2024 ESMO BREAST CANCER

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Trastuzumab deruxtecan vs treatment of physician's choice in patients with HER2+ metastatic breast cancer previously treated with trastuzumab emtansine: updated overall survival results of the randomized, phase 3 DESTINY-Breast02 study

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Declaration of Interests

Dr. Sung-Bae Kim reports:

- **Consulting or advisory role:** AstraZeneca, Beigene, DaeHwah Pharma, Daiichi Sankyo, Ensol Bioscience Inc, ISU Abxis, Lilly, Novartis, and OBI Pharma
- **Research funding (institution):** Novartis and Sanofi-Aventis
- **Stocks or shares:** Genopeaks and Neogene TC

Background

- The aim of the DESTINY-Breast02 study was to assess the efficacy and safety of T-DXd vs TPC in patients with HER2-positive locally advanced or mBC previously treated with T-DM1
- At the primary study analysis of DESTINY-Breast02 (DCO, June 30, 2022), T-DXd showed statistically significant and clinically meaningful improvement in PFS by BICR and OS vs TPC with median follow-up of 20.7 months[1]
  - The primary endpoint, median PFS, was 17.8 months for T-DXd vs 6.9 months for TPC (HR, 0.36; 95% CI, 0.28-0.45; P<0.0001)[1]
  - The key secondary endpoint, median OS, was 39.2 months for T-DXd vs 26.5 months for TPC (HR, 0.66; 95% CI, 0.50-0.86; P=0.0021)[1]

Here we report updated efficacy and safety results of the DESTINY-Breast02 study (DCO, September 29, 2023) with longer follow-up (median, 26.8 months)

BICR, blinded independent central review; DCO, data cutoff; HER2, human epidermal growth factor receptor 2; mBC, metastatic breast cancer; OS, overall survival; PFS, progression-free survival; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

1. Andre F et al. *Lancet.* 2023;401(10390):1773-1785.

DESTINY-Breast02 Study Design

An open-label, randomized, multicenter, phase 3 study (NCT03523585)

Key eligibility criteria[a]

- Centrally confirmed HER2-positive (IHC 3+ or IHC 2+/ISH+) unresectable or metastatic breast cancer
- Documented radiographic progression after most recent treatment
- Previously treated with T-DM1

Stratification factors

- Hormone receptor status
- Prior treatment with pertuzumab
- History of visceral disease

R 2:1

T-DXd
5.4 mg/kg Q3W
(n = 406)

TPC
Per label (n = 202)
• Trastuzumab / Capecitabine
or
• Lapatinib / Capecitabine

Primary endpoint

- PFS (BICR[b])

Key secondary endpoint

- **OS**

Secondary endpoints

- ORR (BICR[b])
- DoR (BICR[b])
- **ORR (investigator)**
- **DoR (investigator)**
- **PFS (investigator)**
- **Safety**

Exploratory endpoint

- **PFS2 (investigator)**

- **Endpoints were evaluated by investigator assessment for this data cutoff because BICR was discontinued after the primary analysis**
- **Baseline characteristics were balanced across treatment arms as reported in the primary analysis[1]**

BICR, blinded independent central review; DoR, duration of response; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PFS2, median PFS from time of randomization to progression on the next line of therapy or death; Q3W, every three weeks; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

Endpoints in bold were evaluated at this updated data cutoff date (September 29, 2023).

[a]Patients with asymptomatic brain metastases (BMs) including locally untreated and treated BMs were allowed in the study. [b]BICR assessed per mRECIST 1.1.

1. Andre F et al. *Lancet*. 2023;401(10390):1773-1785.

Patient Disposition

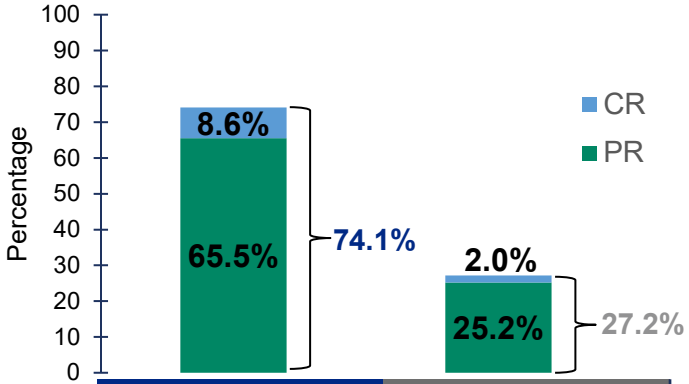
	T-DXd (N = 406)	TPC (N = 202)
Patients randomized, n (%)	406	202
Randomized but not treated	2 (0.5)	7 (3.5)
Median follow-up, months (range)	30.2 (0.8-60.7)	20.5 (0.0-60.6)
Median treatment duration, months (range)	11.3 (0.7-60.7)	~4.5 (0.1-50.6)
Treatment status[a]		
Ongoing	55 (13.6)	0
Discontinued	349 (86.4)	195 (100)
Primary reason for discontinuation from treatment[a]		
Progressive disease	193 (47.8)	144 (73.8)
Adverse event	82 (20.3)	14 (7.2)
Withdrawal by patient	37 (9.2)	17 (8.7)
Clinical progression	26 (6.4)	17 (8.7)
Death	5 (1.2)	1 (0.5)
Lost to follow-up	2 (0.5)	0
Physician decision	2 (0.5)	1 (0.5)
Protocol deviation	1 (0.2)	1 (0.5)
Other	1 (0.2)	0

T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

[a]Percentage calculated using the number of treated patients as denominator.

Confirmed ORR and PFS by Investigator

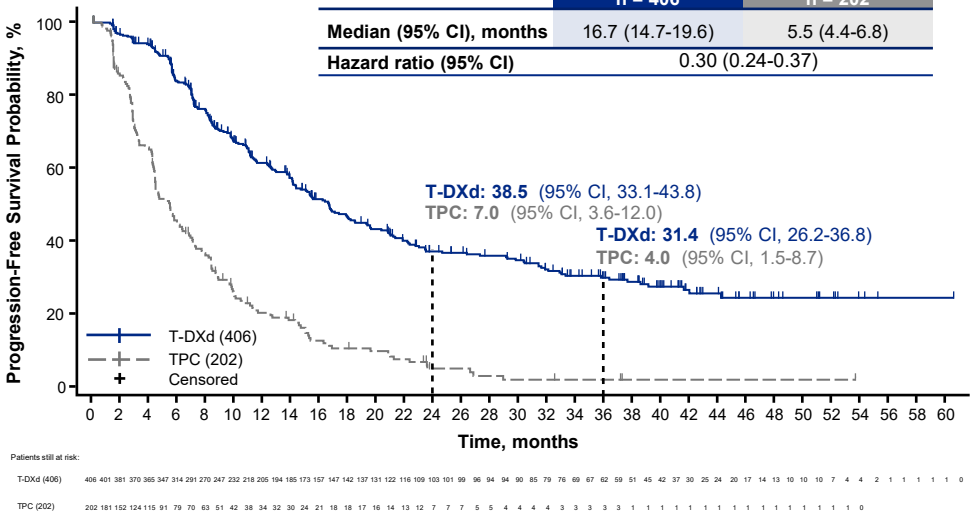
Confirmed ORR[a]



	T-DXd n = 406	TPC n = 202
Other responses, n (%)		
SD	85 (20.9)	98 (48.5)
PD	14 (3.4)	28 (13.9)
NE	6 (1.5)	21 (10.4)
Median DoR,[a] months (95% CI)	19.1 (15.2-25.1)	6.3 (5.1-8.1)

PFS by Investigator

	T-DXd n = 406	TPC n = 202
Median (95% CI), months	16.7 (14.7-19.6)	5.5 (4.4-6.8)
Hazard ratio (95% CI)	0.30 (0.24-0.37)	

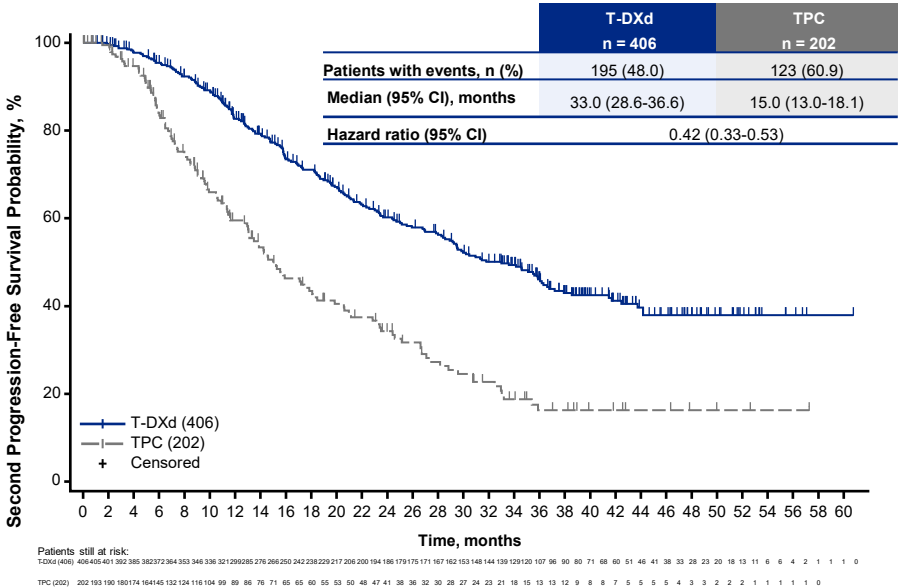


CR, complete response; DoR, duration of response; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.
[a]By investigator assessment.

Post-Trial Anticancer Systemic Treatment and PFS2

	T-DXd n = 406	TPC n = 202
Patients who discontinued treatment,[a] n (%)	**349 (86.0)**	**195 (96.5)**
Patients receiving any post-trial systemic treatment,[b] n (%)	**247 (70.8)**	**148 (75.9)**
Trastuzumab[c]	145 (58.7)	100 (67.6)
HER2 TKI[c]	145 (58.7)	47 (31.8)
Hormone therapy[c]	47 (19.0)	18 (12.2)
Taxane[c]	35 (14.2)	27 (18.2)
T-DXd[c]	32 (13.0)	69 (46.6)
Pertuzumab[c]	21 (8.5)	19 (12.8)
T-DM1[c]	4 (1.6)	5 (3.4)
Other HER2 therapy (except HER2 TKI)[c]	3 (1.2)	9 (6.1)
Other Systemic therapy[c]	208 (84.2)	112 (75.7)
Type of treatment,[b,d] n (%)		
Systemic	247 (70.8)	148 (75.9)
Radiation	43 (12.3)	25 (12.8)
Surgery	10 (2.9)	7 (3.6)

PFS2 by Investigator

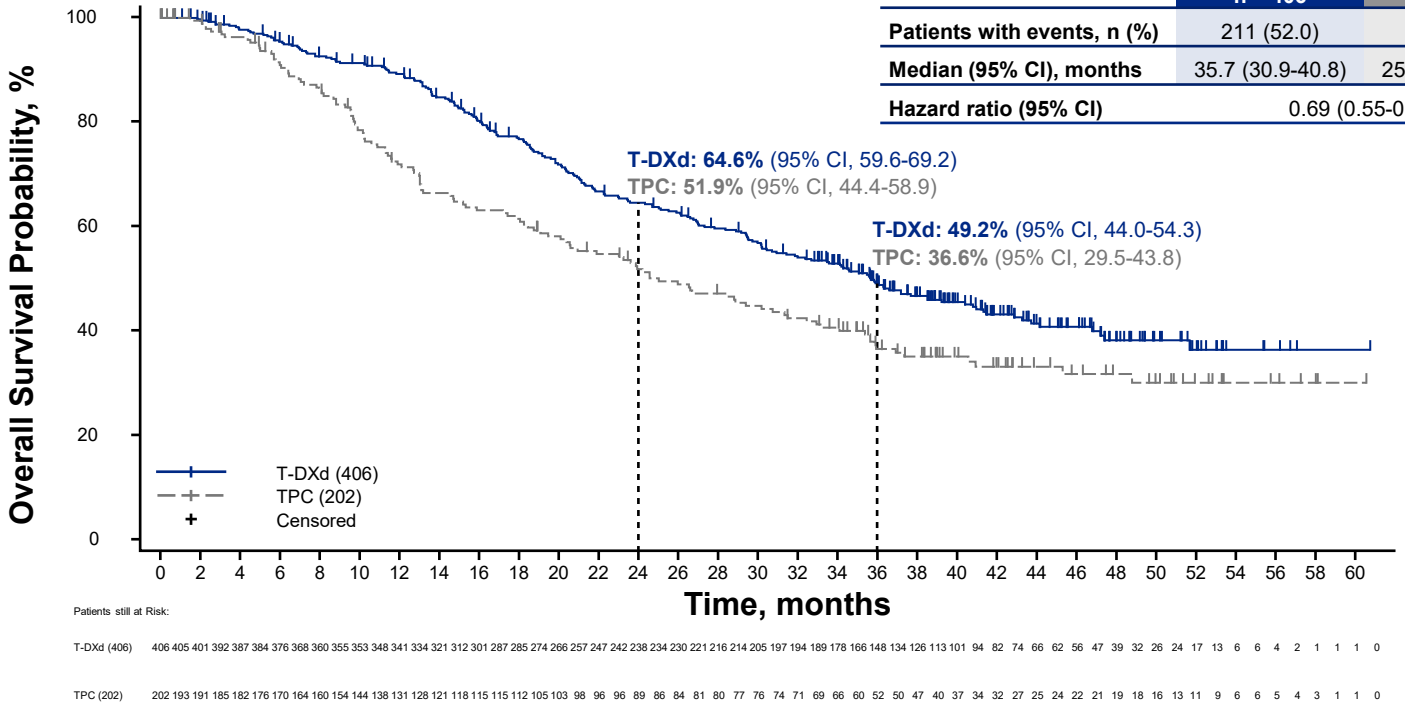


PFS2, progression-free survival from time of randomization to progression on the next line of therapy or death; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice; TKI, tyrosine kinase inhibitor.

[a]Percentage calculated using the number of patients in the full analysis set as the denominator. [b]Percentages are calculated using the number of patients who discontinued treatment as the denominator. [c]Percentages are calculated using the number of patients who received any post-trial systemic treatment as the denominator. [d]Patients may have been treated with more than 1 type of post anti-cancer therapy.

Overall Survival

	T-DXd n = 406	TPC n = 202
Patients with events, n (%)	211 (52.0)	119 (58.9)
Median (95% CI), months	35.7 (30.9-40.8)	25.0 (20.4-31.5)
Hazard ratio (95% CI)	0.69 (0.55-0.86)	



T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

Overall Safety Summary

n (%)	T-DXd (n = 404)[a]	TPC (n = 195)[a]
Any-grade TEAEs	**403 (99.8)**	**185 (94.9)**
Drug-related	394 (97.5)	180 (92.3)
Grade ≥3 TEAEs	**224 (55.4)**	**87 (44.6)**
Drug-related	173 (42.8)	61 (31.3)
Serious AEs	**114 (28.2)**	**46 (23.6)**
Drug-related	47 (11.6)	15 (7.7)
TEAEs associated with drug discontinuation	**87 (21.5)**	**19 (9.7)**
Drug-related	63 (15.6)	10 (5.1)
TEAEs associated with drug interruption	**191 (47.3)**	**90 (46.2)**
Drug-related	136 (33.7)	76 (39.0)
TEAEs associated with dose reduction	**112 (27.7)**	**90 (46.2)**
Drug-related	104 (25.7)	90 (46.2)
TEAEs associated with death	**13 (3.2)**	**7 (3.6)**
Drug-related	4 (1.0)[c]	0

- The most common TEAEs with T-DXd were:
  - Nausea (72.5%)
  - Fatigue[b] (62.4%)
  - Vomiting (38.1%)
- The most common TEAEs with TPC were:
  - Diarrhea (53.8%)
  - Palmar-plantar erythrodysesthesia syndrome (51.3%)
  - Nausea (37.4)%
- There were no new drug-related TEAEs associated with death since the primary analysis[1]
- Overall, the safety profile was consistent with the primary analysis[1]

AE, adverse event; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event; TPC, treatment of physician's choice.
Median treatment duration was 11.3 months (range, 0.7-60.7 months) with T-DXd and ~4.5 months (range, 0.1-50.6 months) with TPC.
[a]The safety analysis set includes all randomly assigned patients who received at least 1 dose of study treatment. [b]Fatigue (fatigue, asthenia, malaise, lethargy). [c]Drug-related TEAEs associated with an outcome of death included pneumonitis (n = 2), acute myeloid leukemia (n = 1), and pneumonia (n = 1).

1. André F et al. *Lancet.* 2023;401(10390):1773-1785.

Adjudicated Drug-Related ILD/Pneumonitis

Adjudicated drug-related ILD/pneumonitis events for the entire study period						
n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade
T-DXd (n = 404)	13 (3.2)	28 (6.9)	3 (0.7)	0	2 (0.5)	46 (11.4)
TPC (n = 195)	0	0	1 (0.5)	0	0	1 (0.5)
Time to first adjudicated drug-related ILD/pneumonitis[a] by worst CTCAE grade in the T-DXd arm						
T-DXd, n (%) (n = 404)	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**	**Any Grade**
≤ 6 months	4 (1.0)	12 (3.0)	1 (2.0)	0	2 (0.5)	19 (4.7)
> 6 to ≤ 12 months	4 (1.0)	8 (2.0)	2 (0.5)	0	0	14 (3.5)
> 12 to ≤ 24 months	4 (1.0)[b]	7 (1.7)[b]	0	0	0	11 (2.7)
> 24 months	1 (0.2)[b]	1 (0.2)[b]	0	0	0	2 (0.5)

- In the T-DXd arm, rates of ILD/pneumonitis increased from 10.4% to 11.4% at this updated DCO[1,2]
  - There were 4 new adjudicated drug-related ILD/pneumonitis events with T-DXd (2 grade 1; 2 grade 2)
- The risk of ILD/pneumonitis with T-DXd did not increase with longer treatment duration; most events occurred within 12 months of treatment initiation
- Median treatment duration was 11.3 months (range, 0.7-60.7 months) with T-DXd and ~4.5 months (range, 0.1-50.6 months) with TPC

CTCAE, common terminology criteria for adverse events; DCO, data cutoff; ILD, interstitial lung disease; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.
Percentages calculated using the number of patients in the Safety Analysis Set as the denominator. This table is based on adjudicated ILD events including all adjudicated as study drug-related ILD by the ILD adjudication committee.
[a]Time to first adjudicated ILD onset (months) = [(onset date of first ILD adjudicated as drug-related - first dose date + 1)/365.25] x 12. [b]Includes 4 additional cases (2 grade 1; 2 grade 2).
1. André F et al. *Lancet*. 2023;401(10390):1773-1785. 2. Krop I et al. Presented at: San Antonio Breast Cancer Symposium 2022; December 6-10, 2022; San Antonio, TX, USA. Presentation GS2-01.

Conclusions

- With longer follow-up, results reinforce the substantial benefit of T-DXd over TPC in patients with HER2-positive mBC previously treated with T-DM1, demonstrated by clinically meaningful improvement in efficacy over TPC
  - Confirmed ORR by investigator was **74.1%** for T-DXd vs **27.2%** for TPC
  - Median PFS by investigator was **16.7** months with T-DXd vs **5.5** months with TPC **(HR, 0.30)**
  - Median OS was **35.7** months with T-DXd vs **25.0** months with TPC; the risk of death was reduced by **31% (HR, 0.69)**

- The safety profile of T-DXd continues to be manageable, with no long-term toxicity observed with longer follow-up
  - There was no observed increased risk of ILD with longer treatment duration

These data confirm the long-term survival benefit, as well as favorable benefit/risk profile of T-DXd in patients with HER2-positive mBC who have been previously treated with T-DM1

HER2, human epidermal growth factor receptor 2; HR, hazard ratio; mBC, metastatic breast cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PFS2, PFS from time of randomization to progression on the next line of therapy or death; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

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&

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Plain Language Summary

DESTINY-Breast02

Why did we perform this research?

- Trastuzumab deruxtecan (T-DXd) is an antibody drug conjugate (ADC) that targets HER2 and is approved for the treatment of patients with unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-positive breast cancer who have received a prior anti-HER2-based regimen or chemotherapy.[1-3] The phase 3 DESTINY-Breast02 study compared the efficacy and safety of T-DXd with the chemotherapy treatment of a physician's choice (TPC) in patients with HER2-positive metastatic breast cancer previously treated with trastuzumab emtansine (T-DM1).[4] In the primary analysis, T-DXd was observed to have a more favorable benefit-risk profile than TPC, with a median follow-up time of 20.7 months.[4] The objective of this analysis was to evaluate updated efficacy and safety results of patients participating in the DESTINY-Breast02 study with extended follow-up .

How did we perform this research?

- Patients with HER2-positive metastatic breast cancer that is resistant or refractory to T-DM1 were eligible for the study.[4] Patients were randomly assigned to receive treatment with T-DXd or TPC.[4] Both patients and investigators knew which treatment they were receiving.[4]

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

- The findings from the extended follow-up were generally consistent with the primary study results;[4] T-DXd showed clinical benefit in efficacy over TPC with no new safety signals observed. In this updated analysis, the rate of ILD/pneumonitis (11.4%), a side effect (treatment-emergent adverse event) of special interest, was similar to the rate observed in the primary analysis (10%).[4] These findings continue to support the use of T-DXd in patients with HER2-positive mBC previously treated with T-DM1.

Where can I access more information?

- To learn more about the DESTINY-Breast02 study, you can visit https://www.clinicaltrials.gov/study/NCT03523585

1. Enhertu® (fam-trastuzumab deruxtecan-nxki) for injection, for intravenous use. Prescribing Information. Daiichi Sankyo, Inc.; Basking Ridge, NJ, USA; 2022. 2. Enhertu® for intravenous drip infusion 100 mg. Prescribing Information. Daiichi Sankyo Inc.; Tokyo, Japan. 3. Enhertu. Summary of product characteristics. Daiichi Sankyo Europe GmbH; 2022 4. André F et al. *Lancet.* 2023;401(10390):1773-1785.

Baseline Characteristics and Prior Therapies[1,2]

	T-DXd (n = 406)	TPC (n = 202)
Age, median (range), years	54.2 (22.4-88.5)	54.7 (24.7-86.5)
Female, n (%)	403 (99.3)	200 (99.0)
Region, n (%)		
Europe	152 (37.4)	78 (38.6)
Asia	112 (27.6)	52 (25.7)
North America	41 (10.1)	23 (11.4)
Rest of World	101 (24.9)	49 (24.3)
HER2 status (IHC),[a] n (%)		
3+	326 (80.3)	159 (78.7)
2+ (ISH+)	79 (19.5)	41 (20.8)
2+ (ISH- or nonevaluable)	1 (0.2)	1 (0.5)
1+ (ISH+)	0	1 (0.5)
ECOG PS, n (%)		
0	228 (56.2)	121 (59.9)
1	177 (43.6)	81 (40.1)
2	1 (0.2)	0
Hormone receptor,[b] n (%)		
Positive	238 (58.6)	118 (58.4)
Negative	165 (40.6)	83 (41.1)

HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ECOG PS, Eastern Cooperative Oncology Group performance status; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

[a]HER2 status as evaluated by central laboratory testing. [b]3 (0.7%) patients in the T-DXd arm and 1 (0.5%) patient in the TPC arm had indeterminate hormone receptor status (neither estrogen receptors nor progesterone receptors positive and estrogen receptors indeterminate or progesterone receptors indeterminate) based on factors reported from EDC.

1. Andre F et al. *Lancet.* 2023;401(10390):1773-1785. 2. Krop I et al. Presented at: San Antonio Breast Cancer Symposium 2022; December 6-10, 2022; San Antonio, TX. Presentation GS2-01.

Baseline Characteristics and Prior Therapies[1,2] Cont.

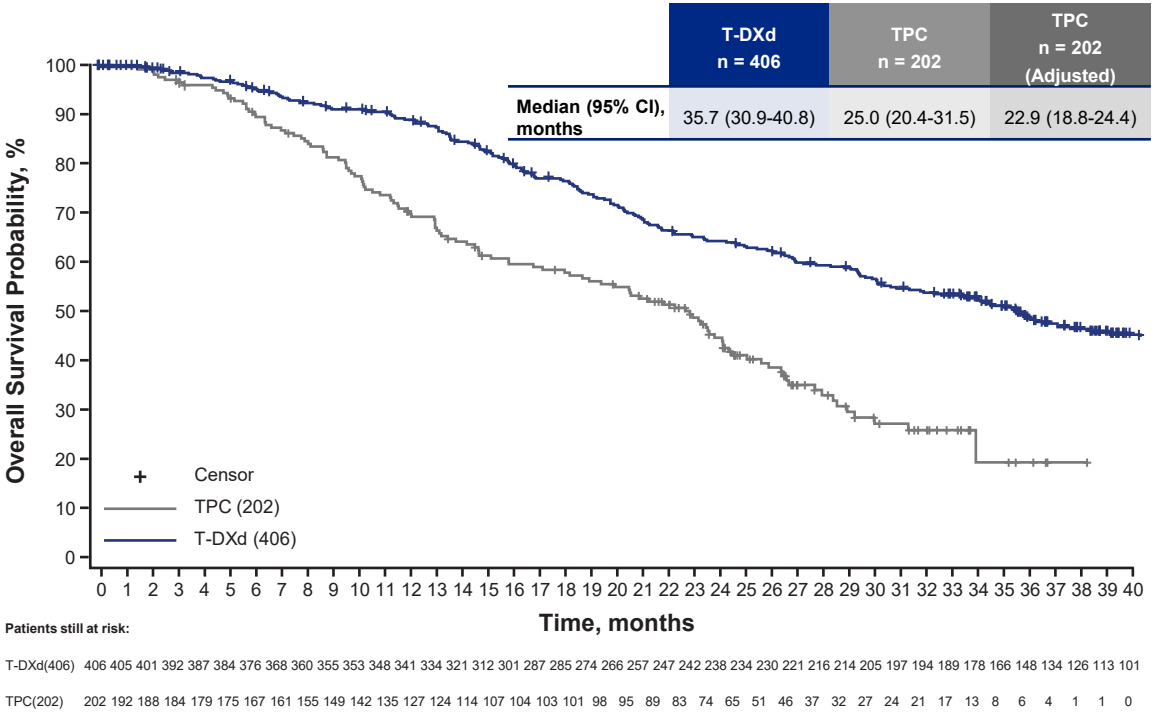
	T-DXd (n = 406)	TPC (n = 202)
Baseline brain metastases,[a] n (%)		
Yes	74 (18.2)	36 (17.8)
No	332 (81.8)	166 (82.2)
History of visceral disease, n (%)		
Yes	316 (77.8)	160 (79.2)
No	90 (22.2)	42 (20.8)
Median number of prior lines of therapy in the metastatic setting, (range)	**2 (0-10)**	**2 (1-8)**
Any prior systemic cancer therapy, n (%)	**406 (100)**	**202 (100)**
Trastuzumab	404 (99.5)	202 (100)
T-DM1	404 (99.5)	202 (100)
Taxane	386 (95.1)	197 (97.5)
Pertuzumab	318 (78.3)	156 (77.2)
Other systemic therapy	289 (71.2)	157 (77.7)
Hormone therapy	164 (40.4)	87 (43.1)
Anti-HER2 TKI	26 (6.4)	17 (8.4)
Other anti-HER2 therapy (except HER2 TKI)	11 (2.7)	6 (3.0)

HER2, human epidermal growth factor receptor 2; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TKI, tyrosine kinase inhibitor; TPC, treatment of physician's choice.

[a]Patients with clinically inactive brain metastases or patients with treated brain metastases that were no longer symptomatic and who require no treatment with corticosteroids or anticonvulsants could be included.

1. Andre F et al. *Lancet.* 2023;401(10390):1773-1785. 2. Krop I et al. Presented at: San Antonio Breast Cancer Symposium 2022; December 6-10, 2022; San Antonio, TX. Presentation GS2-01.

Overall Survival Sensitivity Analysis



- Sensitivity analysis was conducted using rank-preserving structure failure time model to adjust OS in the TPC group for patients who received post-trial T-DXd treatment
- Adjusted median OS was reduced by approximately 2 months (median adjusted OS of 22.9 months) in the TPC group
- The hazard ratio for OS between the T-DXd group and the adjusted TPC group was 0.47 (95% CI, 0.29-0.74)

OS, overall survival, T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

Most Common TEAEs (≥15% in Either Arm) by Preferred or Grouped Term

	T-DXd (n = 404)		TPC (n = 195)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any TEAEs, n (%)	**403 (99.8)**	**224 (55.4)**	**185 (94.9)**	**87 (44.6)**
Nausea	293 (72.5)	27 (6.7)	73 (37.4)	5 (2.6)
Fatigue[a]	252 (62.4)	41 (10.1)	72 (36.9)	2 (1.0)
Vomiting	154 (38.1)	15 (3.7)	25 (12.8)	2 (1.0)
Alopecia	150 (37.1)	1 (0.2)	8 (4.1)	0
Constipation	145 (35.9)	1 (0.2)	21 (10.8)	1 (0.5)
Neutropenia[b]	144 (35.6)	75 (18.6)	23 (11.8)	8 (4.1)
Decreased appetite	126 (31.2)	7 (1.7)	35 (17.9)	1 (0.5)
Anemia[c]	122 (30.2)	37 (9.2)	28 (14.4)	6 (3.1)
Diarrhea	116 (28.7)	11 (2.7)	105 (53.8)	14 (7.2)
Musculoskeletal pain[d]	105 (26.0)	3 (0.7)	35 (17.9)	1 (0.5)
Transaminases increased[e]	95 (23.5)	10 (2.5)	30 (15.4)	3 (1.5)
Abdominal pain[f]	93 (23.0)	4 (1.0)	39 (20.0)	4 (2.1)
Thrombocytopenia[g]	93 (23.0)	11 (2.7)	23 (11.8)	4 (2.1)
Headache[h]	86 (21.3)	1 (0.2)	12 (6.2)	0
Leukopenia[i]	80 (19.8)	29 (7.2)	12 (6.2)	0
Weight decreased	75 (18.6)	2 (0.5)	8 (4.1)	0
Upper respiratory tract infection[j]	74 (18.3)	1 (0.2)	20 (10.3)	0
COVID-19	61 (15.1)	6 (1.5)	5 (2.6)	1 (0.5)
Stomatitis[k]	51 (12.6)	4 (1.0)	40 (20.5)	2 (1.0)
Rash[l]	40 (9.9)	0	32 (16.4)	0
Palmar-plantar erythrodysesthesia syndrome	7 (1.7)	1 (0.2)	100 (51.3)	21 (10.8)

T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event; TPC, treatment of physician's choice.

[a]Fatigue (fatigue, asthenia, malaise, lethargy). [b]Neutropenia (neutrophil count decreased, neutropenia). [c]Anemia (hemoglobin decreased, red blood cell count decreased, anemia, hematocrit decreased). [d]Musculoskeletal pain (back pain, myalgia, pain in extremity, musculoskeletal pain, muscle spasms, bone pain, neck pain, musculoskeletal chest pain, limb discomfort). [e]Transaminases increased (transaminases increased, aspartate aminotransferase increased, alanine aminotransferase increased, gamma-glutamyltransferase increased, liver function test abnormal, hepatic function test abnormal, liver function test increased, hypertransaminasemia). [f]Abdominal pain (abdominal discomfort, abdominal pain, abdominal pain lower, abdominal pain upper, gastrointestinal pain). [g]Thrombocytopenia (platelet count decreased, thrombocytopenia). [h]Headache (migraine, headache, sinus headache). [i]Leukopenia (white blood cell count decreased, leukopenia). [j]Upper respiratory tract infection (influenza, influenza like illness, upper respiratory tract infection, nasopharyngitis, pharyngitis, sinusitis, rhinitis, laryngitis) [k]Stomatitis (stomatitis, aphthous ulcer, mouth ulceration, oral mucosa erosion, oral mucosal blistering, oral mucosal eruption). [l]Rash (rash, rash pustular, rash maculo-papular, rash papular, rash macular, rash pruritic).

Most Common Drug-Related TEAEs Associated with Study Drug Discontinuation

	T-DXd (n = 404)	TPC (n = 195)
Drug-related TEAEs associated with drug discontinuation, n (%)	**63 (15.6)**	**10 (5.1)**
Pneumonitis	25 (6.2)	1 (0.5)
Interstitial lung disease	15 (3.7)	0
Asthenia	3 (0.7)	0
Ejection fraction decreased	2 (0.5)	0
Hepatic cirrhosis	2 (0.5)	0
Pulmonary toxicity	2 (0.5)	0
Skin hyperpigmentation	2 (0.5)	0
Alanine aminotransferase increased	1 (0.2)	0
Ascites	1 (0.2)	0
Aspartate aminotransferase increased	1 (0.2)	0
Electrocardiogram QT prolonged	1 (0.2)	0
Fatigue	1 (0.2)	0
Hemolysis	1 (0.2)	0
Idiopathic interstitial pneumonia	1 (0.2)	0
Lung disorder	1 (0.2)	0
Neutropenia	1 (0.2)	0
Peripheral sensory neuropathy	1 (0.2)	0
Pneumonia	1 (0.2)	0
Pulmonary fibrosis	1 (0.2)	0
Thrombocytopenia	1 (0.2)	0
Abdominal sepsis	0	1 (0.5)
Blood bilirubin increased	0	2 (1.0)
Diarrhea	0	2 (1.0)
Drug eruption	0	1 (0.5)
Palmar-plantar erythrodysesthesia syndrome	0	3 (1.5)
Vomiting	0	1 (0.5)

T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice; TEAE, treatment-emergent adverse event.