular dysfunction, and right ventricular failure
ILD, interstitial lung disease; P, pertuzumab; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

Conclusions

- T-DXd + P demonstrated a **statistically significant and clinically meaningful PFS benefit** by BICR vs THP, which was consistently observed across subgroups
  - Hazard ratio of **0.56** vs THP (**P<0.00001**)
  - Median PFS was **40.7 months (T-DXd + P)** vs **26.9 months (THP)**
- Median DOR of **>3 years with T-DXd + P**, with CRs in **15.1% (T-DXd + P)** vs **8.5% (THP)**
- Early OS data suggest a positive trend favoring T-DXd + P, with a supportive hazard ratio of **0.60** for PFS2
- T-DXd + P safety data were **consistent with known profiles of individual treatments**

PFS by BICR

44%

Reduction in risk of disease progression or death with T-DXd + P vs THP

T-DXd + P demonstrated a statistically significant and clinically meaningful PFS benefit vs THP and may represent a new first-line standard of care for patients with HER2+ a/mBC

a/mBC, advanced/metastatic breast cancer; BICR, blinded independent central review; CR, complete response; DOR, duration of response; HER2+, human epidermal growth factor receptor 2–positive; OS, overall survival; P, pertuzumab; PFS, progression-free survival; PFS2, second progression-free survival; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

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Acknowledgments

Thank you:

- **Patients and their families for their participation**
- **Study site staff for their contributions**
- **Members of the independent data monitoring committee and the interstitial lung disease adjudication committee**

This study was sponsored and designed by:
AstraZeneca
Daiichi Sankyo

Medical writing support was funded by AstraZeneca and provided by: Conor O'Boyle, PhD and Stephen Purver, MChem (Helios Medical Communications, part of Helios Global Group)

Supplementary content is available:
- Plain language summary infographic
- ASCO patient summary