

15:05 – 16:50

Neoadjuvante und post-neoadjuvante Therapie des frühen Mammakarzinoms

Vorsitz: Prof. Dr. Vesna Bjelic-Radisic, Prof. Dr. Jens-Uwe Blohmer

Grundsätze der neoadjuvanten Therapie und Update 2026 (20 Min)

Prof. Dr. Jens Huober

Targets kombinieren – Chemotherapie-freie, neoadjuvante Therapie beim triple-positiven, frühen Brustkrebs (15 Min)

PD Dr. Mattea Reinisch

Moderne Substanzen in der präoperativen endokrinen Therapie (15 Min)

Prof. Dr. Maria Margarete Karsten

Biparatopische HER2-Blockade beim HER2+ frühen Brustkrebs (15 Min)

Dr. Theresa Link

Post-neoadjuvante Therapie beim HER2+ frühen Brustkrebs – wer erhält welche Therapie nach Destiny Breast05/TRUDY (15 Min)

Prof. Dr. Michael Untch

Post-neoadjuvante Therapie beim HER2- frühen Brustkrebs – aktueller Stand und was wir uns erhoffen (15 Min)

Prof. Dr. Frederik Marmé

Fallvorstellung (10 Min)

Prof. Dr. Andreas Hartkopf



Diagnostik und Therapie des Mammakarzinoms

State of the Art

Herausgegeben von
M. Untch, G. Konecny, H. Sittek, M. KeBler,
M. Reiser, H. Hepp



Steinhardt

1997

**„Stirbt der
forschende
Geist, dann
stirbt auch die
Gesellschaft“
Cato der Ältere**

**„ceterum
censeo
Carthaginem
esse delendam”**

ORIGINAL ARTICLE

Survival with Trastuzumab Emtansine in Residual HER2-Positive Breast Cancer

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Priya Rastogi, M.D., Andreas Schneeweiss, M.D., Andres Redondo, M.D., Ph.D.,
Hans H. Fischer, M.D., Véronique D'Hondt, M.D., Ph.D., Alison K. Conlin, M.D.,
Valentina Guarneri, M.D., Ph.D., Irene L. Wapnir, M.D.,
Christian Jackisch, M.D., Ph.D., Claudia
Peter A. Fasching, M.D., Michael P. DiGiovanna,
Pia Wuelfing, M.D., Zhimin Shao, M.D.,
Hervé R. Bonnefoi, M.D., Bryan T. Hennessy, M.D.,
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Beatrice Nyawira, M.D., Eleonora Restuccia, M.D.,
for the KATHERINE Study Investigators

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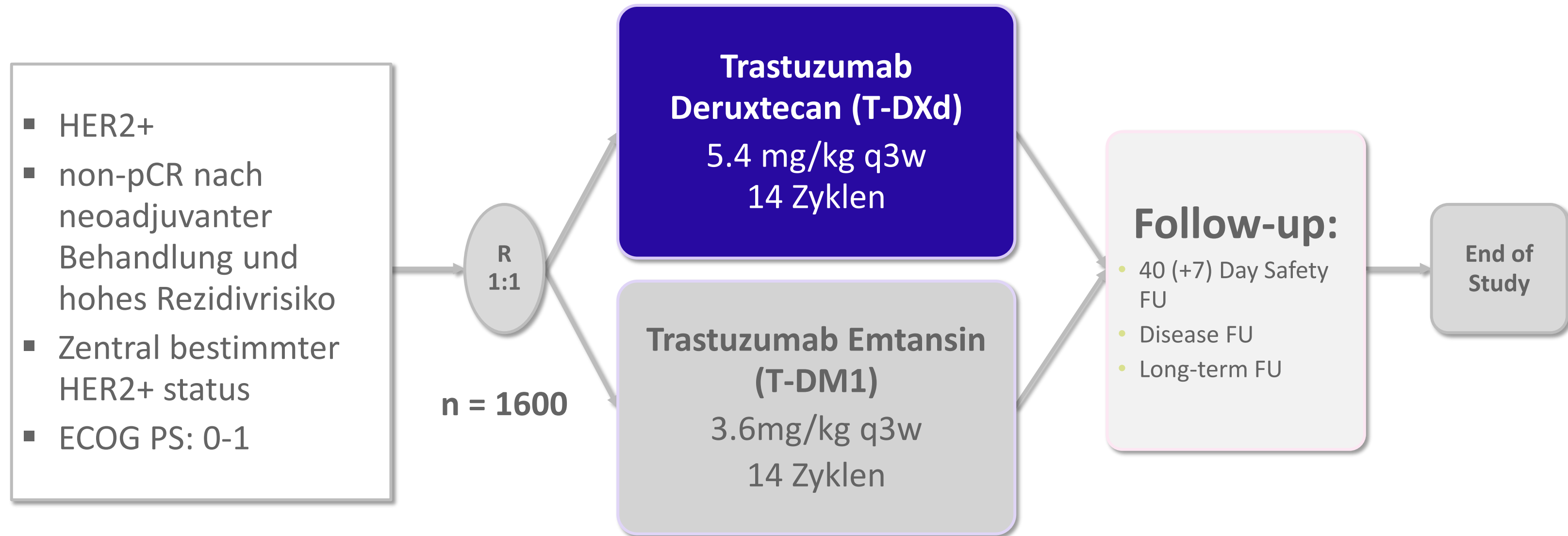
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Trastuzumab Deruxtecan in Residual HER2-Positive Early Breast Cancer

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for the DESTINY-Breast05 Trial Investigators*

Studiendesign

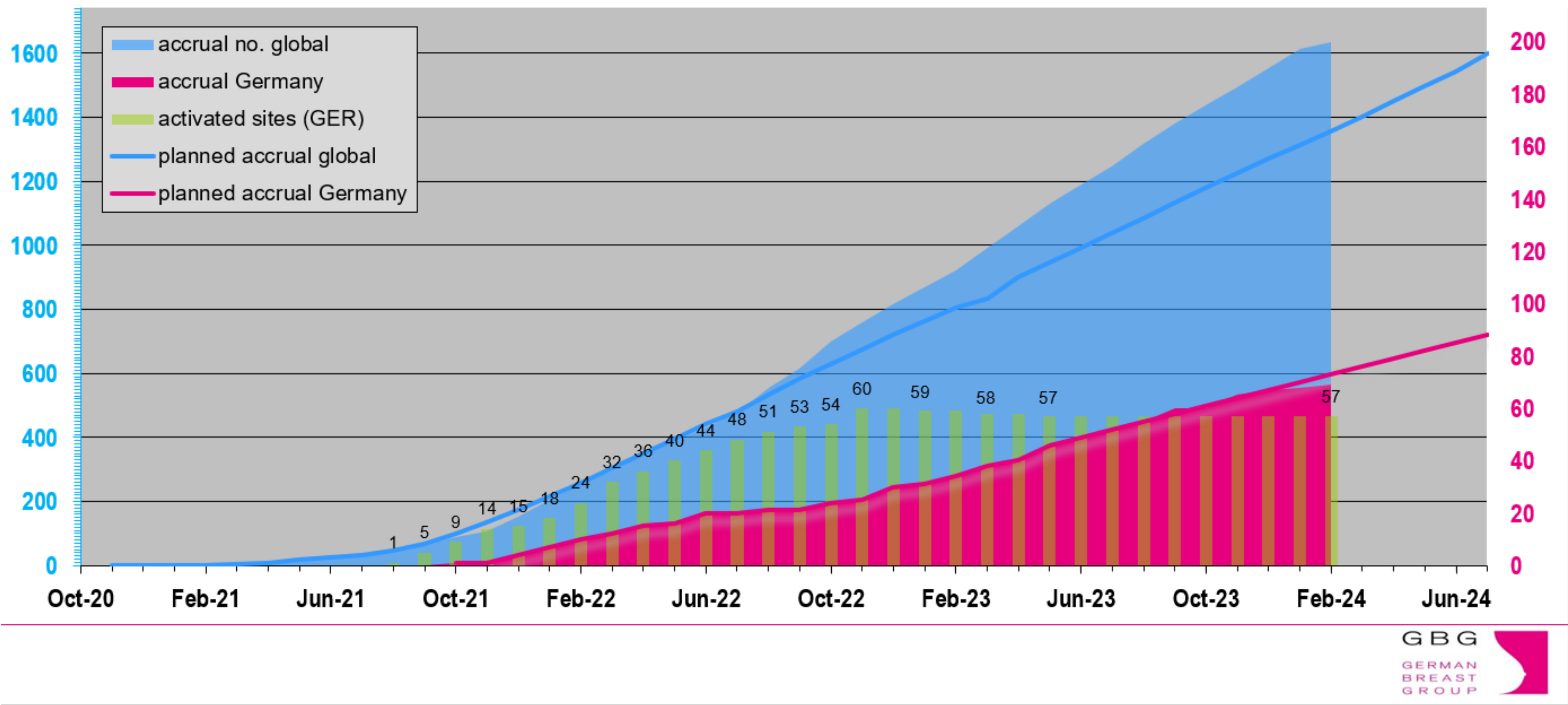


- Randomisierung < 12 Wochen nach Brust-OP
- Adjuvante Radiotherapie und/oder endokrine Therapie per Protokoll und lokalen Richtlinien

Strata:

- Operabel versus Inoperabel
- Nodalstatus nach NACT (positiv versus negativ)
- Hormonrezeptorstatus (positiv versus negativ)
- NACT (einfache Blockade versus doppelte Blockade)

Rekrutierung (Stand FEB-2024)

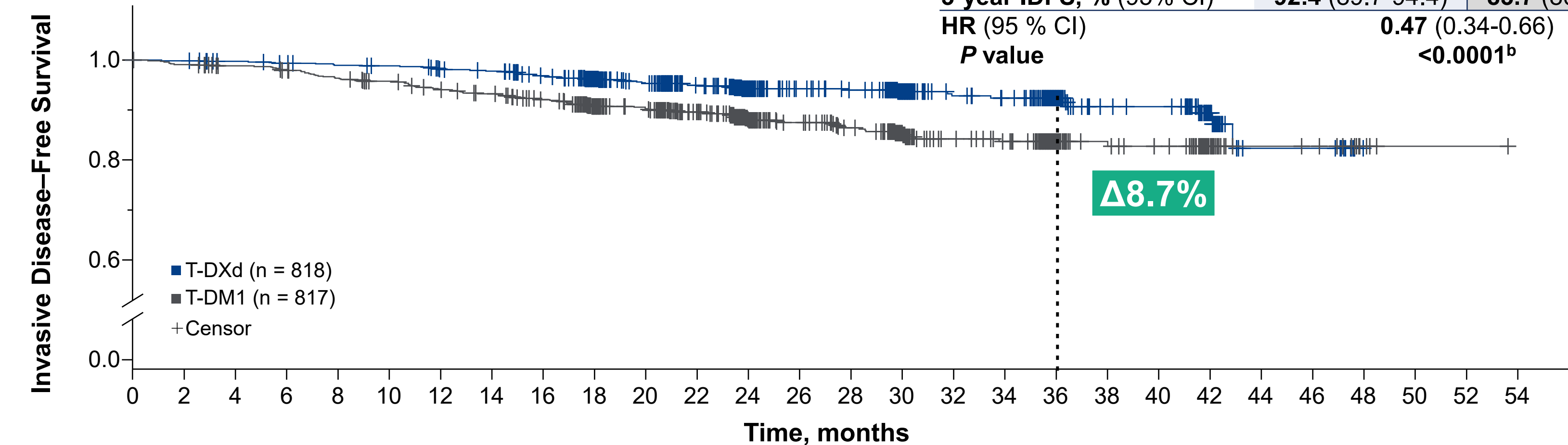


Top-Rekrutierer

Zentrum	Hauptprüfer/in	Patienten pro Zentrum
Frauenklinik der Universität Erlangen	Fasching, Peter	7
Mammazentrum HH am Krankenhaus Jerusalem	Schem, Christian	6
Universitätsfrauenklinik Ulm	Rack, Brigitte	4
Gemeinschaftspraxis Dres. Heinrich / Bangerter	Heinrich, Bernhard	4
Brustzentrum Niederrhein	Gräser, Monika	4

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

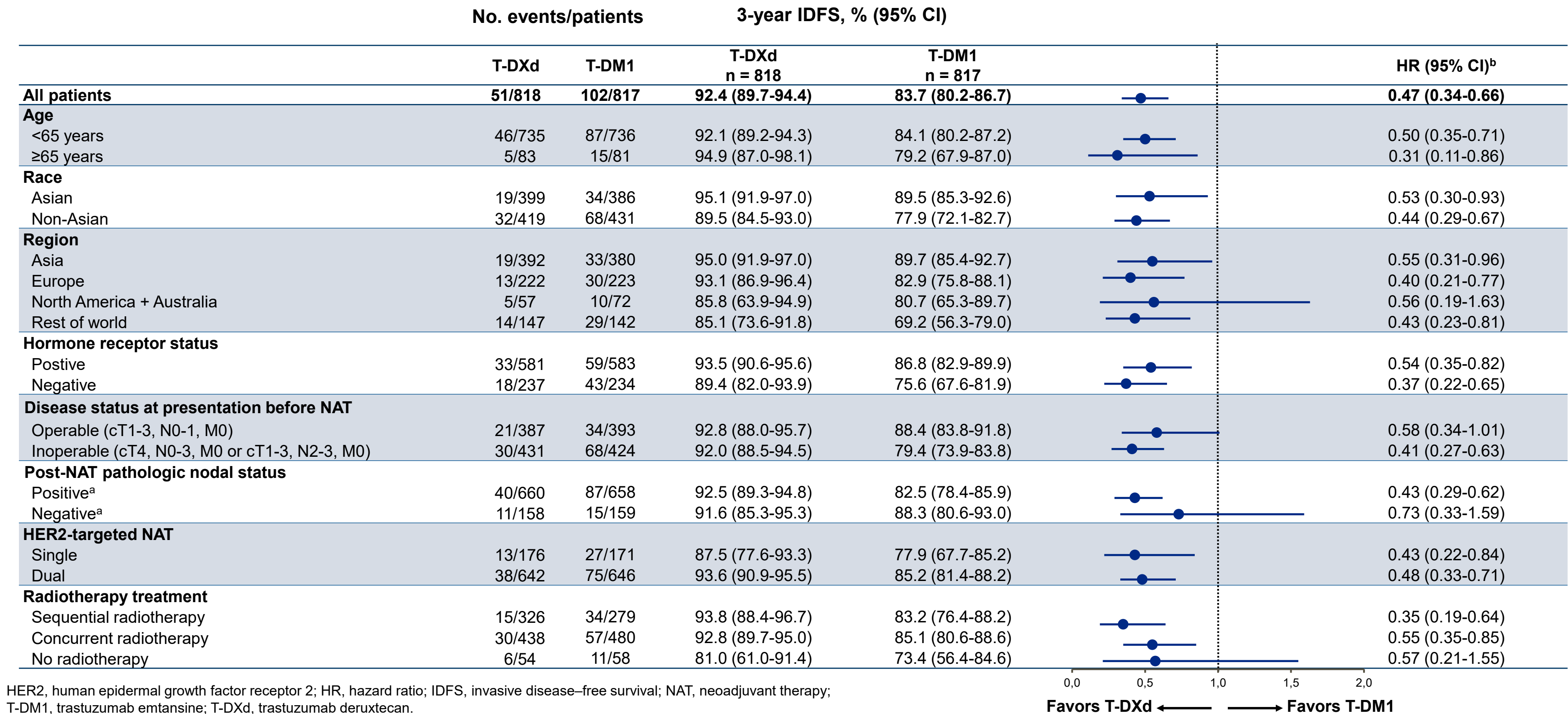
HR, hazard ratio; IDFS, invasive disease-free survival; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
Efficacy stopping boundary, $P = 0.0183$.
^aIDFS is defined as the time from randomization until the date of first occurrence of one of the following events: recurrence of ipsilateral 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.

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Primary endpoint subgroup analysis: IDFS



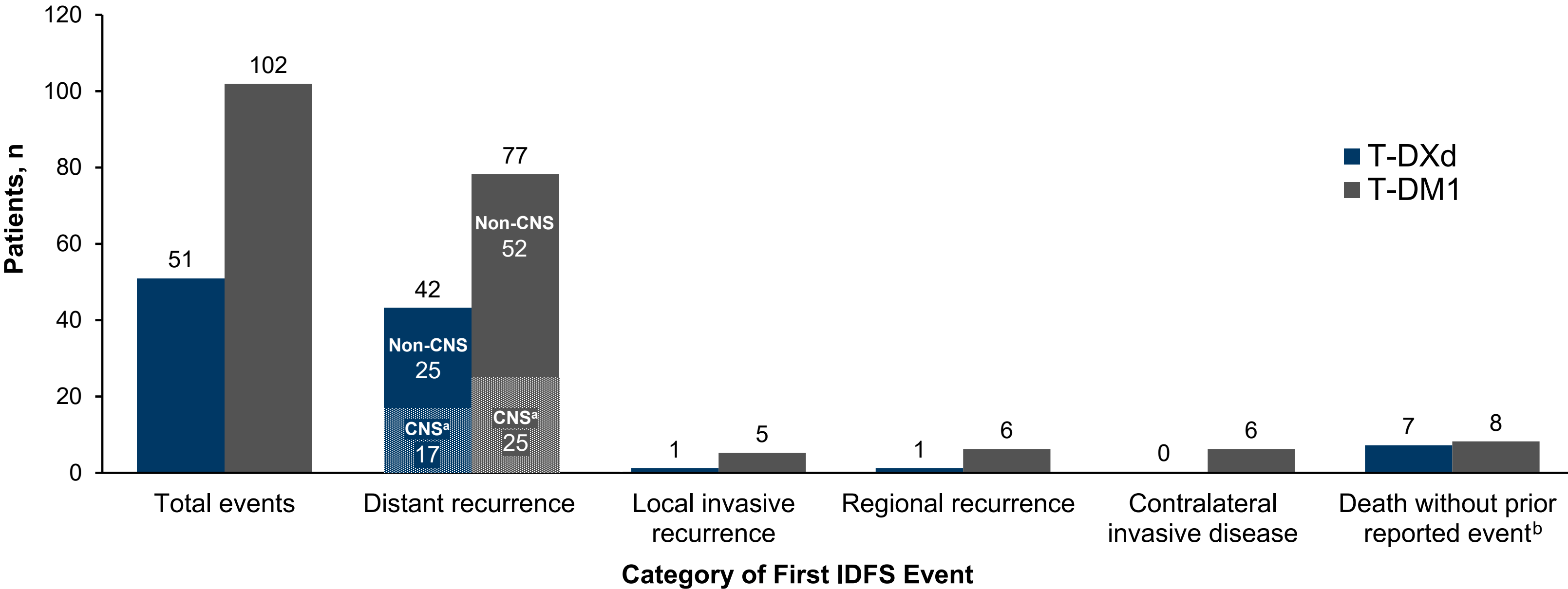
HER2, human epidermal growth factor receptor 2; HR, hazard ratio; IDFS, invasive disease-free survival; NAT, neoadjuvant therapy; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
^aPositive pathologic nodal status defined as ypN1-3 and negative pathologic nodal status defined as ypN0. ^bFrom unstratified Cox proportional hazards model.

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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.
^aCNS as sole site for distant recurrence or one of multiple distance 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.

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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

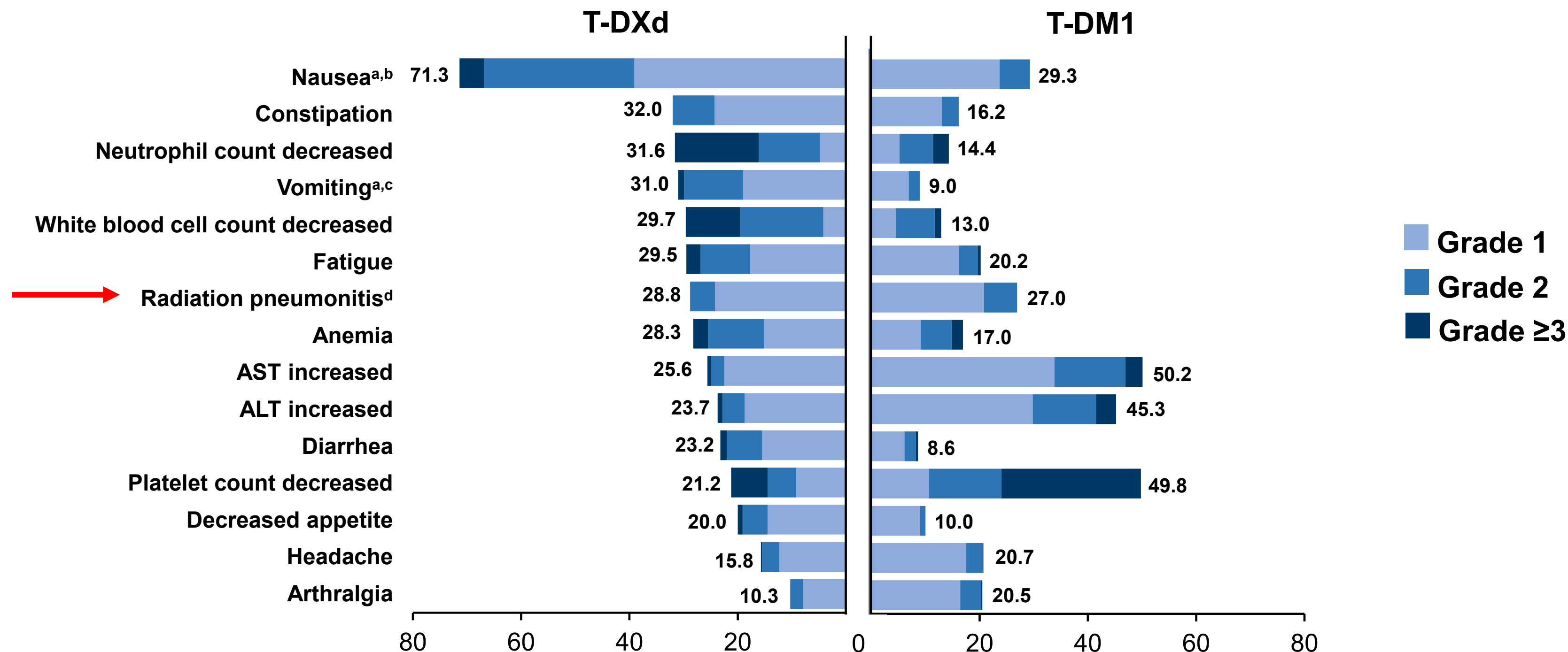
HER2, human epidermal growth factor receptor 2; SOC, standard of care; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

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

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TEAEs in ≥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.

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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.

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DESTINY-BREAST05

VS

KATHERINE: BASELINE CHARACTERISTICS

DESTINY-BREAST05			KATHERINE		
ITT Population	T-DXd (n=818)	T-DM1 (n=817)	ITT Population	T-DM1 (n=743)	Trastuzumab (n=743)
Median age (range), years	50.3 (24-78)	50.6 (21-83)	Median age (range), years	49 (24-79)	49 (23-80)
Hormone Receptor status			Hormone Receptor status		
HR+	581 (71.0)	583 (71.4)	HR+	534 (71.9)	540(72.7)
HR-	237 (29.0)	234 (28.6)	HR-	209 (28.1)	203 (27.3)
HER2 IHC			HER2 IHC		
HER2 3+	676 (82.6)	670 (82.0)	HER2 3+	573 (77.1)	559 (75.2)
HER2 1+/2+	142 (17.4)	147 (18.0)	HER2 0/1+/2+ ISH amplified	170 (22.9)	181 (24.3)
			Unknown	0 (0)	3 (0.4)
Operative Status at Presentation			Operative Status at Presentation		
Operable	387 (47.3)	393 (48.1)	Operable	558 (75.1)	554 (74.4)
Inoperable	431 (52.7)	424 (51.9)	Inoperable	185 (24.9)	190 (25.6)
Post-neoadj tx nodal status			Post-neoadj tx nodal status		
Positive	660 (80.7)	658 (80.5)	Positive	343(46.1)	346 (46.6)
Negative	158 (19.3)	159 (19.5)	Negative	400 (53.8)	397(53.4)
Neoadjuvant HER2 Therapy Approach			Neoadjuvant HER2 Therapy Approach		
Single HER2 targeting	176 (21.5)	171 (20.9)	Single HER2 targeting	600 (80.8)	171 (20.9)
Dual HER2 targeting	642 (78.5)	646 (79.1)	Dual HER2 targeting	143 (19.2)	147 (19.8)
Neoadjuvant Anthracycline use	423 (51.7)	399 (48.8)	Neoadjuvant Anthracycline use	579 (77.9)	564 (75.9)

Fazit

Heilung durch Innovation, Kompetenz
und Partnerschaft – führend in der
Brustkrebs-Forschung

- **Katherine und DB 05 haben in max 30 % unserer Her2 pos Patientinnen ein überlappendes Kollektiv**
- **In der Mehrheit unserer Patientinnen bleibt TDM 1 der Standard der postneoadjuvanten Behandlung bei non pCR nach leitliniengerechter neoadjuvanter Behandlung mit zb 6 mal TCHP bzw 4 mal EC und 12 mal Paclitaxel plus duale anti Her 2 AK**

**Christine Mau, Holger Schultz,
Katja Jugel, Heike Klocke, Katharina Kappo**





Willst du an deine
Lieben denken,
musst du heut' ein
Märzchen
schenken. Es
bringt Glück und
Wohlergehn' und
sagt: "Man kann
den Frühling
schon deutlich
sehn'!"

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)

	T-DXd n = 818	T-DM1 n = 817
Operative status at disease presentation,^c n (%)		
Operable (cT1-3, N0-1, M0)	387 (47.3)	393 (48.1)
Inoperable (cT4, N0-3, M0 or cT1-3, N2-3, M0)	431 (52.7)	424 (51.9)
Post-NAT pathologic nodal status,^c n (%)		
Positive	660 (80.7)	658 (80.5)
Negative	158 (19.3)	159 (19.5)
Neoadjuvant HER2-targeted therapy, n (%)		
Trastuzumab alone	176 (21.5)	171 (20.9)
Trastuzumab + pertuzumab	637 (77.9)	641 (78.5)
Trastuzumab + other HER2-targeted therapy	3 (0.4)	3 (0.4)
Trastuzumab + pertuzumab + other HER2-targeted therapy	2 (0.2)	2 (0.2)
Neoadjuvant chemotherapy, n (%)		
Taxanes	818 (100)	817 (100)
Platinum compounds	386 (47.2)	392 (48.0)
Anthracycline	423 (51.7)	399 (48.8)
Radiotherapy treatment, n (%)		
Adjuvant radiotherapy	764 (93.4)	759 (92.9)
Concurrent	438 (53.5)	480 (58.8)
Sequential	326 (39.9)	279 (34.1)
No radiotherapy	54 (6.6)	58 (7.1)

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.

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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.

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