SINGAPORE 2025 ESMO ASIA

DESTINY Breast09

Trastuzumab deruxtecan (T-DXd) + pertuzumab (P) vs taxane + trastuzumab + pertuzumab (THP) for first-line treatment of Asian patients with HER2+ advanced/metastatic breast cancer: a DESTINY-Breast09 analysis

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Saturday, December 6, 2025

Presentation 88MO

Declaration of interests

Professor Takano, MD, PhD declares financial interests in:

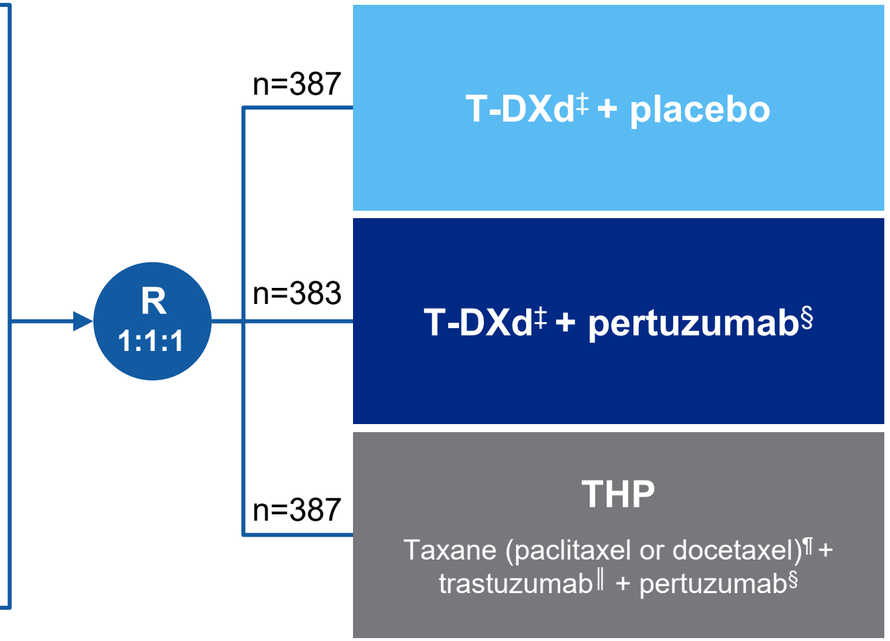
- Daiichi Sankyo
- Chugai Pharmaceutical Co.
- Eli Lilly
- Gilead Sciences

DESTINY-Breast09 study design[1,2]

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

Eligibility criteria

- HER2+ a/mBC
- Asymptomatic/inactive brain mets allowed
- DFI >6 mo from completion of chemotherapy or HER2-targeted therapy in neoadjuvant/adjuvant setting and diagnosis of a/mBC
- 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. Blinded for pertuzumab or placebo 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–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; Q3W, every 3 weeks; QW, once every week; R, randomization; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

1. NCT04784715. Updated. August 1, 2025. Available from: https://clinicaltrials.gov/study/NCT04784715 (Accessed November 3, 2025); 2. Tolaney SM, et al. Oral presentation at ASCO 2025 (Abstract LBA1008)

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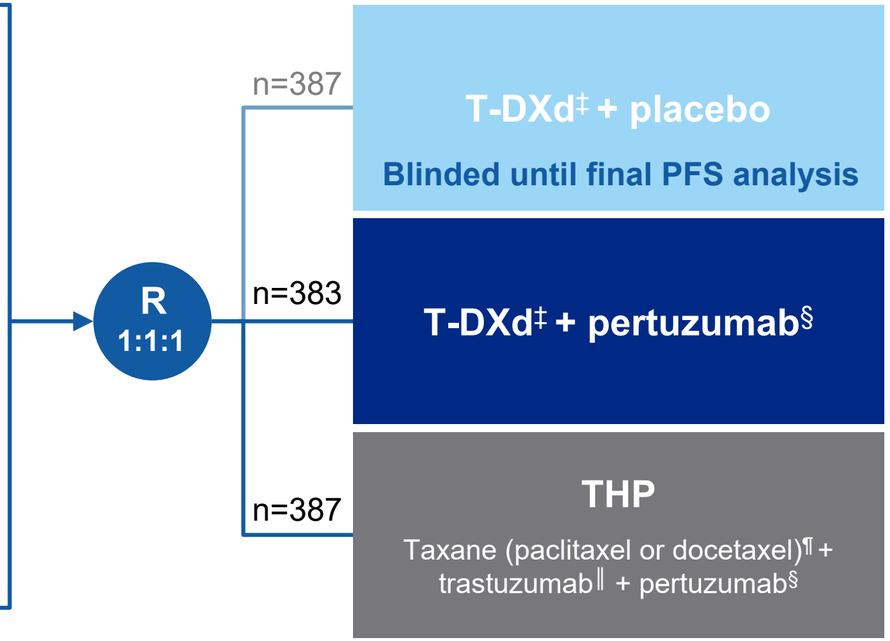

Endpoints

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- HR+ or HR−
- *PIK3CA*m (detected vs non-detected)

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

*Open label for THP arm. Blinded for pertuzumab or placebo 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

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Patient disposition

DESTINY-Breast09

Blinded until final PFS analysis

T-DXd + placebo
(Overall n=387; Asian subgroup n=170)

	Overall population[1]		Asian subgroup	
Screened	1703		728	
Randomized 1:1:1	1157		516	
	T-DXd + P	**THP‡**	**T-DXd + P**	**THP‡**
Randomized, n	383	387	174	172
Treated, n (%)	380 (99.2)	383 (99.0)	174 (100)	171 (99.4)
Ongoing treatment, n (%)	174 (45.8)	128 (33.4)	82 (47.1)	62 (36.3)
Discontinued treatment, %*	**T-DXd**: 59.7†	**Taxane**: 96.3 **Trastuzumab**: 66.6	**T-DXd**: 57.5†	**Taxane**: 93.0 **Trastuzumab**: 63.7
Switched to trastuzumab after discontinuation, %	8.7	N/A	7.5	N/A

- A total of 346 patients were randomized from the following Asian countries/regions: mainland China (155 [44.8%]), Japan (70 [20.2%]), Republic of Korea (56 [16.2%]), Taiwan (31 [9.0%]), and Philippines (34 [9.8%])
- Median duration of follow up: 29.2 months (overall); 30.2 months (Asian subgroup)
- Reasons for treatment discontinuation, baseline characteristics, and prior therapies were generally consistent with the overall population[1]

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% (overall) and 52.9% (Asian) of patients discontinued all treatments*; ‡64.6% (n=250) of patients received docetaxel and 34.4% (n=133) received paclitaxel
P, pertuzumab; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab
1. Tolaney SM, et al. Oral presentation at ASCO 2025 (Abstract LBA1008)

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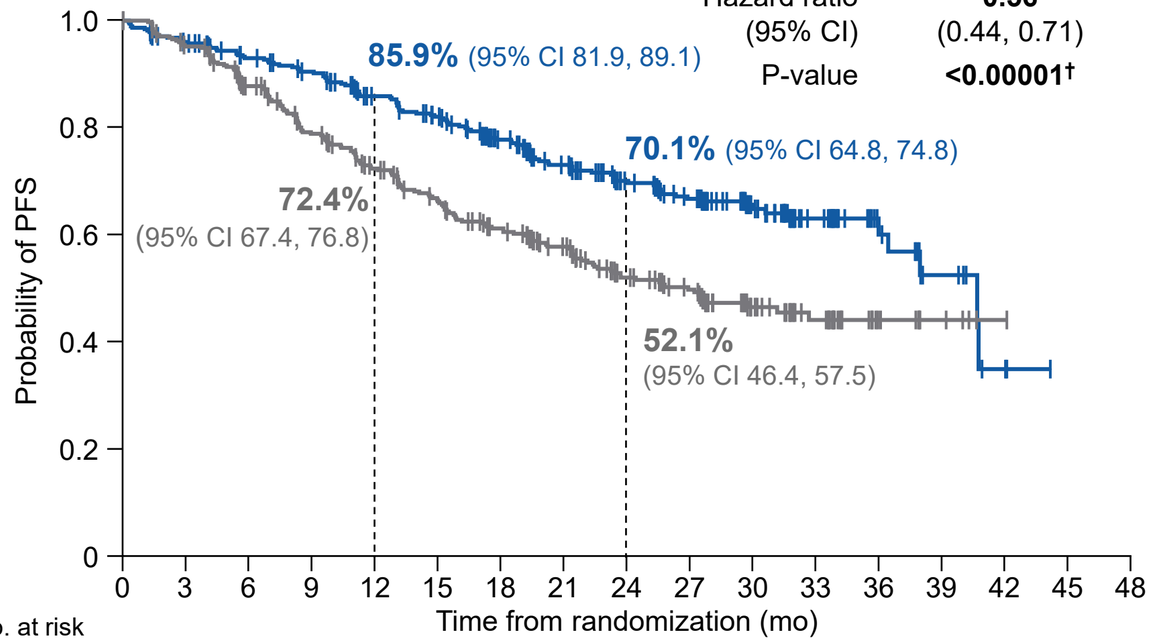
PFS (BICR): primary endpoint

Overall population[1]

	T-DXd + P	THP
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†**	

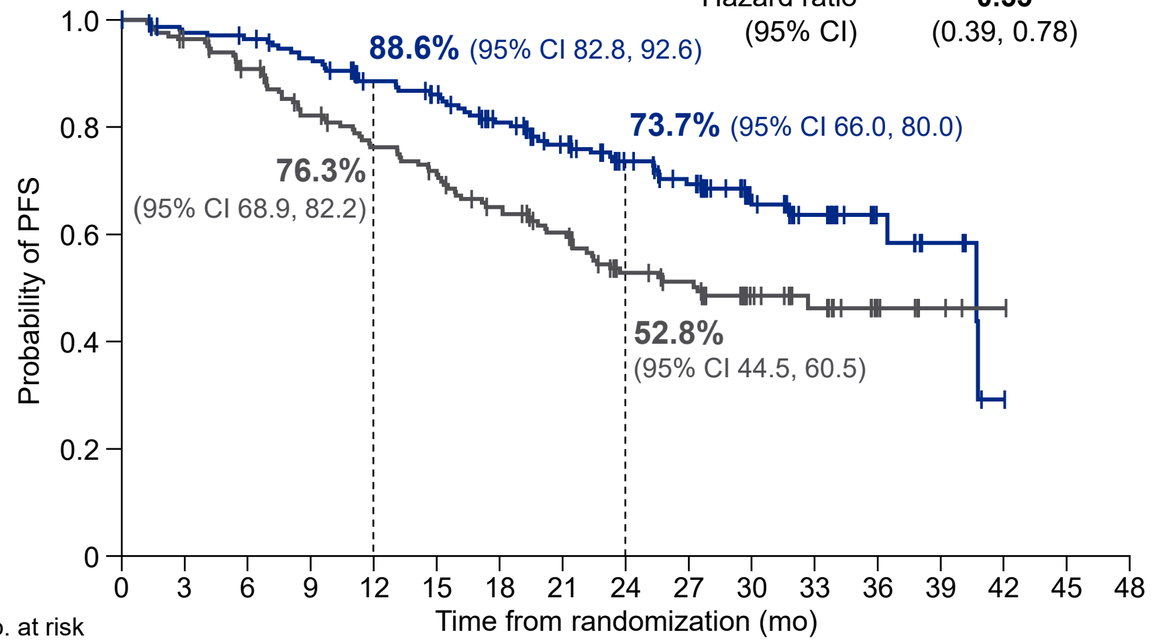


No. at risk

T-DXd + P	383	358	335	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

Asian subgroup

	T-DXd + P	THP
Median, mo (95% CI)	**40.7*** (36.5, NC)	**27.4** (21.5, NC)
Hazard ratio (95% CI)	**0.55** (0.39, 0.78)	



No. at risk

T-DXd + P	174	166	163	155	142	135	120	106	91	79	40	28	12	6	1	0
THP	172	160	147	129	118	110	97	84	64	59	31	21	8	3	1	0

Clinically meaningful improvement in median PFS by BICR with T-DXd + P, consistent with the overall population

*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; NC, not calculable; P, pertuzumab; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

1. Tolaney SM, et al. Oral presentation at ASCO 2025 (Abstract LBA1008)

Toshimi Takano, MD, PhD

Additional efficacy outcomes

	Overall population[1]		Asian subgroup	
	T-DXd + P (n=383)	THP (n=387)	T-DXd + P (n=174)	THP (n=172)
Median OS, mo (95% CI)	NC (NC, NC)	NC (NC, NC)	NC (NC, NC)	NC (NC, NC)
Hazard ratio (95% CI)	0.84 (0.59, 1.19)		0.56 (0.29, 1.02)	
Data maturity	~16%		~12%	
Median PFS (investigator), mo (95% CI)	40.7* (36.5, NC)	20.7 (17.3, 23.5)	40.7* (36.5, NC)	21.5 (19.1, 28.8)
Hazard ratio (95% CI)	0.49 (0.39, 0.61)		0.47 (0.33, 0.65)	
Confirmed ORR (BICR),† % (95% CI)	85.1 (81.2, 88.5)	78.6 (74.1, 82.5)	89.7 (84.1, 93.8)	84.3 (78.0, 89.4)
CR, %	15.1	8.5	17.8	12.8
Median DOR (BICR), mo (95% CI)	39.2 (35.1, NC)	26.4 (22.3, NC)	39.2 (35.1, NC)	26.3 (21.1, NC)
Stable disease, %	9.9	14.5	8.6	11.0
Median PFS2 (investigator),‡ mo (95% CI)	NC (NC, NC)	36.5 (36.1, NC)	NC (39.6, NC)	37.4 (36.5, NC)
Hazard ratio (95% CI)	0.60 (0.45, 0.79)		0.44 (0.28, 0.70)	
Data maturity	~25%		~23%	

T-DXd + P demonstrated improvements across OS, PFS (by investigator), confirmed ORR, DOR, and PFS2

*Median PFS estimate for T-DXd + P is likely to change at updated analysis; †based on RECIST 1.1; response required confirmation after 4 weeks; ‡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

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; PFS, progression-free survival; PFS2, second progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

1. Tolaney SM, et al. Oral presentation at ASCO 2025 (Abstract LBA1008)

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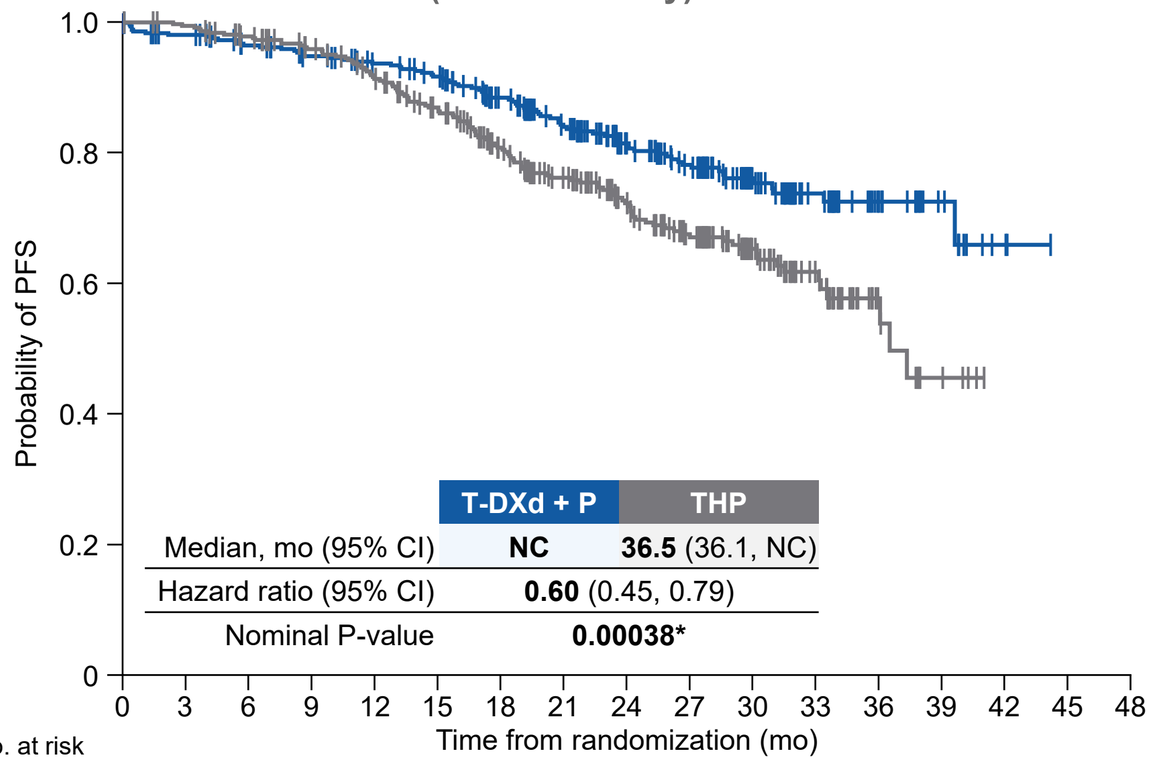
PFS2 (investigator)

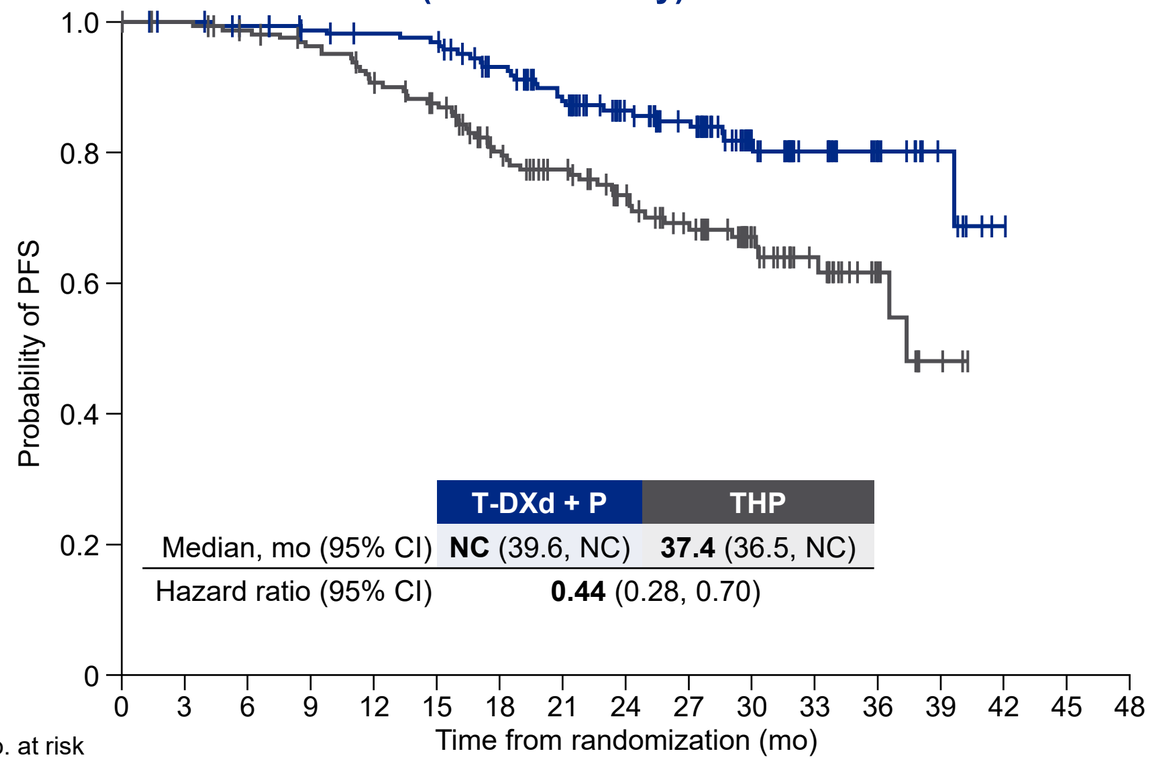
Overall population[1] (~25% maturity)



	T-DXd + P	THP
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

Asian subgroup (~23% maturity)



	T-DXd + P	THP
Median, mo (95% CI)	**NC** (39.6, NC)	**37.4** (36.5, NC)
Hazard ratio (95% CI)	**0.44** (0.28, 0.70)	

No. at risk																
T-DXd + P	174	172	168	163	160	158	144	130	111	97	51	33	18	7	1	0
THP	172	167	162	155	145	136	116	103	86	74	44	28	10	3	0	0

T-DXd + P demonstrated a clinically meaningful improvement in PFS2, consistent with the overall population

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
CI, confidence interval; mo, months; NC, not calculable; P, pertuzumab; PFS, progression-free survival; PFS2, second progression-free survival; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

1. Tolaney SM, et al. Oral presentation at ASCO 2025 (Abstract LBA1008)

Toshimi Takano, MD, PhD

Post-discontinuation therapies

	Overall population[1]		Asian subgroup	
	T-DXd + P (n=383)	THP (n=387)	T-DXd + P (n=174)	THP (n=172)
Received post-discontinuation therapy in second line, n (%)	124 (32.4)	181 (46.8)	63 (36.2)	86 (50.0)
Targeted therapy, n (%)	111 (29.0)	166 (42.9)	59 (33.9)	80 (46.5)
T-DXd	6 (1.6)	39 (10.1)	1 (0.6)	14 (8.1)
T-DM1	7 (1.8)	47 (12.1)	2 (1.1)	23 (13.4)
Trastuzumab-containing regimen*	78 (20.4)	51 (13.2)	38 (21.8)	15 (8.7)
Pertuzumab-containing regimen*	53 (13.8)	34 (8.8)	30 (17.2)	7 (4.1)
Chemotherapy, n (%)	68 (17.8)	57 (14.7)	43 (24.7)	31 (18.0)
Docetaxel	24 (6.3)	8 (2.1)	16 (9.2)	3 (1.7)
Paclitaxel†	18 (4.7)	4 (1.0)	10 (5.7)	1 (0.6)
Capecitabine	24 (6.3)	35 (9.0)	16 (9.2)	23 (13.4)
Endocrine therapy, n (%)	19 (5.0)	13 (3.4)	8 (4.6)	5 (2.9)

Percentages are based on the overall population or patients included in the Asian subgroup. Therapies listed are not exhaustive. Patients may have received more than one type of therapy
*Patients may have received trastuzumab and pertuzumab concurrently; †includes paclitaxel, paclitaxel liposome, and paclitaxel nanoparticle albumin-bound
P, pertuzumab; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab
1. Tolaney SM, et al. Oral presentation at ASCO 2025 (Abstract LBA1008)

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Overall safety summary

	Overall population[1]		Asian subgroup	
	T-DXd + P (n=381)	THP (n=382)	T-DXd + P (n=175)	THP (n=171)
Total treatment duration, median (range), months	21.7 (0.3–44.5)	16.9 (0.7–41.7)	24.2 (0.7–42.7)	19.6 (0.7–41.7)
Treatment duration for T-DXd	20.0 (0.3–44.5)†	N/A	22.8 (0.7–42.7)	N/A
Treatment duration for taxanes	N/A	Doc: 5.5 (0.7–37.4) Pac: 4.4 (0.2–30.7)	N/A	Doc: 6.0 (0.7–37.4) Pac: 6.9 (2.5–30.7)
Number of cycles for taxanes	N/A	Doc: 8 (1–51) Pac: 6 (1–42)	N/A	Doc: 8 (1–51) Pac: 10 (4–42)
Any TEAE, n (%)	380 (99.7)	378 (99.0)	174 (99.4)	170 (99.4)
Possibly treatment-related TEAEs,‡ n (%)	373 (97.9)	369 (96.6)	173 (98.9)	168 (98.2)
Grade ≥3	209 (54.9)	200 (52.4)	101 (57.7)	115 (67.3)
Serious TEAEs, n (%)	103 (27.0)	96 (25.1)	40 (22.9)	39 (22.8)
TEAEs associated with treatment discontinuation,§ n (%)	79 (20.7)	108 (28.3)	36 (20.6)	48 (28.1)
TEAEs associated with dose interruption,§ n (%)	262 (68.8)	187 (49.0)	132 (75.4)	93 (54.4)
TEAEs associated with dose reduction,§ n (%)	175 (45.9)	76 (19.9)	81 (46.3)	35 (20.5)
TEAEs with outcome of death, n (%) Possibly treatment related (investigator assessed)	13 (3.4) 5 (1.3)	3 (0.8) 1 (0.3)	2 (1.1) 0	2 (1.2) 1 (0.6)¶

*Safety analyses included all patients who received at least one dose of study treatment (at least one study drug); †excludes data from the 8.7% (33/380) of treated patients who received trastuzumab after discontinuing T-DXd due to TEAEs; ‡investigator assessed; §dose modifications or discontinuations relate to any component of each arm; ¶owing to anemia

Doc, docetaxel; N/A, not applicable; P, pertuzumab; Pac, paclitaxel; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event; THP, taxane + trastuzumab + pertuzumab

1. Tolaney SM, et al. Oral presentation at ASCO 2025 (Abstract LBA1008)

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Adjudicated drug-related ILD/pneumonitis

Overall population

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)

Asian subgroup

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
T-DXd + P (n=175)	15 (8.6)	17 (9.7)	0	0	1 (0.6)*	33 (18.9)
THP (n=171)	2 (1.2)	1 (0.6)	0	0	0	3 (1.8)

Asian subgroup: Japan

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
T-DXd + P (n=39)	10 (25.6)	3 (7.7)	0	0	0	13 (33.3)
THP (n=31)	1 (3.2)	0	0	0	0	1 (3.2)

Safety analysis set. Adjudicated drug-related ILD/pneumonitis (grouped term) includes chronic obstructive pulmonary disease, interstitial lung disease, organizing pneumonia, pneumonia, and pneumonitis
*Owing to pneumonitis
ILD, interstitial lung disease; P, pertuzumab; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

Toshimi Takano, MD, PhD

Conclusions

In DESTINY-Breast09, **44.9% (n=346) of the overall population (T-DXd + P and THP arms) were from Asian countries/regions** (mainland China, Japan, Republic of Korea, Taiwan, and Philippines)

In the interim analysis, efficacy of T-DXd + P in the Asian subgroup was **consistent with the overall population**

- T-DXd + P demonstrated a **clinically meaningful PFS benefit** by BICR vs THP

There were **no new safety signals** in the Asian subgroup

- Incidence of **adjudicated drug-related ILD/pneumonitis** was comparatively higher in the Asian subgroup, particularly in the Japanese subgroup, than in the overall population

PFS by BICR

	Overall population[1]		Asian subgroup	
	T-DXd + P	THP	T-DXd + P	THP
Median, mo	40.7	26.9	40.7	27.4
Hazard ratio	0.56		0.55	
Reduction in risk of disease progression or death with T-DXd + P vs THP:	**44%**		**45%**	

T-DXd + P demonstrated a clinically meaningful PFS benefit vs THP for Asian patients, further supporting T-DXd + P as a potential first-line treatment option for patients with HER2+ a/mBC

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

1. Tolaney SM, et al. Oral presentation at ASCO 2025 (Abstract LBA1008)

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- Study site staff for their contributions
- Members of the Independent Data Monitoring Committee and the Interstitial Lung Disease Adjudication Committee

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Daiichi Sankyo

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In March 2019, AstraZeneca entered into a global development and commercialization collaboration agreement with Daiichi Sankyo for trastuzumab deruxtecan (T-DXd; DS-8201)

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Scan below to access:

- **Presentation and supplementary slides**
- **Plain language summary infographic**

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Supplementary data

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Saturday, December 6, 2025
Presentation 88MO

Baseline characteristics

	Overall population[1]		Asian subgroup	
	T-DXd + P (n=383)	THP (n=387)	T-DXd + P (n=174)	THP (n=172)
Age, median (range), years	54 (27–85)	54 (20–81)	55 (27–81)	55 (28–77)
Female, n (%)	383 (100)	387 (100)	174 (100)	172 (100)
ECOG performance status, n (%)				
0 (normal activity)	256 (66.8)	246 (63.6)	125 (71.8)	121 (70.3)
1 (restricted activity)	127 (33.2)	141 (36.4)	49 (28.2)	51 (29.7)
HER2 score by central test, n (%)				
IHC 3+	318 (83.0)	315 (81.4)	141 (81.0)	148 (86.0)
IHC <3 / ISH+	62 (16.2)	71 (18.3)	30 (17.2)	23 (13.4)
IHC NR / ISH+	3 (0.8)	1 (0.3)	3 (1.7)	1 (0.6)
HR status, n (%)				
Positive*	207 (54.0)	209 (54.0)	82 (47.1)	79 (45.9)
Negative	176 (46.0)	178 (46.0)	92 (52.9)	93 (54.1)
De-novo disease at diagnosis, n (%)	200 (52.2)	200 (51.7)	88 (50.6)	79 (45.9)
***PIK3CA* mutations detected, n (%)**	116 (30.3)	121 (31.3)	54 (31.0)	58 (33.7)
Brain metastases, n (%)†	25 (6.5)	22 (5.7)	11 (6.3)	4 (2.3)
Visceral metastases, n (%)	281 (73.4)	268 (69.3)	120 (69.0)	121 (70.3)

*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
1. Tolaney SM, et al. Oral presentation at ASCO 2025 (Abstract LBA1008)

Toshimi Takano, MD, PhD

Prior therapies

	Overall population[1]		Asian subgroup	
	T-DXd + P (n=383)	THP (n=387)	T-DXd + P (n=174)	THP (n=172)
(Neo)adjuvant setting, n(%)				
Any (neo)adjuvant treatment	166 (43.3)	169 (43.7)	77 (44.3)	81 (47.1)
Chemotherapy	159 (41.5)	152 (39.3)	72 (41.4)	69 (40.1)
Endocrine therapy	74 (19.3)	85 (22.0)	34 (19.5)	43 (25.0)
Targeted therapy	112 (29.2)	108 (27.9)	52 (29.9)	54 (31.4)
Trastuzumab	110 (28.7)	108 (27.9)	52 (29.9)	54 (31.4)
Pertuzumab	31 (8.1)	24 (6.2)	13 (7.5)	14 (8.1)
T-DM1	3 (0.8)	4 (1.0)	0	0
Pyrotinib	1 (0.3)	1 (0.3)	1 (0.6)	1 (0.6)
CDK4/6 inhibitor	0	1 (0.3)	0	0
First-line a/mBC setting, n (%)				
Endocrine therapy	5 (1.3)	5 (1.3)	1 (0.6)	1 (0.6)

a/mBC, advanced/metastatic breast cancer; CDK4/6, cyclin-dependent kinase; P, pertuzumab; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

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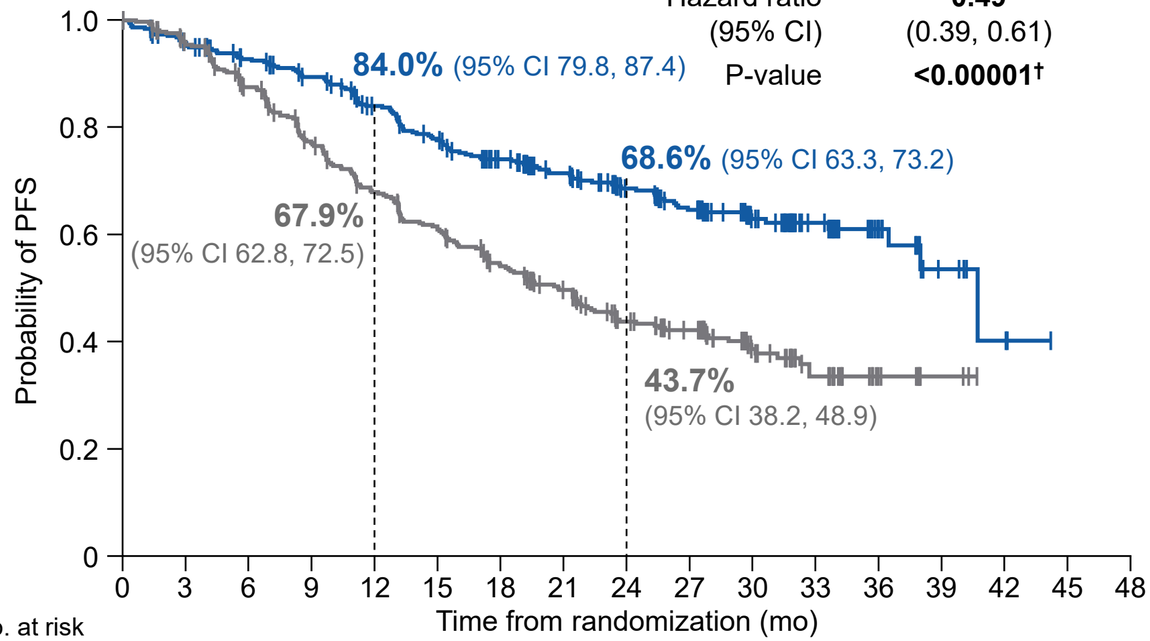
PFS (investigator)

Overall population[1]

	T-DXd + P	THP
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)	
P-value	**<0.00001†**	

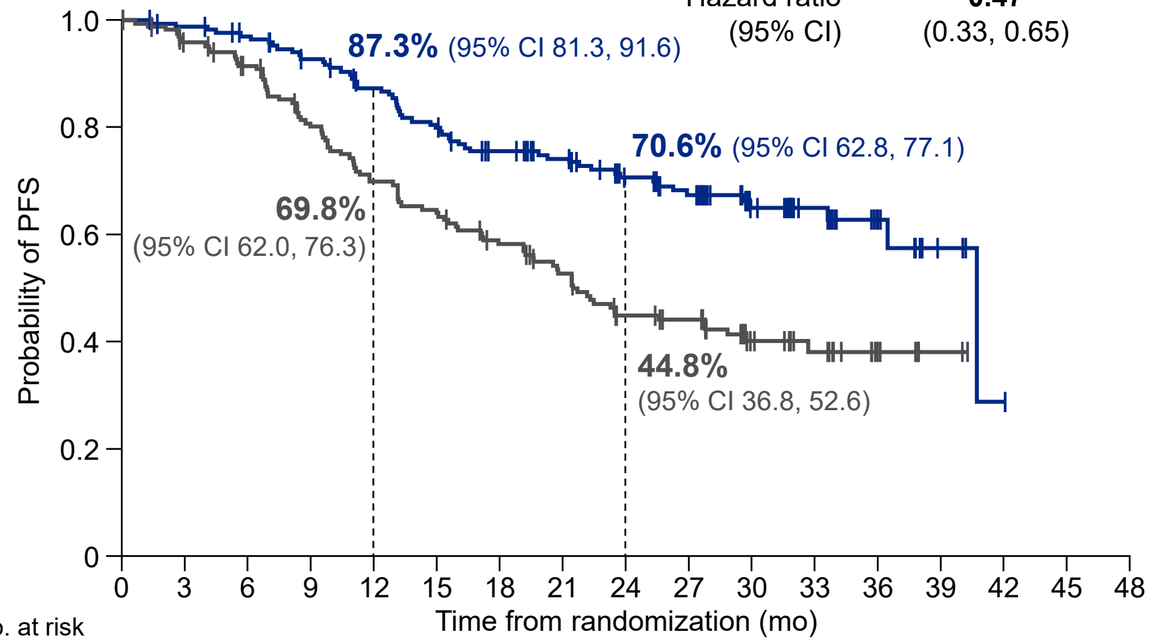


No. at risk

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

Asian subgroup

	T-DXd + P	THP
Median, mo (95% CI)	**40.7*** (36.5, NC)	**21.5** (19.1, 28.8)
Hazard ratio (95% CI)	**0.47** (0.33, 0.65)	



No. at risk

T-DXd + P	174	169	163	153	141	129	117	109	94	82	45	30	14	4	1	0
THP	172	157	146	125	109	100	88	75	58	54	28	20	7	2	1	0

T-DXd + P showed improvement in investigator-assessed PFS, consistent with improvement in PFS by BICR

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

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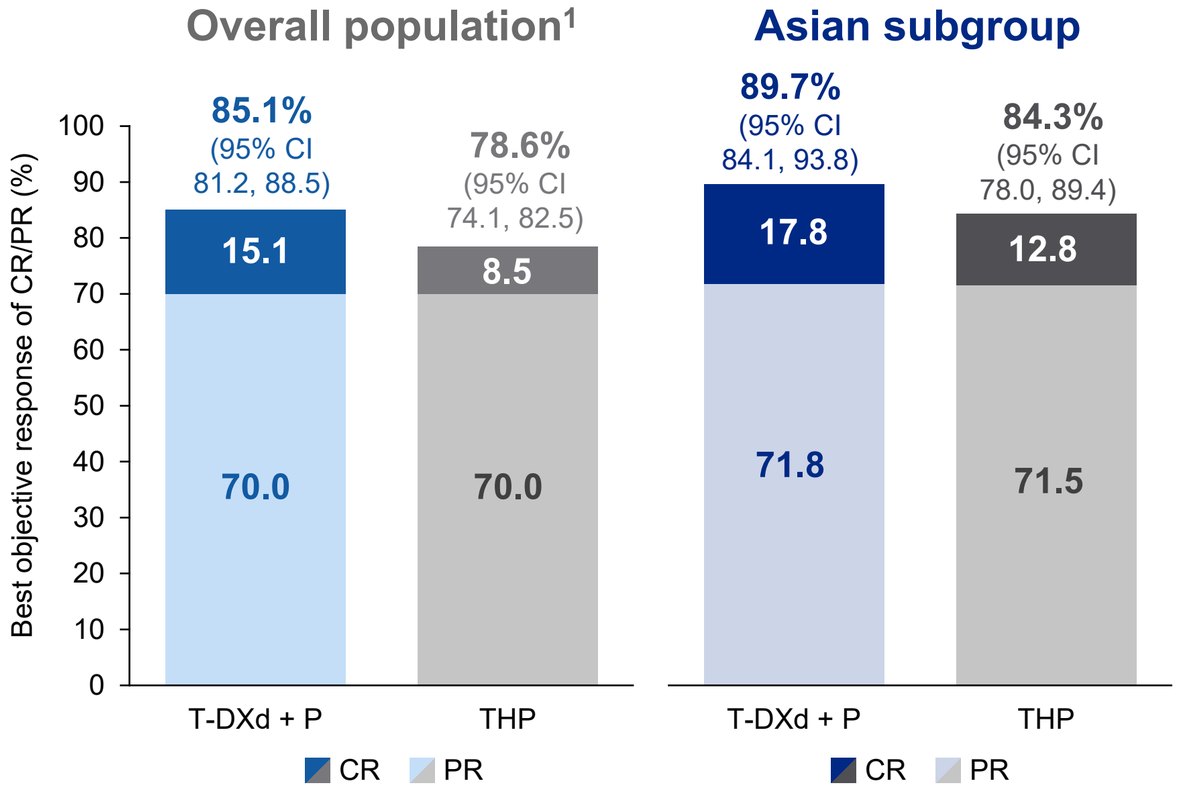
ORR and DOR (BICR)

Confirmed ORR*



DOR

	Overall population[1]		Asian subgroup	
	T-DXd + P (n=383)	THP (n=387)	T-DXd + P (n=174)	THP (n=172)
Median DOR, mo (95% CI)	39.2 (35.1, NC)	26.4 (22.3, NC)	39.2 (35.1, NC)	26.3 (21.1, NC)
Remaining in response at 24 mo (%)	73.3	54.9	74.4	54.6
Stable disease, n (%)	38 (9.9)	56 (14.5)	15 (8.6)	19 (11.0)

Numerically higher ORR and DOR with T-DXd + P vs THP, with efficacy comparable to the overall population

*Based on RECIST 1.1; 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

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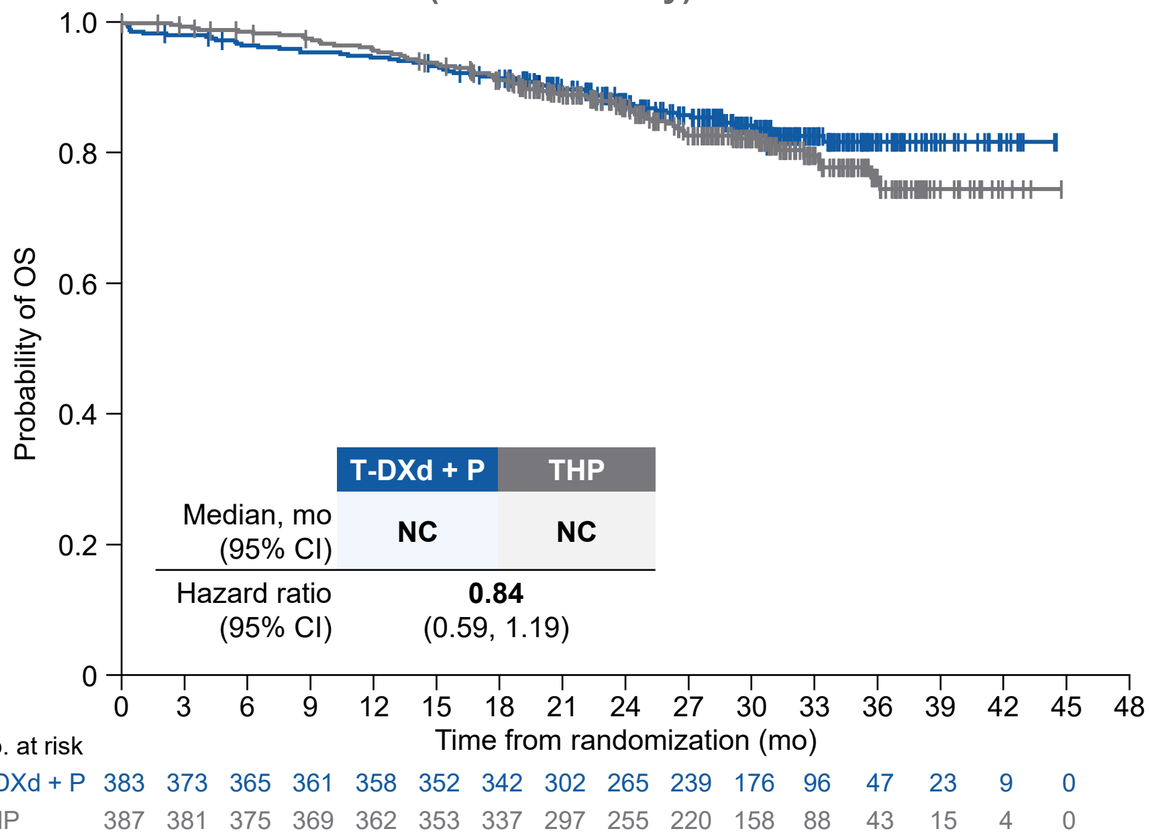
Overall survival

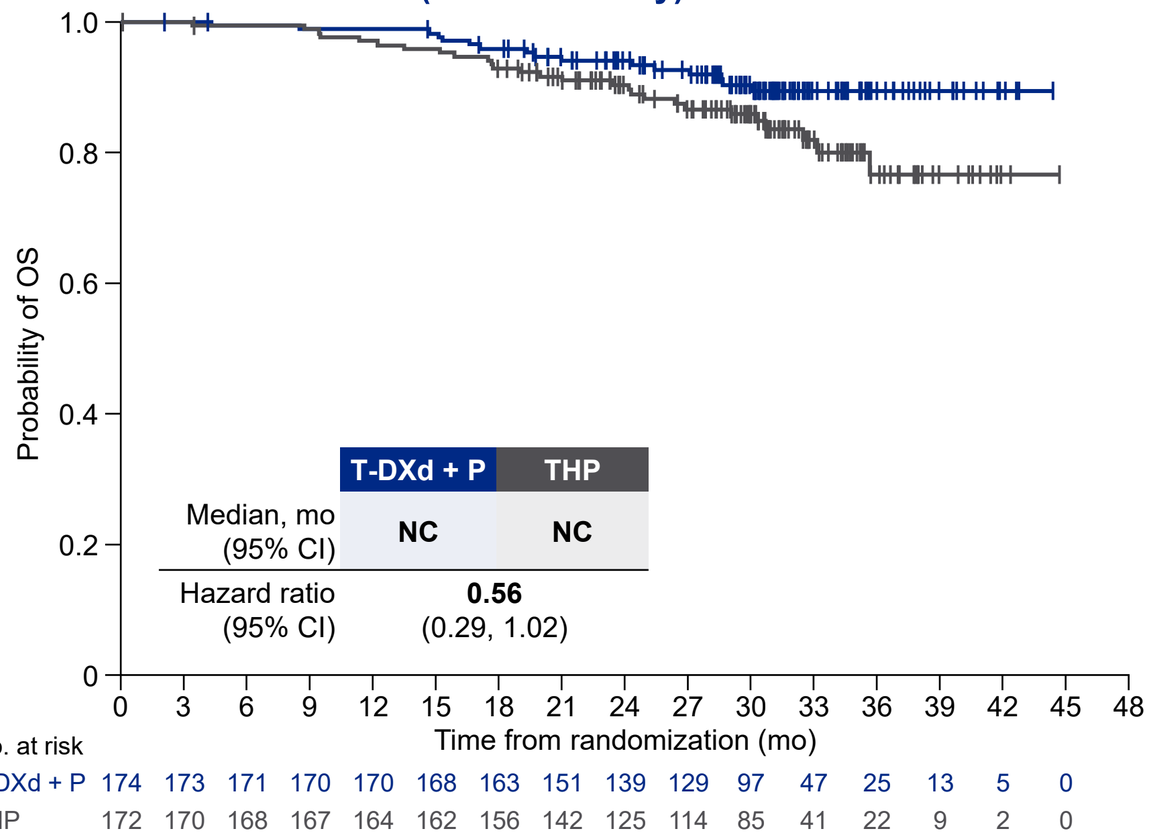
Overall population[1] (~16% maturity)



No. at risk

T-DXd + P	383	373	365	361	358	352	342	302	265	239	176	96	47	23	9	0
THP	387	381	375	369	362	353	337	297	255	220	158	88	43	15	4	0

Asian subgroup (~12% maturity)



No. at risk

T-DXd + P	174	173	171	170	170	168	163	151	139	129	97	47	25	13	5	0
THP	172	170	168	167	164	162	156	142	125	114	85	41	22	9	2	0

Early OS data suggest a positive trend favoring T-DXd + P, similar to the overall population

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

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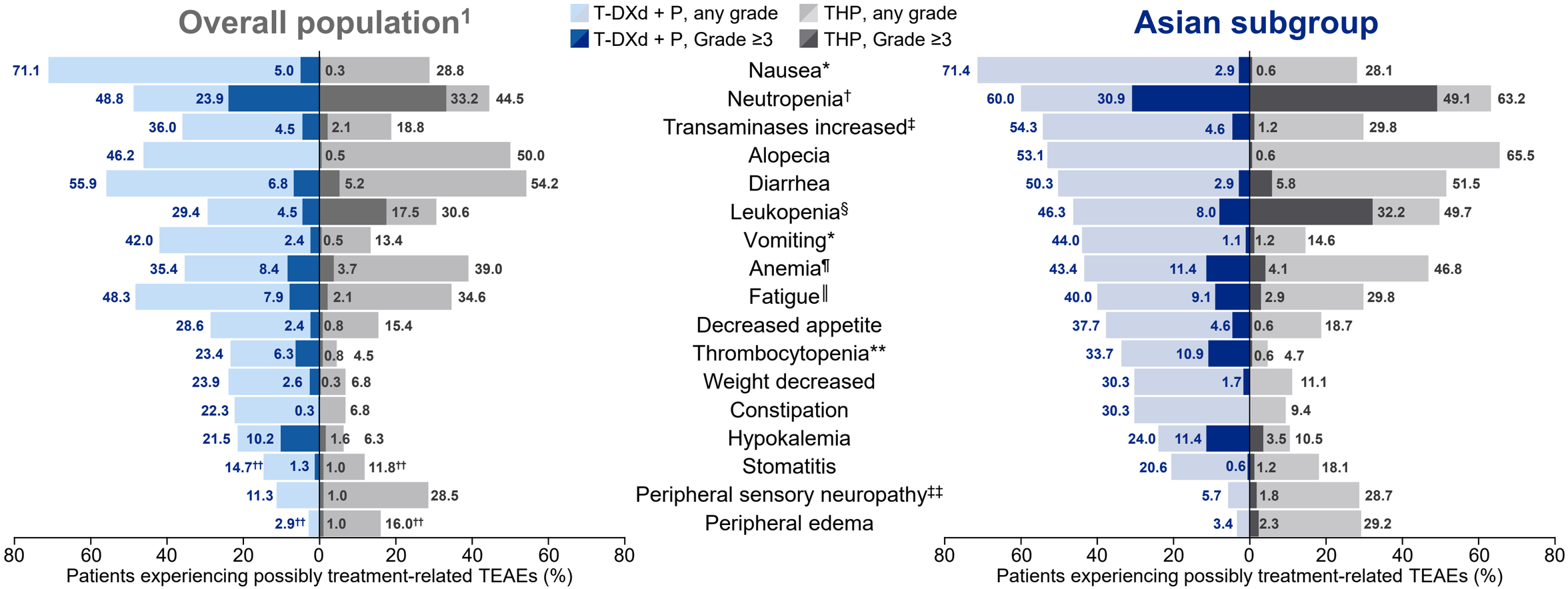
Possibly treatment-related (investigator-assessed) TEAEs in ≥20% of patients (either arm)



*Antiemetic prophylaxis was recommended but not mandated by protocol; †neutropenia (grouped term) includes neutropenia and neutrophil count decreased; ‡transaminases increased (grouped term) includes transaminases increased, aspartate aminotransferase increased, alanine aminotransferase increased, gamma-glutamyl transferase increased, liver function test abnormal, hepatic function abnormal, and liver function test increase; §leukopenia (grouped term) includes: leukopenia and white blood cell count decreased; ¶anemia (grouped term) includes: anemia, hemoglobin decreased, hematocrit decreased, and red blood cell count decreased; ‖fatigue (grouped term) includes fatigue, asthenia, malaise, and lethargy; **thrombocytopenia (grouped term) includes platelet count decreased and thrombocytopenia; ††included for comparison with Asian subgroup; ‡‡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

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What is the purpose of the DESTINY-Breast09 Asian subgroup analysis?

In Asia, the **number of people with breast cancer is increasing**, and more people with breast cancer have a higher-than-normal level of a protein called HER2 (known as '**HER2-positive**') than people in Western populations. **Trastuzumab deruxtecan (T-DXd)** is a **recommended treatment** for people with **HER2-positive advanced/metastatic breast cancer (a/mBC)** once the cancer has worsened while receiving their first treatment.

In **DESTINY-Breast09, T-DXd + pertuzumab** was compared with standard therapy – known as **THP (taxane + trastuzumab + pertuzumab)** – for people with **HER2-positive a/mBC**. This was the first large-scale study investigating the use of T-DXd + pertuzumab as a **first-line treatment** for HER2-positive a/mBC.

In an interim analysis of DESTINY-Breast09 (previously reported), people in the **T-DXd + pertuzumab** arm lived longer without their disease growing, spreading, or getting worse than people in the **THP** arm.

The aim of this analysis was to find out how well T-DXd + pertuzumab worked for people in Asian countries/regions who were included in DESTINY-Breast09

What did this subgroup analysis show?

T-DXd + pertuzumab showed a **similar benefit** for patients in Asian countries/regions to those in the overall population. Participants in the **T-DXd + pertuzumab** arm lived longer without their disease growing, spreading, or getting worse compared with participants in the **THP** arm. Side effects of the treatments were also similar to those seen in the overall population.

How was the DESTINY-Breast09 Asian subgroup analysis carried out?

Start of study

The study included people with:

- Advanced/metastatic breast cancer (a/mBC)
- HER2+ HER2-positive tumors
- **No** prior chemotherapy or HER2-targeted therapy for a/mBC

346 participants were from Asian countries/regions:

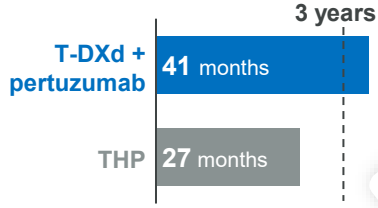
174 people were randomly assigned to **T-DXd + pertuzumab**

172 people were randomly assigned to **THP***

**There was another group of people who received T-DXd without pertuzumab, who will be evaluated versus THP in a future analysis*

Time without progression

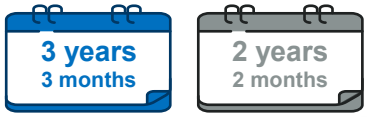
The timepoint after randomization at which half of the participants had cancer progression or died (known as median progression-free survival) was:



Time without progression was similar to the overall population

Duration of response

The expected length of time for which at least half the people who responded to treatment continued to respond (known as median duration of response) was:



for people given **T-DXd + pertuzumab** | for people given **THP**

Duration of response was consistent with the overall population

Response to treatment

The percentage of participants who had at least a 30% decrease in size of tumors (known as objective response rate) was:

~9 in 10 (90%) of those in the **T-DXd + pertuzumab** arm

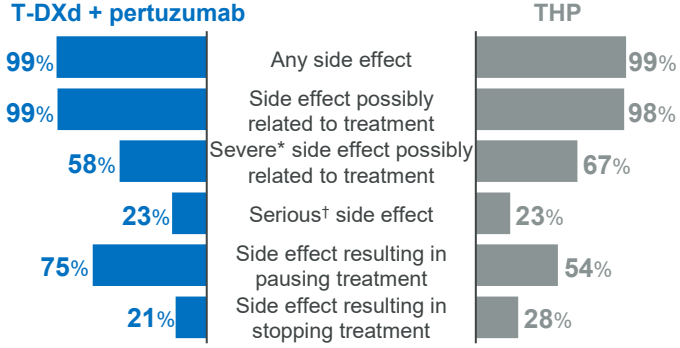
~8 in 10 (84%) of those in the **THP** arm

18% of people given **T-DXd + pertuzumab** and **13%** of people given **THP** had all signs of their cancer disappear (known as complete response)

Response to treatment and complete response were comparable to the overall population

Safety

The proportion of participants who experienced at least one side effect was:



*Interfering with / preventing routine activities, life-threatening, or fatal
†Resulting in negative medical outcomes, such as death or hospitalization

33 (19%) people given **T-DXd + pertuzumab** and **3 (2%)** people given **THP** developed interstitial lung disease (inflammation and/or scarring of the lungs), which was higher than the overall population

Most cases of interstitial lung disease in Asian participants were mild to moderate and almost half occurred in participants from Japan

Safety outcomes were broadly similar to those of the overall population

What's next?

The study will continue to explore T-DXd with and without pertuzumab compared with THP at longer follow up

How do the results of the DESTINY-Breast09 Asian subgroup analysis help to improve the possible treatment options for cancer?

The results demonstrate that T-DXd + pertuzumab can potentially be beneficial for people with HER2-positive a/mBC in Asia, supporting use of this combination as a possible new first-line treatment option

Where can I access more information?

DESTINY-Breast09 ClinicalTrials.gov identifier NCT04784715

This summary is based on an oral presentation by Professor Toshimi Takano at the 2025 European Society for Medical Oncology (ESMO) Asia Congress (Presentation ID 88MO). This summary, and the results of this study, have not yet been peer reviewed. The authors would like to thank the patients and their families who participated in the DESTINY-Breast09 study, and the investigators, co-investigators, and study staff. Date of summary: December 2025. The DESTINY-Breast09 study was sponsored by AstraZeneca. In March 2019, AstraZeneca entered into a global development and commercialization collaboration agreement with Daiichi Sankyo for trastuzumab deruxtecan (T-DXd; DS-8201). This plain language summary was prepared by Hannah Abdly, BSc (Helios Medical Communications, part of Helios Global Group), and was funded by AstraZeneca.