

Trastuzumab deruxtecan (T-DXd) vs trastuzumab emtansine (T-DM1) in patients with high-risk human epidermal growth factor receptor 2–positive (HER2+) primary breast cancer with residual invasive disease after neoadjuvant therapy: Interim analysis of DESTINY-Breast05

Background

- HER2-targeted therapies have greatly improved outcomes for patients with HER2+ eBC^{1,2}
- **In the KATHERINE trial, adjuvant T-DM1 significantly improved IDFS and OS relative to trastuzumab in patients with HER2+ eBC and residual invasive disease following NAT (HR for IDFS, 0.50; 95% CI, 0.39-0.64; $P < 0.001$; HR for OS, 0.66; 95% CI, 0.51-0.87; $P = 0.003$)^{3,4}**
 - However, **subsets of patients presenting with advanced locoregional disease or positive nodal status after NAT had 3-year IDFS rates of 76% and 83%, with 7-year IDFS rates of 67% and 72%, respectively^{4,5}**
 - Furthermore, **adjuvant T-DM1 did not reduce CNS recurrences relative to trastuzumab⁵**
- Therefore, an **unmet medical need** remained even with adjuvant T-DM1 for these high-risk patients in the post-neoadjuvant setting^{3,4}
- **Early phase studies in heavily pretreated HER2+ mBC had demonstrated remarkable activity of T-DXd,⁶ and DESTINY-Breast03 demonstrated superiority of T-DXd relative to T-DM1 in the 2L metastatic setting⁷**

DESTINY-Breast05 is a global, multicenter, randomized, open-label, phase 3 trial to assess efficacy and safety of adjuvant T-DXd vs T-DM1 in high-risk patients with HER2+ eBC and residual invasive disease following neoadjuvant therapy

DESTINY-Breast05 study design

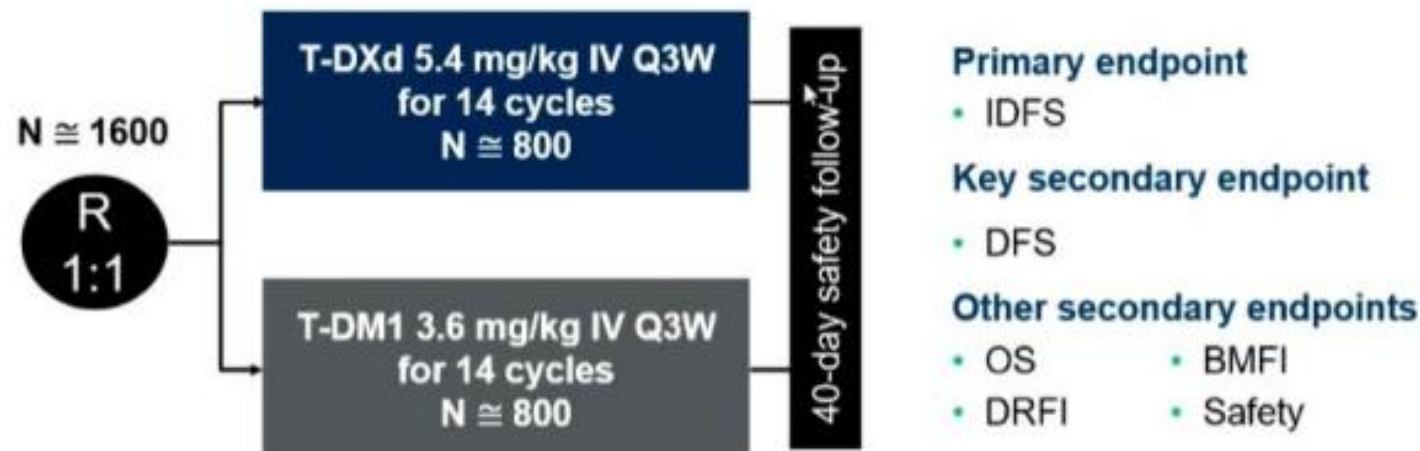
A global, multicenter, randomized, open-label, phase 3 trial (NCT04622319)

Key Eligibility Criteria

- **Residual invasive disease in the breast and/or axillary lymph nodes** after neoadjuvant chemotherapy with HER2-directed therapy (NAT)^a
- **High-risk defined as presentation prior to NAT with:**
 - **Inoperable eBC** (cT4,N0-3,M0 or cT1-3,N2-3,M0) **OR**
 - **Operable eBC** (cT1-3,N0-1,M0) with axillary node-positive disease (ypN1-3) after NAT
- **Centrally confirmed HER2+ (IHC 3+ or ISH+) eBC**
- ECOG PS 0 or 1

Stratification factors

- Extent of disease at presentation (inoperable, operable)
- HER2-targeted NAT (single, dual)
- Hormone receptor status (positive, negative)
- Post-NAT pathologic nodal status (positive, negative)



BMFI, brain metastasis-free interval; CT, computed tomography; eBC, early breast cancer; DCO, data cutoff; DFS, disease-free survival; DRFI, distant recurrence-free interval; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; IDFS, invasive disease-free survival; IHC, immunohistochemistry; ILD, interstitial lung disease; ISH, in situ hybridization; IV, intravenous; NAT, neoadjuvant therapy; OS, overall survival; Q3W, every 3 weeks; R, randomization; RT, radiotherapy; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

^aNAT is defined as ≥16 weeks' NAT with ≥9 weeks trastuzumab ± pertuzumab and ≥9 weeks taxane-based chemotherapy.

DESTINY-Breast05 study design

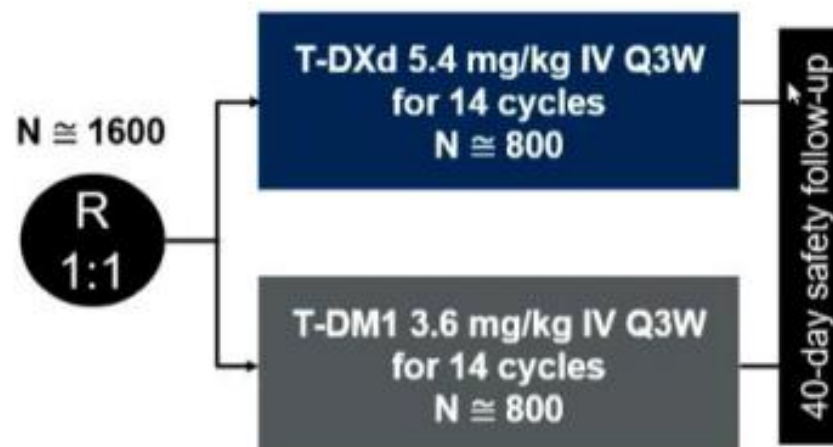
A global, multicenter, randomized, open-label, phase 3 trial (NCT04622319)

Key Eligibility Criteria

- Residual invasive disease in the breast and/or axillary lymph nodes after neoadjuvant chemotherapy with HER2-directed therapy (NAT)^a
- High-risk defined as presentation prior to NAT with:
 - Inoperable eBC (cT4,N0-3,M0 or cT1-3,N2-3,M0)
 - OR
 - Operable eBC (cT1-3,N0-1,M0) with axillary node-positive disease (ypN1-3) after NAT
- Centrally confirmed HER2+ (IHC 3+ or ISH+) eBC
- ECOG PS 0 or 1

Stratification factors

- Extent of disease at presentation (inoperable, operable)
- HER2-targeted NAT (single, dual)
- Hormone receptor status (positive, negative)
- Post-NAT pathologic nodal status (positive, negative)



Primary endpoint

- IDFS

Key secondary endpoint

- DFS

Other secondary endpoints

- OS
- BMFI
- DRFI
- Safety

- Concomitant adjuvant ET was allowed per local practices
- If administered, RT could be initiated concurrent with study therapy or completed prior to initiation of study therapy (sequential) per investigator
- ILD monitoring program for patients treated with RT
 - All patients had baseline non-contrast, low dose (LD) chest CT during screening
 - All RT patients (concurrent and sequential) had LD chest CT 6 weeks after start of study therapy, then every 12 weeks while on therapy, and at 40-day follow-up
 - Sequential RT patients had additional LD chest CT after completion of RT prior to start of study therapy

BMFI, brain metastasis-free interval; CT, computed tomography; eBC, early breast cancer; DCO, data cutoff; DFS, disease-free survival; DRFI, distant recurrence-free interval; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; IDFS, invasive disease-free survival; IHC, immunohistochemistry; ILD, interstitial lung disease; ISH, in situ hybridization; IV, intravenous; NAT, neoadjuvant therapy; OS, overall survival; Q3W, every 3 weeks; R, randomization; RT, radiotherapy; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

^aNAT is defined as ≥16 weeks' NAT with ≥9 weeks trastuzumab ± pertuzumab and ≥9 weeks taxane-based chemotherapy.

Study status and statistical analysis

1600 randomized patients would provide **~80% power** with **~207 IDFS events** to demonstrate a statistically significant difference in IDFS assuming a HR of 0.675, corresponding to an improvement of **3-year IDFS rate from 83.0% projected in the T-DM1 arm to 88.2% in the T-DXd arm**

Study status

- First patient in – Dec 2020
- Last patient randomized – Feb 2024
- Last patient final treatment – Feb 2025
- 481 locations

Statistical analysis

**Interim analysis of IDFS planned at
~70% of the 207 target events**

Interim analysis timeline

- DCO: 2 July 2025
- Events as of DCO: 153 (74% IF)

Multiple testing procedure^a

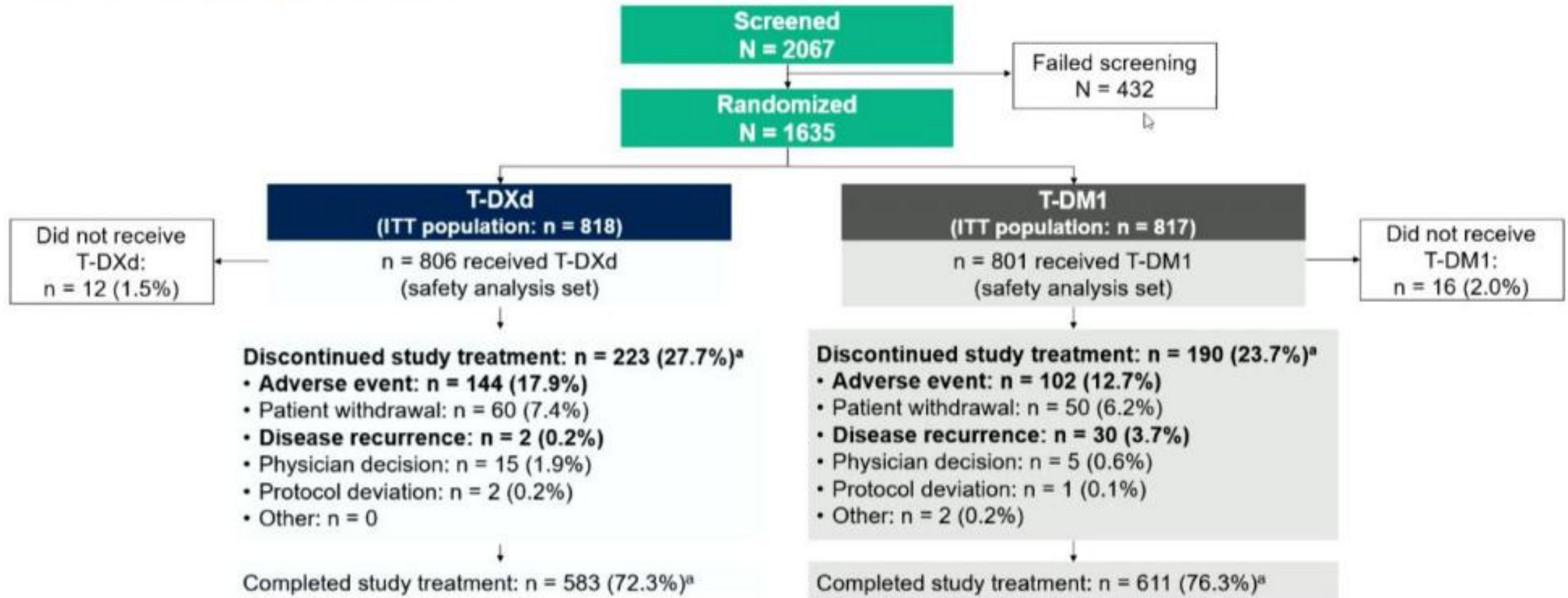
IDFS (alpha = 5%)



DFS (alpha = 5%)

^aSeparate Lan-DeMets alpha-spending functions with O'Brien-Fleming boundaries were used to allocate alpha between interim and final analyses for IDFS and DFS under the hierarchical testing strategy

Patient disposition



Median study duration: 29.9 months (range, 0.3-53.4 months) with T-DXd and 29.7 months (range, 0.1-54.4 months) with T-DM1

ITT, intention-to-treat; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
^aCalculated using the number of patients in the safety analysis set as a denominator

Baseline demographics and clinical characteristics

	T-DXd n = 818	T-DM1 n = 817
Age, median (range), years	50.3 (24-78)	50.6 (21-83)
<65	735 (89.9)	736 (90.1)
≥65	83 (10.1)	81 (9.9)
Female sex, n (%)	814 (99.5)	814 (99.6)
Race		
White	301 (36.8)	333 (40.8)
Black or African American	22 (2.7)	13 (1.6)
Asian	399 (48.8)	386 (47.2)
Other	96 (11.7)	85 (10.4)
Region, n (%)		
Asia	392 (47.9)	380 (46.5)
Europe	222 (27.1)	223 (27.3)
North America + Australia	57 (7.0)	72 (8.8)
Rest of world ^a	147 (18.0)	142 (17.4)
ECOG PS score, n (%)		
0	656 (80.2)	652 (79.8)
1	162 (19.8)	165 (20.2)
HER2 expression,^b n (%)		
IHC 3+	676 (82.6)	670 (82.0)
IHC 2+ and ISH+	129 (15.8)	133 (16.3)
IHC 2+ and ISH-	2 (0.2)	0
IHC 1+ and ISH+	11 (1.3)	14 (1.7)
Hormone receptor status,^c n (%)		
Positive	581 (71.0)	583 (71.4)
Negative	237 (29.0)	234 (28.6)

ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; NAT, neoadjuvant therapy; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

^aIncluded regions: Argentina, Brazil, Chile, Czech Republic, Israel, Mexico, Peru, Poland, Romania, Russian Federation. ^bCentrally confirmed. ^cAs reported in electronic data capture.

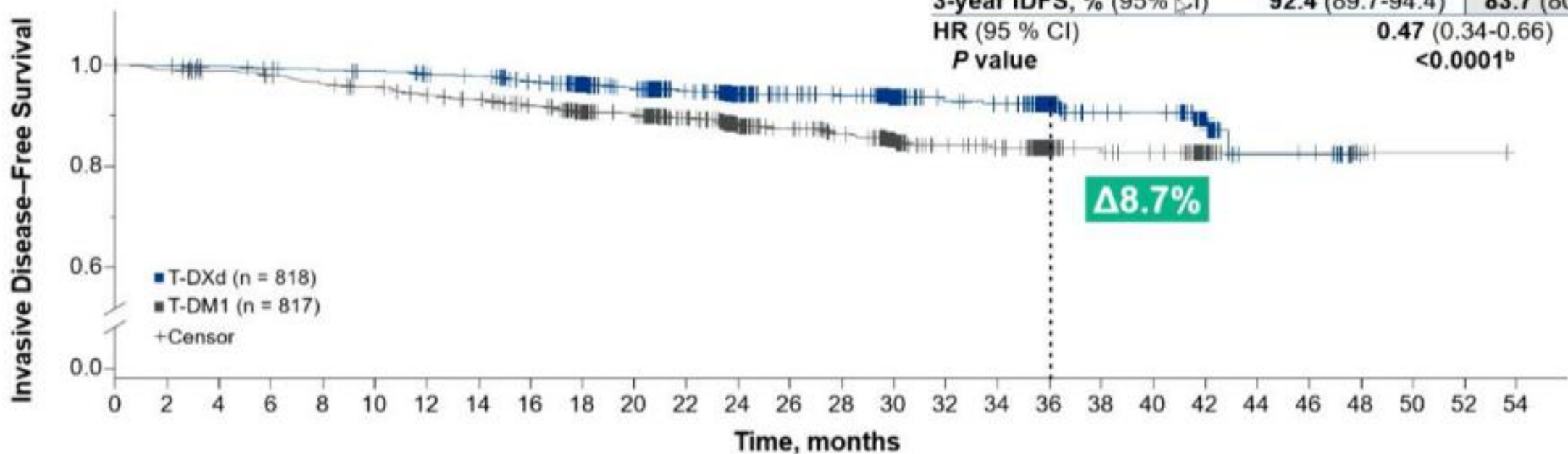
Baseline demographics and clinical characteristics

	T-DXd n = 818	T-DM1 n = 817		T-DXd n = 818	T-DM1 n = 817
Age, median (range), years	50.3 (24-78)	50.6 (21-83)	Operative status at disease presentation,^c n (%)		
<65	735 (89.9)	736 (90.1)	Operable (cT1-3, N0-1, M0)	387 (47.3)	393 (48.1)
≥65	83 (10.1)	81 (9.9)	Inoperable (cT4, N0-3, M0 or cT1-3, N2-3, M0)	431 (52.7)	424 (51.9)
Female sex, n (%)	814 (99.5)	814 (99.6)	Post-NAT pathologic nodal status,^c n (%)		
Race			Positive	660 (80.7)	658 (80.5)
White	301 (36.8)	333 (40.8)	Negative	158 (19.3)	159 (19.5)
Black or African American	22 (2.7)	13 (1.6)	Neoadjuvant HER2-targeted therapy, n (%)		
Asian	399 (48.8)	386 (47.2)	Trastuzumab alone	176 (21.5)	171 (20.9)
Other	96 (11.7)	85 (10.4)	Trastuzumab + pertuzumab	637 (77.9)	641 (78.5)
Region, n (%)			Trastuzumab + other HER2-targeted therapy	3 (0.4)	3 (0.4)
Asia	392 (47.9)	380 (46.5)	Trastuzumab + pertuzumab + other HER2-targeted therapy	2 (0.2)	2 (0.2)
Europe	222 (27.1)	223 (27.3)	Neoadjuvant chemotherapy, n (%)		
North America + Australia	57 (7.0)	72 (8.8)	Taxanes	818 (100)	817 (100)
Rest of world ^a	147 (18.0)	142 (17.4)	Platinum compounds	386 (47.2)	392 (48.0)
ECOG PS score, n (%)			Anthracycline	423 (51.7)	399 (48.8)
0	656 (80.2)	652 (79.8)	Radiotherapy treatment, n (%)		
1	162 (19.8)	165 (20.2)	Adjuvant radiotherapy	764 (93.4)	759 (92.9)
HER2 expression,^b n (%)			Concurrent	438 (53.5)	480 (58.8)
IHC 3+	676 (82.6)	670 (82.0)	Sequential	326 (39.9)	279 (34.1)
IHC 2+ and ISH+	129 (15.8)	133 (16.3)	No radiotherapy	54 (6.6)	58 (7.1)
IHC 2+ and ISH-	2 (0.2)	0			
IHC 1+ and ISH+	11 (1.3)	14 (1.7)			
Hormone receptor status,^c n (%)					
Positive	581 (71.0)	583 (71.4)			
Negative	237 (29.0)	234 (28.6)			

ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; NAT, neoadjuvant therapy; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

^aIncluded regions: Argentina, Brazil, Chile, Czech Republic, Israel, Mexico, Peru, Poland, Romania, Russian Federation. ^bCentrally confirmed. ^cAs reported in electronic data capture.

Primary endpoint: IDFS^a



	T-DXd n = 818	T-DM1 n = 817
Patients with events, n (%)	51 (6.2)	102 (12.5)
3-year IDFS, % (95% CI)	92.4 (89.7-94.4)	83.7 (80.2-86.7)
HR (95 % CI)	0.47 (0.34-0.66)	
P value	<0.0001 ^b	

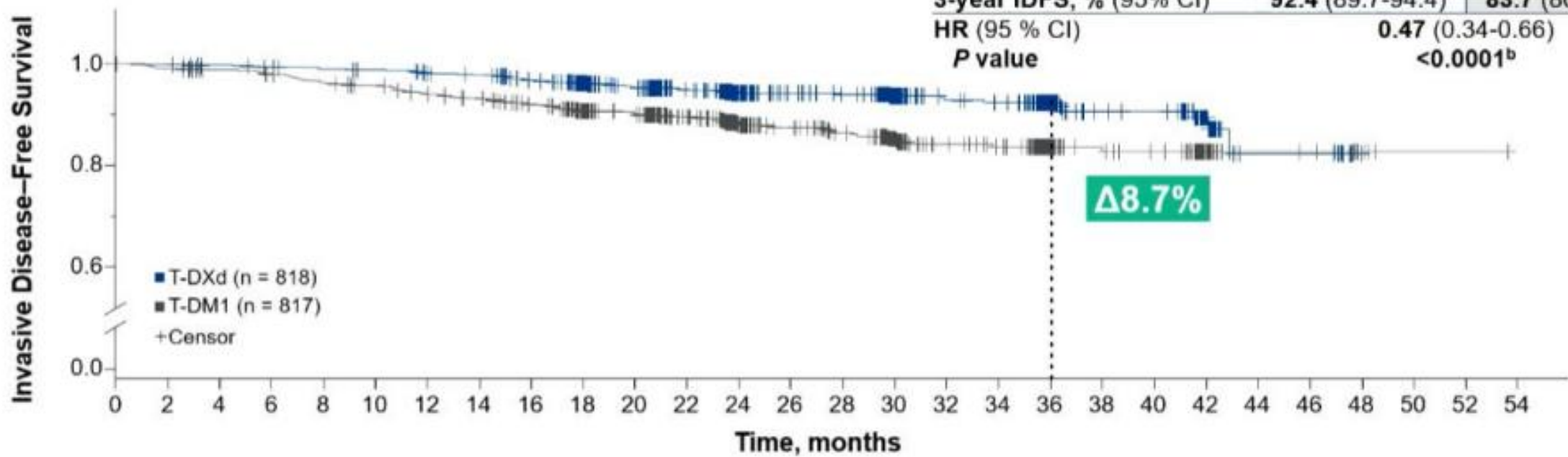
Number at Risk:

T-DXd	818	788	781	776	771	768	758	753	731	684	634	544	440	380	370	275	218	212	129	92	90	46	14	14	0	0	0	0
T-DM1	817	781	769	760	745	734	719	708	687	632	599	527	417	355	337	233	186	177	120	84	79	38	14	13	4	1	1	0

53% reduction in the risk of invasive disease recurrence or death for T-DXd compared with T-DM1

HR, hazard ratio; IDFS, invasive disease-free survival; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
Efficacy stopping boundary, P = 0.0183.
^aIDFS is defined as the time from randomization until the date of first occurrence of one of the following events: recurrence of ipsilateral invasive breast tumor, recurrence of ipsilateral locoregional invasive breast cancer, contralateral invasive breast cancer, a distant disease recurrence, or death from any cause. ^bTwo-sided P value from stratified log-rank test. Hazard ratio and 95% CI from stratified Cox proportional hazards model with stratification factor of operative status at disease presentation.

Primary endpoint: IDFS^a



	T-DXd n = 818	T-DM1 n = 817
Patients with events, n (%)	51 (6.2)	102 (12.5)
3-year IDFS, % (95% CI)	92.4 (89.7-94.4)	83.7 (80.2-86.7)
HR (95 % CI)	0.47 (0.34-0.66)	
P value	<0.0001 ^b	

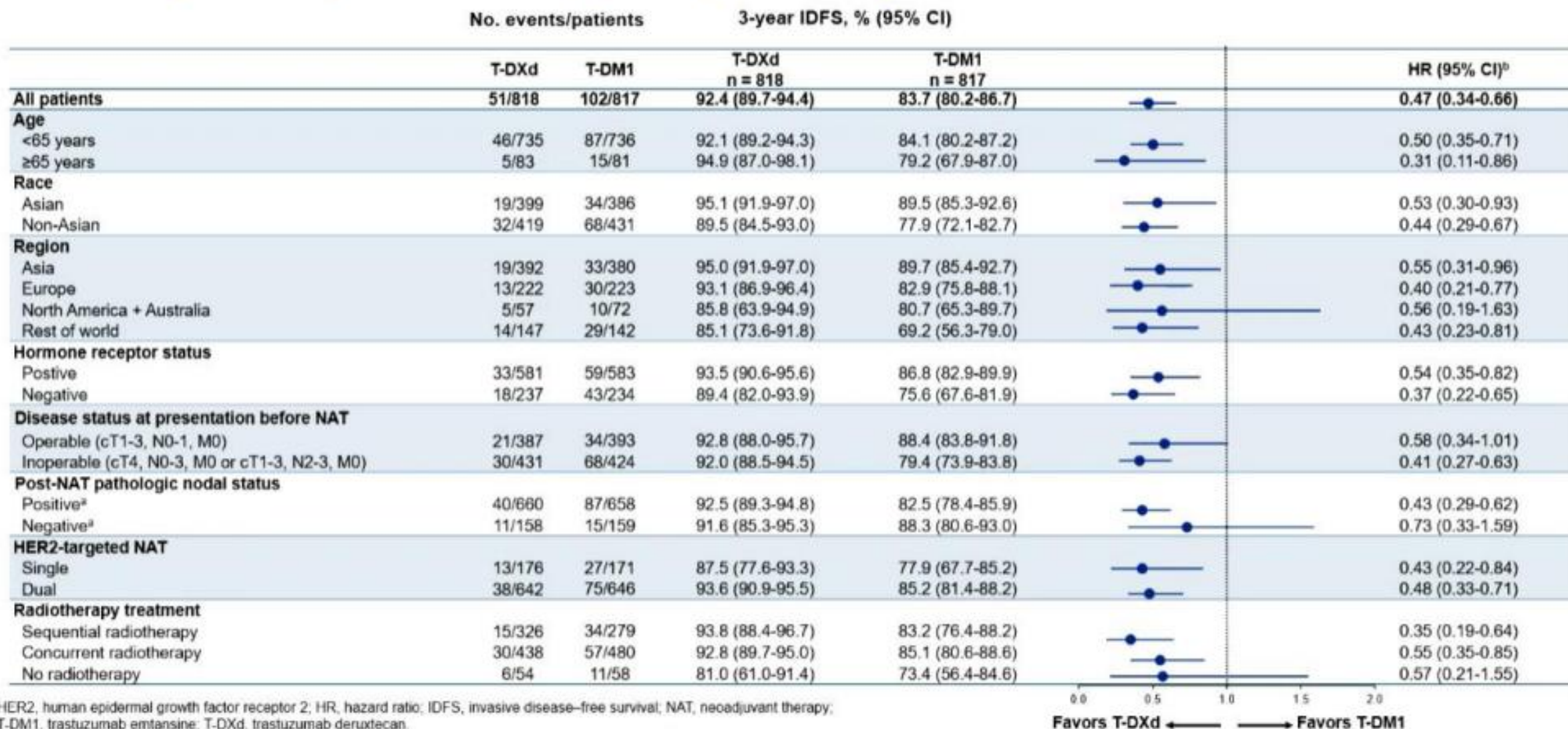
Number at Risk:

T-DXd	818	788	781	776	771	768	758	753	731	684	634	544	440	380	370	275	218	212	129	92	90	46	14	14	0	0	0	0
T-DM1	817	781	769	760	745	734	719	708	687	632	599	527	417	355	337	233	186	177	120	84	79	38	14	13	4	1	1	0

53% reduction in the risk of invasive disease recurrence or death for T-DXd compared with T-DM1

HR, hazard ratio; IDFS, invasive disease-free survival; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
Efficacy stopping boundary, $P = 0.0183$.
^aIDFS is defined as the time from randomization until the date of first occurrence of one of the following events: recurrence of ipsilateral invasive breast tumor, recurrence of ipsilateral locoregional invasive breast cancer, contralateral invasive breast cancer, a distant disease recurrence, or death from any cause. ^bTwo-sided P value from stratified log-rank test. Hazard ratio and 95% CI from stratified Cox proportional hazards model with stratification factor of operative status at disease presentation.

Primary endpoint subgroup analysis: IDFS

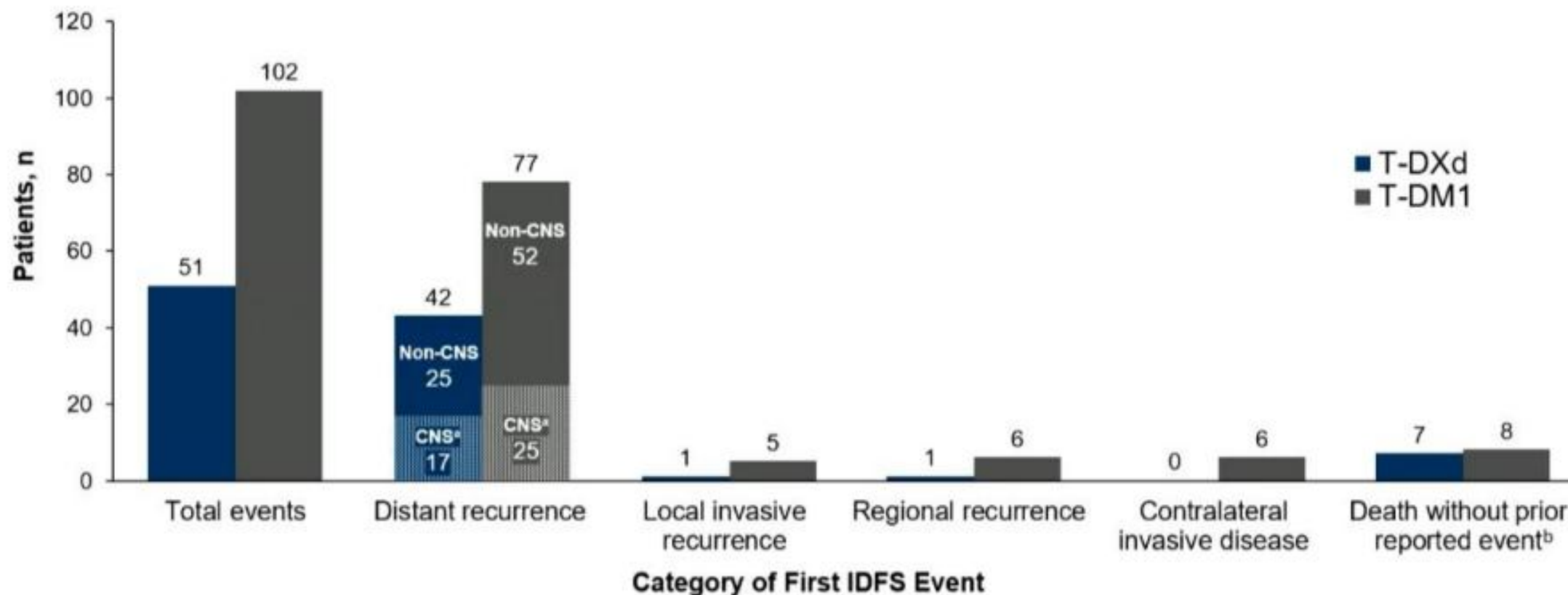


HER2, human epidermal growth factor receptor 2; HR, hazard ratio; IDFS, invasive disease-free survival; NAT, neoadjuvant therapy;

T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

^aPositive pathologic nodal status defined as ypN1-3 and negative pathologic nodal status defined as ypN0. ^bFrom unstratified Cox proportional hazards model.

Categories of first IDFS events



Lower distant and locoregional recurrences were observed with T-DXd vs T-DM1, including CNS recurrences

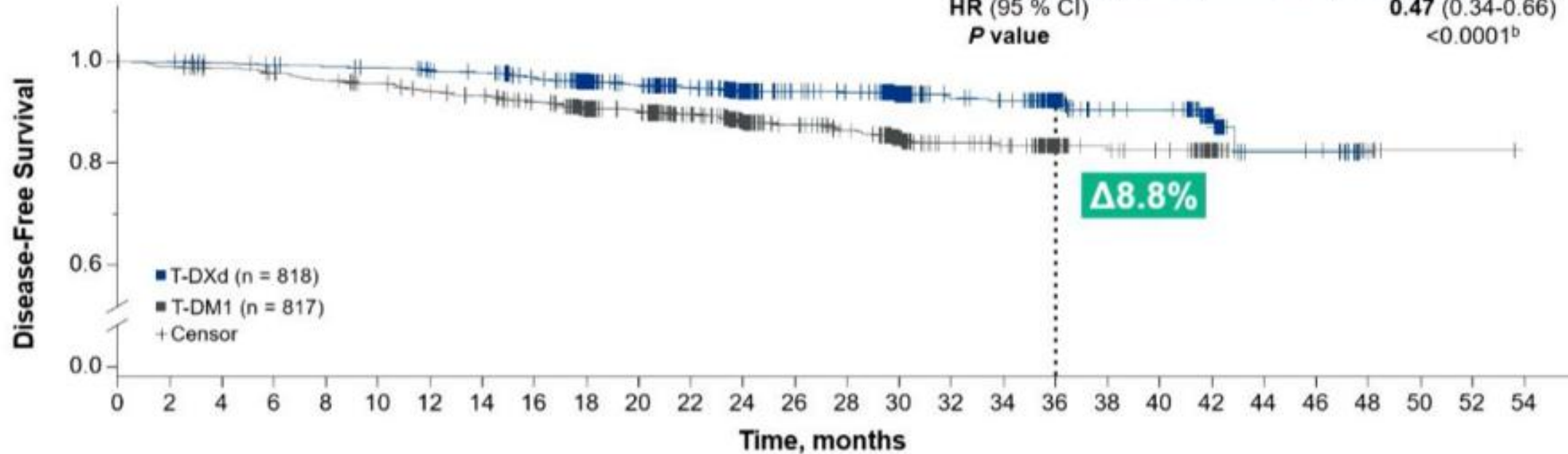
IDFS, invasive disease-free survival; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

Participants who experienced multiple types of IDFS events within 61 days of their first event are reported in the category according to the following hierarchy: distant recurrence CNS, distant recurrence non-CNS, local invasive recurrence, regional recurrence, contralateral breast cancer, and death without a previous event.

*CNS as sole site for distant recurrence or one of multiple distant recurrent sites. ^bCauses of death in the T-DXd arm were 2 drug-related ILD, unrelated respiratory tract infection, acute respiratory failure (outside AE reporting period), acute respiratory distress syndrome (outside AE reporting period), and 2 disease progression, and in the T-DM1 arm were drug-related sepsis, unrelated ovarian cancer, unrelated aneurysm, unrelated pneumothorax, unrelated leiomyosarcoma, self-inflicted gun wound, and 2 disease progression.

Key secondary endpoint: DFS^a

	T-DXd n = 818	T-DM1 n = 817
Patients with events, n (%)	52 (6.4)	103 (12.6)
3-year DFS, % (95% CI)	92.3 (89.5-94.3)	83.5 (79.9-86.4)
HR (95 % CI)	0.47 (0.34-0.66)	
P value	<0.0001 ^b	



Number at Risk:

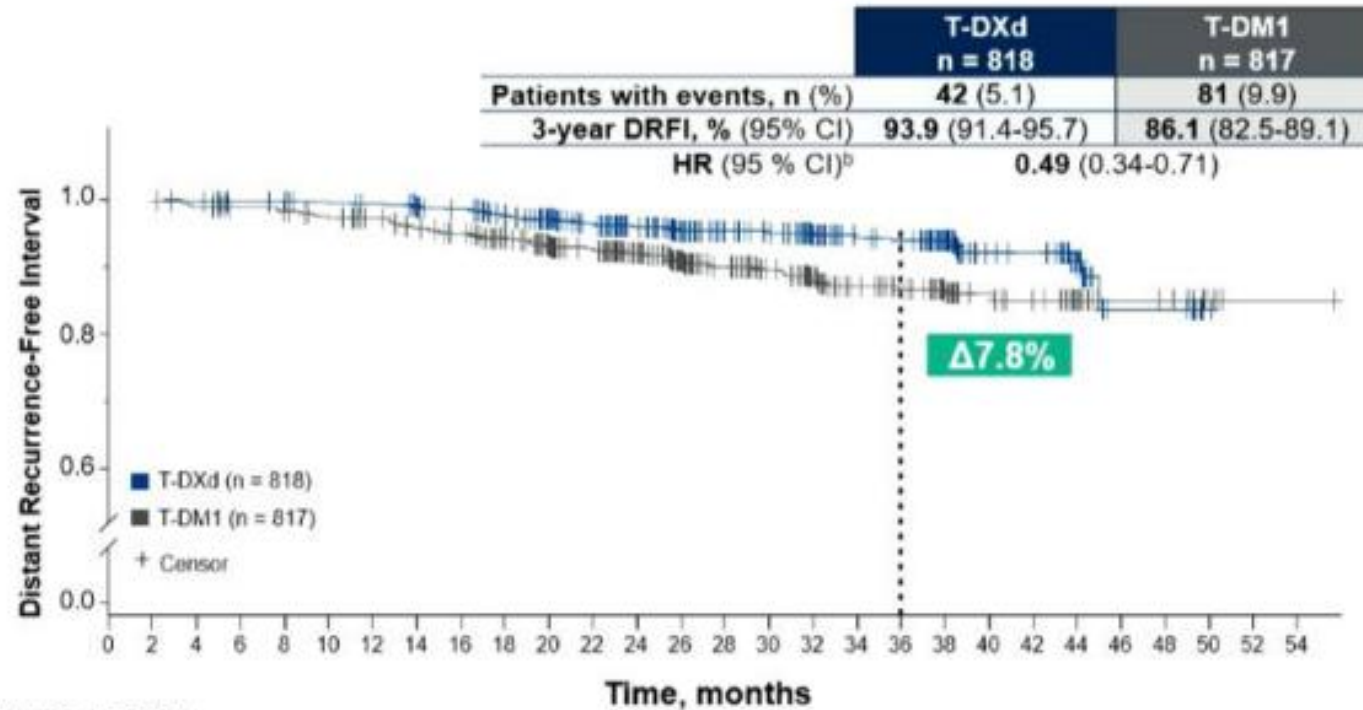
T-DXd	818	788	781	776	771	768	758	753	731	683	633	543	440	380	370	275	218	212	129	92	90	46	14	14	0	0	0	0
T-DM1	817	779	767	757	743	733	718	707	686	631	598	526	416	354	336	233	186	177	120	84	79	38	14	13	4	1	1	0

DFS, disease-free survival; HR, hazard ratio; INV, investigator assessment; STEEP, Standardized Definitions for Efficacy End Points in adjuvant breast cancer trials; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

Efficacy stopping boundary, $P = 0.0144$.

^aDFS defined as the time between randomization and the date of the first occurrence of an IDFS event per STEEP criteria, including second primary non-breast cancer event or contralateral or ipsilateral ductal carcinoma in situ. ^bTwo-sided P value from stratified log-rank test. Hazard ratio and 95% CI from stratified Cox proportional hazards model with stratification factor of operative status at disease presentation.

Secondary endpoints: DRFI^a, BMFI, and OS



Number at Risk:

T-DXd	818	786	778	774	770	767	757	753	731	684	635	545	442	382	372	276	219	213	129	92	90	46	14	14	0	0	0	0
T-DM1	817	780	769	761	746	739	724	713	694	639	606	533	424	362	345	240	192	182	121	84	79	38	14	13	4	1	1	0

	T-DXd n = 818	T-DM1 n = 817
BMFI		
Patients with recurrence in CNS, n (%)	17 (2.1)	26 (3.2)
3-year BMFI rate, % (95% CI)	97.6 (96.2-98.5)	95.8 (93.6-97.2)
HR (95% CI) ^b	0.64 (0.35-1.17)	
OS (2.9% maturity)		
Patient deaths, n (%)	18 (2.2)	29 (3.5)
Survival at 3 years % (95% CI)	97.4 (95.8-98.4)	95.7 (93.5-97.2)
HR (95% CI) ^b	0.61 (0.34-1.10)	

BMFI, brain metastasis-free interval, DRFI, distant recurrence-free interval, HR, hazard ratio, OS, overall survival, T-DM1, trastuzumab emtansine, T-DXd, trastuzumab deruxtecan.

^aDRFI is defined as the time between randomization and the date of distant breast cancer recurrence. ^bHR and 95% CI from stratified Cox proportional hazards model with stratification factor of operative status at disease presentation.

Study treatment exposure

	T-DXd n = 806^a	T-DM1 n = 801^a
Median study treatment duration, months	9.8	9.7
Number of cycles, n (%)		
≥4 cycles	737 (91.4)	747 (93.3)
≥7 cycles	670 (83.1)	704 (87.9)
≥11 cycles	612 (75.9)	649 (81.0)
14 cycles	583 (72.3)	611 (76.3)

- **More than 72% of patients completed the planned 14 cycles of therapy in both arms**
- **Patients discontinuing study prior to 14 cycles were allowed to receive additional HER2-targeted therapy as per SOC to complete up to 14 cycles of HER2-targeted adjuvant therapy**

HER2, human epidermal growth factor receptor 2; SOC, standard of care; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
*All patients who received at least 1 dose of study treatment.

Overall safety summary

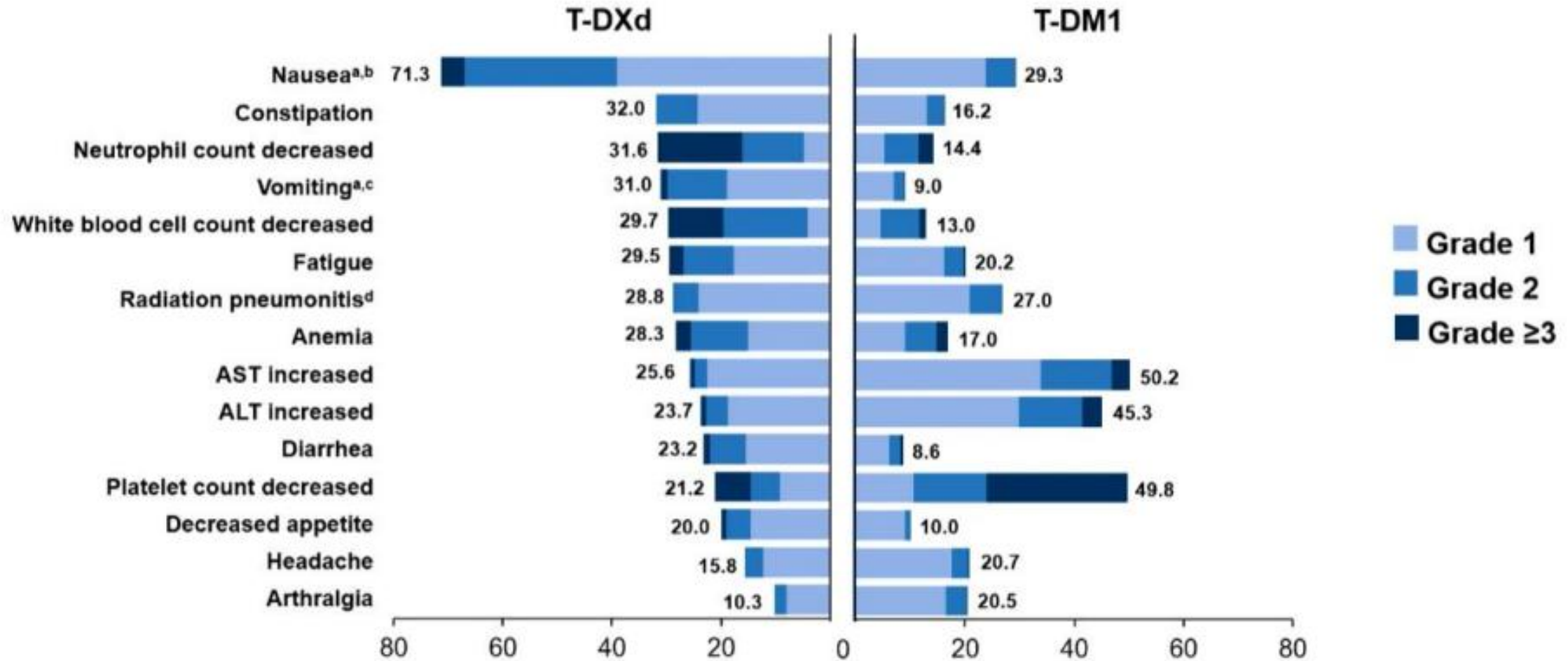
TEAEs, n (%)	T-DXd n = 806 ^a	T-DM1 n = 801 ^a
Any grade	802 (99.5)	788 (98.4)
Grade ≥3	408 (50.6)	416 (51.9)
Serious	140 (17.4)	109 (13.6)
Associated with drug discontinuation	144 (17.9)	103 (12.9)
Drug-related ILD/pneumonitis ^b	87 (10.8)	20 (2.5)
Associated with drug interruptions	400 (49.6)	329 (41.1)
Associated with dose reductions	213 (26.4)	213 (26.6)
Associated with deaths	3 (0.4)	5 (0.6)

- In the T-DXd arm, causes of death (n = 3) were 2 ILD/pneumonitis^c and respiratory tract infection (adjudicated as not ILD)
- In the T-DM1 arm, causes of death (n = 5) were leiomyosarcoma of the uterus, aneurysm, non-neutropenic sepsis, ovarian cancer, and traumatic pneumothorax

ILD, interstitial lung disease; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TEAE, treatment-related adverse event.

^aAll patients who received at least 1 dose of study treatment. ^bInvestigator-assessed as drug-related ILD and pneumonitis per preferred term. ^cInvestigator assessed and adjudication committee confirmed.

TEAEs in $\geq 20\%$ of patients (either arm)



ALT, alanine aminotransferase; AST, aspartate aminotransferase; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event.

^aProphylactic antiemetics were recommended but not mandatory. ^bIn the T-DXd and T-DM1 arms: 39.1% and 23.7% grade 1, 27.8% and 5.5% grade 2, and 4.5% and 0.1% grade 3 events, respectively. ^cIn the T-DXd and T-DM1 arms: 19.0% and 6.9% grade 1, 10.9% and 2.0% grade 2, and 1.1% and 0.1% grade 3 events. ^dIn the T-DXd and T-DM1 arms: 24.2% and 20.8% grade 1, 4.6% and 6.1% grade 2 events.

Adverse events of special interest: ILD/pneumonitis and LV dysfunction

n (%)	Adjudicated Drug-related ILD					
	Any grade	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
T-DXd (n = 806) ^a	77 (9.6)	16 (2.0)	52 (6.5)	7 (0.9)	0	2 (0.2)
T-DM1 (n = 801) ^a	13 (1.6)	8 (1.0)	5 (0.6)	0	0	0

Adjuvant radiotherapy timing (sequential or concurrent) showed no differences in adjudicated drug-related ILD

Similar distributions of any grade adjudicated drug-related ILD events were observed with sequential and concurrent radiotherapy in both treatment arms (T-DXd: 10.7% and 9.6.% vs T-DM1: 2.6% and 1.0%, respectively)

n (%)	LV dysfunction					
	Any grade	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
T-DXd (n = 806) ^a	23 (2.9)	1 (0.1)	20 (2.5)	2 (0.2)	0	0
T-DM1 (n = 801) ^a	14 (1.7)	0	11 (1.4)	3 (0.4)	0	0

CT, computed tomography; ILD, interstitial lung disease; LV, left ventricular; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

^aAll patients who received at least 1 dose of study treatment

Conclusions

- DESTINY-Breast05 demonstrated a **statistically significant and clinically meaningful improvement in IDFS and DFS with T-DXd vs T-DM1 in high-risk^a patients with HER2+ eBC and residual invasive disease after NAT**
- **IDFS benefit was consistent across all prespecified subgroups**
- **Benefit in DRFI with T-DXd was also observed**
- **CNS metastases and deaths were numerically fewer with T-DXd vs T-DM1**
- The overall **safety profile of T-DXd was manageable with no new signals**
 - >72% of patients completed treatment and was comparable in both arms
 - **Adjudicated drug-related ILD was reported in 9.6% of patients receiving T-DXd, with the majority being grade 1 or 2 and reversible**, suggesting that the risk is manageable with appropriate monitoring and timely intervention

**IDFS Benefit T-DXd
versus T-DM1**

**53% reduction in the
risk of invasive
disease recurrence or
death**

**3-year IDFS rate
92.4% versus 83.7%
HR 0.47
P value <0.0001**

Adjuvant T-DXd demonstrated superior efficacy with manageable safety in patients with high-risk HER2+ eBC and residual invasive disease after NAT, representing a potential new standard of care in this post-neoadjuvant setting

DFS, disease-free survival; eBC, early breast cancer; HER2, human epidermal growth factor receptor 2; HR, hazard ratio; IDFS, invasive disease-free survival; ILD, interstitial lung disease; NAT, neoadjuvant therapy; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

^aDefined as cT4, N0-3, M0 or cT1-3, N2-3, M0 at presentation (before NAT) or cT1-3, N0-1, M0, with axillary node-positive disease (ypN1-3) following NAT.