Preventing and Managing Toxicities Associated with Antibody-Drug Conjugates in the Management of Metastatic Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, November 19, 2025

5:00 PM – 6:00 PM ET

Faculty

Lisa A Carey, MD, ScM, FASCO

Rita Nanda, MD

Moderator

Neil Love, MD

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Faculty

Lisa A Carey, MD, ScM, FASCO
L Richardson and Marilyn Jacobs Preyer Distinguished Professor for Breast Cancer Research
University of North Carolina at Chapel Hill
Deputy Director for Clinical Sciences
Lineberger Comprehensive Cancer Center
Chief Clinical Research Officer
Clinical Research Partners
UNC Health
Chapel Hill, North Carolina

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Rita Nanda, MD
Director, Breast Oncology
Associate Professor of Medicine
Section of Hematology/Oncology
The University of Chicago
Chicago, Illinois

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Dr Love — Disclosures

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Dr Carey — Disclosures

No relevant conflicts of interest to disclose

Dr Nanda — Disclosures

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Contracted Research	Arvinas, AstraZeneca Pharmaceuticals LP, Bristol Myers Squibb, Corcept Therapeutics Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, GSK, Merck, Novartis, OBI Pharma Inc, Pfizer Inc, Relay Therapeutics, Sun Pharma Advanced Research Company, Taiho Oncology Inc

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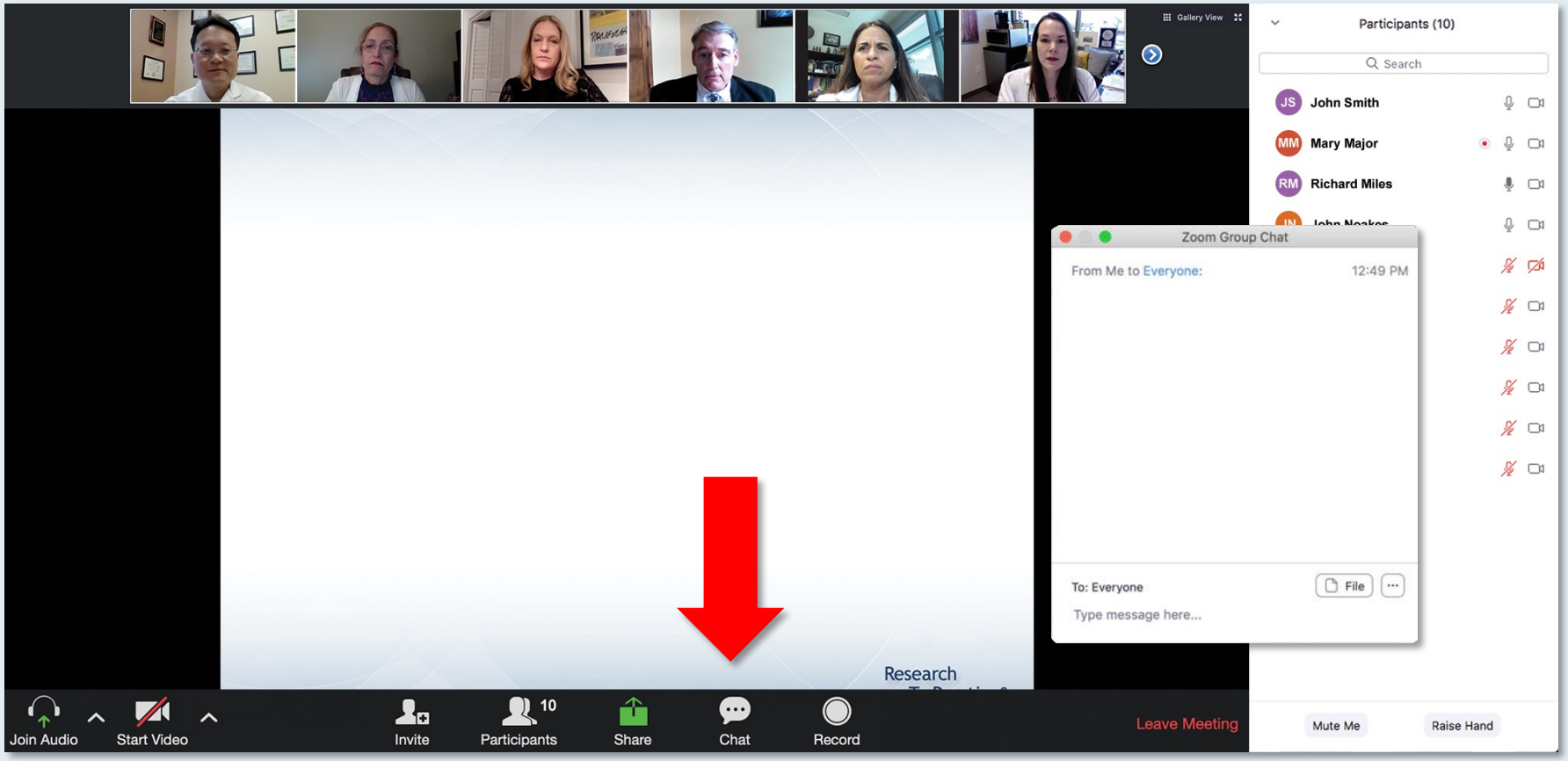

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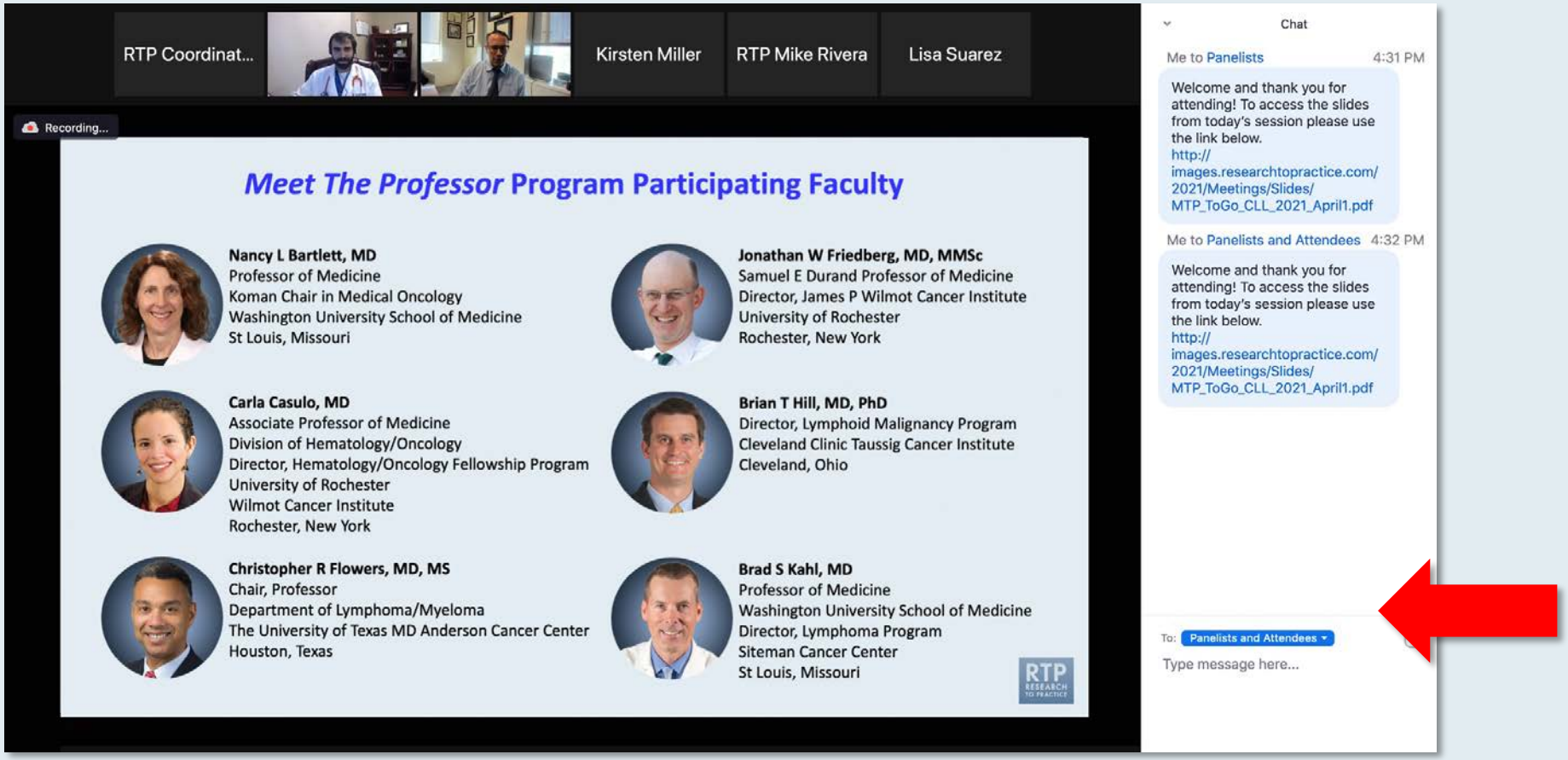

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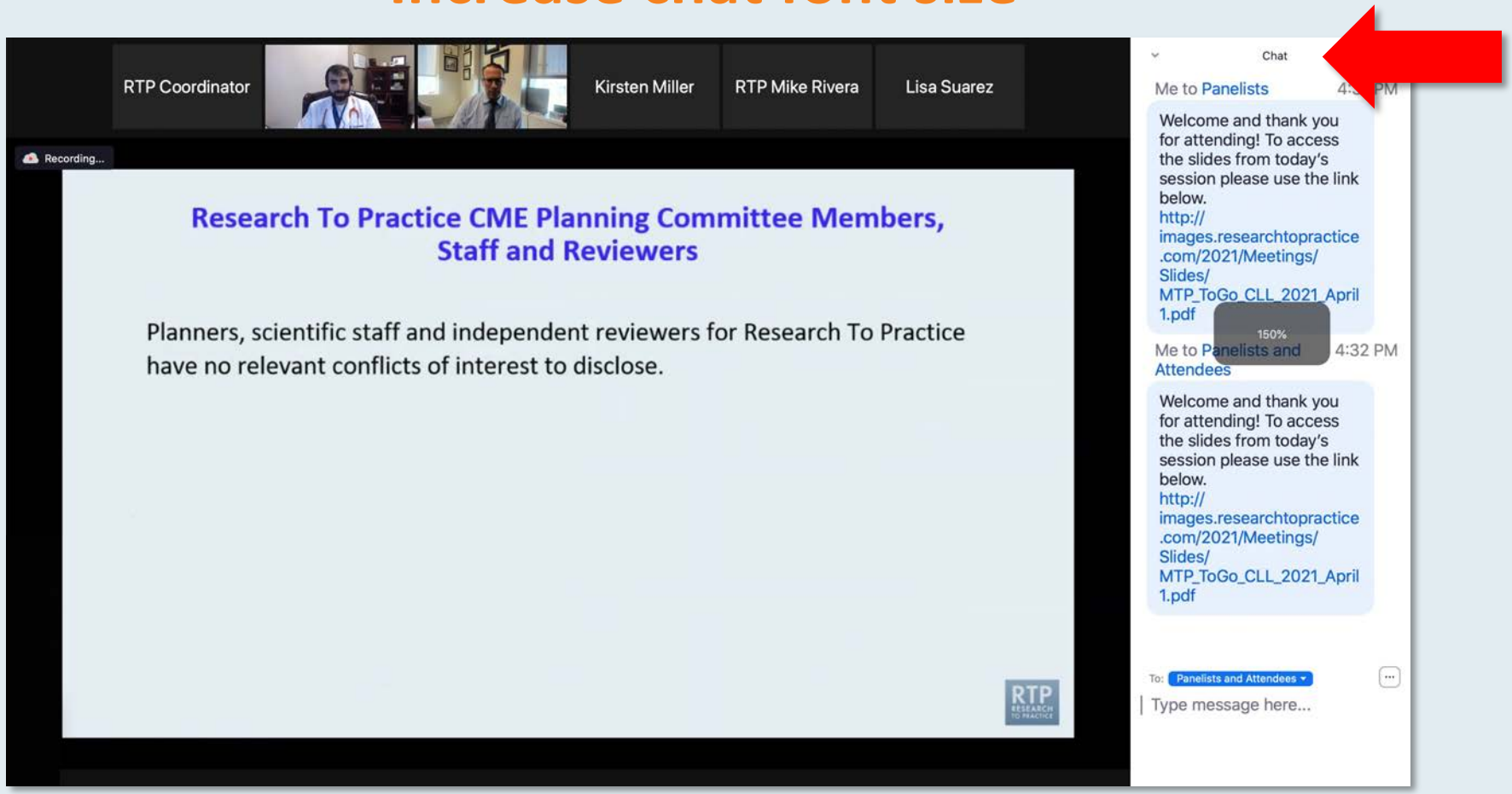

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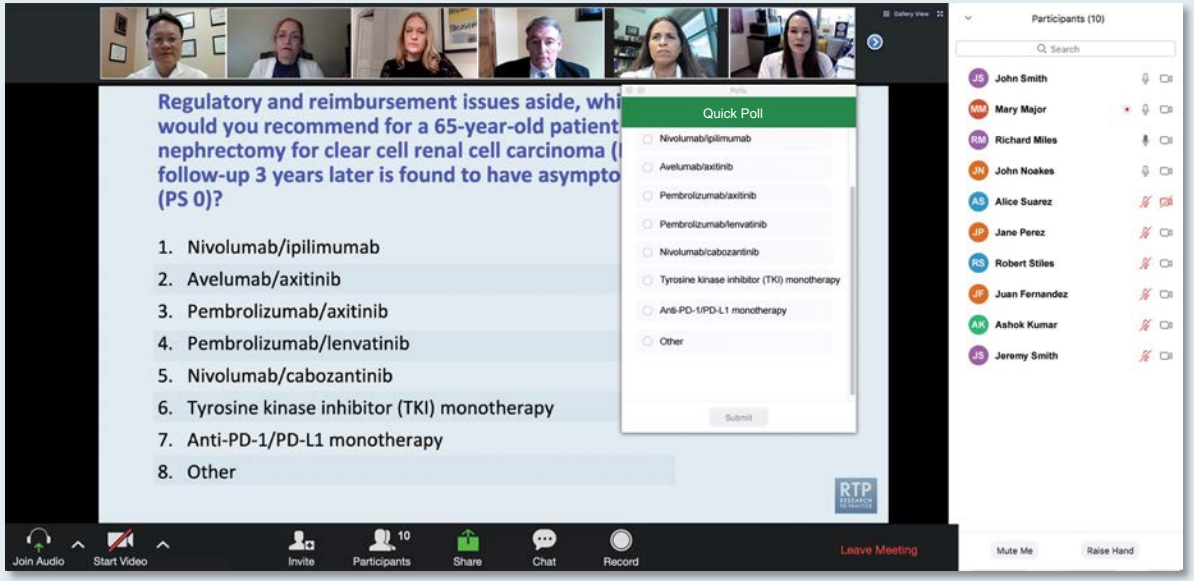

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ER-Positive Metastatic Breast Cancer — A Roundtable Discussion on the Current and Future Role of Oral SERDs

PROF FRANCOIS-CLEMENT BIDARD
INSTITUT CURIE

DR REBECCA SHATSKY
UNIVERSITY OF CALIFORNIA
SAN DIEGO MOORES CANCER CENTER

DR HOPE S RUGO
CITY OF HOPE COMPREHENSIVE CANCER CENTER

DR SETH WANDER
MASSACHUSETTS GENERAL HOSPITAL

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Cancer Conference Update: ESMO Congress 2025 — Urothelial Bladder Cancer and Prostate Cancer

A CME/MOC-Accredited Live Webinar

Thursday, November 20, 2025
5:00 PM – 6:00 PM ET

Faculty

Terence Friedlander, MD
Rana R McKay, MD

Moderator

Neil Love, MD

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Exciting CME Events You Do Not Want to Miss

A Friday Satellite Symposium Series Preceding the 67th ASH Annual Meeting

Friday, December 5, 2025

Acute Myeloid Leukemia
7:30 AM – 9:30 AM ET

Myelofibrosis and Systemic Mastocytosis
3:15 PM – 5:15 PM ET

Chronic Lymphocytic Leukemia
11:30 AM – 1:30 PM ET

Follicular Lymphoma and Diffuse Large B-Cell Lymphoma
7:00 PM – 9:00 PM ET

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Cases from the Community: Investigators Discuss the Optimal Management of Breast Cancer

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Antibody-Drug Conjugates for Metastatic Breast Cancer

Tuesday, December 9, 2025

7:00 PM – 8:30 PM CT

HER2-Positive Breast Cancer

Wednesday, December 10, 2025

7:00 PM – 9:00 PM CT

Endocrine-Based Therapy

Thursday, December 11, 2025

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Moderator

Neil Love, MD

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Hematologic Cancers: A 3-Part ASH 2025 Review

A CME/MOC-Accredited Webinar Series

Relapsed/Refractory Multiple Myeloma

Monday, December 15, 2025

5:00 PM – 6:00 PM ET

Immune Thrombocytopenia

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5:00 PM – 6:30 PM ET

Bispecific Antibodies in Lymphoma

Wednesday, December 17, 2025

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Grand Rounds

CME/MOC-Accredited Interactive Series

November 2025 to April 2026

Three Series

Optimizing Treatment for Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia

Optimizing the Use of Novel Therapies for Patients with Diffuse Large B-Cell Lymphoma

Optimizing Therapy for Patients with Hormone Receptor-Positive Localized Breast Cancer

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Save The Date

Fifth Annual
National General Medical Oncology Summit

A Multitumor CME/MOC-, NCPD- and ACPE-Accredited Educational Conference Developed in Partnership with Florida Cancer Specialists & Research Institute

Friday to Sunday, April 24 to 26, 2026

The Ritz-Carlton Orlando, Grande Lakes | Orlando, Florida

Moderated by Neil Love, MD

Thank you for joining us! Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us.

Information on how to obtain CME, ABIM MOC and ABS credit will be provided at the conclusion of the activity in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

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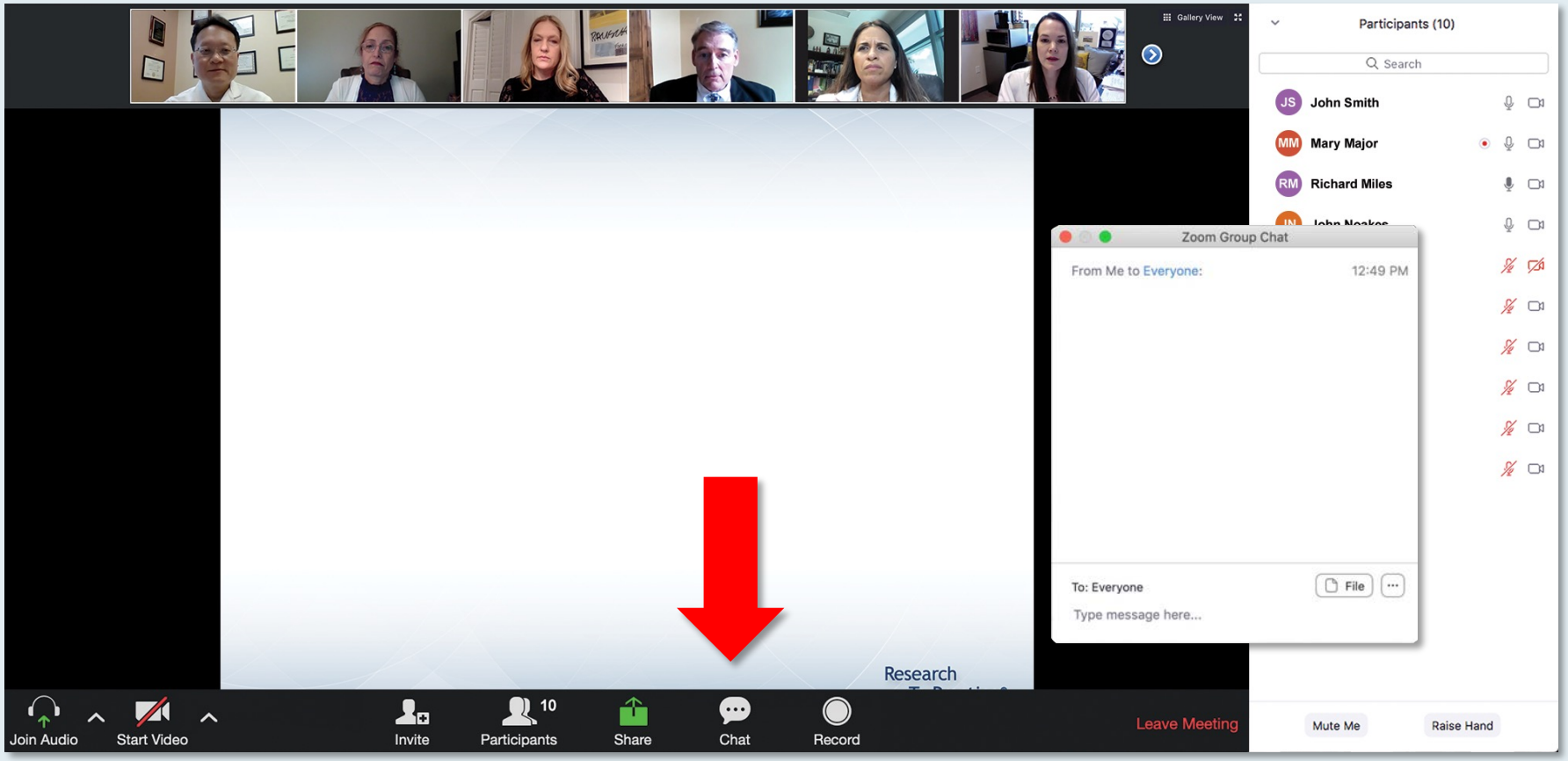

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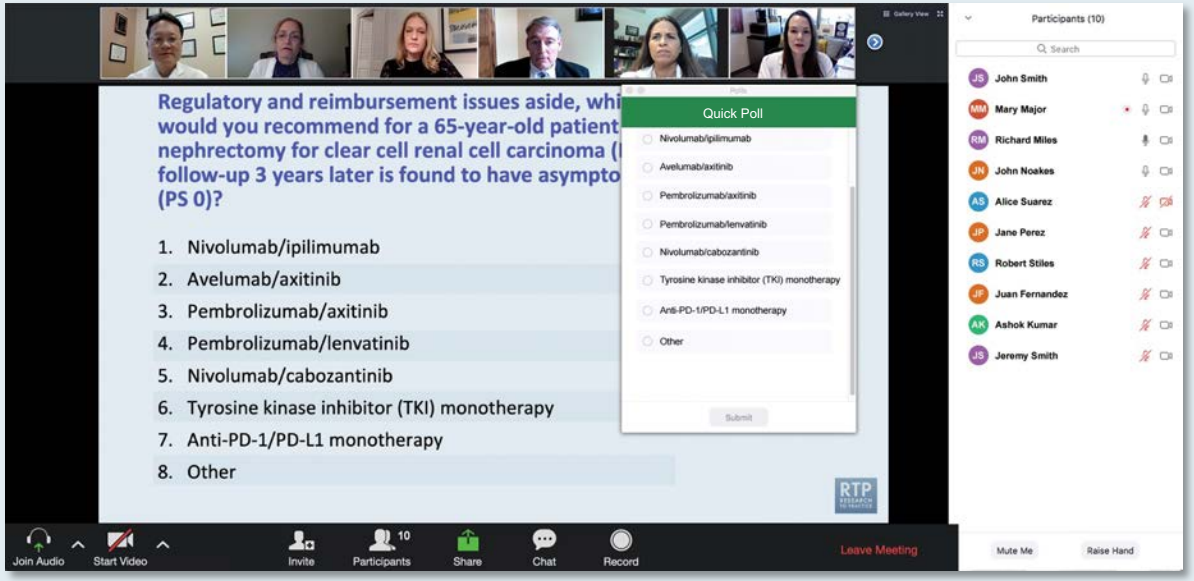

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Dr Carey — Disclosures

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Contributing General Medical Oncologists

Laila Agrawal, MD
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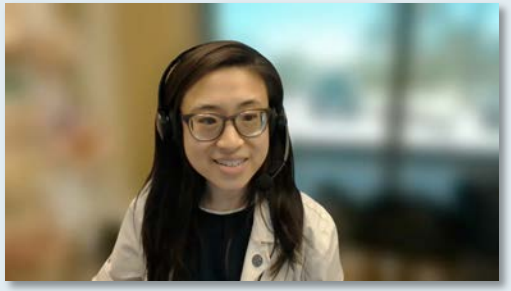
Oncology Specialists of Charlotte
Charlotte, North Carolina

Ranju Gupta, MD
Lehigh Valley Topper Cancer Institute
Bethlehem, Pennsylvania



Kimberly Ku, MD
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Erik Rupard, MD
Penn State Cancer Institute
Reading, Pennsylvania

Richard Zelkowitz, MD
Hartford HealthCare Cancer Institute
Bridgeport, Connecticut

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Agenda

Introduction	Overview: Molecular basis of antibody-drug conjugate (ADC) toxicities — Sequencing of ADCs and mechanisms of resistance
Case 1	Dr Zelkowitz – 68-year-old woman
■ Data Review: TROP2-targeted ADCs (sacituzumab govitecan, Dato-DXd, sac TMT)	
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Case 3	Dr Agrawal – 83-year-old woman
Case 4	Dr Favaro – 70-year-old woman
■ Data Review: Trastuzumab deruxtecan	
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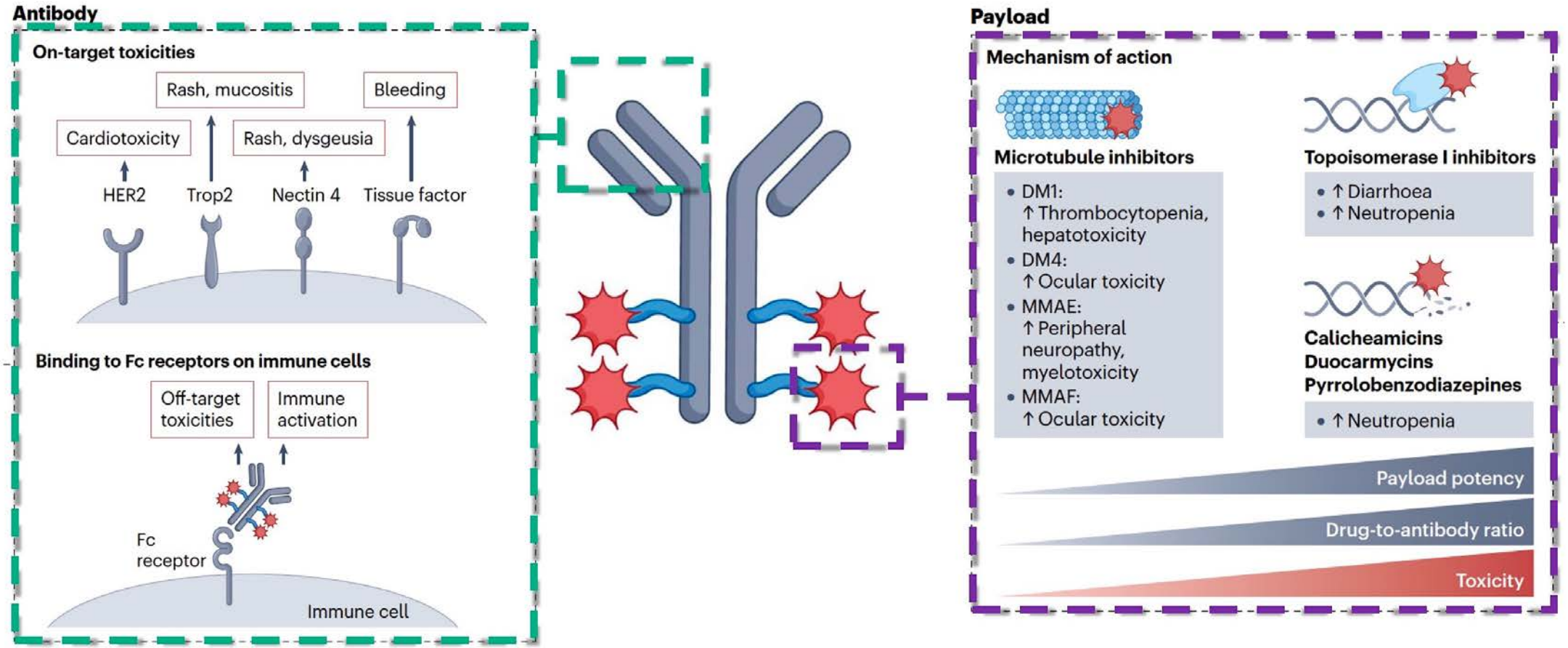
ASCO/ESMO 2025 ADC Clinical Trial Bonanza

- Cortes JC et al. Primary results from ASCENT-03: A randomized phase III study of sacituzumab govitecan (SG) vs chemotherapy (chemo) in patients (pts) with previously untreated advanced triple-negative breast cancer (TNBC) who are unable to receive PD-(L)1 inhibitors (PD-[L]1i). ESMO 2025;Abstract LBA20.
- Tolaney SM et al. Sacituzumab govitecan (SG) + pembrolizumab (pembro) vs chemotherapy (chemo) + pembro in previously untreated PD-L1–positive advanced triple-negative breast cancer (TNBC): Primary results from the randomized phase 3 ASCENT-04/KEYNOTE-D19 study. ASCO 2025;Abstract LBA109.
- Dent R et al. First-line (1L) datopotamab deruxtecan (Dato-DXd) vs chemotherapy in patients with locally recurrent inoperable or metastatic triple-negative breast cancer (mTNBC) for whom immunotherapy was not an option: Primary results from the randomised, phase III TROPION-Breast02 trial. ESMO 2025;Abstract LBA21.
- Li M et al. Sacituzumab tirumotecan (sac-TMT) vs investigator's choice of chemotherapy (ICC) in previously treated locally advanced or metastatic hormone receptor-positive, HER2-negative (HR+/HER2-) breast cancer (BC): Results from the randomized, multi-center phase III OptiTROP-Breast02 study. ESMO 2025;Abstract LBA23.

ASCO/ESMO 2025 ADC Clinical Trial Bonanza (Continued)

- Tolaney SM et al. Trastuzumab deruxtecan (T-DXd) + pertuzumab (P) vs taxane + trastuzumab + pertuzumab (THP) for first-line (1L) treatment of patients (pts) with human epidermal growth factor receptor 2–positive (HER2+) advanced/metastatic breast cancer (a/mBC): Interim results from DESTINY-Breast09. ASCO 2025;Abstract LBA1008.
- Geyer C et al. Trastuzumab deruxtecan (T-DXd) vs trastuzumab emtansine (T-DM1) in patients (pts) with high-risk human epidermal growth factor receptor 2–positive (HER2+) primary breast cancer (BC) with residual invasive disease after neoadjuvant therapy (tx): Interim analysis of DESTINY-Breast05. ESMO 2025;Abstract LBA1.
- Harbeck N et al. DESTINY-Breast11: Neoadjuvant trastuzumab deruxtecan alone (T-DXd) or followed by paclitaxel + trastuzumab + pertuzumab (T-DXd-THP) vs SOC for high-risk HER2+ early breast cancer (eBC). ESMO 2025;Abstract 2910O.

Mechanisms of ADC Toxicity



Szabados B. ESMO 2025.

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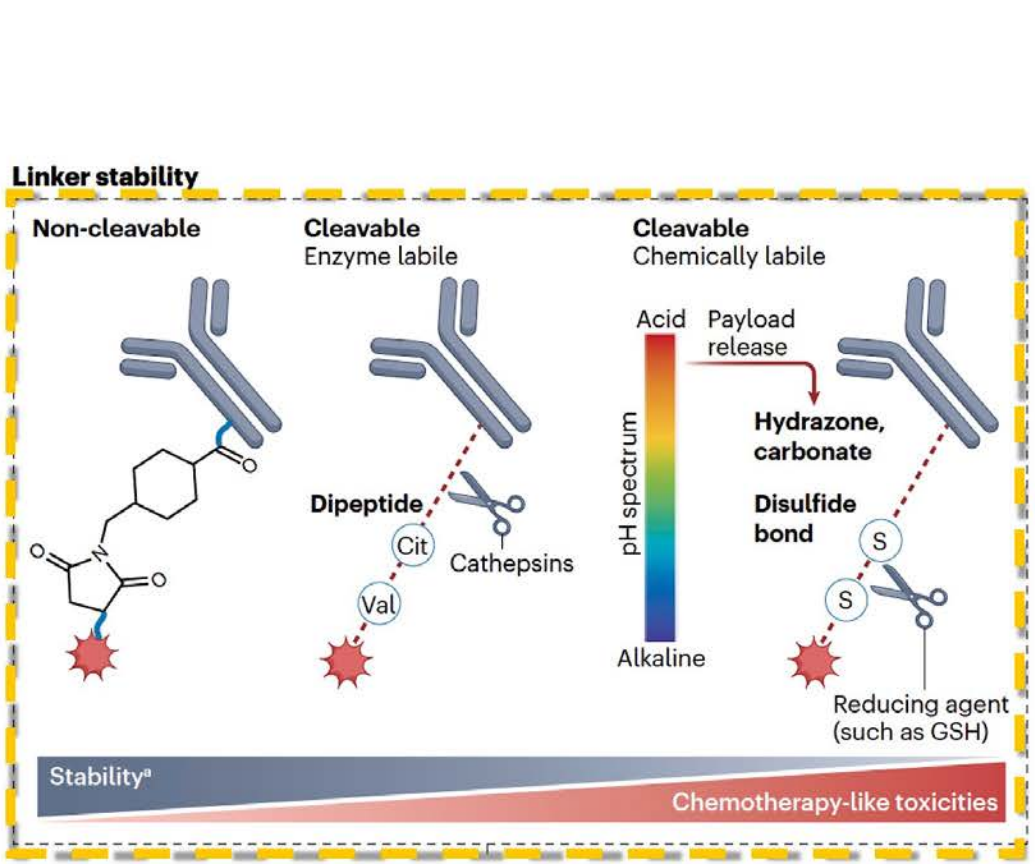
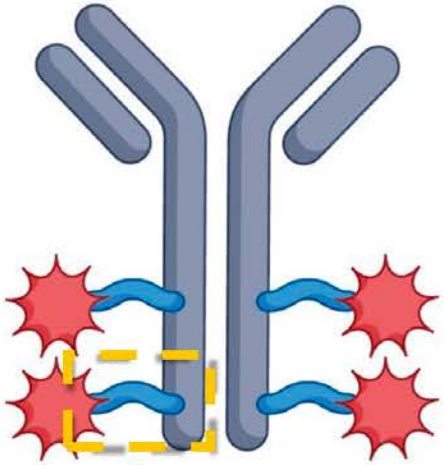
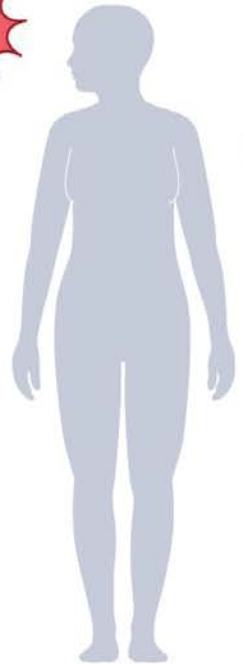
Mechanisms of ADC Toxicity (Continued)







Patient–related factors

- Baseline organ function
- Comorbidities
- Pharmacogenomic polymorphisms
- Body composition
- Ethnicity

Bernadett Szabados MD

Tarantino et al. Nat Rev Clin Oncol 2023

BERLIN 2025 ESMO congress

Szabados B. ESMO 2025.

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Case Presentation: 68-year-old woman with localized TNBC develops myocarditis during neoadjuvant chemotherapy/pembrolizumab

Dr Richard Zelkowitz (Bridgeport, Connecticut)

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Abstract LBA20

BERLIN 2025 ESMO congress

Primary Results From ASCENT-03: A Randomized Phase 3 Study of Sacituzumab Govitecan vs Chemotherapy in Patients With Previously Untreated Metastatic Triple-Negative Breast Cancer Who Are Unable to Receive PD-(L)1 Inhibitors

Javier Cortés[1-5], Aditya Bardia[6], Kevin Punie[7], Carlos Barrios[8], Sara Hurvitz[9], Andreas Schneeweiss[10], Joohyuk Sohn[11], Eriko Tokunaga[12], Adam Brufsky[13], Yeon Hee Park[14], Binghe Xu[15], Roberto Hegg[16], Mafalda Oliveira[17], Alessandra Fabi[18], Natalya Vaksman[19], Theresa Valdez[19], Xinrui Zhang[19], Catherine Lai[19], Sara M Tolaney[20]

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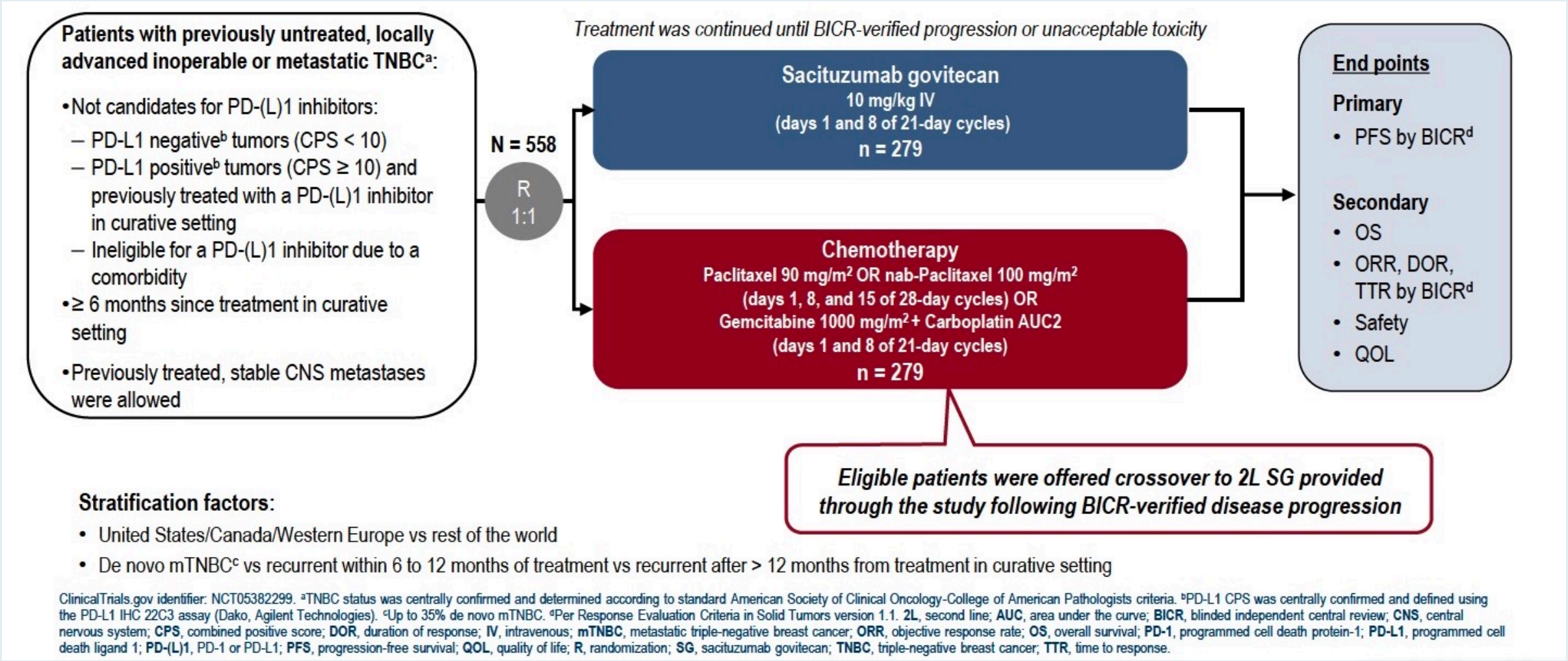
Sunday, October 19, 2025; 9:15-9:25 am
LBA 20

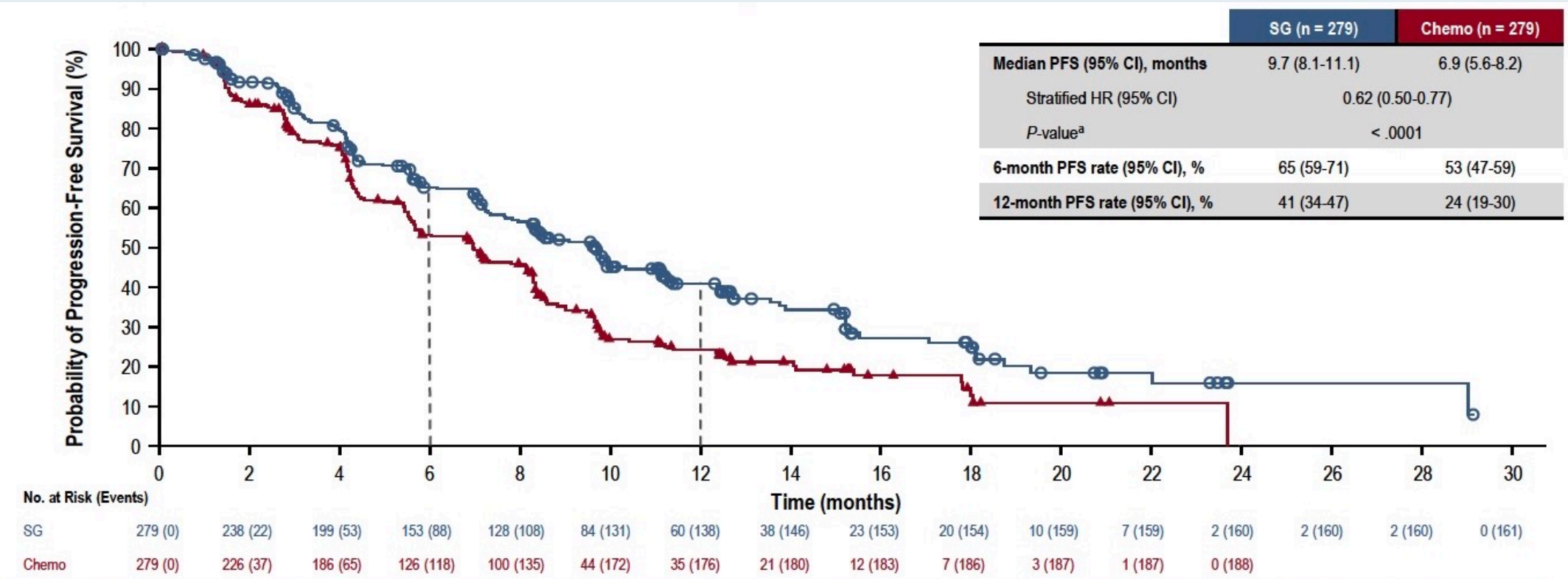
Phase III ASCENT-03 Study Design



ClinicalTrials.gov identifier: NCT05382299. [a]TNBC status was centrally confirmed and determined according to standard American Society of Clinical Oncology-College of American Pathologists criteria. [b]PD-L1 CPS was centrally confirmed and defined using the PD-L1 IHC 22C3 assay (Dako, Agilent Technologies). [c]Up to 35% de novo mTNBC. [d]Per Response Evaluation Criteria in Solid Tumors version 1.1. **2L**, second line; **AUC**, area under the curve; **BICR**, blinded independent central review; **CNS**, central nervous system; **CPS**, combined positive score; **DOR**, duration of response; **IV**, intravenous; **mTNBC**, metastatic triple-negative breast cancer; **ORR**, objective response rate; **OS**, overall survival; **PD-1**, programmed cell death protein-1; **PD-L1**, programmed cell death ligand 1; **PD-(L)1**, PD-1 or PD-L1; **PFS**, progression-free survival; **QOL**, quality of life; **R**, randomization; **SG**, sacituzumab govitecan; **TNBC**, triple-negative breast cancer; **TTR**, time to response.

Cortés J et al. ESMO 2025;Abstract LBA20.

Phase III ASCENT-03: PFS by BICR



	SG (n = 279)	Chemo (n = 279)
Median PFS (95% CI), months	9.7 (8.1-11.1)	6.9 (5.6-8.2)
Stratified HR (95% CI)	0.62 (0.50-0.77)	
P-value[a]	< .0001	
6-month PFS rate (95% CI), %	65 (59-71)	53 (47-59)
12-month PFS rate (95% CI), %	41 (34-47)	24 (19-30)

SG demonstrated statistically significant and clinically meaningful improvement in PFS vs chemo by BICR analysis, with a 38% reduction in risk of disease progression or death

Data cutoff date: April 2, 2025. [a]Two-sided *P*-value from stratified log-rank test.
BICR, blinded independent central review; **chemo**, chemotherapy; **HR**, hazard ratio; **PFS**, progression-free survival; **SG**, sacituzumab govitecan.

Cortés J et al. ESMO 2025;Abstract LBA20.

Phase III ASCENT-03: Safety Summary

Safety population	SG (n = 275)	Chemo (n = 276)	
Treatment component	SG	Taxane	Gemcitabine/ Carboplatin
All treated patients, n	275	154	122
Median duration of treatment, months (range)	8.3 (< 0.1-28.7)	6.3 (< 0.1-24.2)	5.8 (< 0.1-23.1)

TEAEs, n (%)	SG (n = 275)	Chemo (n = 276)
Any TEAE	273 (99)	269 (97)
Grade ≥ 3 TEAEs	181 (66)	171 (62)
Treatment-related	167 (61)	147 (53)
Treatment-emergent SAE	71 (26)	67 (24)
Treatment-related	46 (17)	37 (13)
TEAEs leading to treatment discontinuation	10 (4)	33 (12)
TEAEs leading to dose interruption	181 (66)	171 (62)
TEAEs leading to dose reduction	101 (37)	124 (45)
TEAEs leading to death	7 (3)	1 (< 1)
Treatment-related	6 (2)	1 (< 1)

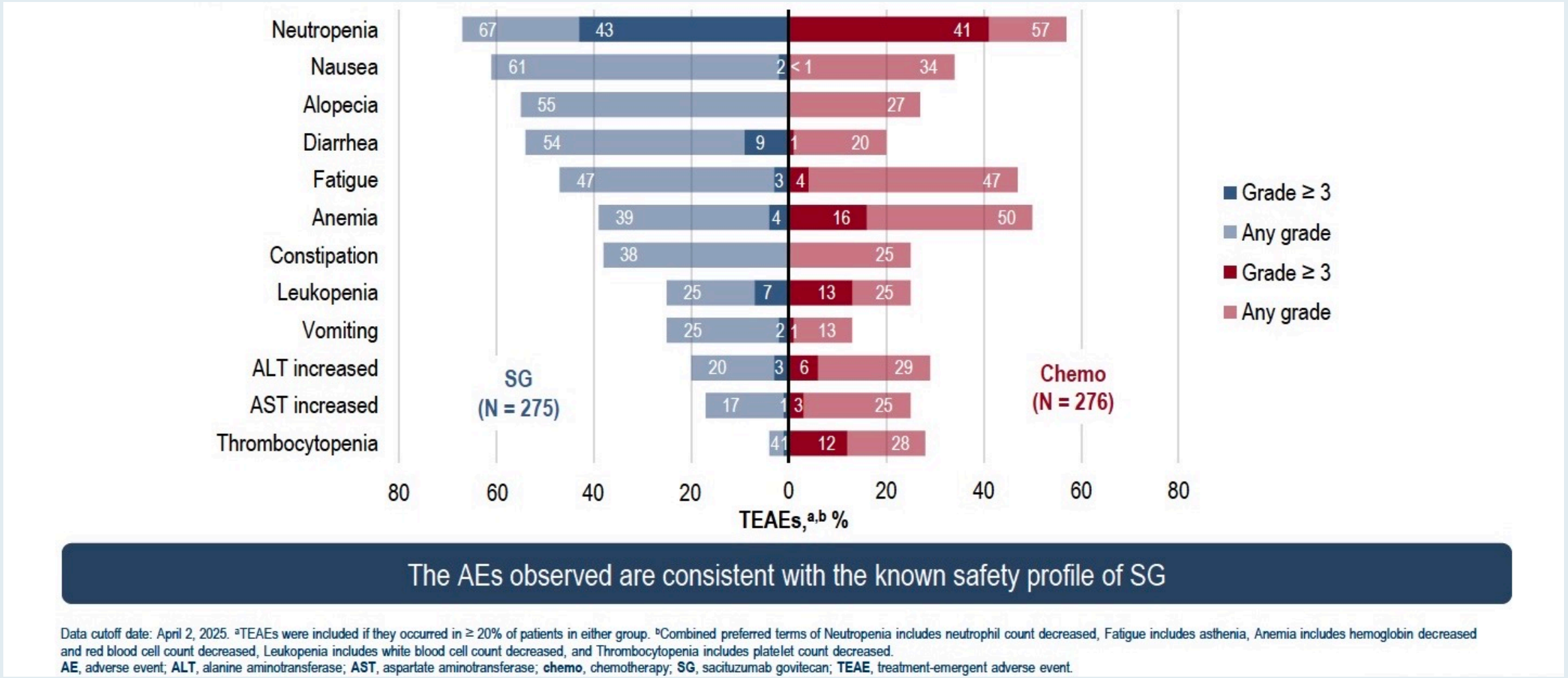
All treatment-related deaths with SG were due to infections; 5 infections were secondary to neutropenia. None of the 5 patients, who had risk factors for febrile neutropenia, received prophylaxis with G-CSF

Rates of grade ≥ 3 TEAEs and treatment-emergent SAEs were similar for both groups.
TEAEs leading to dose reduction or treatment discontinuation were lower with SG vs chemo

Data cutoff date: April 2, 2025. TEAEs were defined as any AEs that began or worsened on or after the first dose date of study drug up to 30 days after the last dose date of study drug or the initiation of subsequent anticancer therapy (including crossover treatment), whichever occurs first.
AE, adverse event; **chemo**, chemotherapy; **G-CSF**, granulocyte-colony stimulation factor; **SAE**, serious adverse event; **SG**, sacituzumab govitecan; **TEAE**, treatment-emergent adverse event.

Cortés J et al. ESMO 2025;Abstract LBA20.

Phase III ASCENT-03: Common AEs



The AEs observed are consistent with the known safety profile of SG

Data cutoff date: April 2, 2025. [a]TEAEs were included if they occurred in ≥ 20% of patients in either group. [b]Combined preferred terms of Neutropenia includes neutrophil count decreased, Fatigue includes asthenia, Anemia includes hemoglobin decreased and red blood cell count decreased, Leukopenia includes white blood cell count decreased, and Thrombocytopenia includes platelet count decreased.
AE, adverse event; **ALT**, alanine aminotransferase; **AST**, aspartate aminotransferase; **chemo**, chemotherapy; **SG**, sacituzumab govitecan; **TEAE**, treatment-emergent adverse event.

Cortés J et al. ESMO 2025;Abstract LBA20.

RTP RESEARCH TO PRACTICE

Sacituzumab Govitecan vs Chemotherapy as First Therapy After Endocrine Therapy in HR+/HER2– (IHC 0, 1+, 2+/ISH–) Metastatic Breast Cancer: Primary Results from ASCENT-07

Jhaveri K et al.

SABCS 2025;Abstract GS1-10.

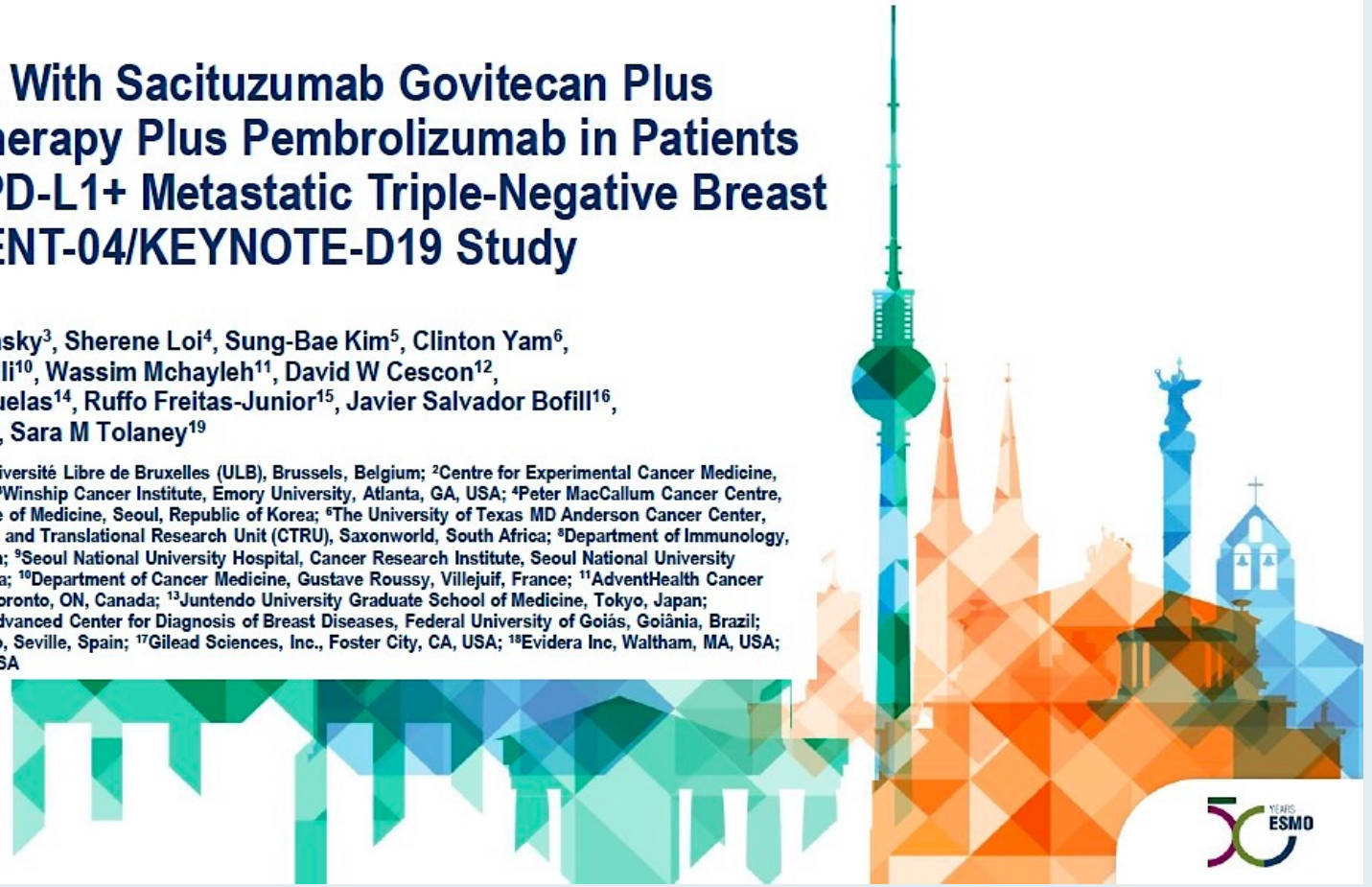
Abstract LBA22

BERLIN 2025 ESMO congress

Patient-Reported Outcomes With Sacituzumab Govitecan Plus Pembrolizumab vs Chemotherapy Plus Pembrolizumab in Patients With Previously Untreated PD-L1+ Metastatic Triple-Negative Breast Cancer in the Phase 3 ASCENT-04/KEYNOTE-D19 Study

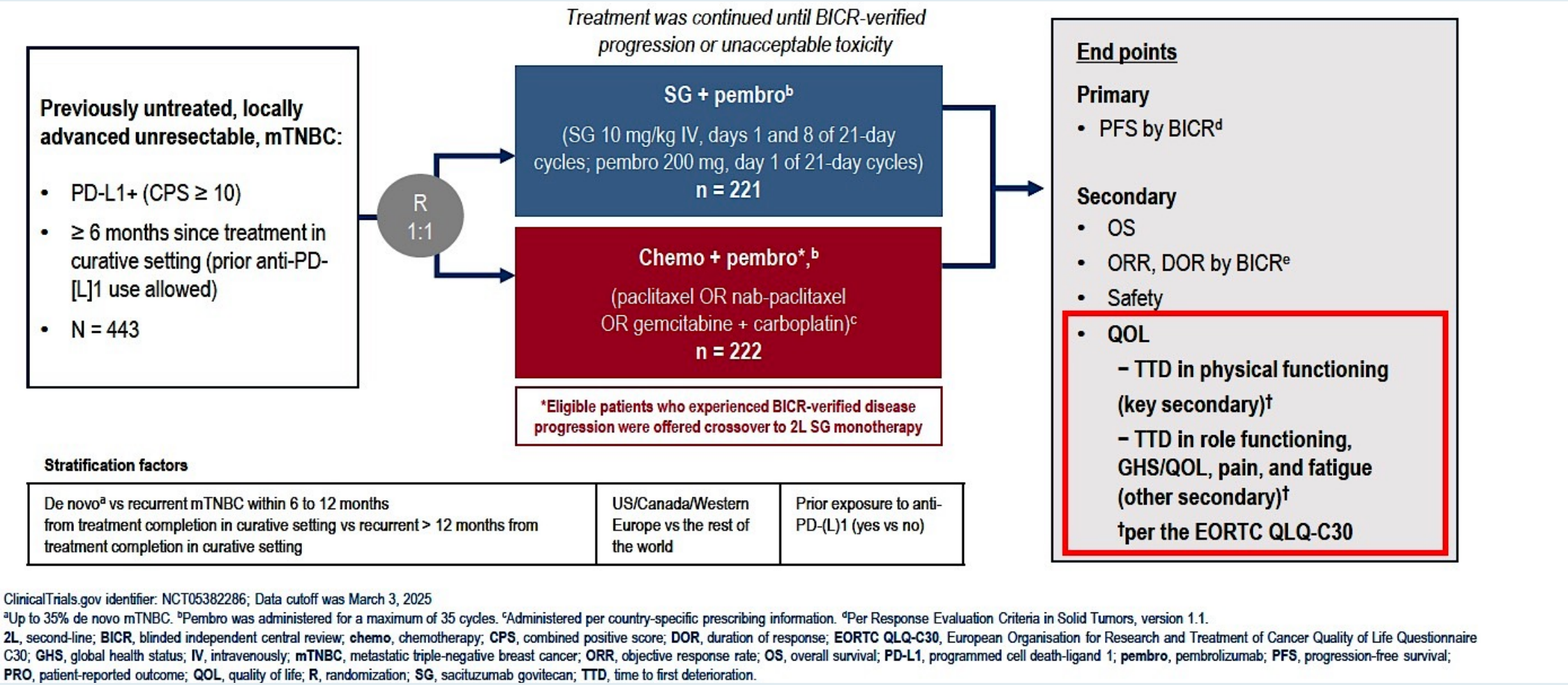
Evandro de Azambuja[1], Peter Schmid[2], Kevin Kalinsky[3], Sherene Loi[4], Sung-Bae Kim[5], Clinton Yam[6], Bernardo Rapoport[7,8], Seock-Ah Im[9], Barbara Pistilli[10], Wassim Mchayleh[11], David W Cescon[12], Junichiro Watanabe[13], Manuel Alejandro Lara Bañuelas[14], Ruffo Freitas-Junior[15], Javier Salvador Bofill[16], Xue Wang[17], Yiran Zhang[17], Ling Shi[18], Ann Chen[17], Sara M Tolaney[19]

[1]Institut Jules Bordet, Hôpital Universitaire de Bruxelles (H.U.B) and Université Libre de Bruxelles (ULB), Brussels, Belgium; [2]Centre for Experimental Cancer Medicine, Barts Cancer Institute, Queen Mary University of London, London, UK; [3]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [4]Peter MacCallum Cancer Centre, Melbourne, Australia; [5]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [6]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [7]The Medical Oncology Centre of Rosebank, Clinical and Translational Research Unit (CTRU), Saxonworld, South Africa; [8]Department of Immunology, Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa; [9]Seoul National University Hospital, Cancer Research Institute, Seoul National University College of Medicine, Seoul National University, Seoul, Republic of Korea; [10]Department of Cancer Medicine, Gustave Roussy, Villejuif, France; [11]AdventHealth Cancer Institute, Orlando, FL, USA; [12]Princess Margaret Cancer Centre, UHN, Toronto, ON, Canada; [13]Juntendo University Graduate School of Medicine, Tokyo, Japan; [14]SCIENTIA Investigación Clínica S.C., Chihuahua, Mexico; [15]CORA – Advanced Center for Diagnosis of Breast Diseases, Federal University of Goiás, Goiânia, Brazil; [16]Medical Oncology Department, Hospital Universitario Virgen del Rocio, Seville, Spain; [17]Gilead Sciences, Inc., Foster City, CA, USA; [18]Evidera Inc, Waltham, MA, USA; [19]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA



Monday, October 20, 2025; 10:15 – 10:20 AM
LBA 22

Phase III ASCENT-04/KEYNOTE-D19 Study Design



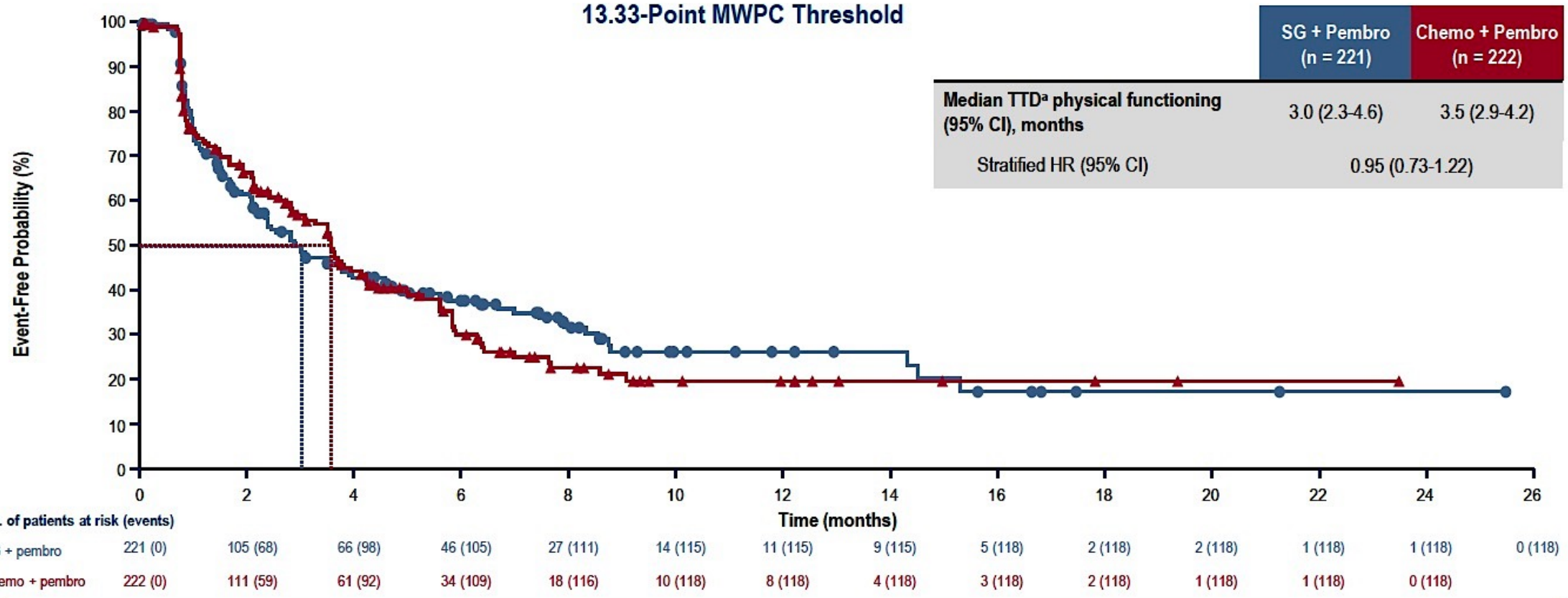
ClinicalTrials.gov identifier: NCT05382286; Data cutoff was March 3, 2025

[a]Up to 35% de novo mTNBC. [b]Pembro was administered for a maximum of 35 cycles. [c]Administered per country-specific prescribing information. [d]Per Response Evaluation Criteria in Solid Tumors, version 1.1.

2L, second-line; **BICR**, blinded independent central review; **chemo**, chemotherapy; **CPS**, combined positive score; **DOR**, duration of response; **EORTC QLQ-C30**, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30; **GHS**, global health status; **IV**, intravenously; **mTNBC**, metastatic triple-negative breast cancer; **ORR**, objective response rate; **OS**, overall survival; **PD-L1**, programmed cell death-ligand 1; **pembro**, pembrolizumab; **PFS**, progression-free survival; **PRO**, patient-reported outcome; **QOL**, quality of life; **R**, randomization; **SG**, sacituzumab govitecan; **TTD**, time to first deterioration.

de Azambuja E et al. ESMO 2025;Abstract LBA22.

Phase III ASCENT-04/KEYNOTE-D19: Time to First Deterioration in Physical Function



	SG + Pembro (n = 221)	Chemo + Pembro (n = 222)
Median TTD[a] physical functioning (95% CI), months	3.0 (2.3-4.6)	3.5 (2.9-4.2)
Stratified HR (95% CI)	0.95 (0.73-1.22)	

TTD in physical functioning was maintained in the SG + pembro group and comparable between treatment groups

[a]TTD defined as the time between randomization and the assessment at which a patient first experienced a worsening exceeding prespecified MWPC from BL or death.

BL, baseline; **chemo**, chemotherapy; **CI**, confidence interval; **HR**, hazard ratio; **MWPC**, meaningful within-patient change; **pembro**, pembrolizumab; **SG**, sacituzumab govitecan; **TTD**, time to first deterioration.

de Azambuja E et al. ESMO 2025;Abstract LBA22.

Phase III ASCENT-04/KEYNOTE-D19 Trial: Overall Safety Summary

ITT population	SG + Pembro (n = 221)		Chemo + Pembro (n = 222)	
Treatment component	SG	Pembro	Chemo	Pembro
All treated patients, n	221	221	220	220
Median duration of treatment, mo (range)	8.9 (0.0-27.1)	8.5 (0.0-26.8)	6.2 (0.0-26.3)	6.4 (0.0-25.6)

n (%)	SG + Pembro (n = 221)	Chemo + Pembro (n = 220)
Any TEAE	220 (> 99)	219 (> 99)
Grade ≥ 3	158 (71)	154 (70)
Treatment-emergent SAE	84 (38)	68 (31)
Treatment-related	61 (28)	42 (19)
TEAEs leading to treatment discontinuation[a]	26 (12)	68 (31)
TEAEs leading to dose interruption	171 (77)	162 (74)
TEAEs leading to dose reduction[b]	78 (35)	96 (44)
TEAEs leading to death[c]	7 (3)	6 (3)
Treatment-related	3 (1)	1 (< 1)

Despite longer duration of treatment with SG + pembro, rates of grade ≥ 3 AEs were similar for both groups. TEAEs leading to dose reduction or treatment discontinuation were lower with SG + pembro

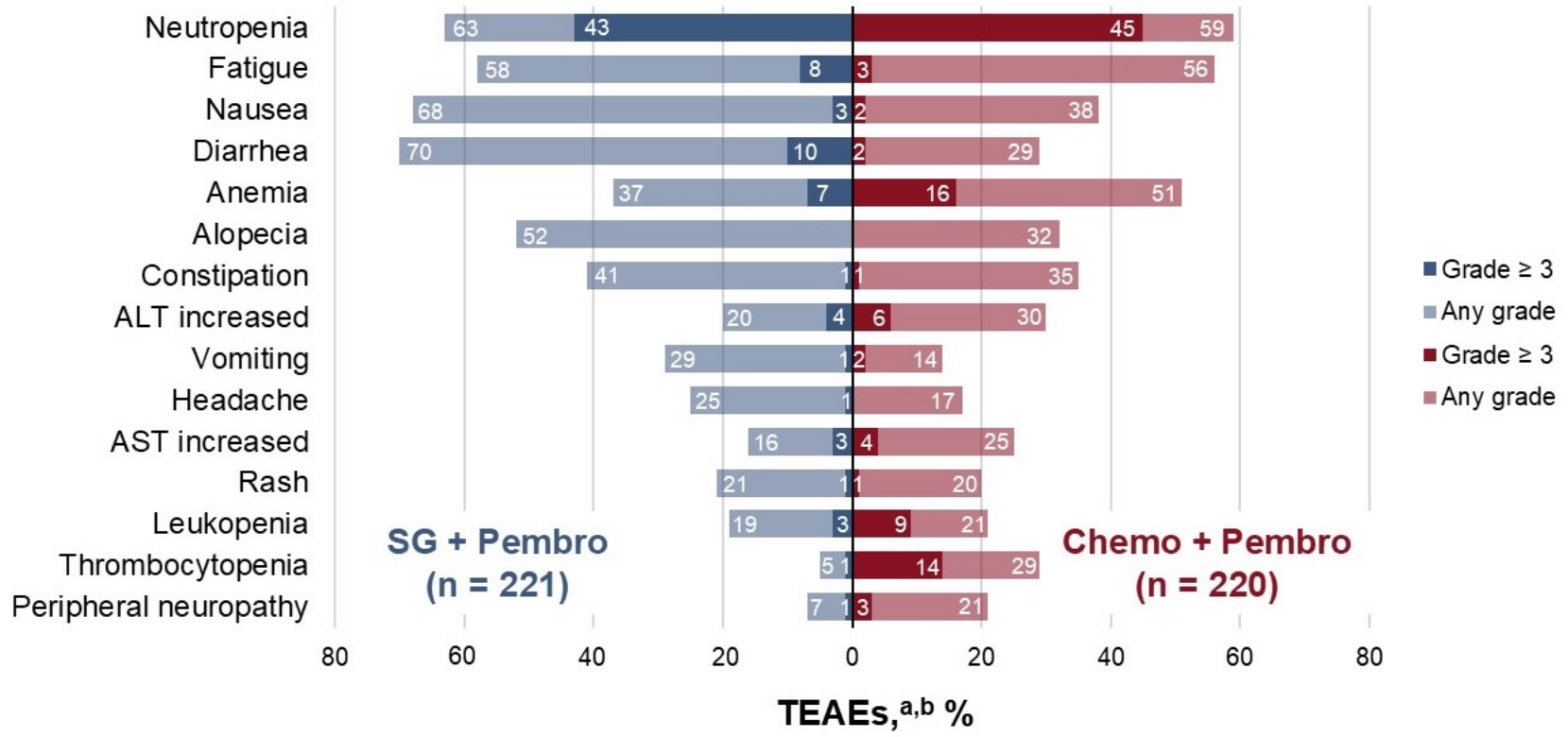
TEAEs were defined as any adverse events that began or worsened on or after the first dose date of study drug up to 30 days (or up to 90 days for SAEs) after the last dose date of study drug or the initiation of subsequent anticancer therapy (including crossover treatment), whichever occurred first. Data cutoff date: March 3, 2025.

[a]The most common any-grade TEAEs that led to treatment discontinuation were pneumonitis (1%) for the SG + pembro group and neuropathy peripheral (5%), pneumonitis (3%), and thrombocytopenia (3%) for the chemo + pembro group. [b]There was no dose reduction for pembrolizumab per the protocol. [c]TEAEs leading to death were pneumonia, sepsis, neutropenic sepsis, pulmonary embolism, and suicide (1 each), as well as 2 deaths of unknown cause in the SG + pembro group, and cardiac arrest, large intestine perforation, pneumonia, sepsis, post-procedural complication, and death of unknown cause (1 each) in the chemo + pembro group.

Chemo, chemotherapy; pembro, pembrolizumab; SAE, serious adverse event; SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event.

Tolaney SM et al. ASCO 2025;Abstract LBA109.

Phase III ASCENT-04/KEYNOTE-D19: Common AEs



The AEs observed are consistent with the known profiles of both SG and pembro

TEAEs were defined as any adverse events that began or worsened on or after the first dose date of study drug up to 30 days (or up to 90 days for SAEs) after the last dose date of study drug or the initiation of subsequent anticancer therapy (including crossover treatment), whichever occurred first. Data cutoff date: March 3, 2025.

[a]TEAEs were included if they occurred in ≥ 20% of patients in either arm. [b]Combined preferred terms of Neutropenia includes neutrophil count decreased, Leukopenia includes white blood cell count decreased, Anemia includes hemoglobin decreased and red blood cell count decreased, Thrombocytopenia includes platelet count decreased, Fatigue includes asthenia.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; chemo, chemotherapy; pembro, pembrolizumab; SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event.

Tolaney SM et al. ASCO 2025;Abstract LBA109.

Phase III ASCENT-04/KEYNOTE-D19: AEs of Special Interest

	AESI,[a] n (%)	SG + Pembro (n = 221)		Chemo + Pembro (n = 220)	
		Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
SG AESIs	Neutropenia[b]	143 (65)	104 (47)	132 (60)	100 (45)
	Hypersensitivity[b]	43 (19)	4 (2)	51 (23)	5 (2)
	Serious infections secondary to neutropenia[b]	6 (3)	5 (2)	3 (1)	3 (1)
	Diarrhea (Grade 3 or higher)	N/A	22 (10)	N/A	5 (2)
Pembro AESIs	Overall	30 (14)	9 (4)	56 (26)	16 (7)
	Infusion reactions (not immune-mediated)[a]	11 (5)	3 (1)	19 (9)	5 (2)
	Pneumonitis[b]	5 (2)	3 (1)	10 (5)	2 (1)
	Colitis[b]	4 (2)	1 (< 1)	1 (< 1)	1 (< 1)
	Hypothyroidism[b]	4 (2)	0	19 (9)	0
	Hypophysitis[b]	2 (1)	0	2 (1)	0
	Hyperthyroidism[b]	2 (1)	0	5 (2)	0
	Severe skin reactions,[b] including Stevens-Johnson syndrome and toxic epidermal necrolysis	2 (1)	2 (1)	2 (1)	2 (1)
	Hepatitis[b]	1 (< 1)	0	2 (1)	2 (1)
	Adrenal insufficiency[b]	1 (< 1)	0	2 (1)	1 (< 1)
	Pancreatitis[b]	0	0	2 (1)	2 (1)

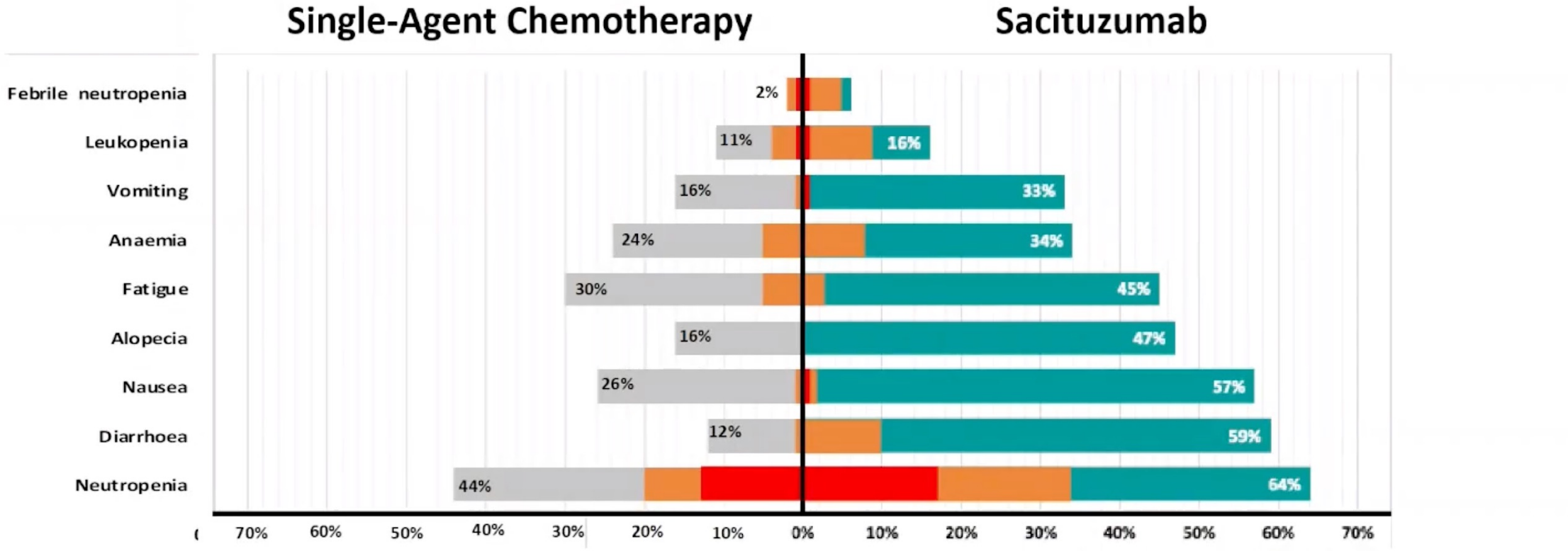
AESIs were consistent with the known safety profiles of each agent; no new safety concerns were observed and no increased rates of AESIs were observed when combining SG with pembro

AESIs were adverse events determined based on a prespecified list of Medical Dictionary for Regulatory Activities (MedDRA) terms, which was updated with each new version of MedDRA. Immune-mediated adverse events were determined based on a prespecified list of Medical Dictionary for Regulatory Activities (MedDRA) terms, which was updated with each new version of MedDRA and specified as immune-mediated by the investigator. Data cutoff date: March 3, 2025.
[a]AESIs observed in ≥1% of patients in either group are presented; [b]Grouped term.
AESI, adverse event of special interest; chemo, chemotherapy; pembro, pembrolizumab; SG, sacituzumab govitecan.

Tolaney SM et al. ASCO 2025;Abstract LBA109.

RTP RESEARCH TO PRACTICE

Safety of Sacituzumab versus Treatment of Physician's Choice in the ASCENT Trial



~5% of patients in both arms discontinued for any adverse reaction[1]

- Neutropenia or febrile neutropenia did not lead to any permanent discontinuation
- No patients discontinued treatment because of diarrhoea

The most frequently reported AEs leading to dose reduction were neutropenia (6.3%) and diarrhoea (3.3%)[3]

Bardia A, et al. ESMO 2020; Abstract LBA17.; Bardia A, et al, NEJM 2021

Schmid P. ESMO Breast 2025.

RTP RESEARCH TO PRACTICE

Management of Sacituzumab Govitecan-Induced Diarrhea

Loperamide

1. Early Intervention (provide patient with medication prophylactically)
2. 4 mg followed by 2 mg with every episode (max 16 mg/d)
3. Discontinue 12h after diarrhea resolves

In selected cases

1. Octreotide: 100-150ug TDS
2. Fluoroquinolones: If >24h, ANC <500 or fever
3. Atropine: If cholinergic response (rare)

	Grade 1	Grade 2	Grade 3	Grade 4
Description	1-3	4-6	>6 or hospitalisation	Life threatening
SG	Continue	Continue	Hold until <G2	
Dose reduction	N/A	N/A	• 1st occurrence: 25% • 2nd occurrence: 50% • 3rd occurrence: Discontinue	

Schmid P. ESMO Breast 2025.

RTP RESEARCH TO PRACTICE

Articles

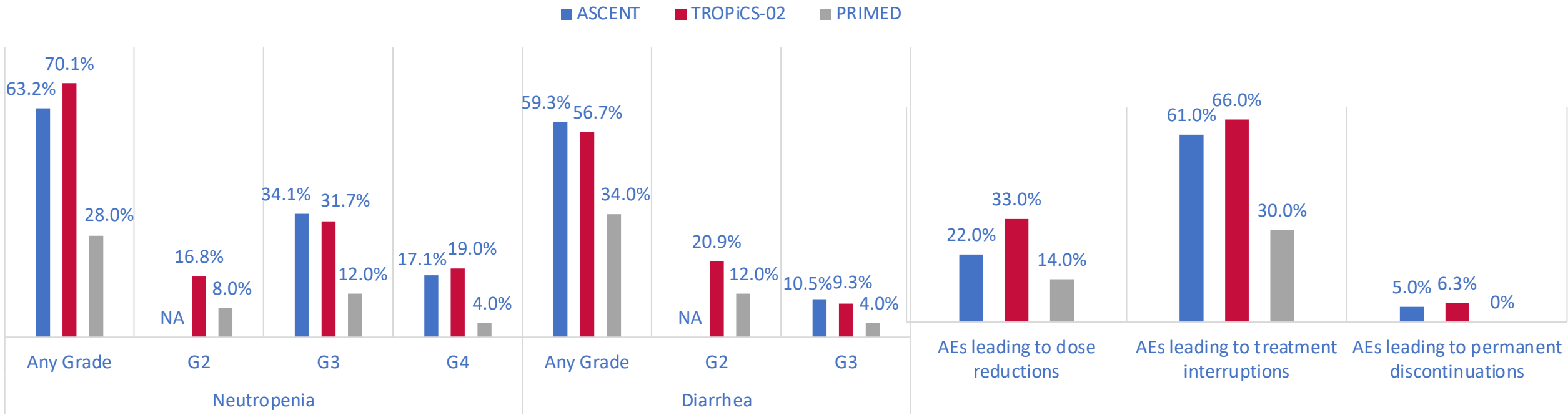
Prevention of sacituzumab govitecan-related neutropenia and diarrhea in patients with HER2-negative advanced breast cancer (PRIMED): an open-label, single-arm, phase 2 trial

José Manuel Pérez-García,[a,b,u] María Gion,[a,c,d,u] Manuel Ruiz-Borrego,[e] Isabel Blancas,[f,g,h] Elena López-Miranda,[a,c,u] Salvador Blanch,[i] Sabela Recalde,[j] Cristina Reboredo Rendo,[k] Xavier González,[l] Nerea Ancizar,[m] Serafin Morales,[n] Patricia Cortez,[d,o] Zuzanna Piwowarska,[a,u] Eileen Shimizu,[a,u] José Antonio Guerrero,[a,u] Miguel Sampayo-Cordero,[a,u] Alejandro Martínez-Bueno,[p] Javier Cortés,[a,b,d,q,r,u] and Antonio Llombart-Cussac[a,s,t,u,*]

EClinicalMedicine 2025;85:103309.

Rates of Neutropenia and Diarrhea in ASCENT, TROPiCS-02, and PRIMED

AEs Leading to Dose Reductions, Rx Interruptions, and Permanent D/C in ASCENT, TROPiCS-02, and PRIMED



50 patients; loperamide 4 mg day 2,3,4 then 9, 10, 11; G-CSF SC day 3, 4 and 10, 11

G, grade; NA, not available.
Pérez-García JM, et al. Presented at 2024 ASCO Annual Meeting. Abstract 1101.

Courtesy of Hope S Rugo, MD

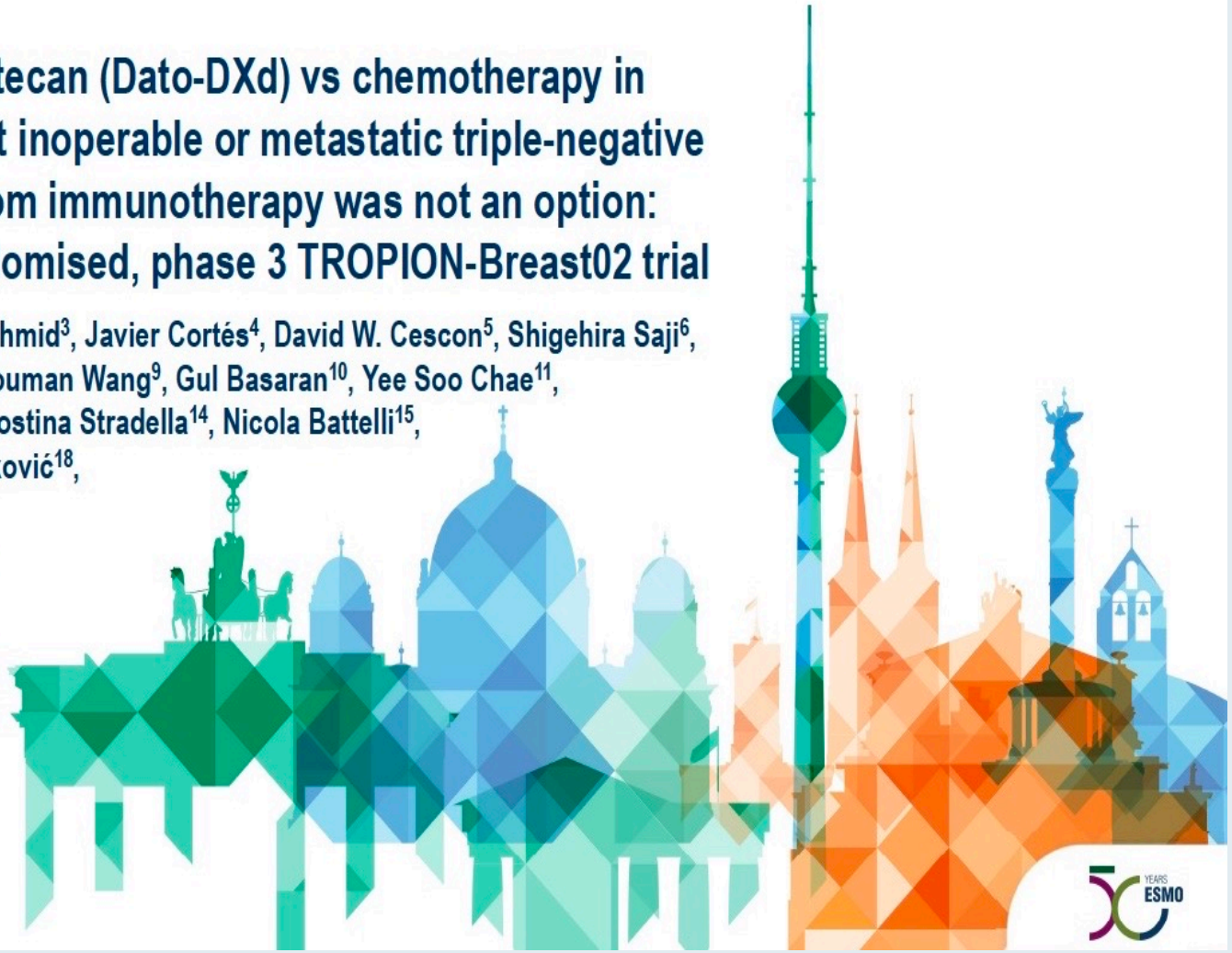
Abstract LBA21

BERLIN 2025 ESMO congress

First-line datopotamab deruxtecan (Dato-DXd) vs chemotherapy in patients with locally recurrent inoperable or metastatic triple-negative breast cancer (TNBC) for whom immunotherapy was not an option: Primary results from the randomised, phase 3 TROPION-Breast02 trial

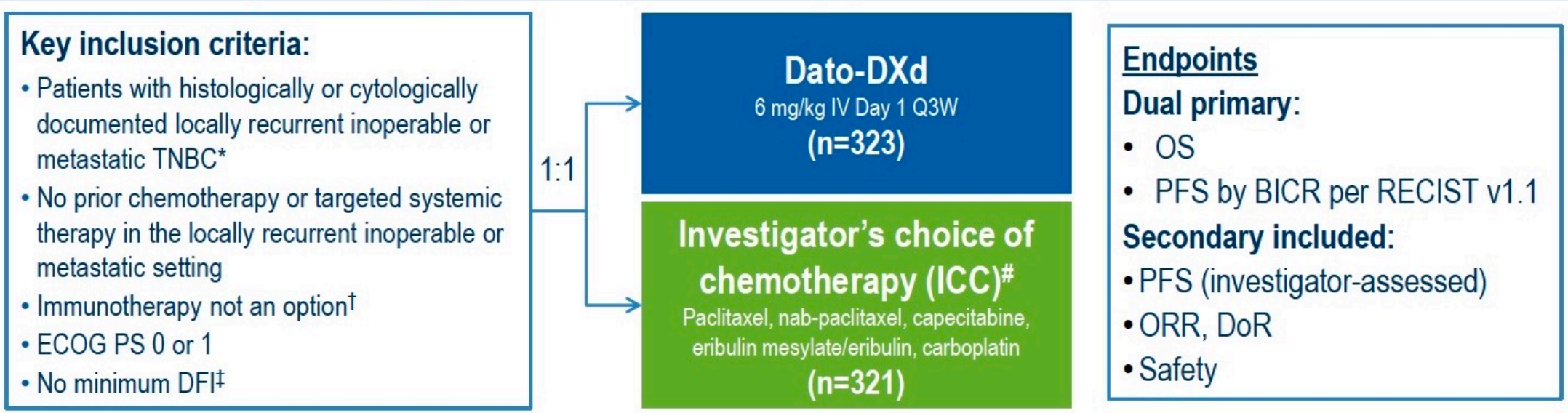
Rebecca A. Dent[1], Zhimin Shao[2], Peter Schmid[3], Javier Cortés[4], David W. Cescon[5], Shigehira Saji[6], Kyung Hae Jung[7], Thomas Bachelot[8], Shouman Wang[9], Gul Basaran[10], Yee Soo Chae[11], Rofhiwa Mathiba[12], Shin-Cheh Chen[13], Agostina Stradella[14], Nicola Battelli[15], Naoki Niikura[16], Kechen Zhao[17], Petra Vuković[18], Micah J. Maxwell[19], Tiffany A. Traina[20]

[1]National Cancer Center Singapore, Singapore; [2]Fudan University Shanghai Cancer Center, Fudan, China; [3]Centre for Experimental Cancer Medicine, Barts Cancer Institute, Queen Mary University of London, London, UK; [4]International Breast Cancer Center (IBCC), Pangaea Oncology, Barcelona, Spain; [5]Princess Margaret Cancer Centre, Toronto, ON, Canada; [6]Fukushima Medical University, Fukushima, Japan; [7]Asan Medical Center – University of Ulsan College of Medicine, Seoul, Republic of Korea; [8]Centre Léon Bérard, Lyon, France; [9]Xiangya Hospital of Central South University, Changsha, China; [10]MAA Acibadem University, School of Medicine, Medical Oncology Department, Istanbul, Türkiye; [11]Kyungpook National University Chilgok Hospital, Kyungpook National University School of Medicine, Kyungpook, Republic of Korea; [12]Charlotte Maxeke Johannesburg Academic Hospital, Johannesburg, South Africa; [13]Chang Gung Medical Foundation – Taipei Chang Gung Memorial Hospital, Taipei City, Taiwan; [14]Institut Catala d'Oncologia - Hospital Duran i Reynals (ICO L'Hospitalet), Barcelona, Spain; [15]Ospedale Generale Provinciale Macerata, Macerata, Italy; [16]Tokai University School of Medicine, Kanagawa, Japan; [17]Biometrics, Late-Stage Development, Oncology R&D, AstraZeneca, Wilmington, DE, USA; [18]Clinical Development, Late-Stage Development, Oncology R&D, AstraZeneca, Cambridge, UK; [19]Clinical Development, Late-Stage Development, Oncology R&D, AstraZeneca, Gaithersburg, MD, USA; [20]Memorial Sloan Kettering Cancer Center (MSKCC), New York, NY, USA



RTP RESEARCH TO PRACTICE

Phase III TROPION-Breast02 Study Design



Randomisation stratified by:

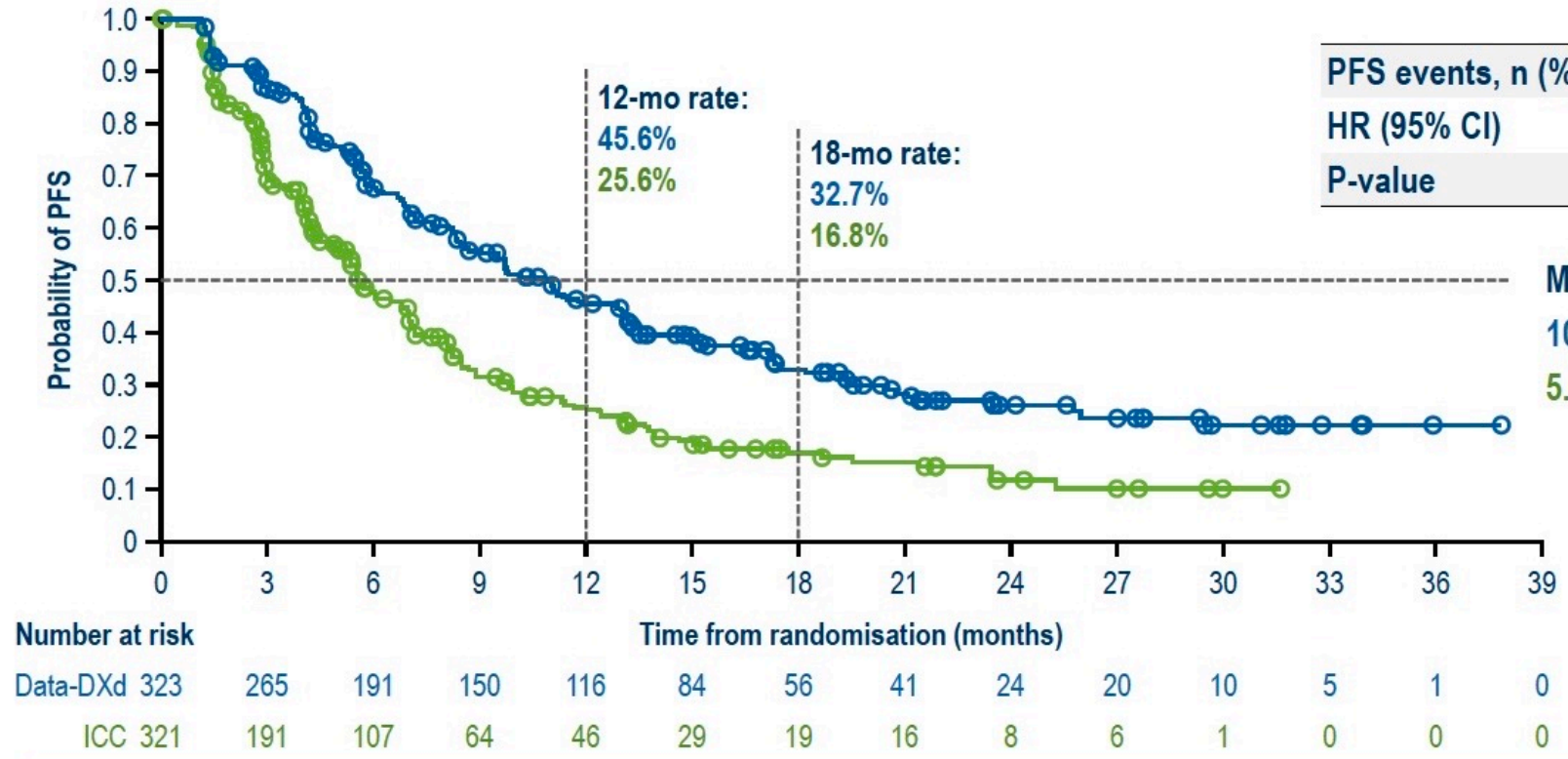
- Geographic region (US/Canada/Europe vs other geographic regions)
- PD-L1 status (high [CPS ≥10] vs low [CPS <10])§
- DFI history (*de novo* vs prior DFI 0–12 months vs prior DFI >12 months)¶

- Treatment continued until investigator-assessed RECIST v1.1 progressive disease, unacceptable toxicity, or another discontinuation criterion was met
- Following progression or discontinuation of study treatment, patients could receive subsequent therapies, including approved ADCs or chemotherapy, at the investigator's discretion‖

*According to ASCO/CAP criteria. †Including patients with PD-L1-low tumours, or patients with PD-L1-high tumours with (a) disease relapse after prior PD-(L)1 inhibitor therapy for early-stage breast cancer, (b) comorbidities precluding PD-(L)1 inhibitor therapy, or (c) no regulatory access to PD-(L)1 inhibitor therapy. ‡DFI defined as time between date of completion of treatment with curative intent and date of first documented local or distant disease recurrence. §Recruitment of patients with PD-L1-high tumours who would otherwise be eligible for pembrolizumab if regulatory access was available was capped at ~10% of randomised patients. ¶Recruitment of patients with DFI 0–12 months was capped at ~20% of randomised patients. #If no prior taxane, or prior taxane in the (neo)adjuvant setting and DFI >12 months: paclitaxel 80 mg/m² IV, D1, 8, 15, Q3W, or nab-paclitaxel 100 mg/m² IV, D1, 8, 15, Q4W; if prior taxane and DFI 0–12 months: capecitabine 1000 or 1250 mg/m² orally twice daily, D1–14, Q3W (dose determined by standard institutional practice), or eribulin mesylate 1.4 mg/m² / eribulin 1.23 mg/m² IV, Day 1, 8, Q3W, or carboplatin AUC6 IV, D1, Q3W. ‖In the Dato-DXd vs ICC arm, 65% vs 72% of patients received any subsequent therapy in any treatment line; 14% vs 30% received a subsequent ADC (sacituzumab govitecan, sacituzumab tirumotecan, trastuzumab deruxtecan).

Dent R et al. ESMO 2025;Abstract LBA21.

Phase III TROPION-Breast02: PFS by BICR



	Dato-DXd	ICC
PFS events, n (%)	199 (62)	209 (65)
HR (95% CI)	0.57 (0.47–0.69)	
P-value	<0.0001	

Median PFS (95% CI)

10.8 mo (8.6–13.0)

5.6 mo (5.0–7.0)

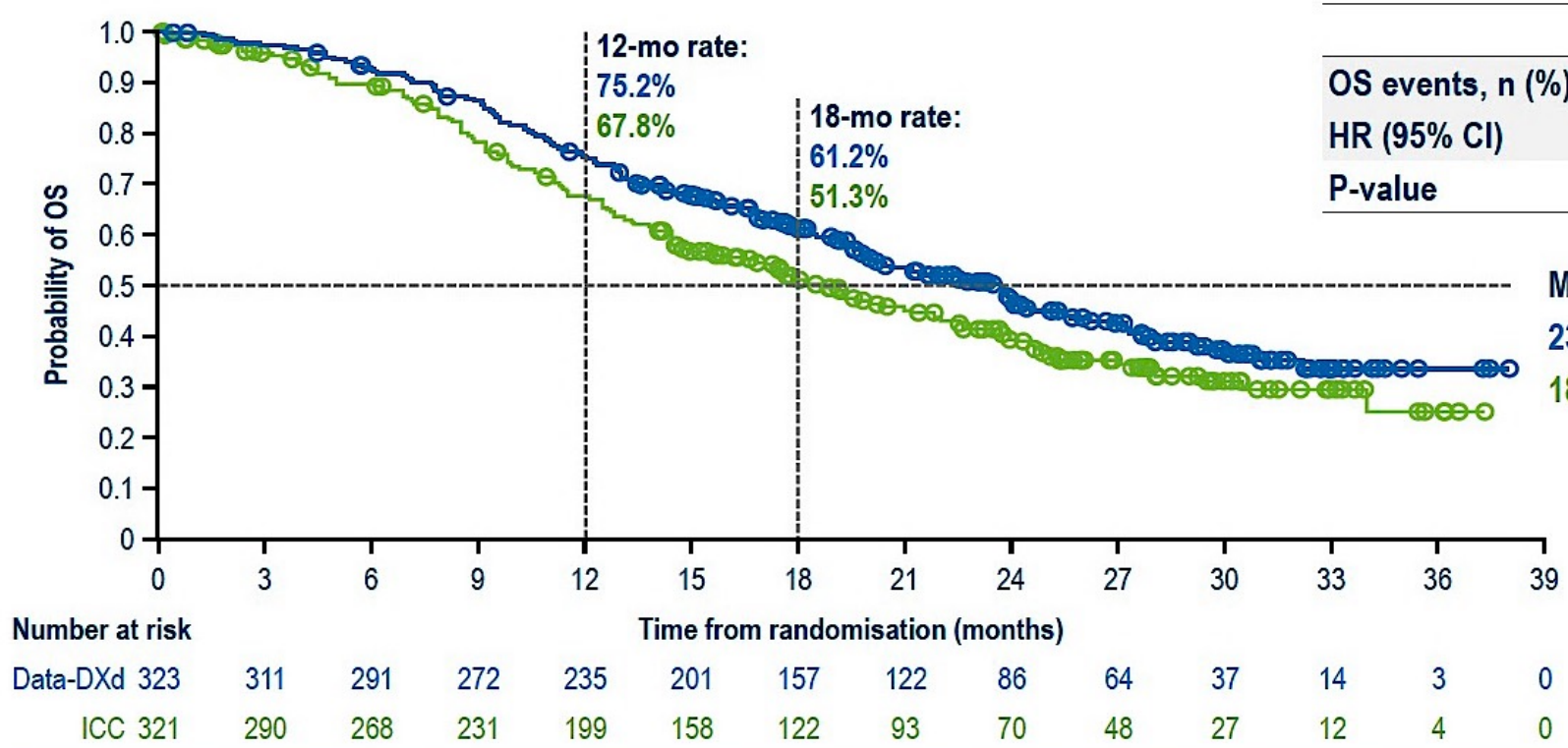
Δ 5.3 mo*

Dato-DXd demonstrated a statistically significant and clinically meaningful improvement in PFS compared with ICC, reducing the risk of progression or death by 43%

Dent R et al. ESMO 2025;Abstract LBA21.

RTP RESEARCH TO PRACTICE

Phase III TROPION-Breast02: Overall Survival (OS)



	Dato-DXd	ICC
OS events, n (%)	168 (52)	181 (56)
HR (95% CI)	0.79 (0.64–0.98)	
P-value	0.0291	

Median OS (95% CI)

23.7 mo (19.8–25.6)

18.7 mo (16.0–21.8)

Δ 5.0 mo

Dato-DXd demonstrated a statistically significant and clinically meaningful improvement in OS compared with ICC, reducing the risk of death by 21%

Dent R et al. ESMO 2025;Abstract LBA21.

RTP RESEARCH TO PRACTICE

Phase III TROPION-Breast02: Overall Safety Summary

- **Median total treatment duration:**
  - **Dato-DXd: 8.5 months** (range 0.7–38.0)
  - **ICC: 4.1 months** (range 0.1–32.0)
- **Patients with total exposure >12 months:**
  - **Dato-DXd: 35.1%**
  - **ICC: 9.4%**

Treatment-related AEs, n (%)	Dato-DXd (n=319)	ICC (n=309)
Any grade	296 (93)	257 (83)
Grade ≥3	105 (33)	89 (29)
Serious TRAEs	29 (9)	26 (8)
Associated with dose interruption	76 (24)	60 (19)
Associated with dose reduction	85 (27)	56 (18)
Associated with discontinuation	14 (4)	23 (7)
Associated with death	0	0

Despite more than double the median duration of treatment in the Dato-DXd arm, rates of grade ≥3 and serious treatment-related AEs were similar, and discontinuations were lower, with Dato-DXd vs ICC

Dent R et al. ESMO 2025;Abstract LBA21.

Phase III TROPION-Breast02: Common AEs

Treatment-related AEs, n (%)	Dato-DXd (n=319)		ICC (n=309)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Dry eye*	76 (24)	4 (1)	9 (3)	0
Stomatitis	182 (57)	27 (8)	27 (9)	0
Nausea	142 (45)	2 (<1)	53 (17)	2 (<1)
Constipation	72 (23)	1 (<1)	31 (10)	0
Vomiting	65 (20)	4 (1)	23 (7)	1 (<1)
Decreased appetite	49 (15)	1 (<1)	20 (6)	1 (<1)
Neutropenia†	39 (12)	10 (3)	90 (29)	40 (13)
Anaemia‡	48 (15)	6 (2)	64 (21)	10 (3)
Leukopenia§	27 (8)	3 (<1)	55 (18)	13 (4)
Peripheral neuropathy¶	14 (4)	0	75 (24)	5 (2)
Alopecia	130 (41)	0	96 (31)	1 (<1)‖
Fatigue#	101 (32)	8 (3)	86 (28)	9 (3)

*In the Dato-DXd arm only, ophthalmologic assessments were required every 3 cycles while on therapy; this was not required in the ICC arm. For all patients in both arms, ophthalmologic assessments were required at baseline, as clinically indicated, and at end of therapy.
†Grouped term comprising preferred terms of neutropenia and neutrophil count decreased. ‡Grouped term comprising preferred terms of haemoglobin decreased, red blood cell count decreased, anaemia, and haematocrit decreased. §Grouped term comprising preferred terms of white blood cell count decreased and leukopenia. ¶Grouped term comprising preferred terms of neuropathy peripheral, peripheral motor neuropathy, polyneuropathy, paraesthesia, and peripheral sensory neuropathy. #Grouped term comprising preferred terms of fatigue, asthenia, and malaise.
‖Per Common Terminology Criteria for Adverse Events version 5.0, the maximum grade for alopecia is grade 2.

Dent R et al. ESMO 2025;Abstract LBA21.

Phase III TROPION-Breast02: AEs of Special Interest with Dato-DXd

AESI category, n (%) Preferred term*	Dato-DXd (n=319)			ICC (n=309)		
	Grade 1	Grade 2	Grade ≥3	Grade 1	Grade 2	Grade ≥3
Oral mucositis/stomatitis†	78 (24)	87 (27)	27 (8)	22 (7)	8 (3)	0
Stomatitis	72 (23)	83 (26)	27 (8)	19 (6)	8 (3)	0
Ocular surface events‡§	76 (24)	50 (16)	23 (7)	9 (3)	5 (2)	1 (<1)
Dry eye	51 (16)	21 (7)	4 (1)	6 (2)	3 (1)	0
Keratitis	21 (7)	14 (4)	7 (2)	1 (<1)	0	0
Conjunctivitis	7 (2)	13 (4)	1 (<1)	0	0	0
Adjudicated drug-related ILD/pneumonitis¶	1 (<1)	7 (2)	1 (<1)#	1 (<1)	1 (<1)	0

Treatment-related oral mucositis/stomatitis:

- In the Dato-DXd arm, events led to dose interruption, reduction, and discontinuation in 11 (3%), 36 (11%), and 0 patients, respectively
- Grade ≥2 events resolved to grade ≤1 in 103/114 patients (90%) at data cutoff

Treatment-related ocular surface events:

- In the Dato-DXd arm, events led to dose interruption, reduction, and discontinuation in 18 (6%), 14 (4%), and 3 (<1%) patients, respectively
- Grade ≥2 events resolved to grade ≤1 in 49/73 patients (67%) at data cutoff

*Details for preferred terms included if reported in ≥20 patients in either arm. †Comprising the preferred terms of aphthous ulcer, mouth ulceration, oral pain, oropharyngeal pain, pharyngeal inflammation, and stomatitis. ‡Comprising the preferred terms of acquired corneal dystrophy, blepharitis, conjunctivitis, corneal disorder, corneal epithelium defect, corneal erosion, corneal exfoliation, corneal lesion, corneal toxicity, dellen, dry eye, keratitis, keratopathy, lacrimation increased, limbal stem cell deficiency, meibomian gland dysfunction, photophobia, punctate keratitis, ulcerative keratitis, vision blurred, visual acuity reduced, visual impairment, and xerophthalmia. §In the Dato-DXd arm only, ophthalmologic assessments were required every 3 cycles while on therapy; this was not required in the ICC arm. For all patients in both arms, ophthalmologic assessments were required at baseline, as clinically indicated, and at end of therapy. ¶Comprising the preferred terms of interstitial lung disease and pneumonitis. #Grade 5 – this event was characterised by the investigator as grade 3 pneumonitis, with death assessed as related to breast cancer.

Dent R et al. ESMO 2025;Abstract LBA21.

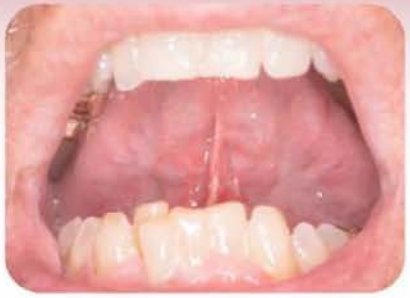
Datopotamab Deruxtecan Toxicities: Mucositis

STEP 1: Prophylaxis

Initiate daily oral care plan prior to administration of first Dato-DXd dose

- **Gently brushing** teeth after meals and at bedtime using a soft toothbrush and a **bland fluoride-containing toothpaste**
- **Daily flossing**, unless it causes pain or bleeding
- Daily use of a **steroid-containing mouthwash**[a,b]
- **Cryotherapy** should be considered
- **Education** on the importance of oral hygiene, hydration, and lubrication of the oral mucosa and **adherence to oral care plan**

STEP 2: Monitor



Bernadett Szabados MD

STEP 3: Manage

Supportive care

- Increase frequency of bland mouthwashes to up to every hour, if necessary
- As soon as oral pain, inflammation, and/or ulceration develops, strongly consider using a steroid-containing mouthwash[a]
- Provide pain management
- Consider referral to a dentist, oral surgeon, oral medicine expert, or dermatologist for severe or persistent events

Grading and dose modifications

Grade 1
- Maintain dose

Grade 2
- Consider a dose delay or reduction if clinically indicated

Grade 3
- If prophylactic/supportive medications have not yet been optimized, delay dose until event has been resolved to ≤ grade 1 or baseline, optimize medications, then maintain dose
- If prophylactic/supportive medications have already been optimized, delay dose until resolved to ≤ grade 1 or baseline, and then reduce dose by 1 level

Grade 4
- Discontinue Dato-DXd

Meric-Bernstam et al., ASCO GU 2025

BERLIN 2025 ESMO congress

Szabados B. ESMO 2025.

RTP RESEARCH TO PRACTICE

Abstract LBA23

BERLIN 2025 ESMO congress

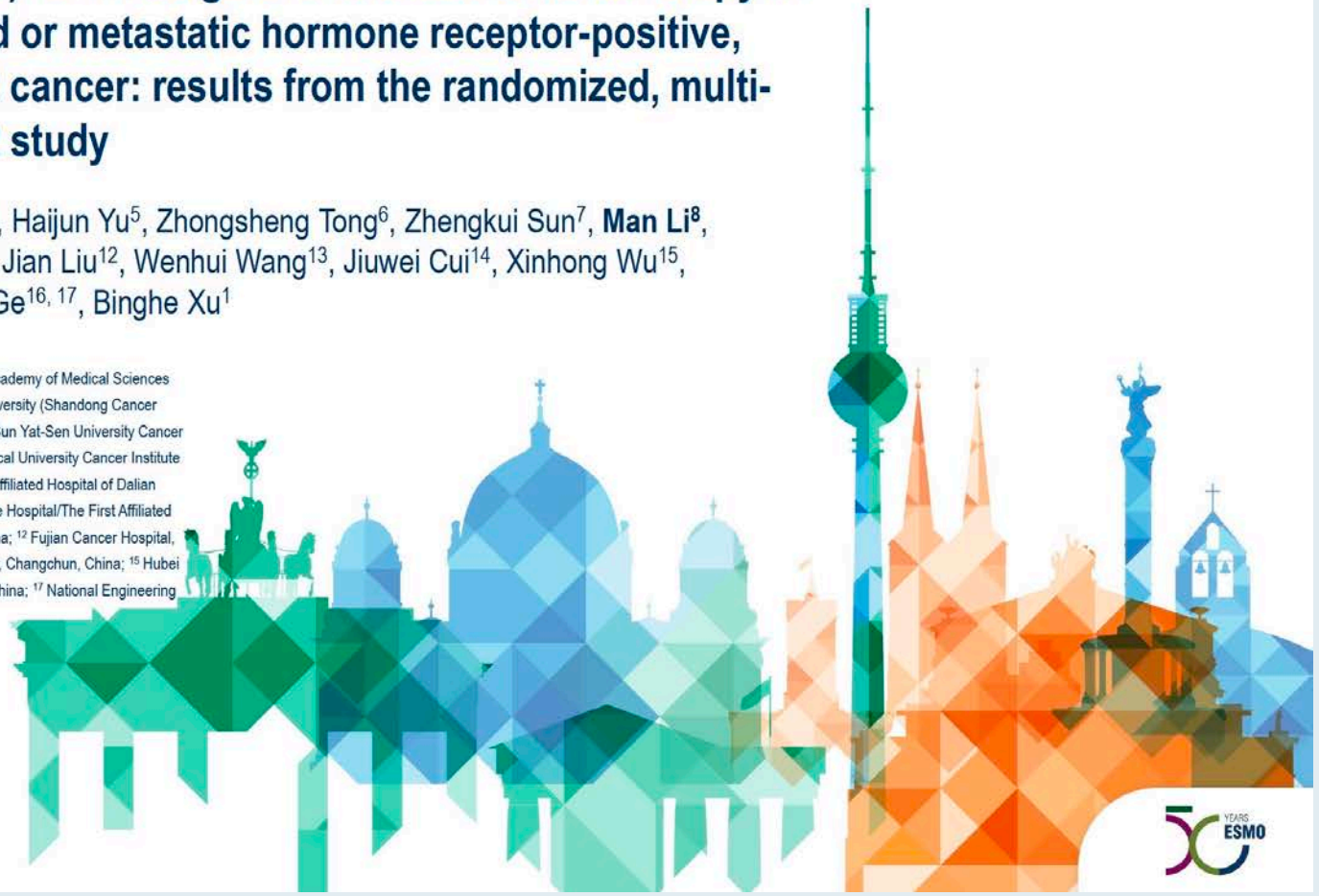
Sacituzumab tirumotecan (sac-TMT) vs investigator's choice of chemotherapy in previously treated locally advanced or metastatic hormone receptor-positive, HER2-negative (HR+/HER2-) breast cancer: results from the randomized, multi-center phase 3 OptiTROP-Breast02 study

Ying Fan[1], Huihui Li[2], Hao Wang[3], Shusen Wang[4], Haijun Yu[5], Zhongsheng Tong[6], Zhengkui Sun[7], **Man Li[8]**, Xiying Shao[9], Yongmei Yin[10], Quchang Ouyang[11], Jian Liu[12], Wenhui Wang[13], Jiuwei Cui[14], Xinhong Wu[15], Gesha Liu[16], Yina Diao[16], Xiaoping Jin[16], Junyou Ge[16, 17], Binghe Xu[1]

[1] National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [2] Cancer Hospital of Shandong First Medical University (Shandong Cancer Institute, Shandong Cancer Hospital), Jinan, China; [3] Sichuan Cancer Hospital, Chengdu, China; [4] Sun Yat-Sen University Cancer Center, Guangzhou, China; [5] Zhongnan Hospital of Wuhan University, Wuhan, China; [6] Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; [7] Jiangxi Provincial Cancer Hospital, Nanchang, China; [8] The Second Affiliated Hospital of Dalian Medical University, Dalian, China; [9] Zhejiang Cancer Hospital, Hangzhou, China; [10] Jiangsu Province Hospital/The First Affiliated Hospital with Nanjing Medical University, Nanjing, China; [11] Hunan Cancer Hospital, Changsha, China; [12] Fujian Cancer Hospital, Fuzhou, China; [13] Weifang People's Hospital, Weifang, China; [14] The First Hospital of Jilin University, Changchun, China; [15] Hubei Cancer Hospital, Wuhan, China; [16] Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd., Chengdu, China; [17] National Engineering Research Center of Targeted Biologics, Chengdu, China.

Presenter: Professor Man Li

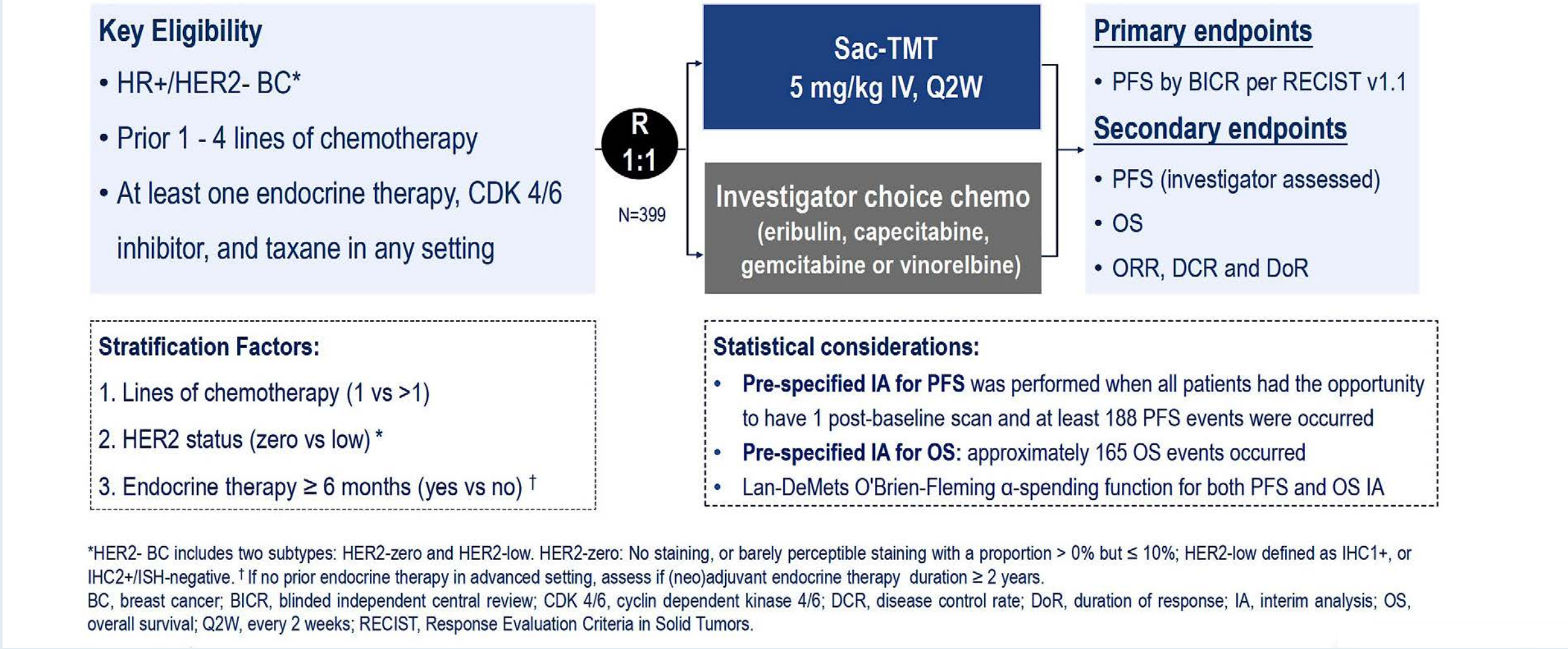
The Second Affiliated Hospital of Dalian Medical University, Dalian, China



Sat, 18.10.2025

RTP RESEARCH TO PRACTICE

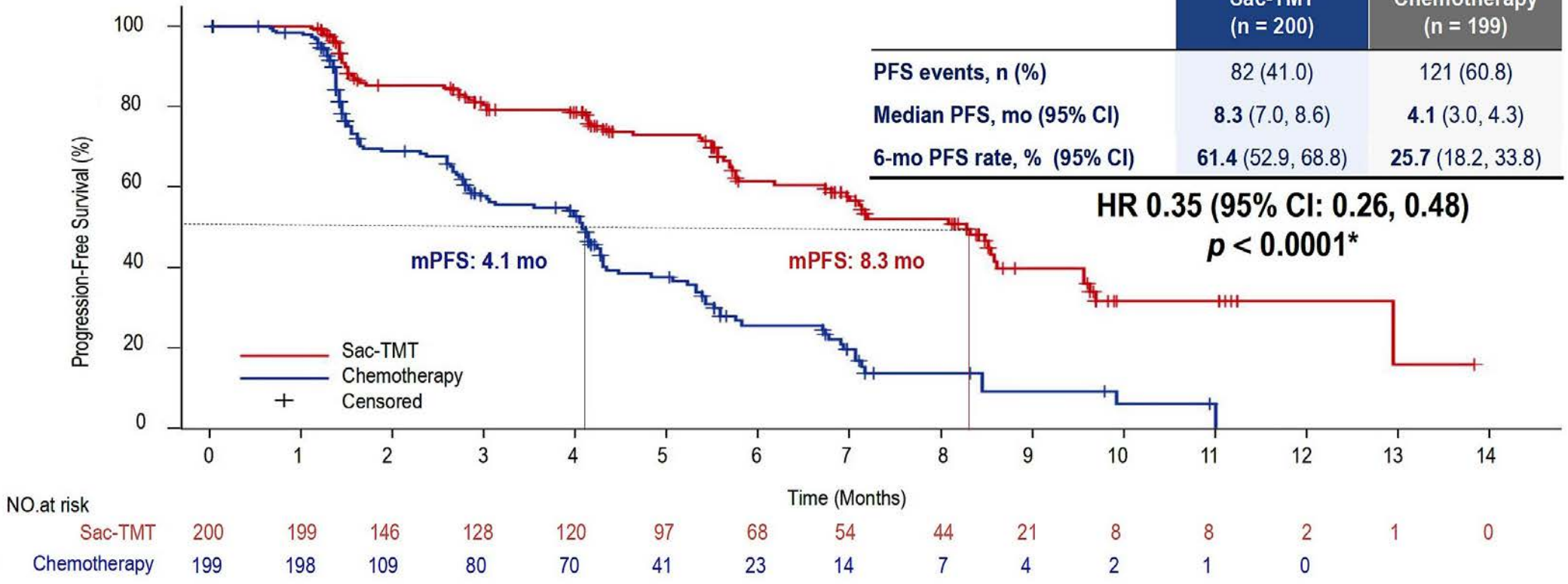
Phase III OptiTROP-Breast02 Study Design



*HER2- BC includes two subtypes: HER2-zero and HER2-low. HER2-zero: No staining, or barely perceptible staining with a proportion > 0% but ≤ 10%; HER2-low defined as IHC1+, or IHC2+/ISH-negative. † If no prior endocrine therapy in advanced setting, assess if (neo)adjuvant endocrine therapy duration ≥ 2 years.
BC, breast cancer; BICR, blinded independent central review; CDK 4/6, cyclin dependent kinase 4/6; DCR, disease control rate; DoR, duration of response; IA, interim analysis; OS, overall survival; Q2W, every 2 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

Li M et al. ESMO 2025;Abstract LBA23.

Phase III OptiTROP-Breast02: PFS by BICR



	Sac-TMT (n = 200)	Chemotherapy (n = 199)
PFS events, n (%)	82 (41.0)	121 (60.8)
Median PFS, mo (95% CI)	**8.3** (7.0, 8.6)	**4.1** (3.0, 4.3)
6-mo PFS rate, % (95% CI)	**61.4** (52.9, 68.8)	**25.7** (18.2, 33.8)

HR 0.35 (95% CI: 0.26, 0.48)
p* < 0.0001

The investigator-assessed PFS was consistent with BICR: HR 0.39 (95% CI: 0.30, 0.52)

* Based on pre-specified PFS IA, one-sided *P* value was less than the pre-specified efficacy boundary to achieve statistically significant improvement (one-sided alpha level of 0.010 determined by the O'Brien-Fleming alpha spending function).

BICR = blinded independent central review

Li M et al. ESMO 2025;Abstract LBA23.

Phase III OptiTROP-Breast02: Overall Safety Summary

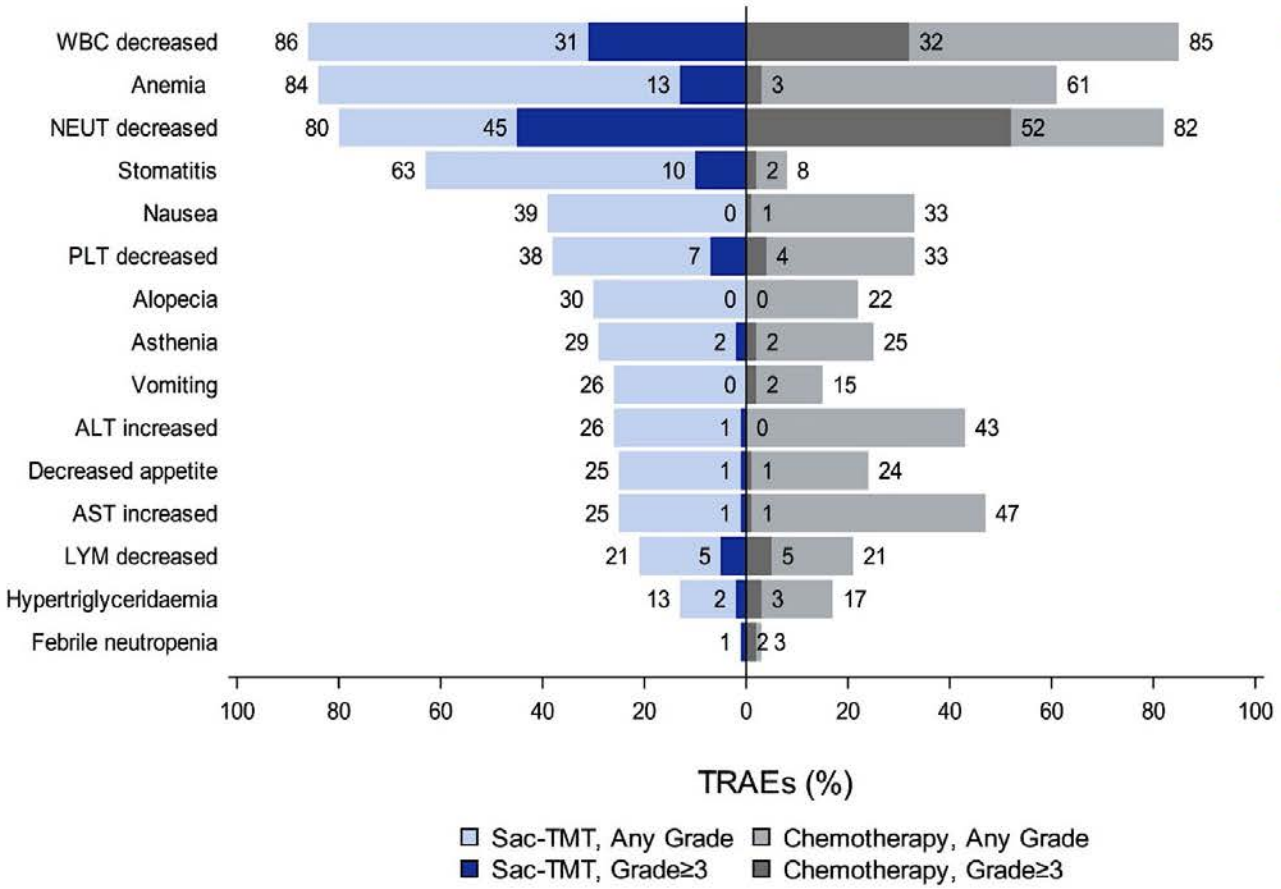
TRAEs, n (%)	Sac-TMT (n = 200)	Chemotherapy (n = 196)
All grades	199 (99.5)	195 (99.5)
Grade ≥ 3	124 (62.0)	127 (64.8)
Serious TRAEs	25 (12.5)	29 (14.8)
Associated with dose interruption	80 (40.0)	89 (45.4)
Associated with dose reduction	63 (31.5)	54 (27.6)
Associated with discontinuation	0	1 (0.5)
Associated with death	0	0

Data cutoff date: Jan 22, 2025.
TRAEs, treatment-related adverse events.

- The incidence of all-grade and grade ≥ 3 TRAEs was similar between the two groups, which were predominantly hematological AEs.
- Incidence of dose reductions was similar between the two groups.
- In the sac-TMT group, there were no TRAEs leading to discontinuation and no treatment-related deaths.

Li M et al. ESMO 2025;Abstract LBA23.

Phase III OptiTROP-Breast02: Safety



- The most common TRAEs for both sac-TMT and chemotherapy were hematologic toxicities.
- Grade ≥ 3 diarrhea occurred in **1.0%** of patients in the sac-TMT group.
- Low ocular surface toxicity (11.5% dry eyes, 4.0% corneal disease, all grade 1-2) observed in the sac-TMT group.
- ILD/pneumonitis occurred in **1.5% and 1.0%** of patients (**all grade 1-2**) in the sac-TMT and chemotherapy groups.

* Summary of TRAEs that occurred in either treatment group at an incidence of ≥ 20% for any grade or ≥ 2% for grade ≥ 3.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; ILD, interstitial lung disease; LYM, lymphocyte count; NEUT, neutrophil count; PLT, platelet count; WBC, white blood cell.

Li M et al. ESMO 2025;Abstract LBA23.

Agenda

Introduction	Overview: Molecular basis of antibody-drug conjugate (ADC) toxicities — Sequencing of ADCs and mechanisms of resistance
Case 1	Dr Zelkowitz – 68-year-old woman
■ Data Review: TROP2-targeted ADCs (sacituzumab govitecan, Dato-DXd, sac TMT)	
Case 2	Dr Gupta – 74-year-old woman
Case 3	Dr Agrawal – 83-year-old woman
Case 4	Dr Favaro – 70-year-old woman
■ Data Review: Trastuzumab deruxtecan	
Case 5	Dr Rupard – 78-year-old woman
Case 6	Dr Ku – 72-year-old woman
■ Data Review: Other HER2-targeted agents	

RTP RESEARCH TO PRACTICE

Case Presentation: 74-year-old woman with recurrent ER-neg, HER2-low, PD-L1-pos mBC with disease progression on *nab* paclitaxel/atezolizumab responds to sacituzumab govitecan

Dr Ranju Gupta (Bethlehem, Pennsylvania)

RTP RESEARCH TO PRACTICE

Agenda

Introduction	Overview: Molecular basis of antibody-drug conjugate (ADC) toxicities — Sequencing of ADCs and mechanisms of resistance
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■ Data Review: Other HER2-targeted agents	

RTP
RESEARCH
TO PRACTICE

Case Presentation: 83-year-old woman with recurrent ER+, HER2-low (IHC 1+) mBC with disease progression on T-DXd then receives datopotamab deruxtecan and has pulmonary symptoms

Dr Laila Agrawal (Louisville, Kentucky)

RTP
RESEARCH
TO PRACTICE

Agenda

Introduction	Overview: Molecular basis of antibody-drug conjugate (ADC) toxicities — Sequencing of ADCs and mechanisms of resistance
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TO PRACTICE

ER-Positive, HER2-Negative or Low Metastatic Breast Cancer (mBC): Sequencing of Systemic Therapies After Endocrine Treatment

ER-positive, HER2-low

- Trastuzumab deruxtecan versus TROP2-targeted ADC (sacituzumab govitecan, datopotamab deruxtecan)
- Capecitabine
- Other chemotherapy

ER-positive, HER2-negative

- Sacituzumab govitecan versus datopotamab deruxtecan
- Capecitabine
- Other chemotherapy

Clinical factors

- PS, comorbidities
- Tumor-related symptoms
- Visceral, CNS disease
- Prior systemic treatment

RTP RESEARCH TO PRACTICE

ER-Negative, HER2-Negative or Low, PD-L1-Positive mBC: Sequencing of Systemic Therapies

ER-negative, HER2-low, PD-L1-positive (immunotherapy)

- Trastuzumab deruxtecan versus TROP2-targeted ADC (sacituzumab govitecan, datopotamab deruxtecan)
- Capecitabine
- Other chemotherapy

ER-negative, HER2-negative, PD-L1-positive (immunotherapy)

- Sacituzumab govitecan versus datopotamab deruxtecan
- Capecitabine
- Other chemotherapy

Clinical factors

- PS, comorbidities
- Tumor-related symptoms
- Visceral, CNS disease
- Prior systemic treatment

ER-Negative, HER2-Negative or Low, PD-L1-Negative mBC: Sequencing of Systemic Therapies

ER-negative, HER2-low, PD-L1-negative

- Trastuzumab deruxtecan versus TROP2-targeted ADC (sacituzumab govitecan, datopotamab deruxtecan)
- Capecitabine
- Other chemotherapy

ER-negative, HER2-negative, PD-L1-negative

- Sacituzumab govitecan versus datopotamab deruxtecan
- Capecitabine
- Other chemotherapy

Clinical factors

- PS, comorbidities
- Tumor-related symptoms
- Visceral, CNS disease
- Prior systemic treatment

RTP RESEARCH TO PRACTICE

Case Presentation: 70-year-old woman with recurrent ER+, HER2-low (IHC 1+) mBC including bladder metastases has disease progression after palbociclib/letrozole then capivasertib/fulvestrant then *nab* paclitaxel

Dr Justin Favaro (Charlotte, North Carolina)

RTP RESEARCH TO PRACTICE

Abstract LBA18

BERLIN 2025 ESMO congress

DESTINY Breast09

Trastuzumab deruxtecan (T-DXd) + pertuzumab vs taxane + trastuzumab + pertuzumab (THP) for patients with HER2+ advanced/metastatic breast cancer: additional analyses of DESTINY-Breast09 in key subgroups of interest

Sibylle Loibl, MD, PhD

University Hospital Goethe, University Frankfurt/M, GBG Neu-Isenburg, Germany

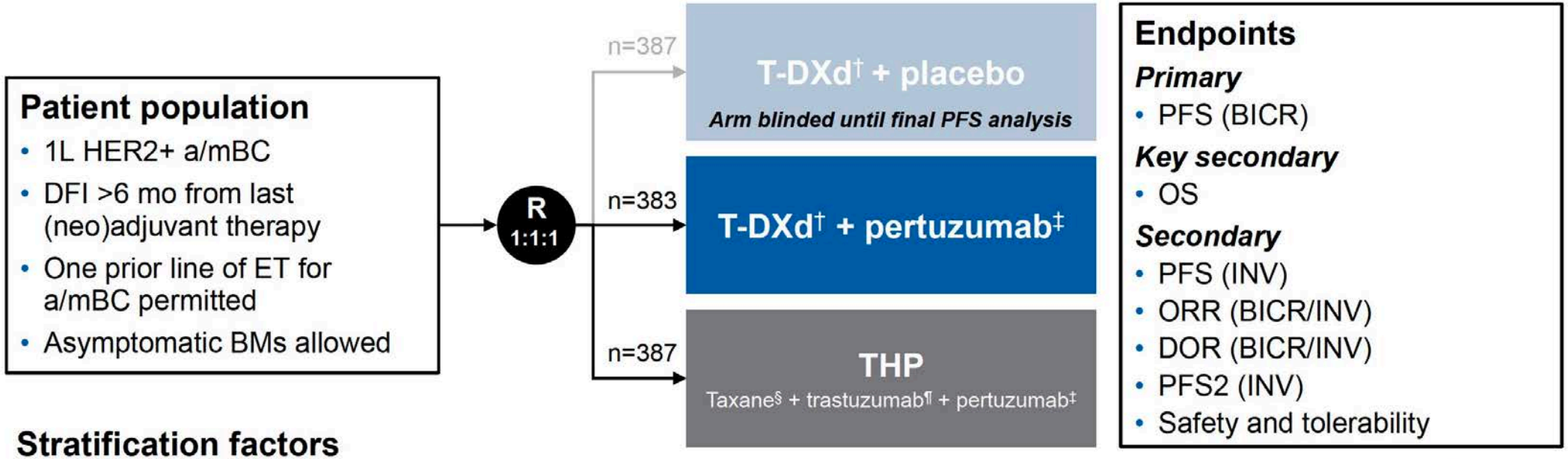
Co-authors: Zefei Jiang, Romualdo Barroso-Sousa, Yeon Hee Park, Cristina Saura, Mothaffar F Rimawi, Andreas Schneeweiss, Masakazu Toi, Seock-Ah Im, Zhongsheng Tong, Umut Demirci, Cynthia Villarreal-Garza, Chiun-Sheng Huang, Toshimi Takano, Valentina Guarneri, Shoubhik Mondal, Doudou Huang, Angela Zeng, Sara M Tolaney

On behalf of the DESTINY-Breast09 investigators

Sunday, October 19, 2025
Presentation LBA18

RTP RESEARCH TO PRACTICE

Phase III DESTINY-Breast09 Study Design



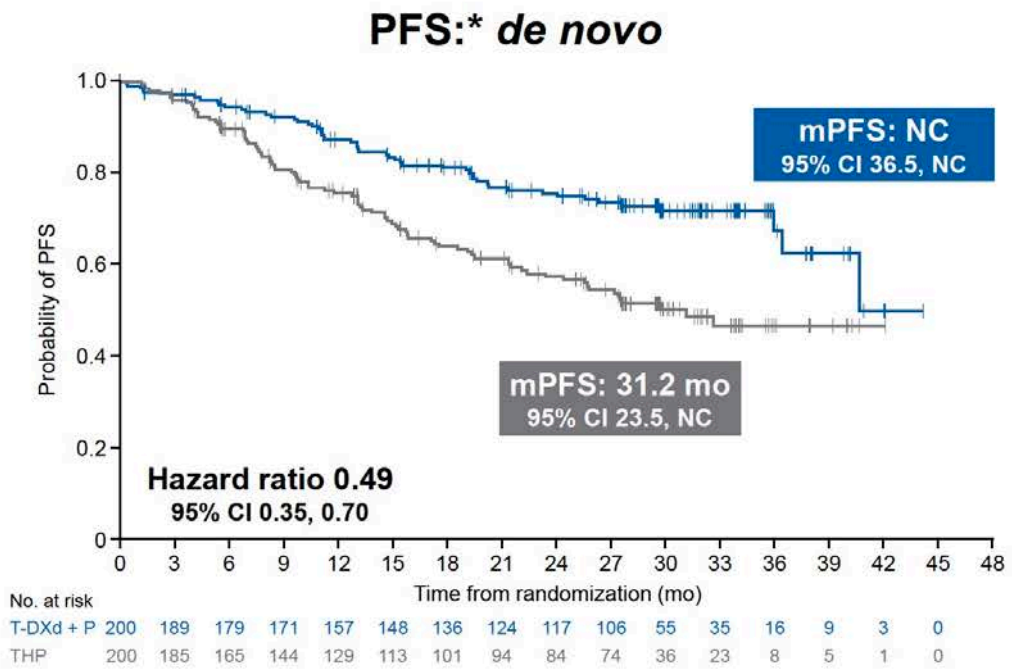
*Open label for THP arm, double blinded for pertuzumab in experimental arms; †5.4 mg/kg Q3W; ‡840 mg loading dose, then 420 mg Q3W; §paclitaxel 80 mg/m² QW or 175 mg/m² Q3W, or docetaxel 75 mg/m² Q3W for a minimum of six cycles or until intolerable toxicity; ¶8 mg/kg loading dose, then 6 mg/kg Q3W; ‖without loading dose

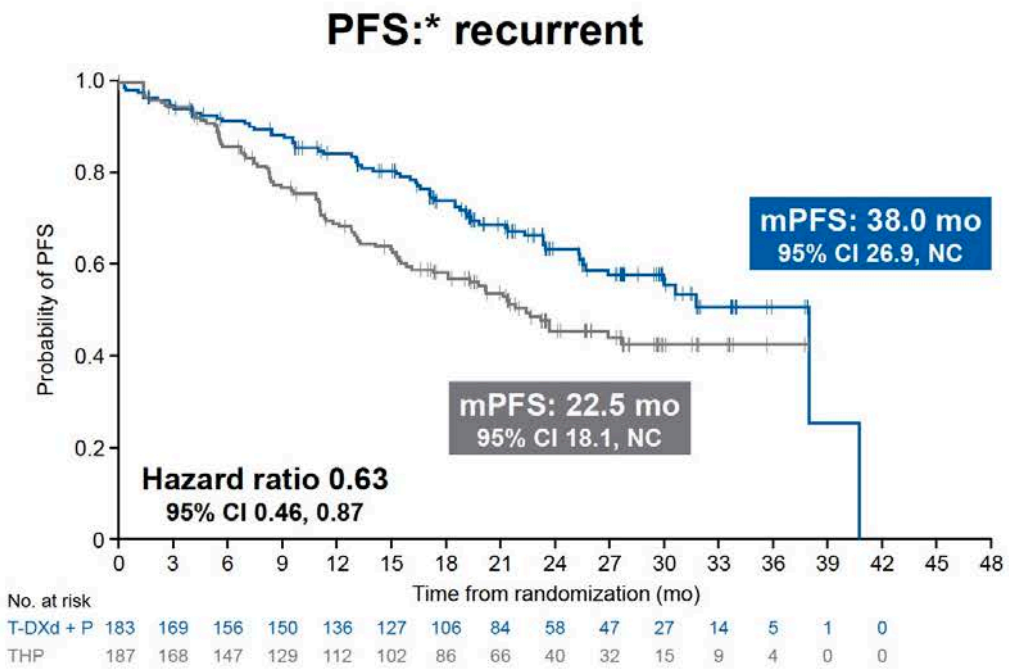
1L, first-line; AE, adverse event; a/mBC, advanced/metastatic breast cancer; BICR, blinded independent central review; BM, brain metastasis; DFI, disease-free interval; DOR, duration of response; ET, endocrine therapy; HER2+, human epidermal growth factor receptor 2–positive; HR+/−, hormone receptor–positive/–negative; ILD, interstitial lung disease; INV, investigator; mo, months; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PFS2, second progression-free survival; *PIK3CA*m, *PIK3CA* mutation; Q3W, every 3 weeks; QW, once weekly; R, randomization; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

1. Tolaney SM, et al. Oral presentation at ASCO 2025 (Abstract LBA1008); 2. NCT04784715. Updated. August 1, 2025. Available from: https://clinicaltrials.gov/study/NCT04784715 (Accessed October 15, 2025)

Loibl S et al. ESMO 2025;Abstract LBA18.

Phase III DESTINY-Breast09: PFS by Treatment Status



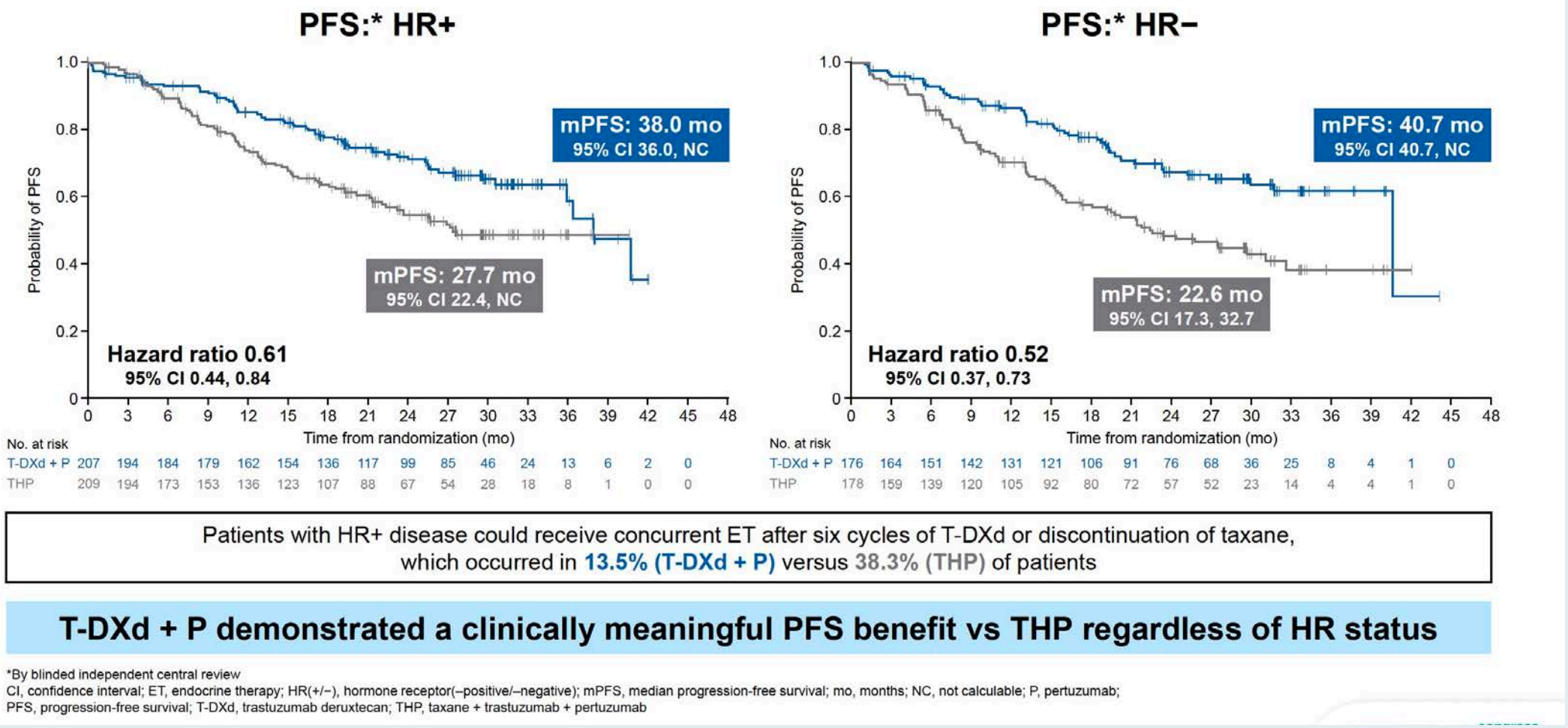


T-DXd + P demonstrated a clinically meaningful PFS benefit vs THP regardless of de-novo or recurrent status

*By blinded independent central review
CI, confidence interval; mPFS, median progression-free survival; mo, months; NC, not calculable; P, pertuzumab; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

Loibl S et al. ESMO 2025;Abstract LBA18.

Phase III DESTINY-Breast09: PFS by HR Status



Patients with HR+ disease could receive concurrent ET after six cycles of T-DXd or discontinuation of taxane, which occurred in **13.5% (T-DXd + P)** versus **38.3% (THP)** of patients

T-DXd + P demonstrated a clinically meaningful PFS benefit vs THP regardless of HR status

*By blinded independent central review
CI, confidence interval; ET, endocrine therapy; HR(+/−), hormone receptor(–positive/–negative); mPFS, median progression-free survival; mo, months; NC, not calculable; P, pertuzumab; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

Loibl S et al. ESMO 2025;Abstract LBA18.

RTP RESEARCH TO PRACTICE

Phase III DESTINY-Breast09 Trial Interim Results: 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)

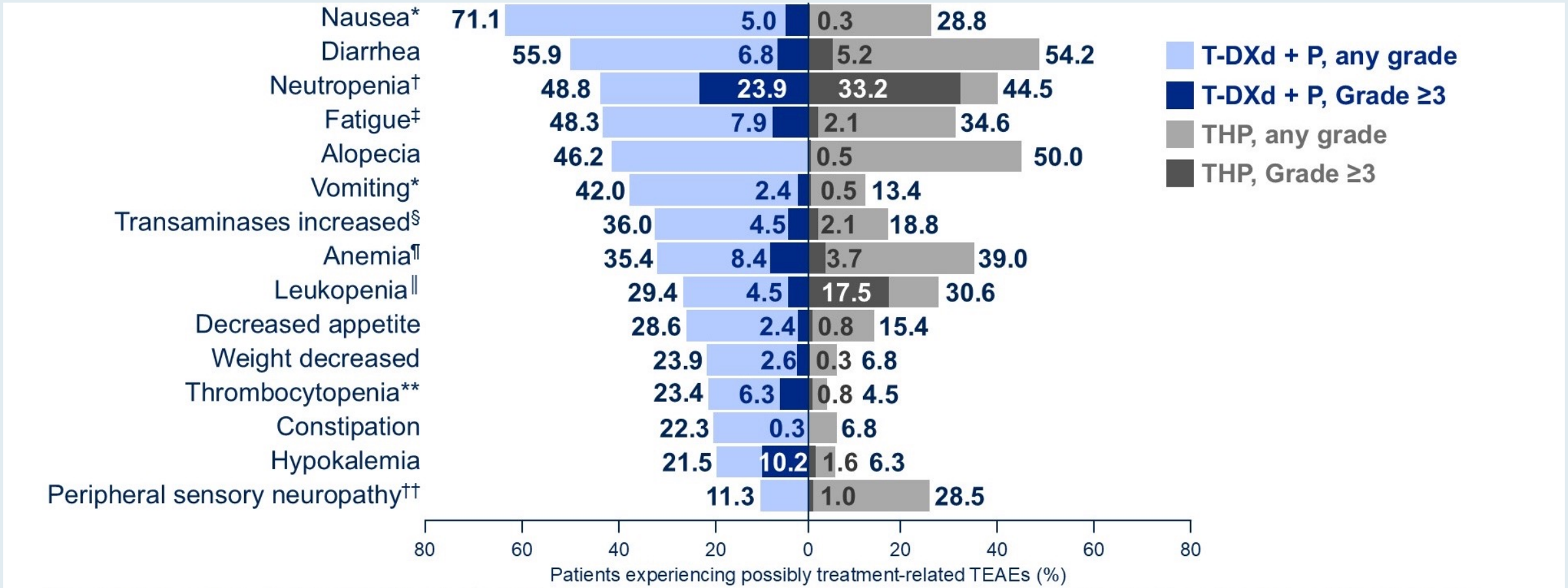
*Safety analyses included all patients who received at least one dose of study treatment (at least one study drug); †dose modifications or discontinuations relate to any component of each arm; ‡treatment-related TEAEs with outcome of death were pneumonitis (n=1), sepsis (n=1), septic shock (n=1), febrile 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

Tolaney SM et al. ASCO 2025;Abstract LBA1008.

RTP RESEARCH TO PRACTICE

Phase III DESTINY-Breast09 Interim Results: Common Adverse Events



*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

Tolaney SM et al. ASCO 2025;Abstract LBA1008.

RTP RESEARCH TO PRACTICE

Phase III DESTINY-Breast09 Interim Results: AEs 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†

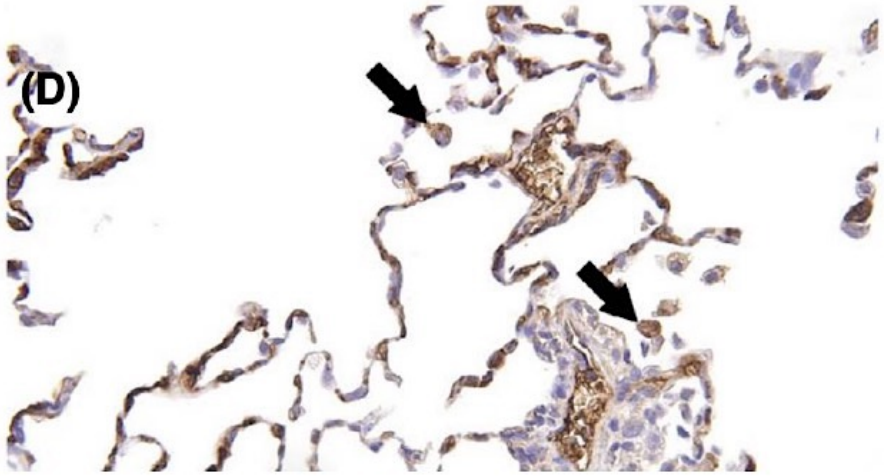
n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
T-DXd + P (n=381)	4 (1.0)	30 (7.9)	7 (1.8)	1 (0.3)	0	42 (11.0)
THP (n=382)	1 (0.3)	19 (5.0)	7 (1.8)	0	0	27 (7.1)

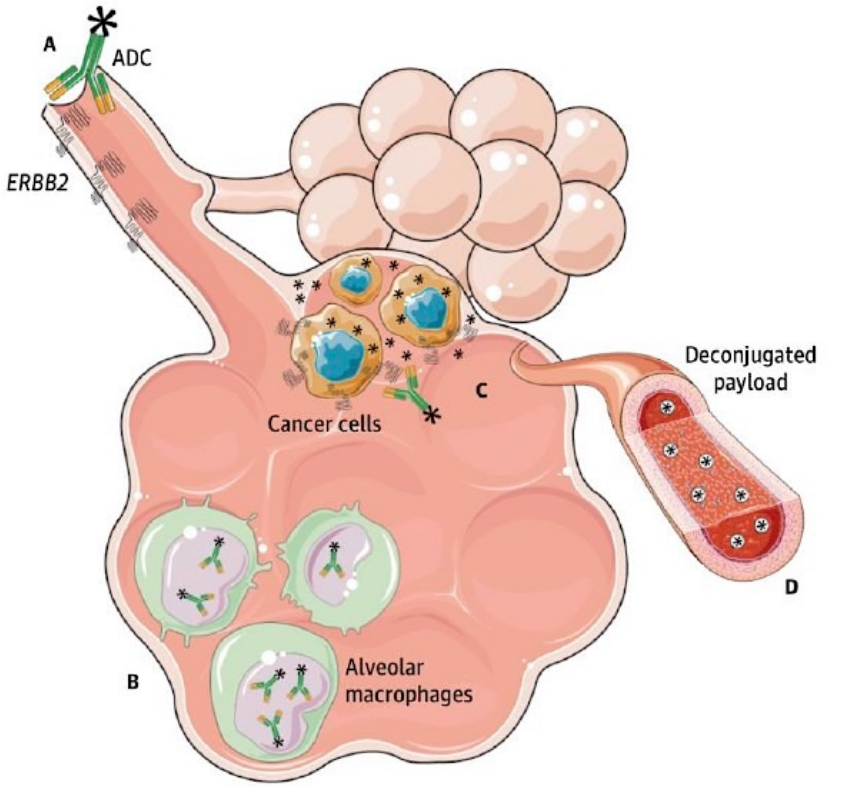
Safety analysis set
*Adjudicated drug-related ILD/pneumonitis (grouped term) includes: chronic obstructive pulmonary disease, interstitial lung disease, organizing pneumonia, pneumonia, and pneumonitis, †left ventricular dysfunction (grouped term) includes: potential heart failure, cardiac failure, cardiac 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

Tolaney SM et al. ASCO 2025;Abstract LBA1008.

Lung Toxicity

- Alveolar macrophages express high amounts of FcγR and were positive for DXd by IHC





Tarantino, JAMA Oncology 2021
Kumagai, Canc Science 2020

Curigliano G. ESMO Breast 2025.

Management of ILD

Routine Monitoring

1. Monitor for symptoms (cough, dyspnea, pyrexia)
2. Review every 4-6 weeks
3. Monitor SpO2 (examine if drop by 2-4% for 1-3d)
4. CT scans every 9-12 weeks

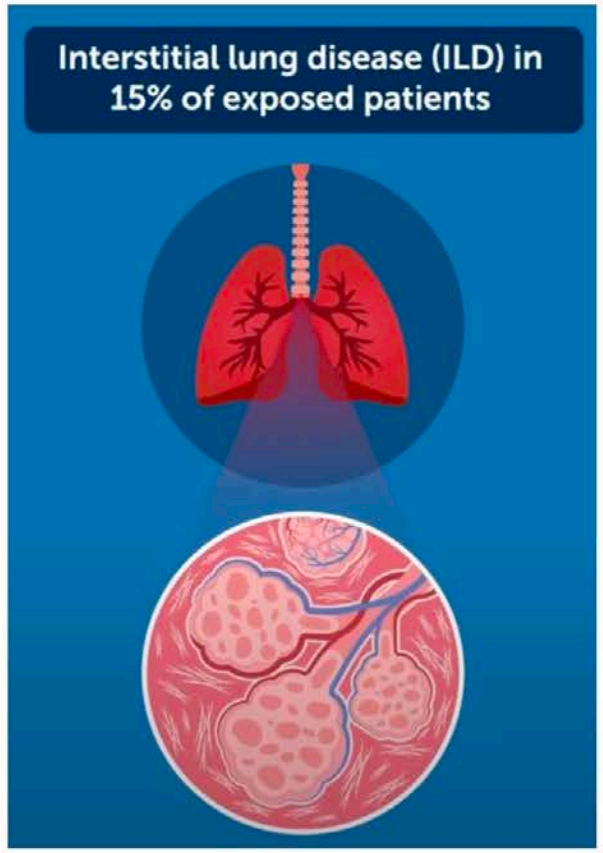
Diagnostic if ILD suspected

1. Lung function test
2. CT chest scan (ideally high-resolution CT)
3. Possibly Bronchoscopy
4. Bloods, blood and sputum cultures

	Grade 1	Grade 2	Grade 3/4
Description	Asymptomatic (diagnostic observations only)	Symptomatic; limiting instrument. ADL	Severe symptoms; limiting self-care ADL; oxygen (G3); Life-threatening (G4)
T-DXd	Hold (restart if resolved within 49 days, otherwise discontinue)	Discontinue	Discontinue
Dose reduction	Same dose if ≤28d, lower dose if > 28d	N/A	N/A
Steroids	0.5 mg/kg /day	≥1 mg/kg/day	Methylprednisolone i.v. 500-1000 mg/d for 3d, followed by ≥1 mg/kg/d prednisolone for 14d
Escalation	If worsens despite initiation of steroids, follow Grade 2 guidelines	if not better within 5d: Increase dose or switch to IV	if not better within 5d: Infliximab, IVIG or MMF
Duration	Until improvement, followed by gradual taper over ≥4 weeks	For at least 14d or until complete resolution of clinical and chest CT findings then gradually taper (for at least 4wks)	

Schmid P. ESMO Breast 2025.

T-DXd Toxicities: ILD



Bernadett Szabados MD

The Five"S" Rules

SCREENING	• Careful patient selection • Regular clinical assessments to exclude signs/symptoms of ILD.
SCANNING	• High-resolution CT scans of the chest. • A baseline scan is recommended, with repeat scans to be performed every 6-12 weeks.
SYNERGY	• Minimizing the risk of ILD involves teamwork • Educating patients and all the care team • Multidisciplinary management once ILD is suspected.
SUSPENDING TREATMENT	• T-DXd should always be interrupted if ILD is suspected; • Tt can only be restarted in the case of asymptomatic ILD that fully resolves.
STEROIDS	• The mainstay for treating T-DXd–induced ILD remains corticosteroids, with the dose to be adapted to the toxicity grade

Tarantino et al., JCO Oncology Practice, 2023

BERLIN 2025 ESMO congress

Szabados B. ESMO 2025

RTP RESEARCH TO PRACTICE

Management of Left Ventricular Ejection Fraction (LVEF) Changes Associated with T-DXd

Routine Monitoring

1. LVEF assessment at baseline
2. Repeat LVEF every 3 months

	LVEF >45%	LVEF 40-45%	LVEF <40%
Decrease from BL <10%	Continue	Continue. Repeat LVEF after 3 weeks	• Hold T-DXd. • Repeat LVEF after 3 weeks. • If confirmed, discontinue
Decrease from BL 10-20%	Continue	• Hold T-DXd. • Repeat LVEF after 3 weeks. • If not recovered to within 10% from BL, discontinue. • If recovered, resume at same dose	
Decrease from BL >20%	• Hold T-DXd. • Repeat LVEF after 3 weeks. • If confirmed, discontinue		

Discontinue if symptomatic congestive heart failure

Schmid P. ESMO Breast 2025.

RTP RESEARCH TO PRACTICE

Abstract LBA1

BERLIN 2025 ESMO congress

DESTINY Breast05

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

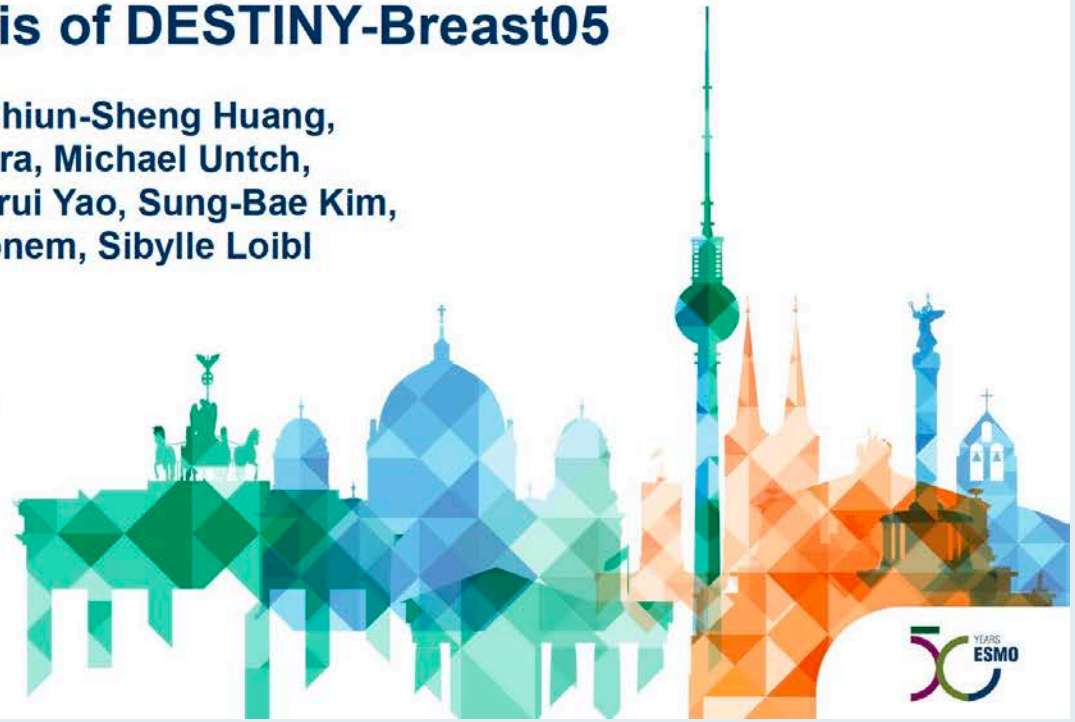
Charles E Geyer Jr,[a,b] Yeon Hee Park, Zhiming Shao, Chiun-Sheng Huang, Carlos Barrios, Jame Abraham, Aleix Prat, Naoki Niikura, Michael Untch, Seock-Ah Im, Wei Li, Huiping Li, Yongsheng Wang, Herui Yao, Sung-Bae Kim, Elton Mathias, Yuta Sato, Wenjing Lu, Hanan Abdel-Monem, Sibylle Loibl

On behalf of the DESTINY-Breast05 investigators

[a]NSABP Foundation, Pittsburgh, PA, USA
[b]University of Pittsburgh Hillman Cancer Center, Pittsburgh, PA, USA

Saturday, October 18, 2025
Presentation LBA1

NSABP National Surgical Adjuvant Breast and Bowel Project · GBG German Breast Group · AGO-B Breast Study Group · SOLTI



50 YEARS ESMO

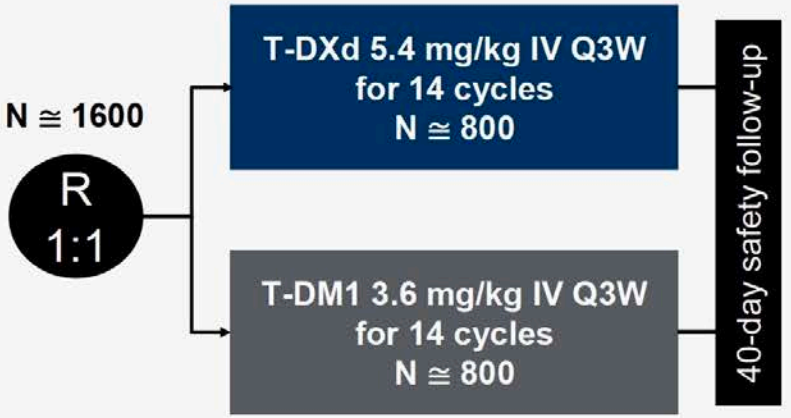
RTP RESEARCH TO PRACTICE

Phase III DESTINY-Breast05 Study Design

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

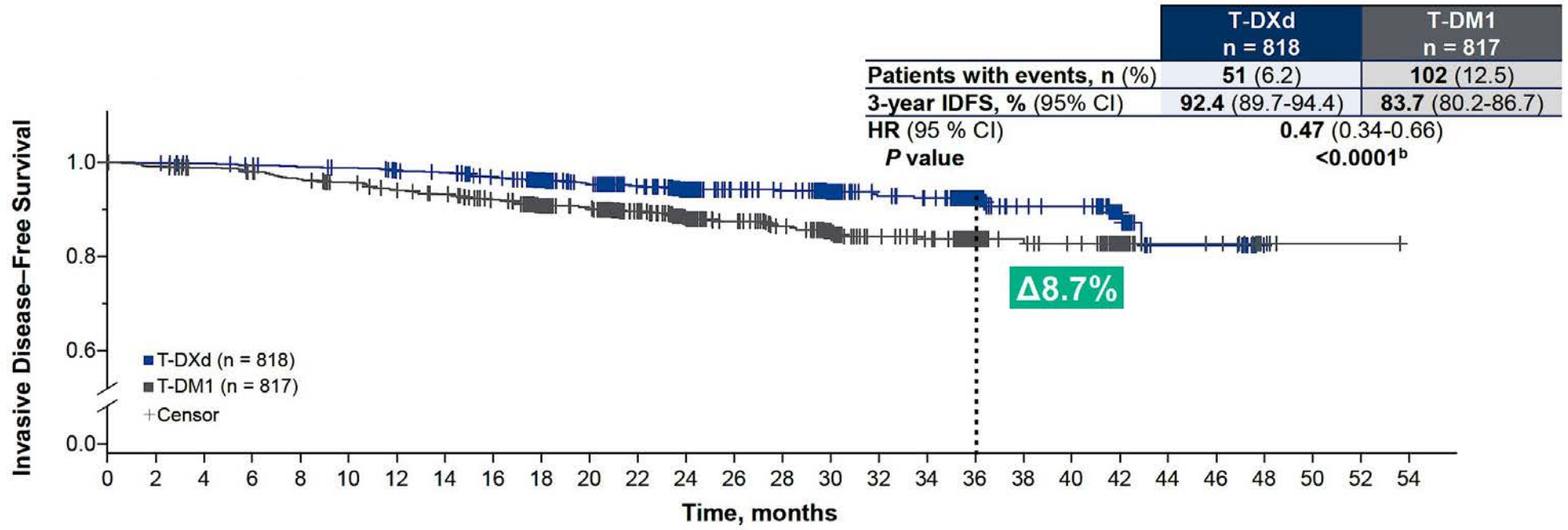
Other secondary endpoints
- OS
- DRFI
- BMFI
- Safety

- **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.
[a]NAT is defined as ≥16 weeks' NAT with ≥9 weeks trastuzumab ± pertuzumab and ≥9 weeks taxane-based chemotherapy.

Geyer CE et al. ESMO 2025;Abstract LBA1.

Phase III DESTINY-Breast05: Primary Endpoint Invasive Disease-Free Survival (IDFS)



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.
[a]IDFS 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. [b]Two-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.

Geyer CE et al. ESMO 2025;Abstract LBA1.

Phase III DESTINY-Breast05: Safety Summary

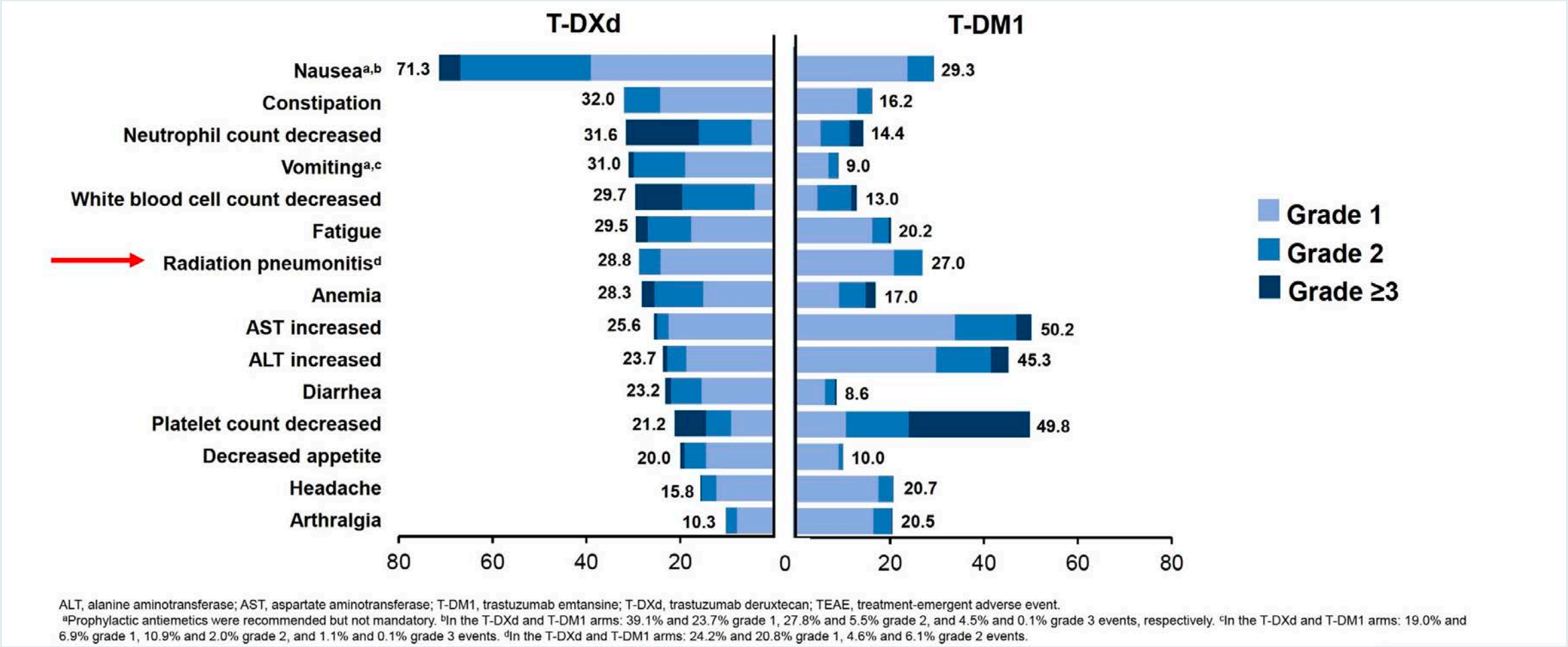
TEAEs, n (%)	T-DXd n = 806[a]	T-DM1 n = 801[a]
Any grade	802 (99.5)	788 (98.4)
Grade ≥3	**408 (50.6)**	**416 (51.9)**
Serious	**140 (17.4)**	**109 (13.6)**
Associated with drug discontinuation	**144 (17.9)**	**103 (12.9)**
Drug-related ILD/pneumonitis[b]	**87 (10.8)**	**20 (2.5)**
Associated with drug 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.
[a]All patients who received at least 1 dose of study treatment. [b]Investigator-assessed as drug-related ILD and pneumonitis per preferred term. [c]Investigator assessed and adjudication committee confirmed.

Geyer CE et al. ESMO 2025;Abstract LBA1.

Phase III DESTINY-Breast05: Common Adverse Events



ALT, alanine aminotransferase; AST, aspartate aminotransferase; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event.
[a]Prophylactic antiemetics were recommended but not mandatory. [b]In 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. [c]In 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. [d]In the T-DXd and T-DM1 arms: 24.2% and 20.8% grade 1, 4.6% and 6.1% grade 2 events.

Geyer CE et al. ESMO 2025;Abstract LBA1.

Phase III DESTINY-Breast05: AEs of Special Interest

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

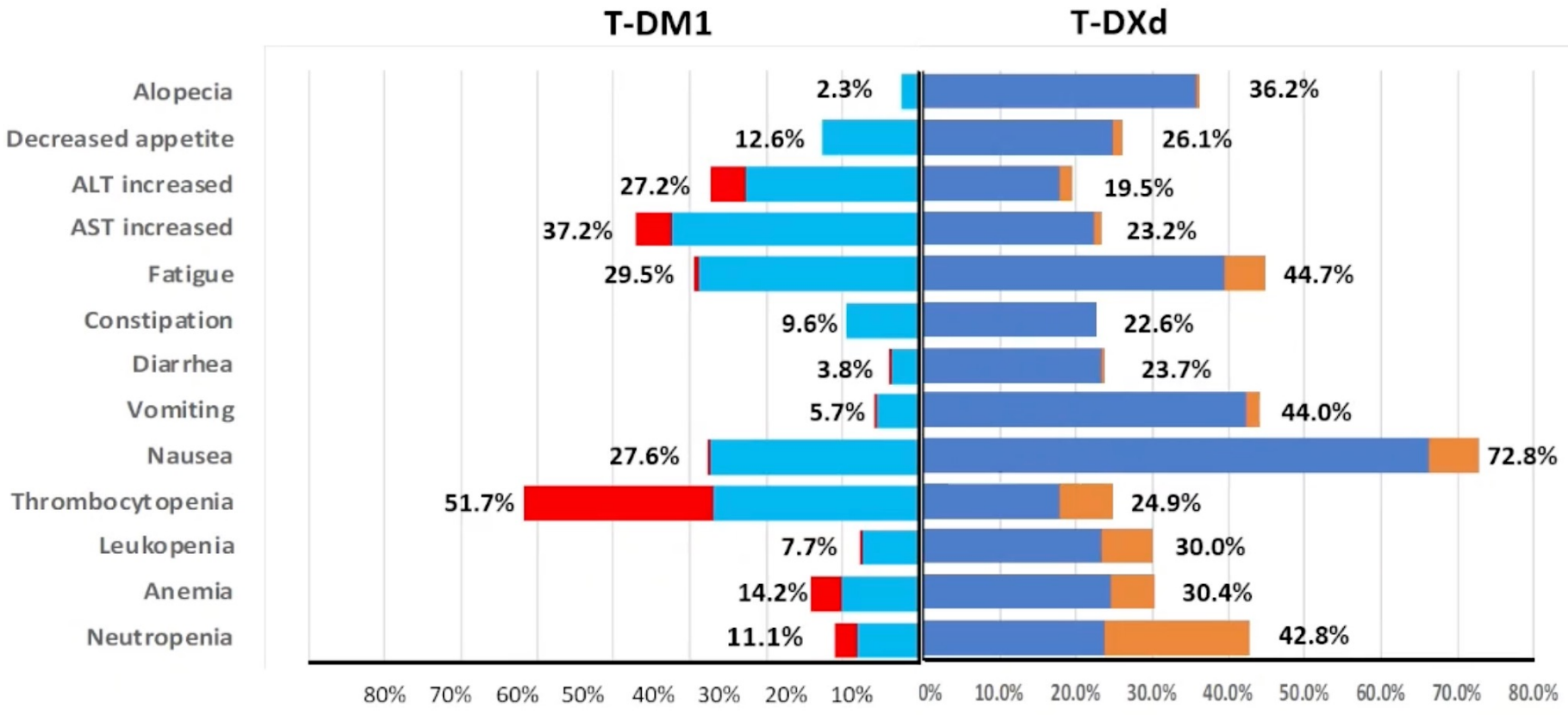
Similar distributions of any grade adjudicated drug-related ILD events were observed with sequential and concurrent radiotherapy in both treatment arms (T-DXd: 10.7% and 9.6.% vs T-DM1: 2.6% and 1.0%, respectively)

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.
[a]All patients who received at least 1 dose of study treatment.

Geyer CE et al. ESMO 2025;Abstract LBA1.

Safety of T-DXd versus T-DM1



Cortes, ESMO 2021
Hurvitz. SABCS 2021

Schmid P. ESMO Breast 2025.

Abstract 291O

BERLIN 2025 ESMO congress

DESTINY Breast11

DESTINY-Breast11: neoadjuvant trastuzumab deruxtecan alone or followed by paclitaxel + trastuzumab + pertuzumab vs ddAC-THP for high-risk HER2+ early breast cancer

Nadia Harbeck

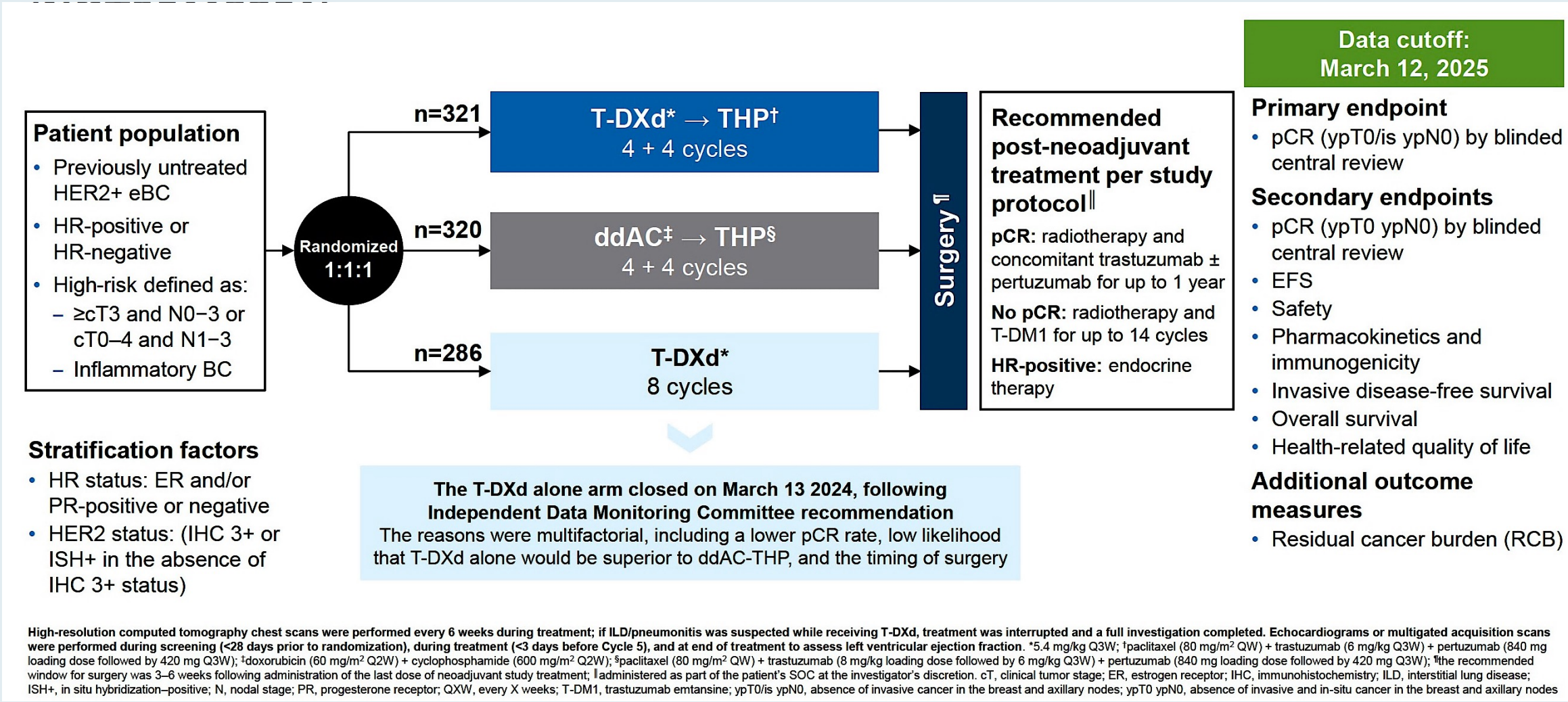
Breast Center, Department of OB&GYN and CCC Munich,
LMU University Hospital, Munich, Germany

Co-authors: Shanu Modi, Lajos Pusztai, Shinji Ohno, Jiong Wu, Sung-Bae Kim, Alessandra Fabi, Xuchen Cao, Rona Joseph, Rubi Li, Bogdan Żurawski, Santiago Escrivá-de-Romaní, Shin-Cheh Chen, Catherine Kelly, Giuseppe Curigliano, William Fraser Symmans, Shoubhik Mondal, Shahana Safdar, Pia Herbolsheimer, Jean-François Boileau
On behalf of the DESTINY-Breast11 investigators

Saturday October 18, 2025
Presentation 291O

RTP RESEARCH TO PRACTICE

Phase III DESTINY-Breast11 Study Design

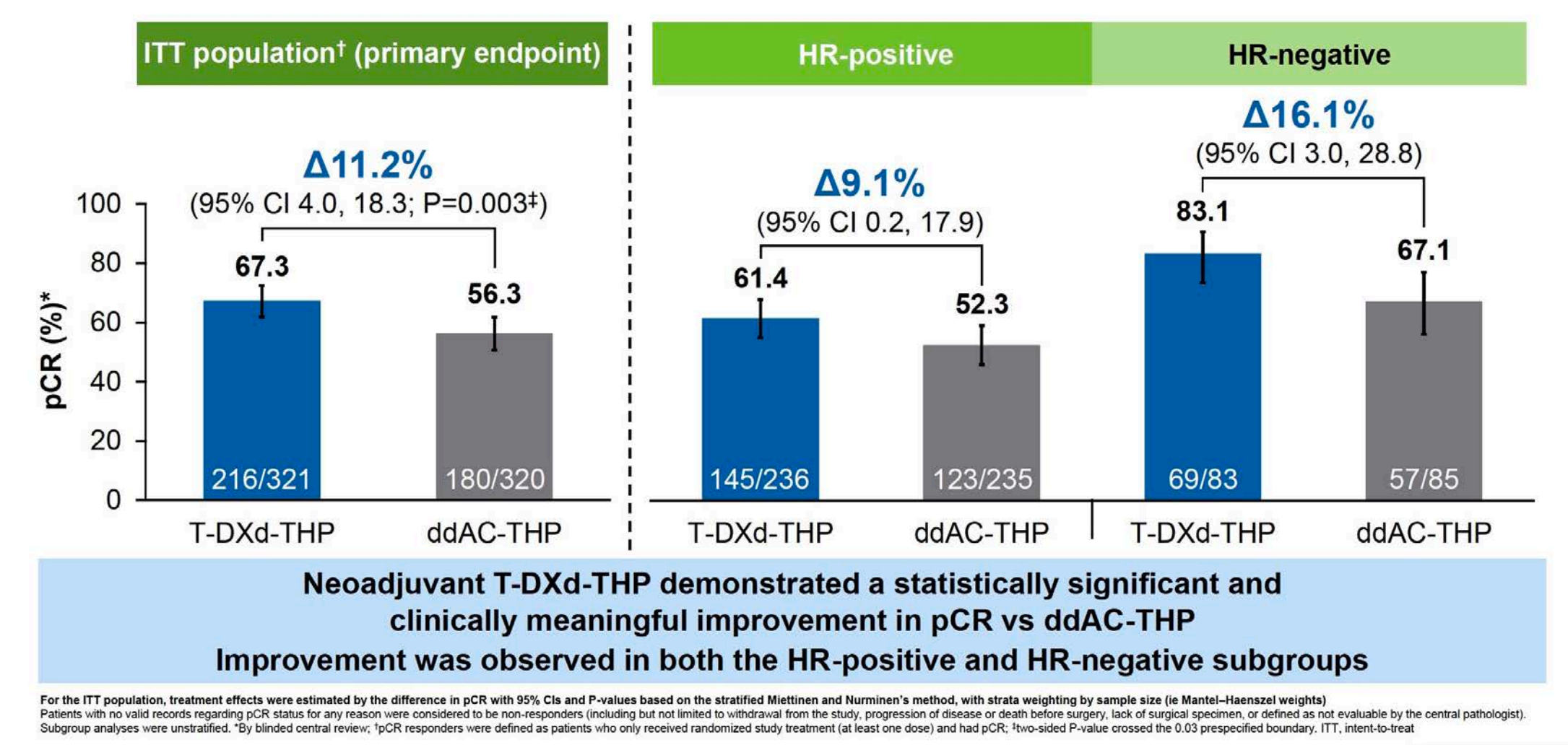


High-resolution computed tomography chest scans were performed every 6 weeks during treatment; if ILD/pneumonitis was suspected while receiving T-DXd, treatment was interrupted and a full investigation completed. Echocardiograms or multigated acquisition scans were performed during screening (<28 days prior to randomization), during treatment (<3 days before Cycle 5), and at end of treatment to assess left ventricular ejection fraction. *5.4 mg/kg Q3W; †paclitaxel (80 mg/m^2 QW) + trastuzumab (6 mg/kg Q3W) + pertuzumab (840 mg loading dose followed by 420 mg Q3W); ‡doxorubicin (60 mg/m^2 Q2W) + cyclophosphamide (600 mg/m^2 Q2W); §paclitaxel (80 mg/m^2 QW) + trastuzumab (8 mg/kg loading dose followed by 6 mg/kg Q3W) + pertuzumab (840 mg loading dose followed by 420 mg Q3W); ¶the recommended window for surgery was 3–6 weeks following administration of the last dose of neoadjuvant study treatment; ‖administered as part of the patient's SOC at the investigator's discretion. cT, clinical tumor stage; ER, estrogen receptor; IHC, immunohistochemistry; ILD, interstitial lung disease; ISH+, in situ hybridization–positive; N, nodal stage; PR, progesterone receptor; QXW, every X weeks; T-DM1, trastuzumab emtansine; ypT0/is ypN0, absence of invasive cancer in the breast and axillary nodes; ypT0 ypN0, absence of invasive and in-situ cancer in the breast and axillary nodes

ddAC = dose-dense doxorubicin and cyclophosphamide; THP = paclitaxel, trastuzumab and pertuzumab

Harbeck N et al. ESMO 2025;Abstract 291O.

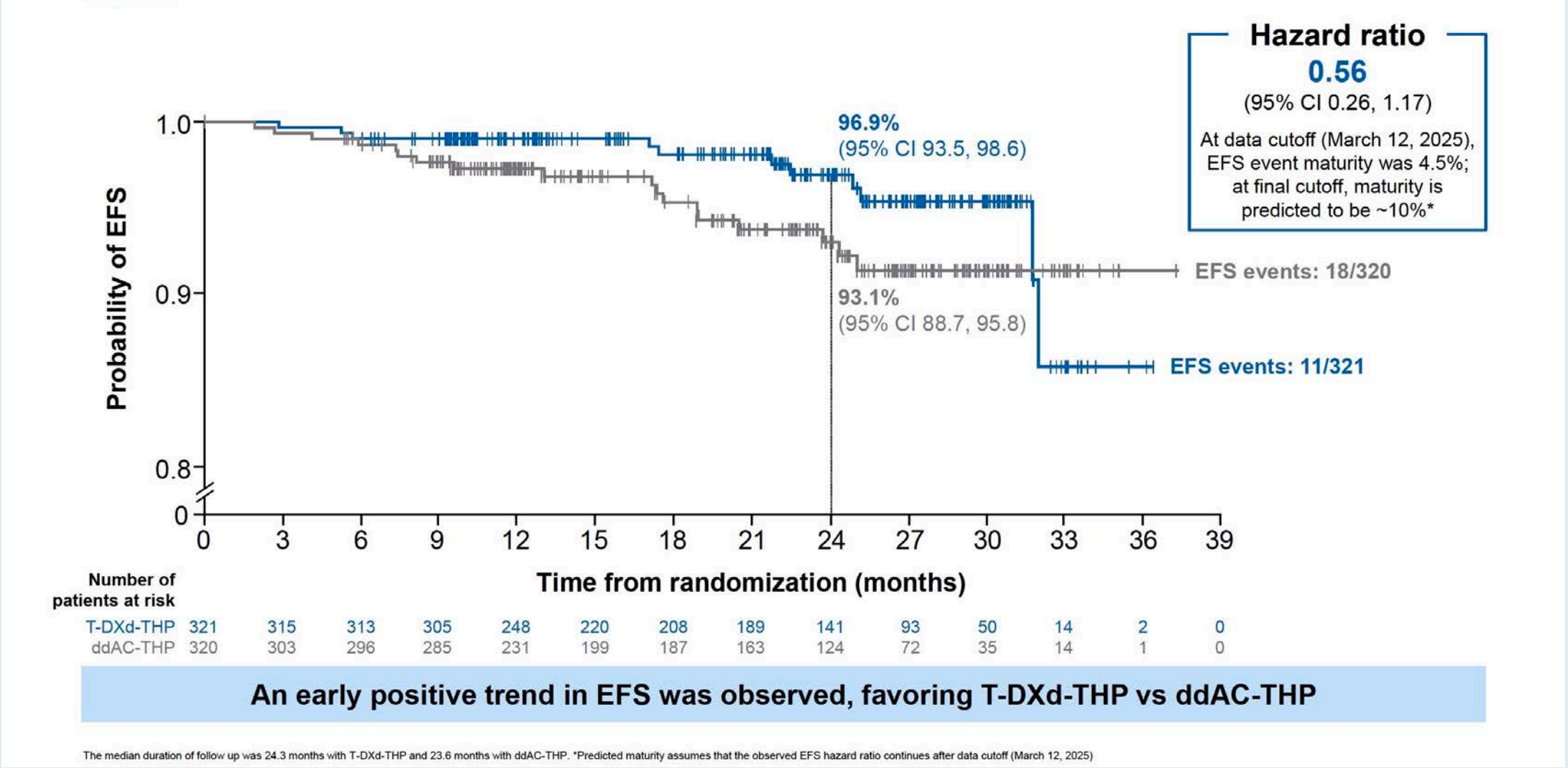
Phase III DESTINY-Breast11: Primary Endpoint pCR



pCR = pathological complete response

Harbeck N et al. ESMO 2025;Abstract 291O.

Phase III DESTINY-Breast11: Event-Free Survival (EFS)



Harbeck N et al. ESMO 2025;Abstract 291O.

Phase III DESTINY-Breast11: Overall Safety Summary

n (%)	T-DXd-THP (n=320)*	ddAC-THP (n=312)*
Any AE	314 (98.1)	308 (98.7)
Grade ≥3	120 (37.5)	174 (55.8)
Any serious AE	34 (10.6)	63 (20.2)
AE leading to any dose reduction	58 (18.1)	60 (19.2)
AE leading to any drug interruption	121 (37.8)	170 (54.5)
AE leading to any treatment discontinuation	45 (14.1)	31 (9.9)
Any AE with outcome of death†	2 (0.6)	2 (0.6)
AE of special interest		
Drug-related adjudicated ILD/pneumonitis	14 (4.4)	16 (5.1)
Grade ≥3	2 (0.6)	6 (1.9)
Grade 5	1 (0.3)	1 (0.3)
Left ventricular dysfunction	4 (1.3)	19 (6.1)
Grade ≥3	1 (0.3)	6 (1.9)
Grade 5	0	0
AE leading to surgical delay‡	11 (3.4)	8 (2.6)

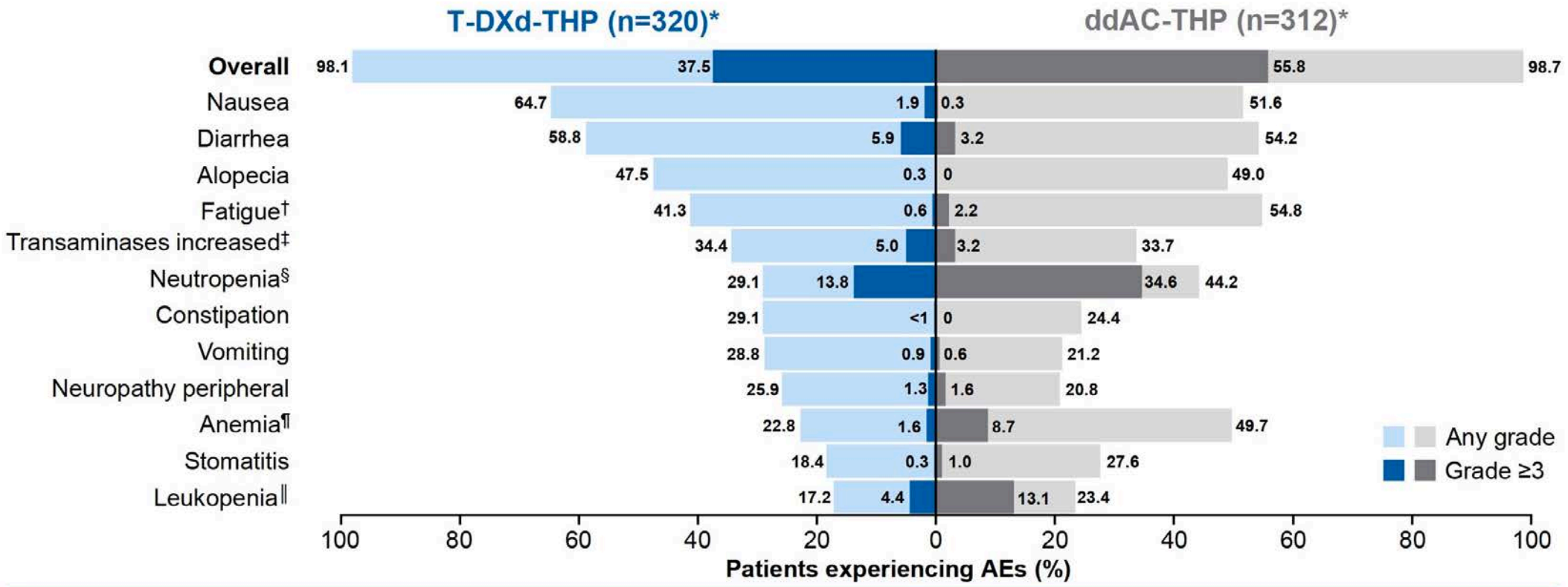
The overall safety profile of T-DXd-THP was favorable vs ddAC-THP, with reduced rates of Grade ≥3 AEs, serious AEs, treatment interruptions, and left ventricular dysfunction

ILD incidence was low and similar in both arms

High-resolution computed tomography chest scans were performed every 6 weeks during treatment; if ILD/pneumonitis was suspected while receiving T-DXd, treatment was interrupted and a full investigation completed. Echocardiograms or multigated acquisition scans were performed during screening (<28 days prior to randomization), during treatment (<3 days before Cycle 5), and at end of treatment to assess left ventricular ejection fraction. Median total treatment duration of whole regimen was 24.1 months (T-DXd-THP), and 21.0 months (ddAC-THP). *Safety analyses included all patients who received at least one dose of any study treatment; †T-DXd-THP arm: death of unknown cause (n=1), drug-related pneumonitis adjudicated by the Independent ILD Adjudication Committee (n=1); ddAC-THP arm: investigator-determined drug-related bacterial encephalitis (n=1), drug-related pneumonitis adjudicated by the ILD Adjudication Committee (n=1); ‡defined as surgery not occurring within 3–6 weeks after the last cycle of neoadjuvant treatment

Harbeck N et al. ASCO 2025;Abstract 291O.

Phase III DESTINY-Breast11: Common Adverse Events



T-DXd-THP had fewer any-grade and Grade ≥3 hematological and fatigue events than ddAC-THP
Aside from nausea, gastrointestinal toxicity was comparable between arms

*Safety analyses included all patients who received at least one dose of any study treatment; †grouped term: fatigue, asthenia, malaise, and lethargy; ‡grouped term: transaminases increased, aspartate transaminase increased, alanine transaminase increased, gamma-glutamyl transferase increased, liver function test abnormal, hypertransaminasemia, hepatic function abnormal, and liver function test increased; §grouped term: neutrophil count decreased and neutropenia; ¶grouped term: hemoglobin decreased, red blood cell count decreased, and anemia and hematocrit decreased; ‖grouped term: white blood cell count decreased and leukopenia. TEAE, treatment-emergent adverse event

Harbeck N et al. ESMO 2025;Abstract 291O.

Efficacy and Safety of Neoadjuvant Trastuzumab Deruxtecan versus Standard of Care Chemotherapy plus Trastuzumab plus Pertuzumab in HER2+ Early Breast Cancer: WSG-ADAPT-HER2-IV

Harbeck N et al.

San Antonio Breast Cancer Symposium 2025;Abstract GS1-02.

Agenda

Introduction	Overview: Molecular basis of antibody-drug conjugate (ADC) toxicities — Sequencing of ADCs and mechanisms of resistance
Case 1	Dr Zelkowitz – 68-year-old woman
■ Data Review: TROP2-targeted ADCs (sacituzumab govitecan, Dato-DXd, sac TMT)	
Case 2	Dr Gupta – 74-year-old woman
Case 3	Dr Agrawal – 83-year-old woman
Case 4	Dr Favaro – 70-year-old woman
■ Data Review: Trastuzumab deruxtecan	
Case 5	Dr Rupard – 78-year-old woman
Case 6	Dr Ku – 72-year-old woman
■ Data Review: Other HER2-targeted agents	

Case Presentation: 78-year-old woman with ER+, HER2-low mBC with disease progression after 1 year of ribociclib/letrozole then receives sacituzumab govitecan

Dr Erik Rupard (Reading, Pennsylvania)

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Agenda

Introduction	Overview: Molecular basis of antibody-drug conjugate (ADC) toxicities — Sequencing of ADCs and mechanisms of resistance
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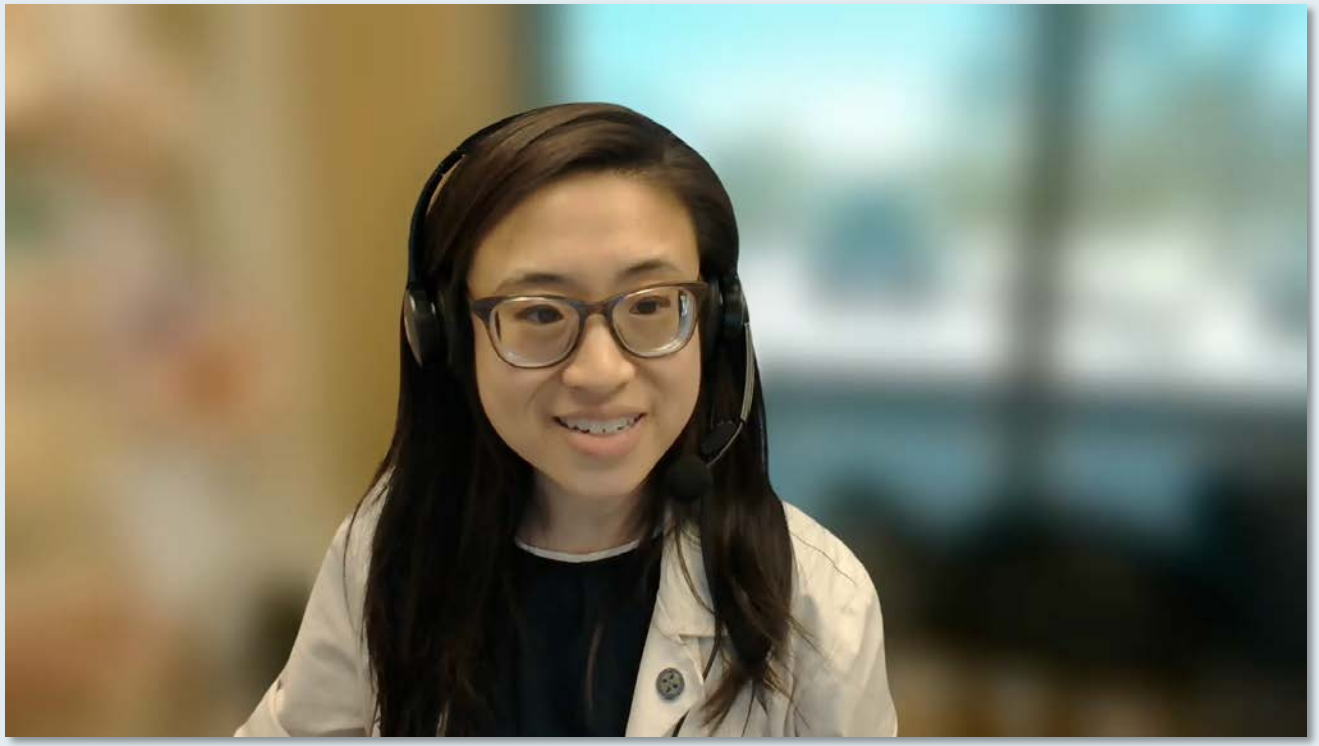
Case 5	Dr Rupard – 78-year-old woman
Case 6	Dr Ku – 72-year-old woman
■ Data Review: Other HER2-targeted agents	

Case Presentation: 72-year-old woman with recurrent ER+, HER2-low (IHC 1+) mBC receives T-DXd and has concerning pulmonary symptoms but without diagnostic imaging findings



Dr Kimberly Ku (Bloomington, Illinois)

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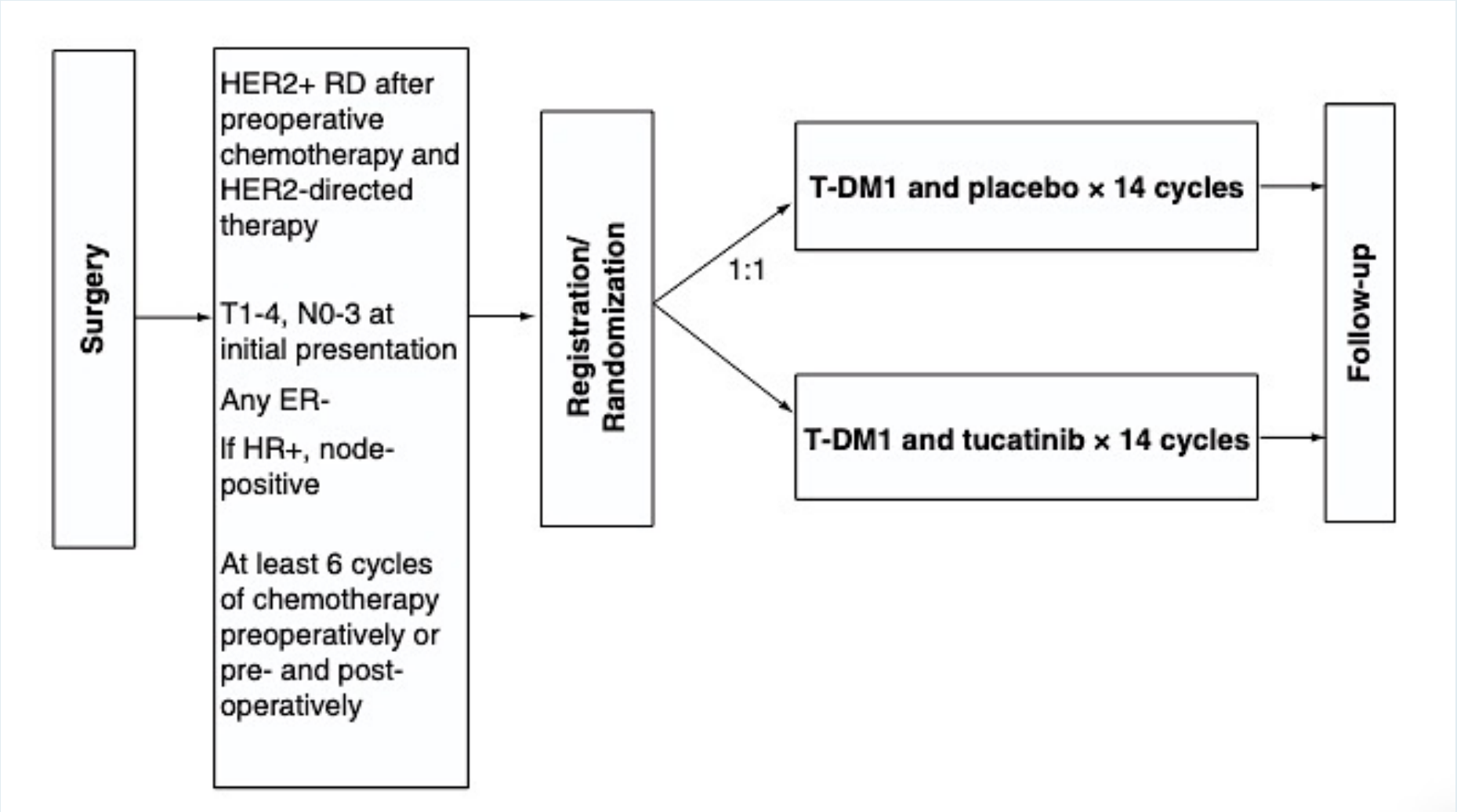
CompassHER2 RD (A011801) Phase III Trial Design



RD = residual disease

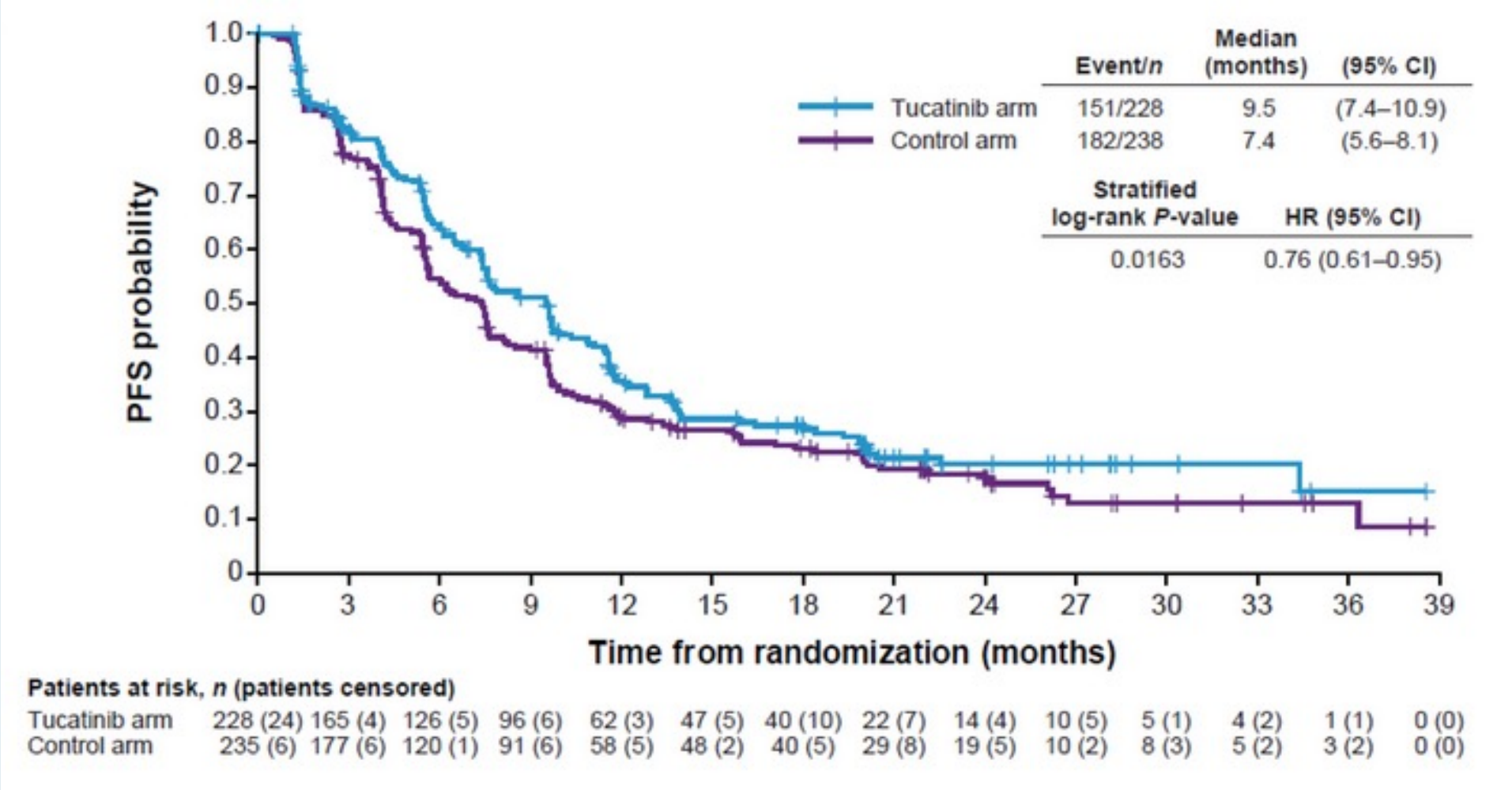
O'Sullivan CC et al. *Future Oncol* 2021;17(34):4665-76.

Tucatinib and Trastuzumab Emtansine for Patients with Previously Treated HER2-Positive Locally Advanced and Metastatic Breast Cancer: Primary Analysis of the Randomized Phase III Trial HER2CLIMB-02

Hurvitz S et al.

Ann Oncology 2025. November 17 (Article in Press)

HER2CLIMB-02 Primary Analysis: PFS with Tucatinib and T-DM1 for Previously Treated HER2-Positive Locally Advanced and Metastatic Breast Cancer



Hurvitz SA et al. *Ann Oncol* 2025;November 17 (Article in press).

HER2CLIMB-02 Safety Summary

Events, *n* (%)	Tucatinib arm (*n* = 231)	Control arm (*n* = 233)
Any TEAE	230 (99.6)	233 (100)
Grade ≥3 TEAE	159 (68.8)	96 (41.2)
Any TESAE	70 (30.3)	52 (22.3)
TEAE leading to death	3 (1.3)	2 (0.9)
Patients who discontinued any treatment due to TEAE	51 (22.1)	27 (11.6)
Discontinued tucatinib or placebo due to TEAE	40 (17.3)	16 (6.9)
Discontinued T-DM1 due to TEAE	47 (20.3)	26 (11.2)

TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event; T-DM1, trastuzumab emtansine.

Hurvitz SA et al. *Ann Oncol* 2025;November 17 (Article in press).

Her2climb-05: A Randomized, Double-Blind, Phase 3 Study of Tucatinib versus Placebo in Combination with Trastuzumab and Pertuzumab as Maintenance Therapy for Her2+ Metastatic Breast Cancer

Hamilton E et al.

San Antonio Breast Cancer Symposium 2025;Abstract GS1-01.

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Exciting CME Events You Do Not Want to Miss

A Friday Satellite Symposium Series Preceding the 67th ASH Annual Meeting

Friday, December 5, 2025

Acute Myeloid Leukemia
7:30 AM – 9:30 AM ET

Myelofibrosis and Systemic Mastocytosis
3:15 PM – 5:15 PM ET

Chronic Lymphocytic Leukemia
11:30 AM – 1:30 PM ET

Follicular Lymphoma and Diffuse Large B-Cell Lymphoma
7:00 PM – 9:00 PM ET

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Thank you for joining us!

Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open for 5 minutes after the meeting ends.

Information on how to obtain CME, ABIM MOC and ABS credit is provided in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

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