Selection and Sequencing of Therapy for Metastatic Triple-Negative Breast Cancer

A CME/MOC-Accredited Live Webinar

Thursday, August 28, 2025
5:00 PM – 6:00 PM ET

Faculty

Ana C Garrido-Castro, MD
Professor Peter Schmid, FRCP, MD, PhD

Moderator

Neil Love, MD

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Faculty

Ana C Garrido-Castro, MD
Assistant Professor of Medicine
Harvard Medical School
Director, Triple-Negative Breast Cancer Research
Susan F Smith Center for Women's Cancers
Department of Medical Oncology
Dana-Farber Cancer Institute
Boston, Massachusetts

Professor Peter Schmid, FRCP, MD, PhD
Lead, Centre of Experimental Cancer Medicine
Barts Cancer Institute
London, United Kingdom

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

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Dr Love — Disclosures

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Prof Schmid — Disclosures

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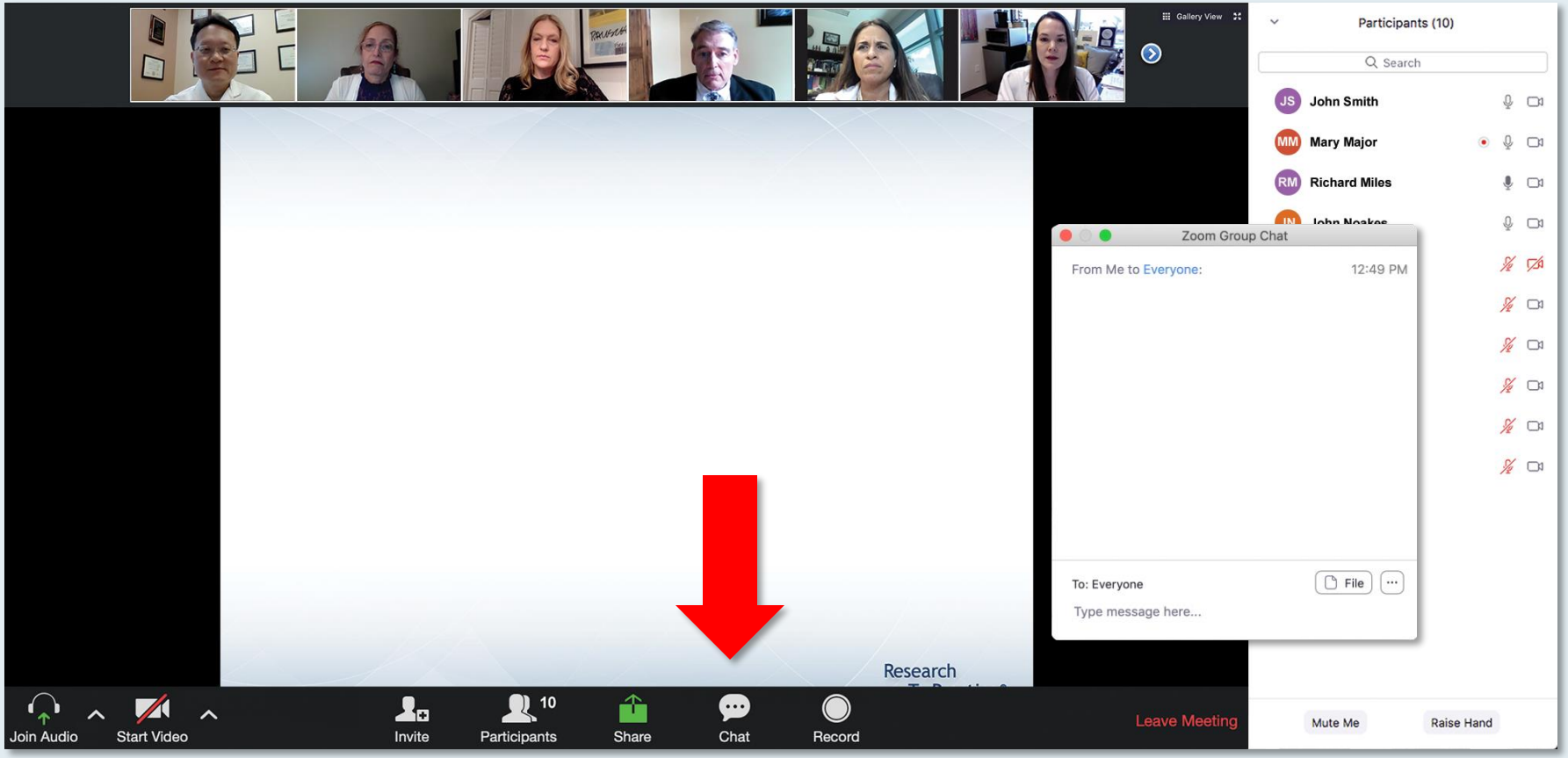

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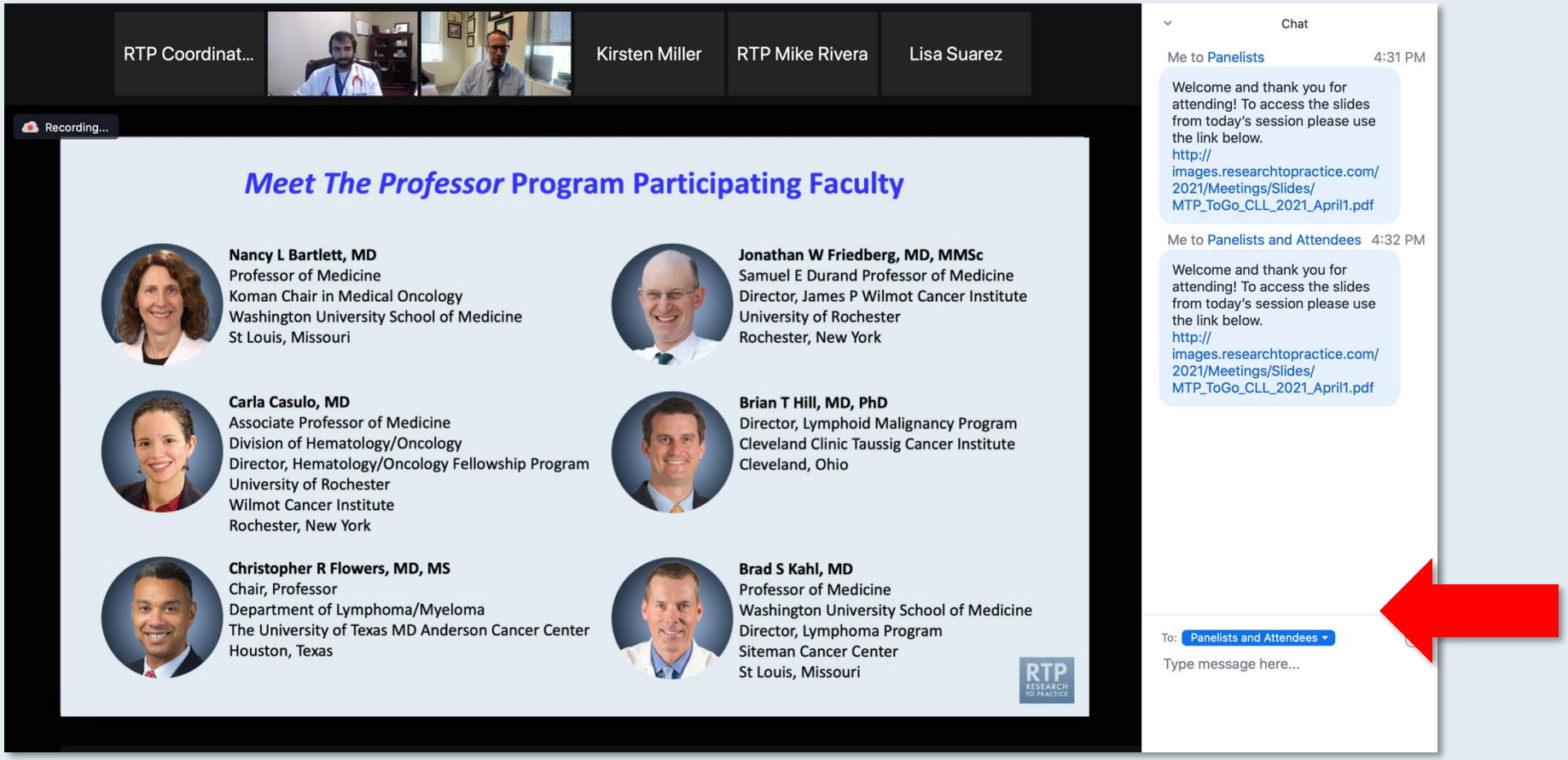

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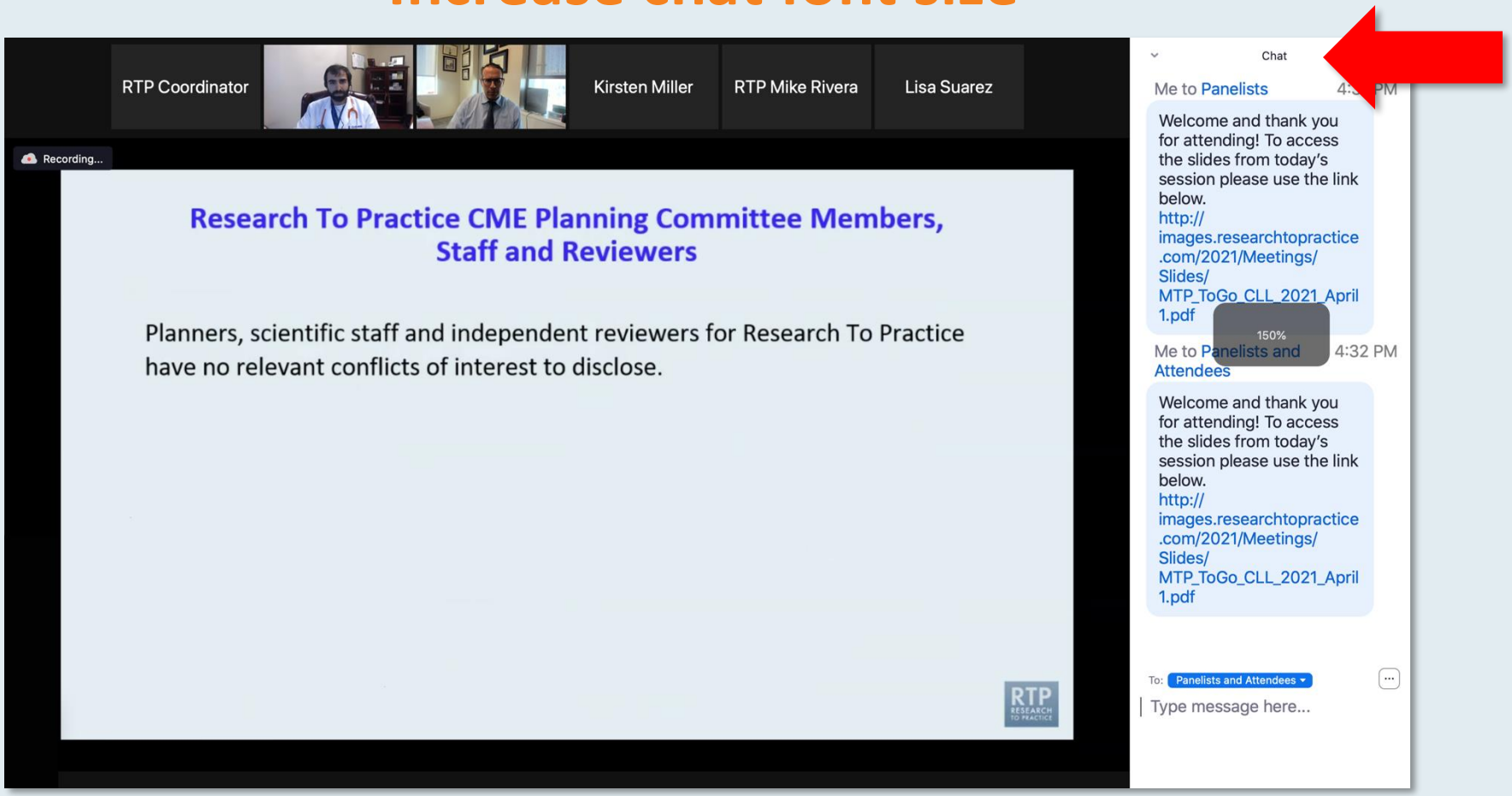

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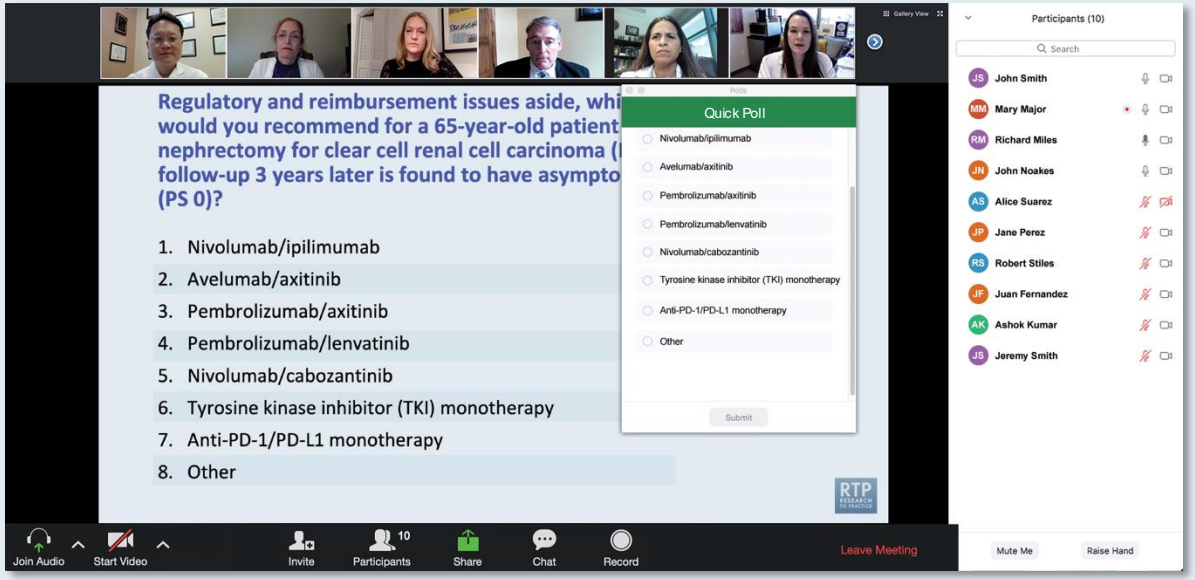
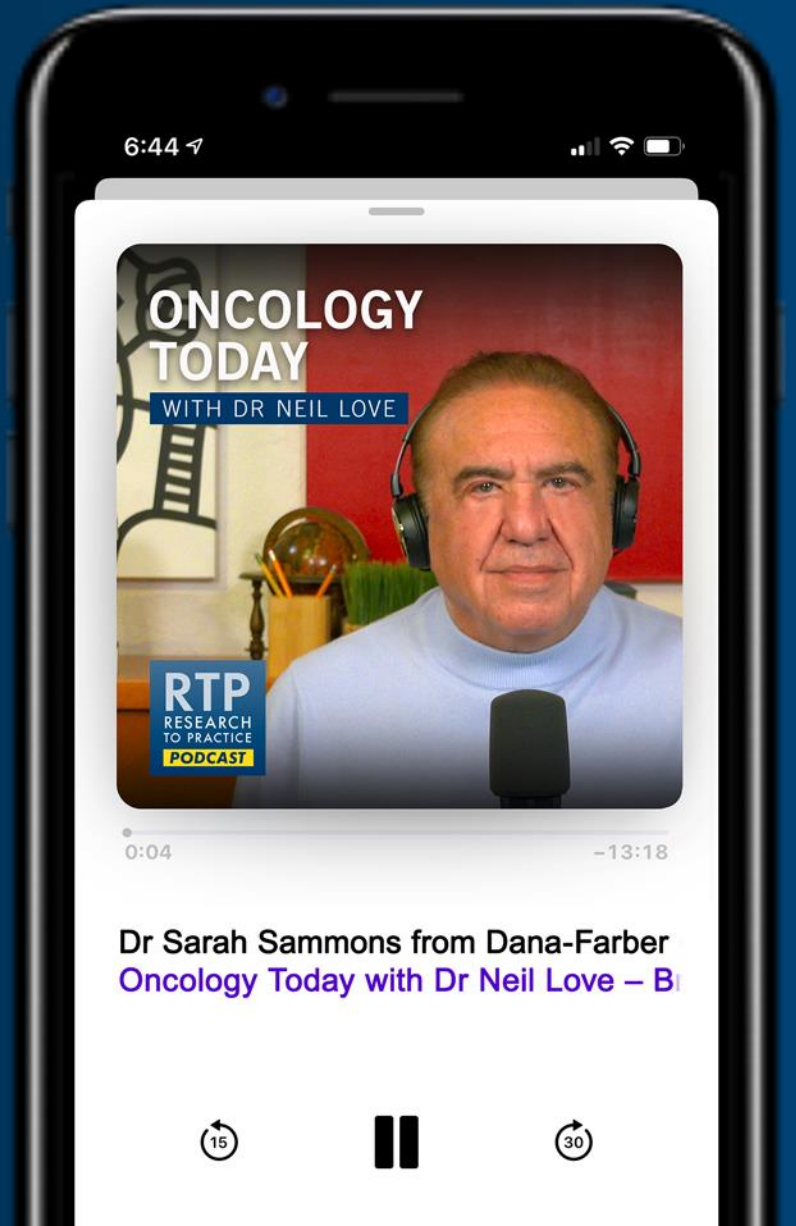


Brain Metastases with HER2-Positive Breast Cancer — An Interview with Dr Sarah Sammons on Optimal Management Approaches

DR SARAH SAMMONS
DANA-FARBER CANCER INSTITUTE



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Consensus or Controversy? Clinical Investigators Provide Perspectives on the Current and Future Care of Patients with Relapsed/Refractory Multiple Myeloma

Part 1 of a 2-Part CME/MOC-, NCPD- and ACPE-Accredited Satellite Symposium Series During the Society of Hematologic Oncology 2025 Annual Meeting

Thursday, September 4, 2025
6:42 PM – 7:42 PM CT

Faculty

Meletios-Athanasios (Thanos) C Dimopoulos, MD
Hans Lee, MD
Noopur Raje, MD

Moderator

Joseph Mikhael, MD, MEd

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Consensus or Controversy? Clinical Investigators Provide Perspectives on the Current and Future Care of Patients with Follicular Lymphoma

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Friday, September 5, 2025

11:47 AM – 12:47 PM CT

Faculty

Jennifer Crombie, MD

Laurie H Sehn, MD, MPH

Moderator

Jeremy S Abramson, MD, MMSc

RTP RESEARCH TO PRACTICE

The Implications of Recent Datasets for the Current and Future Management of Non-Hodgkin Lymphoma

A CME/MOC-Accredited Live Webinar

Wednesday, September 17, 2025
5:00 PM – 6:00 PM ET

Faculty

Carla Casulo, MD
Brad S Kahl, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Data + Perspectives: Clinical Investigators Explore the Application of Recent Datasets in Current Oncology Care

A Multitumor Symposium in Partnership with Florida Cancer Specialists & Research Institute

Saturday, October 11, 2025
7:15 AM – 12:30 PM ET

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

Faculty

Emmanuel S Antonarakis, MD
Matthew P Goetz, MD
Christopher Lieu, MD
Matthew Lunning, DO
Heather McArthur, MD, MPH
Sonali M Smith, MD
John Strickler, MD
Additional faculty to be announced.

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Patients

Wednesday, October 22, 2025
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Clinicians

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Loretta J Nastoupil, MD

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RTP RESEARCH TO PRACTICE

Addressing Current Knowledge and Practice Gaps in the Community — Optimizing the Use of Oral Selective Estrogen Receptor Degraders for Metastatic Breast Cancer, Part 2

A CME/MOC-Accredited Live Webinar

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5:00 PM – 6:00 PM ET

Faculty

Rinath M Jeselsohn, MD

Joyce O'Shaughnessy, MD

Moderator

Neil Love, MD

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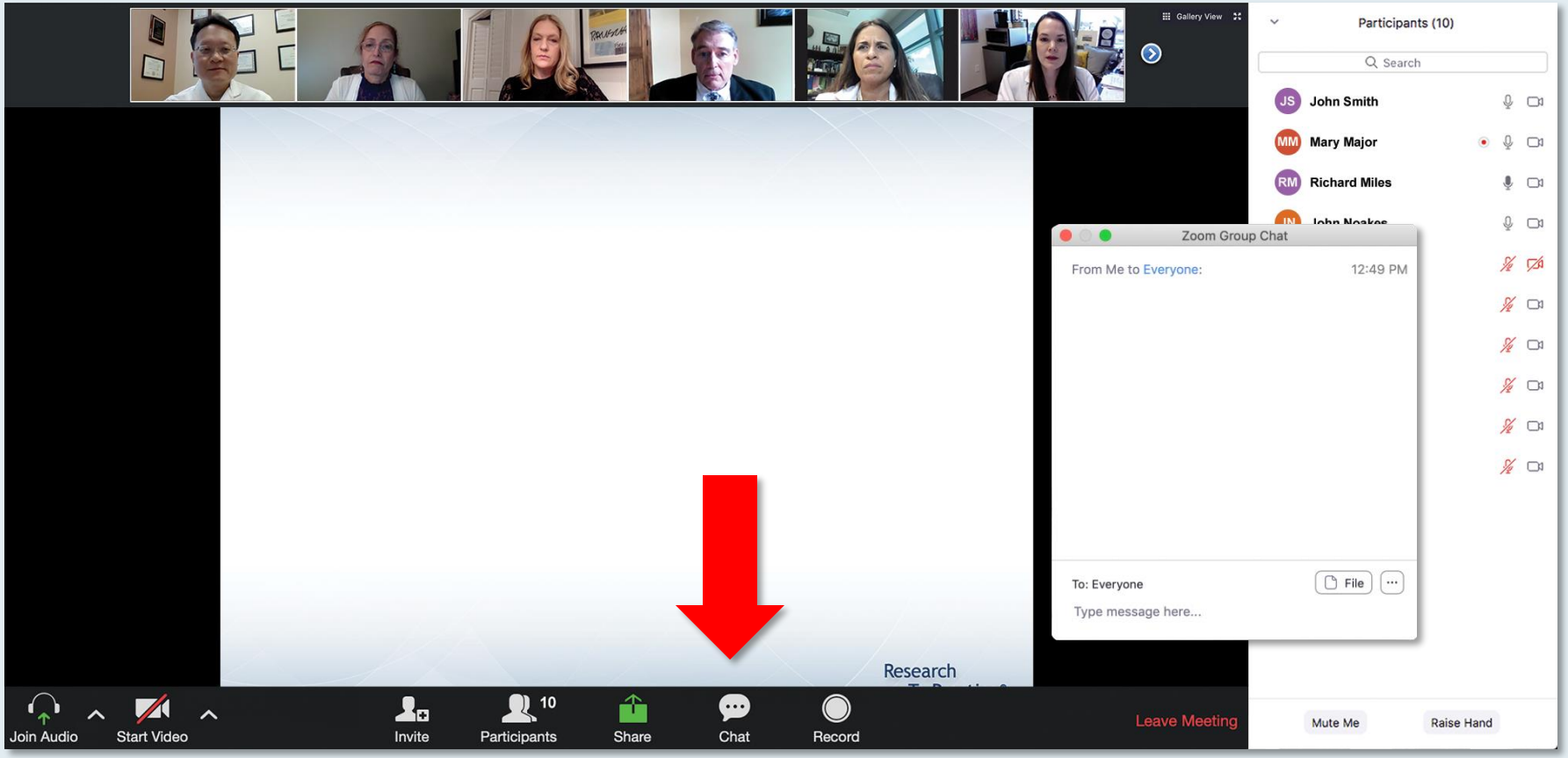

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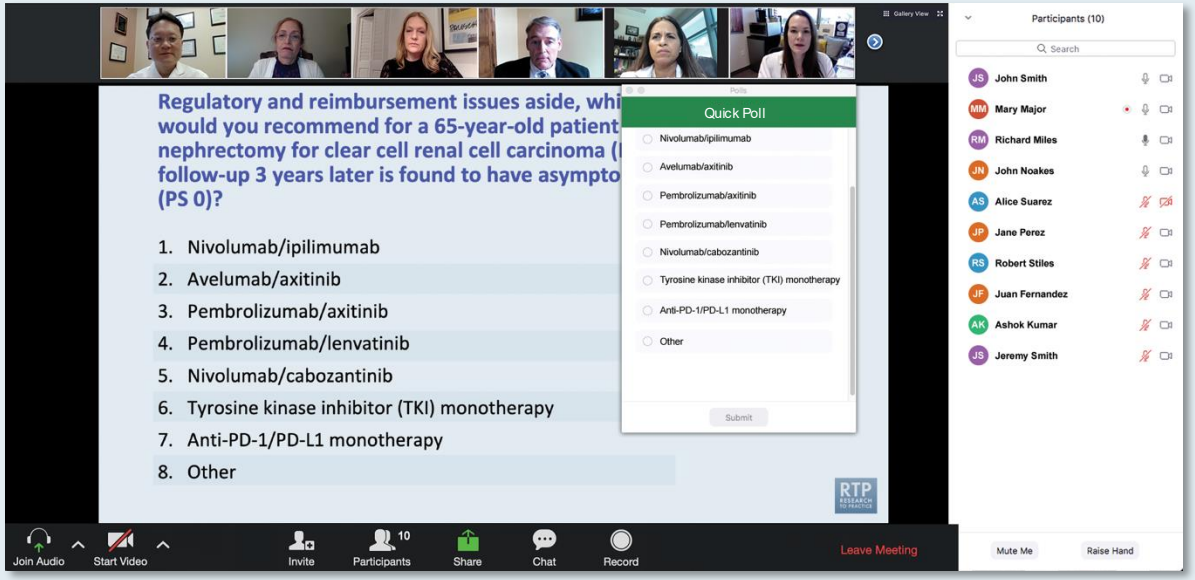

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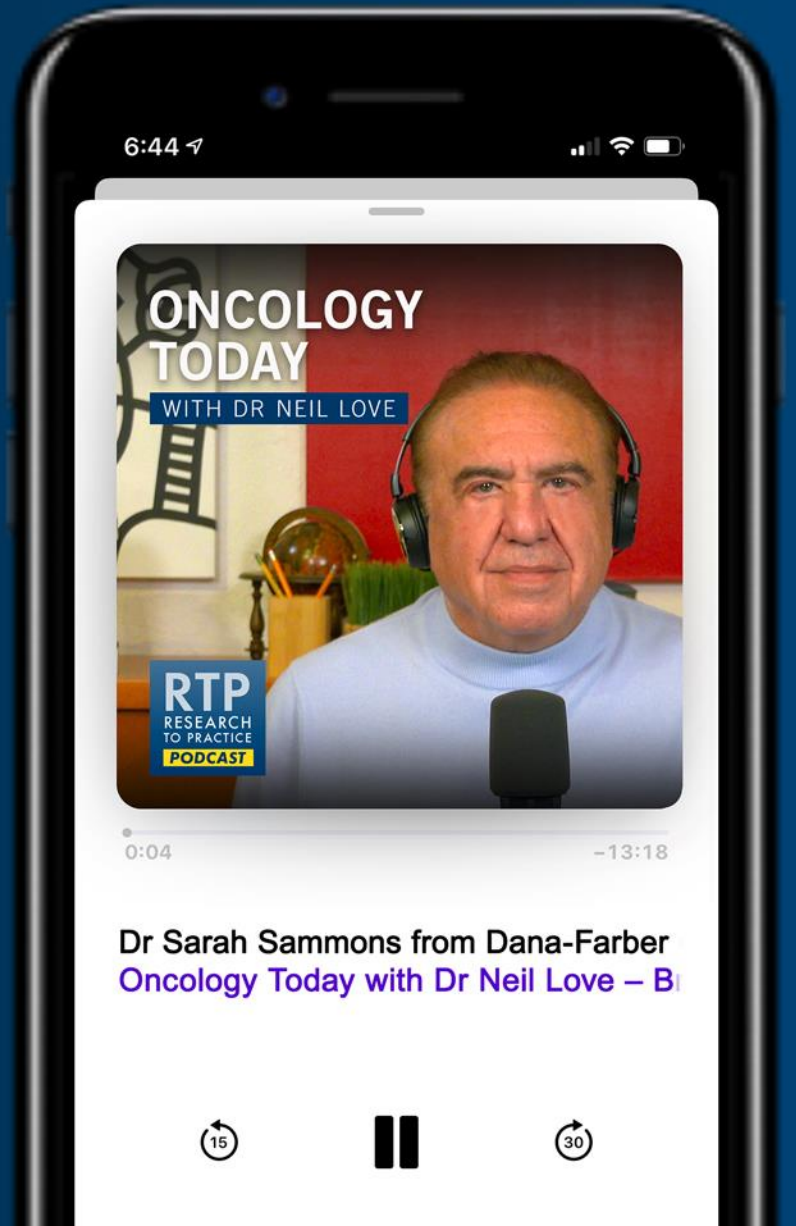

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	Year	Month
Total (hours)	280	24
Recordings	93	7
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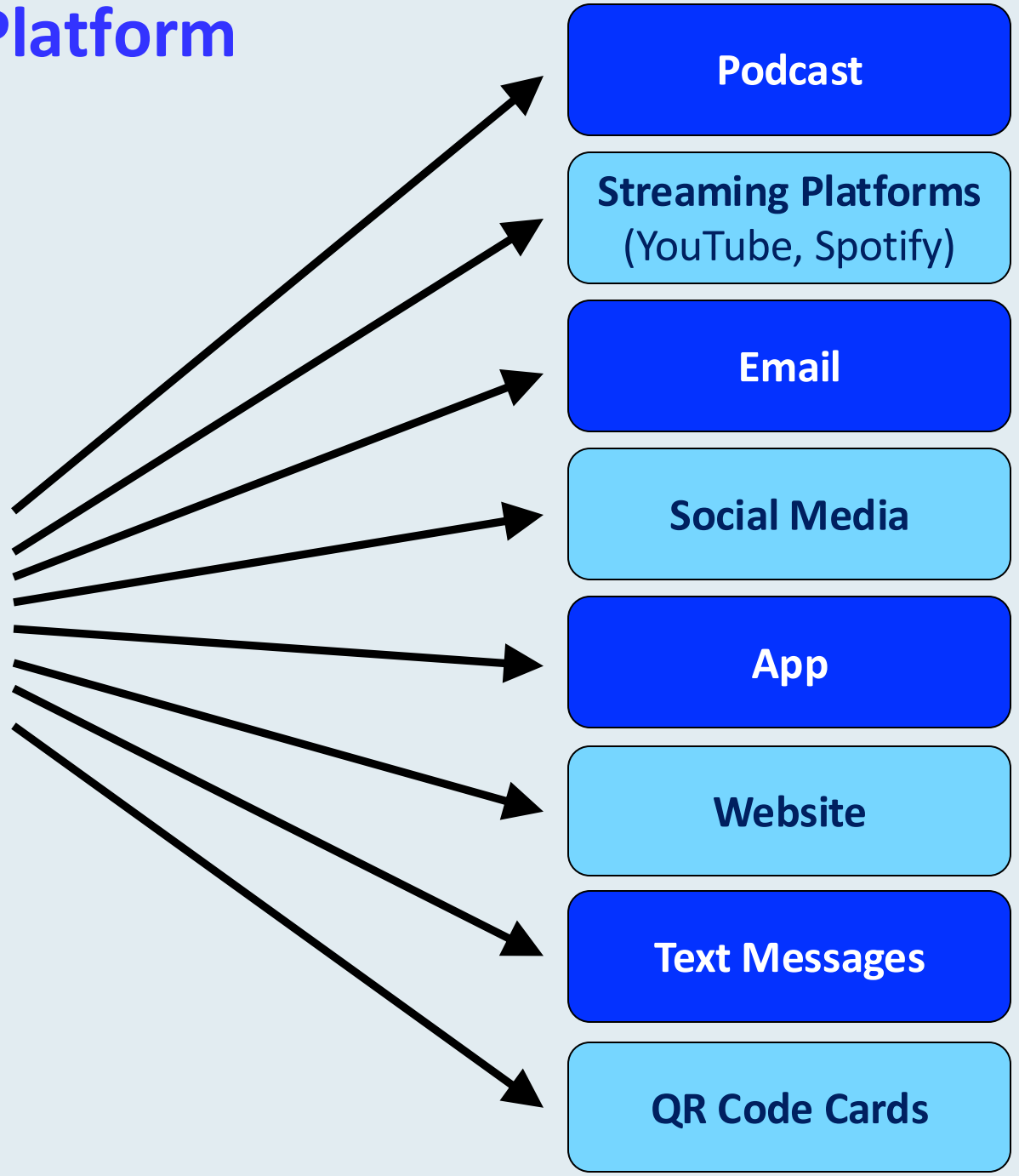

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Contributing General Medical Oncologists

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Medical Group
Fountain Valley, California

Richard Zelkowitz, MD
Hartford HealthCare Cancer Institute
Bridgeport, Connecticut

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Agenda

Introduction: Legendary Figures in Breast Cancer Research

Case 1: Dr Favaro – 82-year-old woman, a current smoker with PMH of myocardial infarction and stroke, develops recurrent TNBC

Case 2: Dr Rudolph – 67-year-old woman with mTNBC (PD-L1 20%) receives chemotherapy/ pembrolizumab followed by sacituzumab govitecan

Case 3: Dr Zelkowitz – 68-year-old woman with localized TNBC develops myocarditis during neoadjuvant chemotherapy/pembrolizumab

Case 4: Dr Gupta – 64-year-old woman with recurrent ER-negative, HER2-low, PI3K-mutant mTNBC

Case 5: Dr Lee – 63-year-old woman with recurrent TNBC confined to contralateral neck nodes

Case 6: Dr Rodriguez – 43-year-old woman with mTNBC s/p multiple lines of chemotherapy receives sacituzumab govitecan

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Case 8: Dr Rudolph – 68-year-old woman with mTNBC experiences severe diarrhea with sacituzumab govitecan

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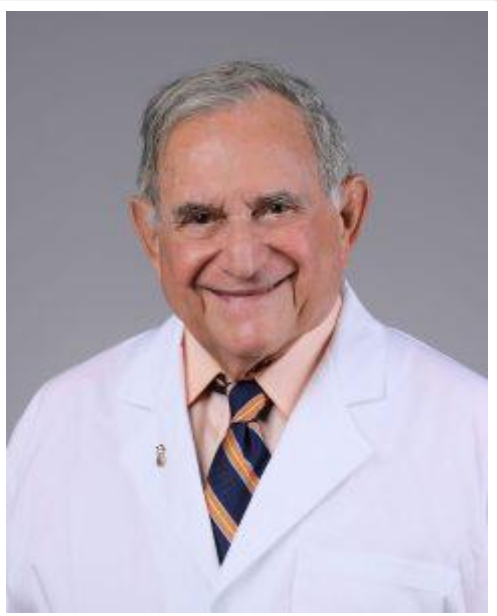
Dan Marino

Bernie Kosar



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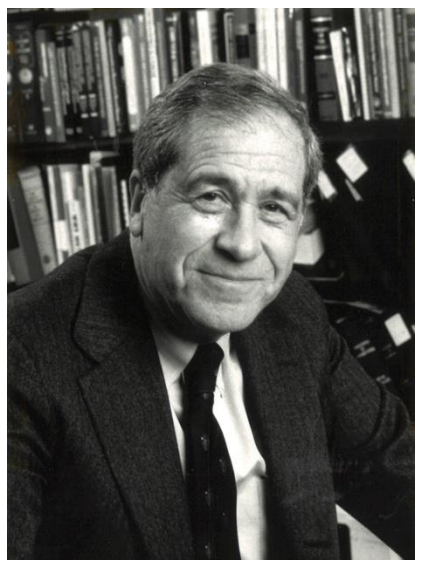
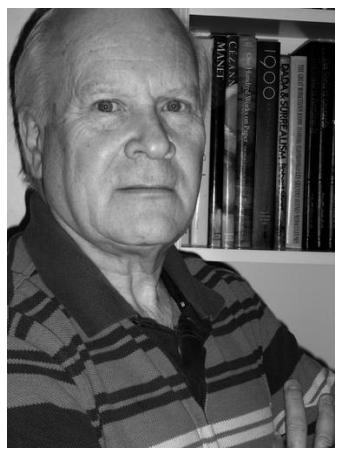
Richard Peto

Larry Norton



Bernard Fisher

Gianni Bonadonna



Michael Baum

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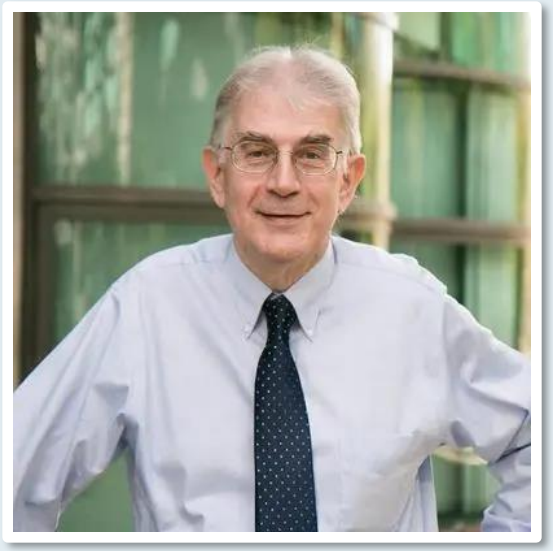

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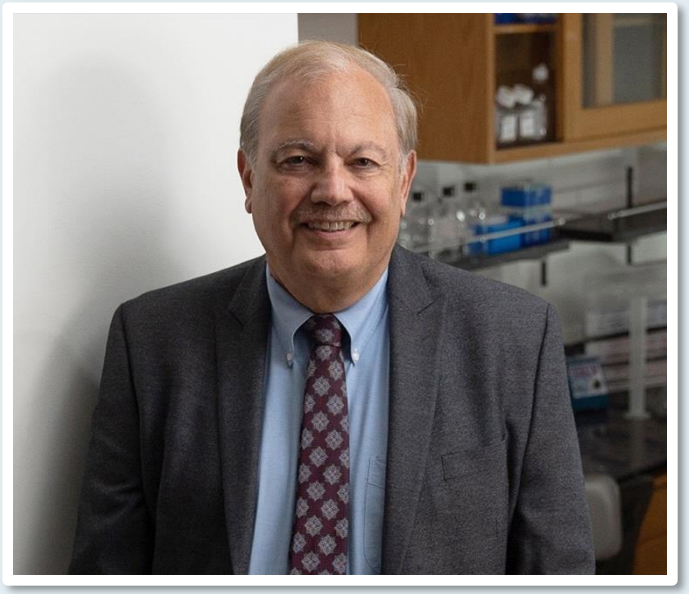
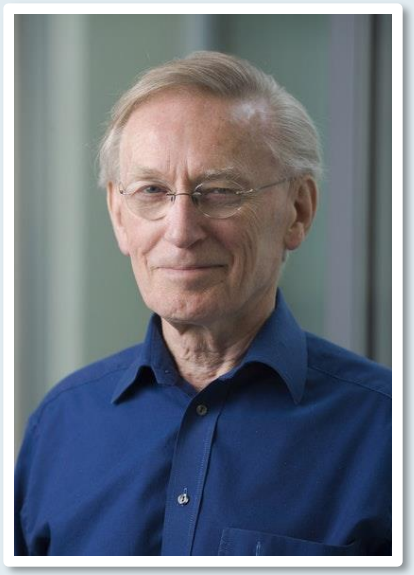


Dennis Slamon



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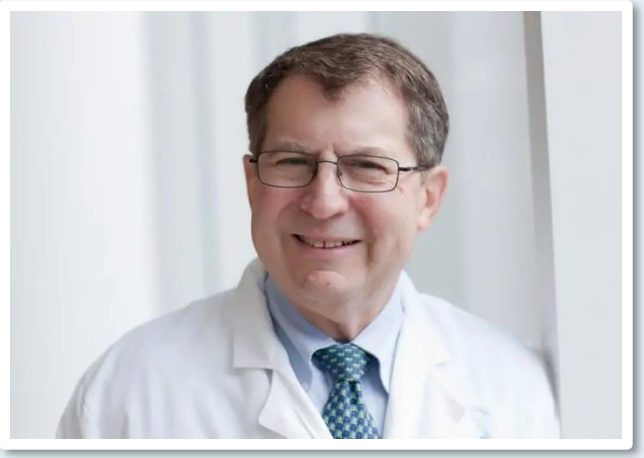
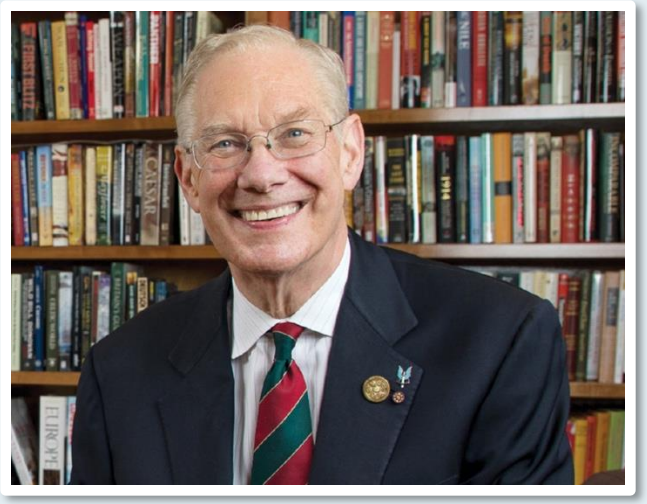


Hyman Muss



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Case 8: Dr Rudolph – 68-year-old woman with mTNBC experiences severe diarrhea with sacituzumab govitecan

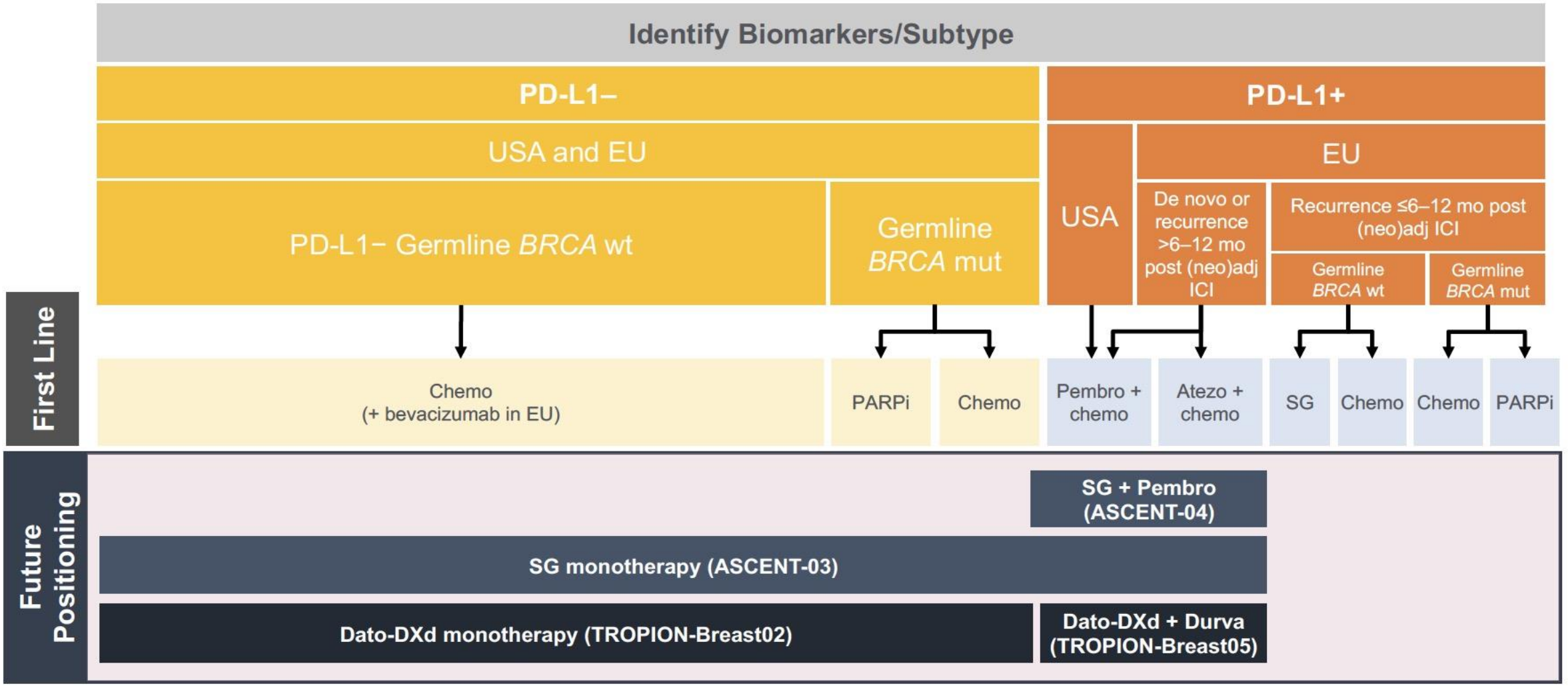
RTP RESEARCH TO PRACTICE

Case Presentation: 82-year-old woman, a current smoker with PMH of myocardial infarction and stroke, develops recurrent TNBC

Dr Justin Favaro (Charlotte, North Carolina)

RTP RESEARCH TO PRACTICE

NCCN and ESMO Guidelines for 1L



1L, first line; atezo, atezolizumab; chemo, chemotherapy; Dato-DXd, datopotamab deruxtecan; durva, durvalumab; ESMO, European Society for Medical Oncology; EU, European Union; ICI, immune checkpoint inhibitor; mo, months; mTNBC, metastatic triple-negative breast cancer; mut, mutation; NCCN, National Comprehensive Cancer Network; (neo)adj, neoadjuvant or adjuvant; PARPi, poly (ADP-ribose) polymerase inhibitor; PD-L1−/+, programmed cell death ligand 1-negative/positive; pembro, pembrolizumab; SG, sacituzumab govitecan; wt, wild-type.

Courtesy of Sara M Tolaney, MD, MPH

ORIGINAL ARTICLE

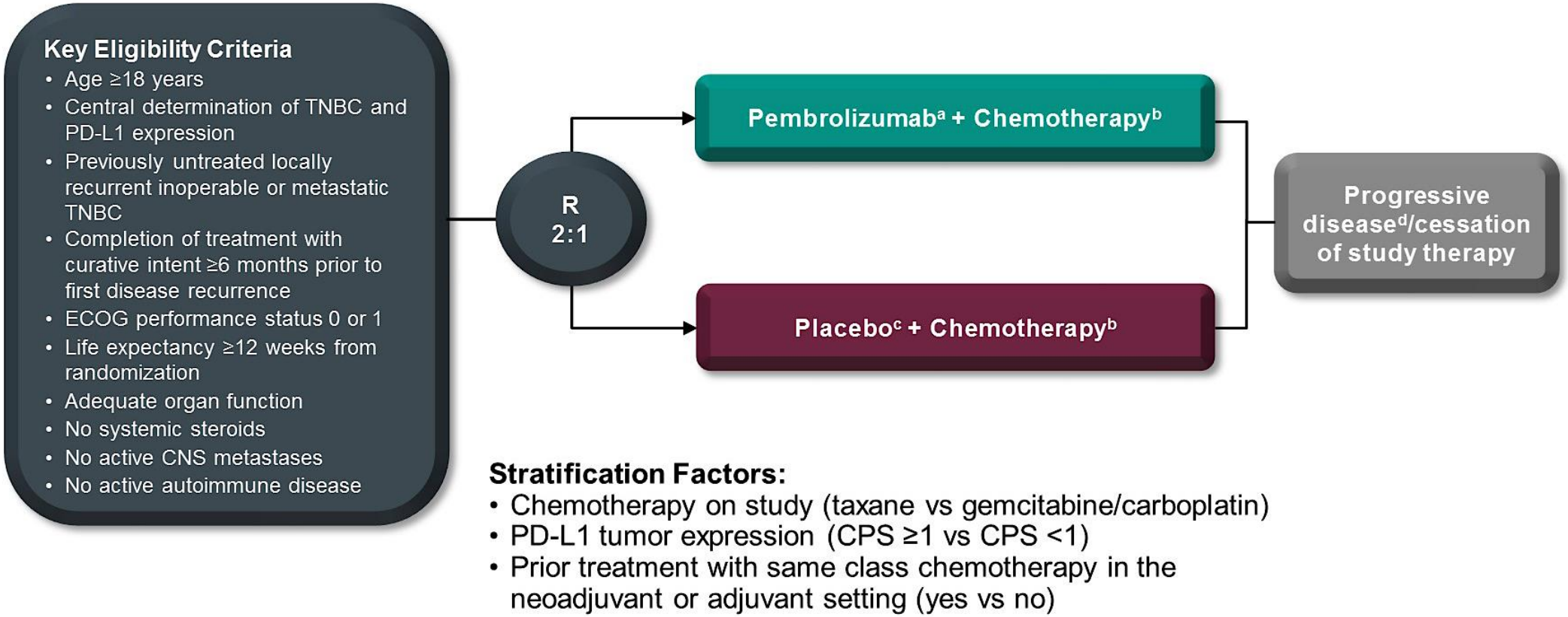
Pembrolizumab plus Chemotherapy in Advanced Triple-Negative Breast Cancer

J. Cortes, H.S. Rugo, D.W. Cescon, S.-A. Im, M.M. Yusof, C. Gallardo, O. Lipatov, C.H. Barrios, J. Perez-Garcia, H. Iwata, N. Masuda, M. Torregroza Otero, E. Gokmen, S. Loi, Z. Guo, X. Zhou, V. Karantza, W. Pan, and P. Schmid, for the KEYNOTE-355 Investigators*

N Engl J Med 2022;387(3):217-26.

RTP RESEARCH TO PRACTICE

Phase III KEYNOTE-355 Study Design



[a]Pembrolizumab 200 mg intravenous (IV) every 3 weeks (Q3W)
[b]Chemotherapy dosing regimens are as follows:
Nab-paclitaxel 100 mg/m^2 IV on days 1, 8, and 15 every 28 days
Paclitaxel 90 mg/m^2 IV on days 1, 8, and 15 every 28 days
Gemcitabine 1000 mg/m^2/carboplatin AUC 2 on days 1 and 8 every 21 days

[c]Normal saline
[d]Treatment may be continued until confirmation of progressive disease
CNS=central nervous system; ECOG=Eastern Cooperative Oncology Group; PD-L1=programmed death ligand 1; R=randomized; TNBC=triple-negative breast cancer

Cortes J et al. *N Engl J Med* 2022;387(3):217-26.

TROP2-directed ADCs

	Sacituzumab govitecan (IMMU-132)	Datopotamab deruxtecan (DS-1062a)	Sacituzumab tirumotecan (MK-2870)
Antibody	hRS7 Humanized IgG1 mAb	MAAP-9001a Humanized IgG1 mAb	hRS7 Humanized IgG1 mAb
Payload	SN38 (DNA Topoisomerase I inhibitor)	DXd (DNA Topoisomerase I inhibitor)	KL610023 (DNA Topoisomerase I inhibitor)
Linker cleavage	Enzymatic and pH-dependent	Enzymatic	Enzymatic and pH-dependent
Bystander effect	Yes	Yes	Yes
DAR	7.6	4	7.4
Half-life	11-14h	~5 days	57h
Dosing	D1, D8 of Q3W schedule	Q3W	Q2W

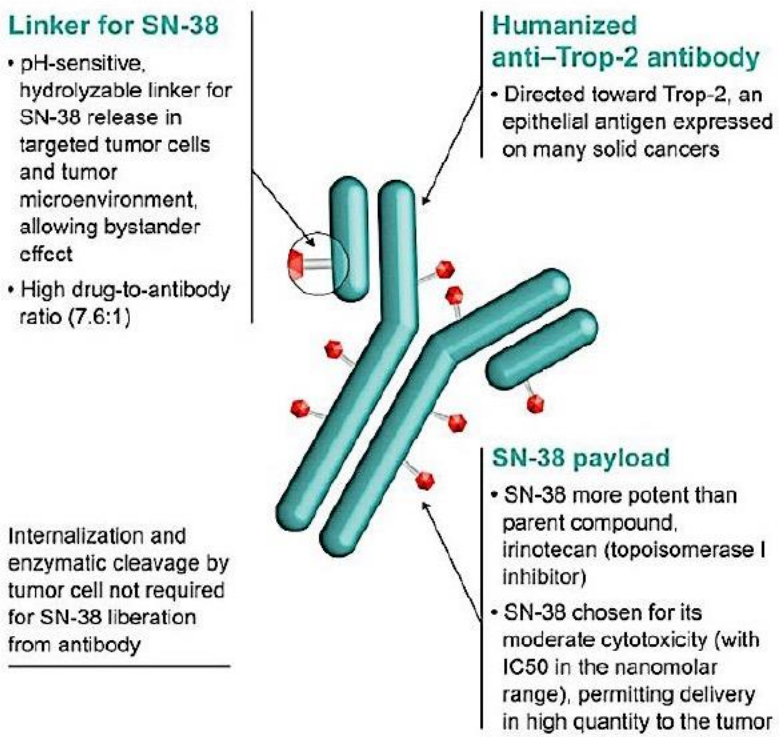
Courtesy of Sara M Tolaney, MD, MPH

Sands J et al. ASCO 2018; Okajima D et al. ASCO 2018; Bardia A et al. ESMO Breast Cancer 2021; Cheng Y et al. Front Oncol 2022.

ADCs in metastatic triple-negative breast cancer

- Targeting Trop2 in mTNBC

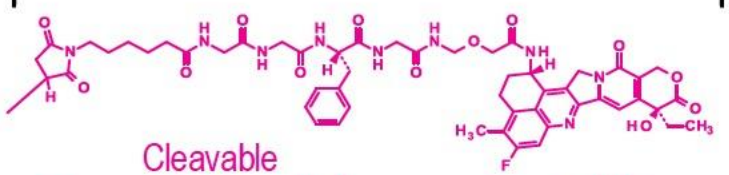
Sacituzumab govitecan



Datopotamab deruxtecan

- Payload mechanism of action: Topo-I inhibitor*
- High potency payload*
- Optimised drug to antibody ratio ≈4*†
- Payload with short systemic half-life*†
- Stable linker-payload*
- Tumour-selective cleavable linker*
- Bystander antitumour effect*

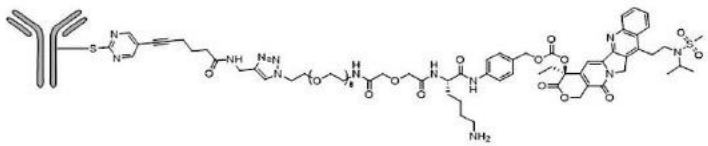
Deruxtecan



Cleavable tetrapeptide-based linker

Topo-I inhibitor payload (DXd)

Sacituzumab tirumotecan (SKB264/MK-2870)



- anti-TROP2 ADC
- Sulfonyl pyrimidine-CL2A-carbonate linker
- **Payload**: belotecan-derivative topoisomerase I inhibitor
- **DAR**: 7.4

Courtesy of Rebecca A Dent, MD, MSc

Several Phase 3 clinical trials are evaluating the use of ADCs ± immunotherapy in 1L mTNBC

Target	Trial	Intervention	Control arm
TROP2	**PD-L1–negative or PD-L1/PD-1 inhibitor-ineligible population**		
	ASCENT-03[3]	Sacituzumab govitecan	**TPC** (gemcitabine/carboplatin, paclitaxel, or nab-paclitaxel)
	TROPION Breast-02[4]	Datopotamab deruxtecan	**ICC** (paclitaxel, nab-paclitaxel, carboplatin, capecitabine or eribulin mesylate)
	TroFuse-011[5]	Sacituzumab tirumotecan† ± pembrolizumab	**TPC** (gemcitabine and carboplatin, paclitaxel, or nab-paclitaxel)
	SKB264-III-11[6]	Sacituzumab tirumotecan†	**ICC** (paclitaxel, nab-paclitaxel, capecitabine, eribulin, or carboplatin)
	PD-L1+ population		
	ASCENT-04[7]	Sacituzumab govitecan + pembrolizumab	**TPC** (gemcitabine and carboplatin, paclitaxel, or nab-paclitaxel) + pembrolizumab
	TROPION Breast-05[8]	Datopotamab deruxtecan ± durvalumab	**ICC** (paclitaxel, nab-paclitaxel or gemcitabine + carboplatin) + pembrolizumab

ADCs (T-DXd and SG) are approved globally as monotherapy in previously treated mTNBC; SG, Dato-DXd and Sac-TMT are being evaluated in 1L mTNBC[2,5–9]

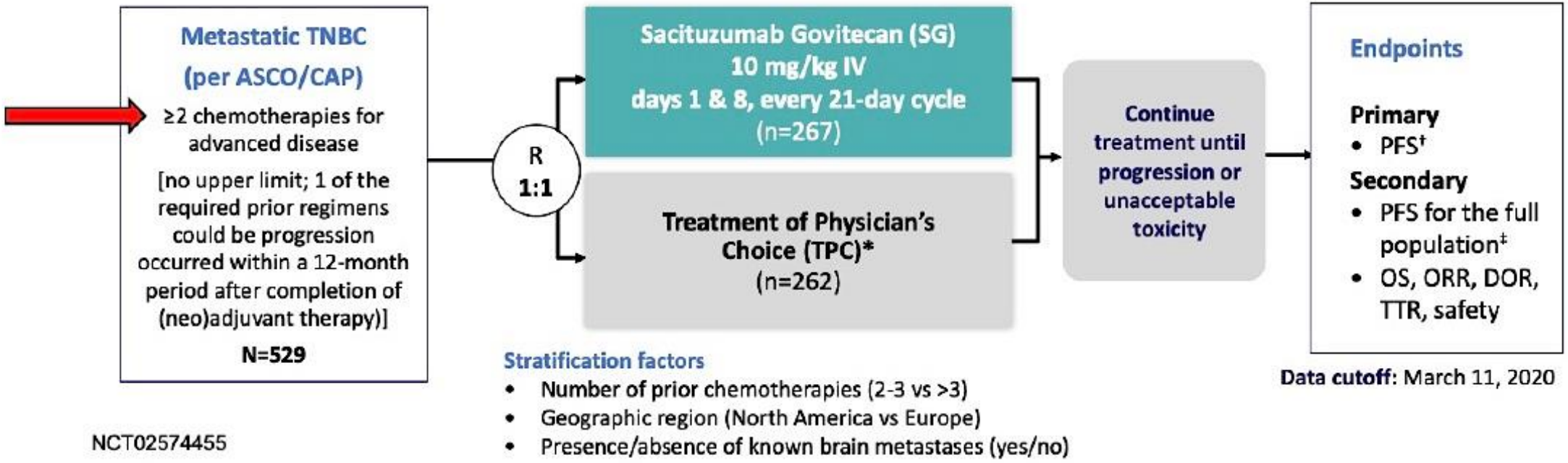
Courtesy of Rebecca A Dent, MD, MSc

OPEN ACCESS | CLINICAL TRIAL UPDATES | February 29, 2024

Final Results From the Randomized Phase III ASCENT Clinical Trial in Metastatic Triple-Negative Breast Cancer and Association of Outcomes by Human Epidermal Growth Factor Receptor 2 and Trophoblast Cell Surface Antigen 2 Expression

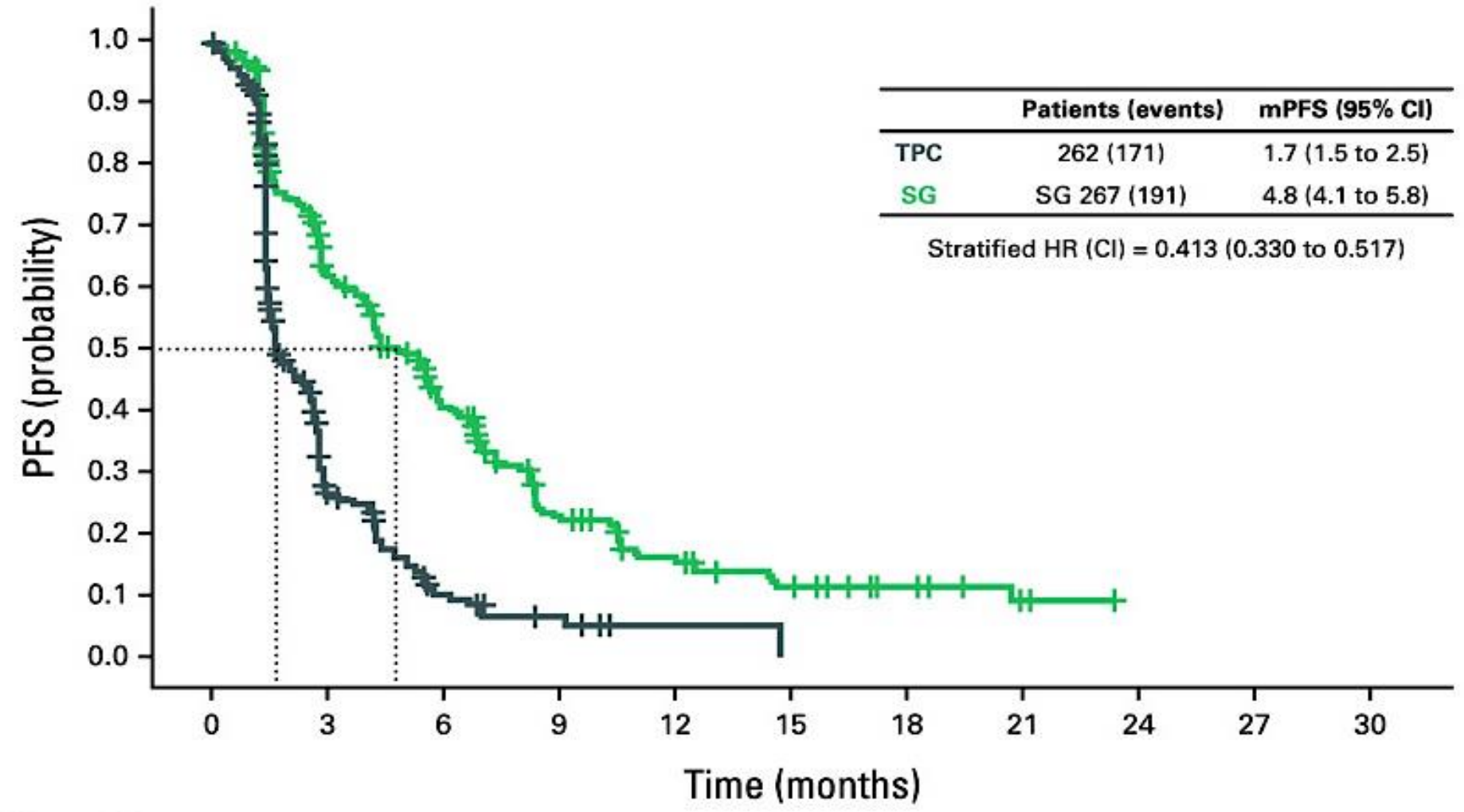
Authors: Aditya Bardia, MD, MPH, Hope S. Rugo, MD, Sara M. Tolaney, MD, MPH, Delphine Loirat, PhD, MD, Kevin Punie, MD, Mafalda Oliveira, MD, PhD, Adam Brufsky, MD, PhD, ... SHOW ALL ... , and Sara A. Hurvitz, MD, FACP | AUTHORS INFO & AFFILIATIONS

Phase III ASCENT Study Design



Bardia A et al. *J Clin Oncol* 2024.

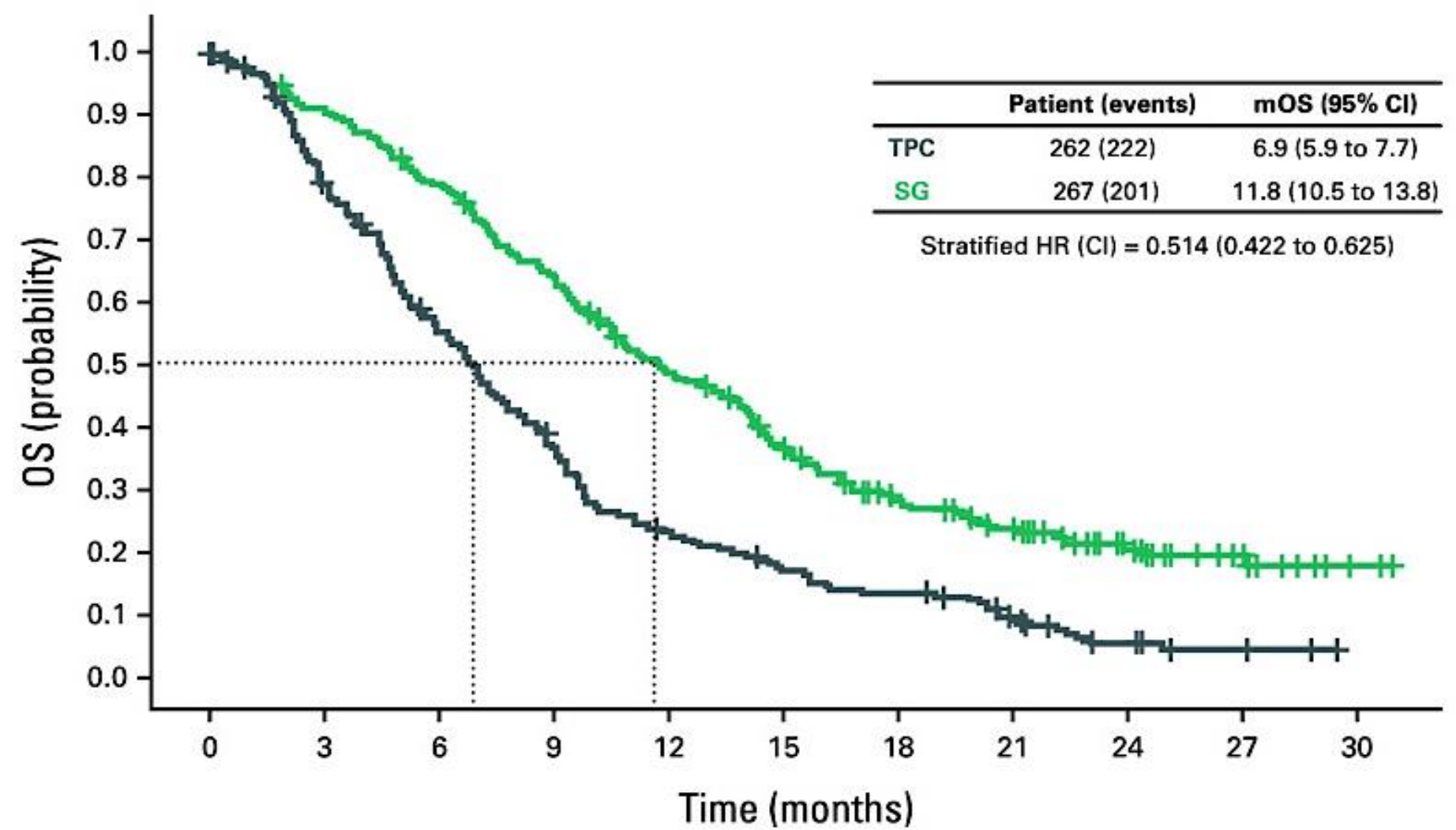
Phase III ASCENT: Progression-Free Survival (PFS)



mPFS = median progression-free survival

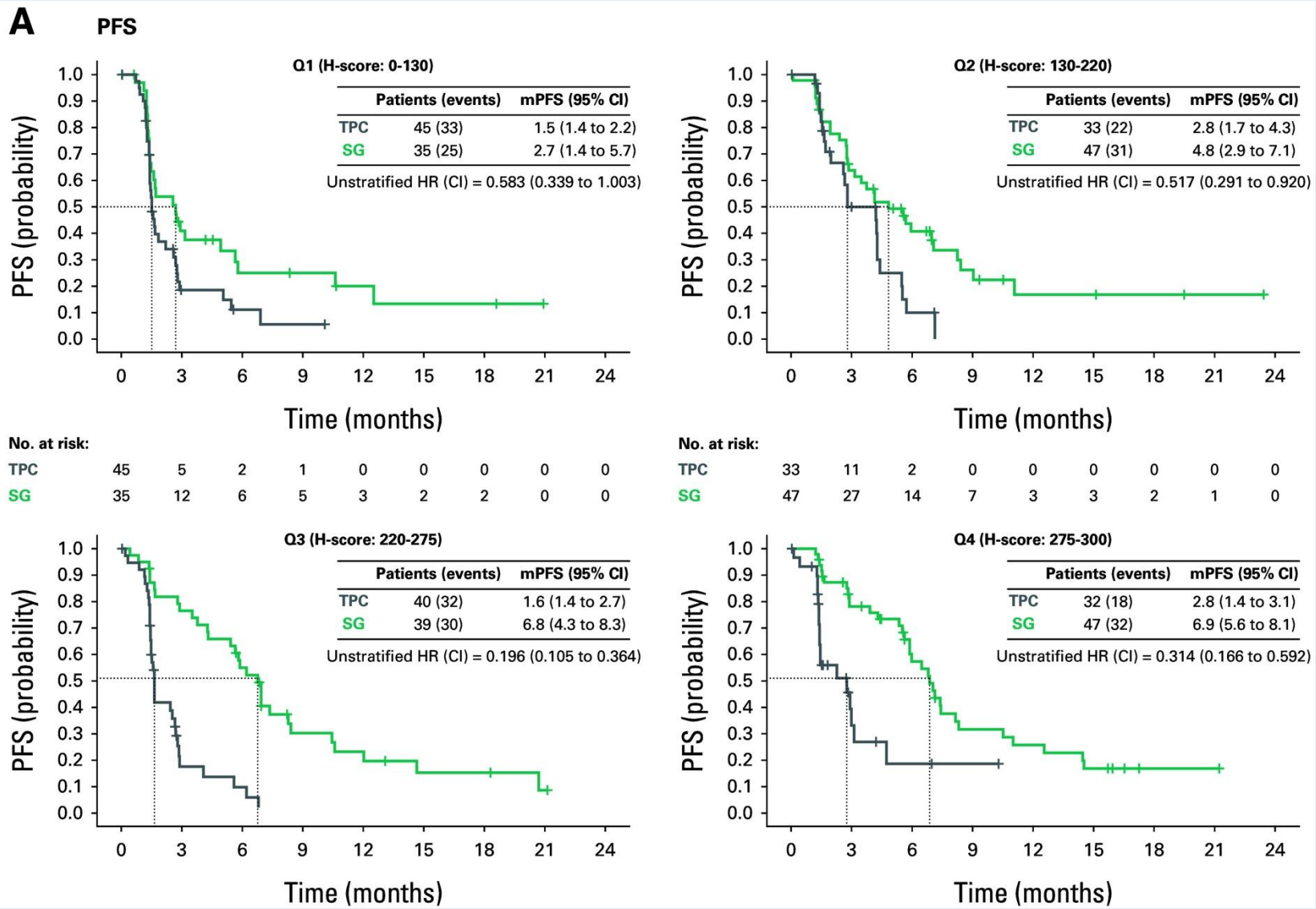
Bardia A et al. *J Clin Oncol* 2024.

Phase III ASCENT: Overall Survival (OS)



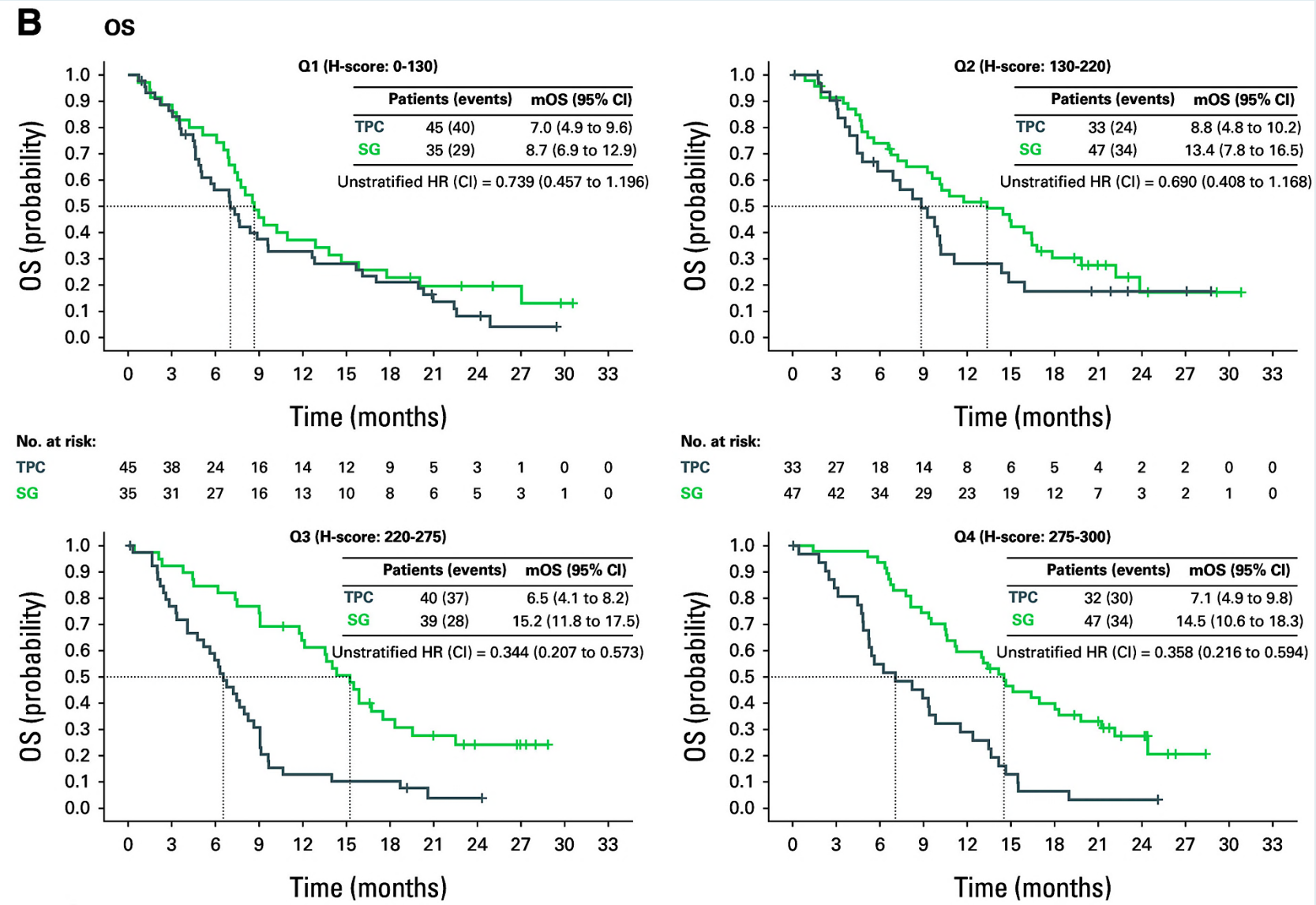
Bardia A et al. *J Clin Oncol* 2024.

Phase III ASCENT: PFS by TROP2 Expression



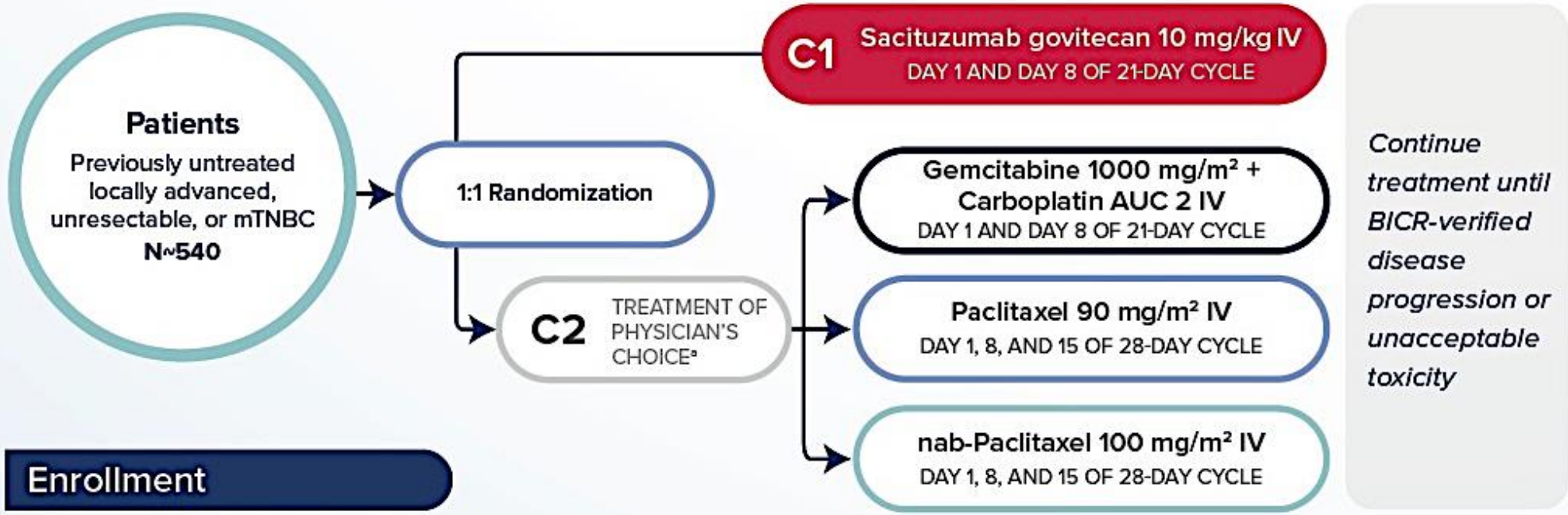
Bardia A et al. *J Clin Oncol* 2024.

Phase III ASCENT: OS by TROP2 Expression



Bardia A et al. *J Clin Oncol* 2024.

Phase III ASCENT-03 Study Design



Study Population 1L mTNBC

- Previously untreated locally advanced, unresectable, or metastatic TNBC
- PD-L1- by 22C3 CPS <10 or PD-L1+ by 22C3 CPS ≥10 in patients previously treated with an aPD-(L)1 agent in the curative setting
- ≥6 months since treatment in the curative setting
- Prior aPD-(L)1 use allowed in the curative setting
- PD-L1 and TNBC status centrally confirmed

[a]Crossover to SG in eligible patients allowed after BICR-verified disease progression.

www.clinicaltrials.gov. NCT05382299. Accessed August 2025.

ASCENT-03: First-Line Sacituzumab Govitecan Demonstrates Highly Statistically Significant and Clinically Meaningful Improvement in PFS for Patients with mTNBC Who Are Not Candidates for Checkpoint Inhibitors

Press Release: May 23, 2025

"[The manufacturer] announced positive topline results from the Phase 3 ASCENT-03 study of sacituzumab govitecan-hziy. The study met its primary endpoint, demonstrating a highly statistically significant and clinically meaningful improvement in progression-free survival (PFS) compared to chemotherapy in patients with first-line metastatic triple-negative breast cancer (mTNBC) who are not candidates for PD-1/PD-L1 inhibitors, meaning they are PD-L1 negative or are ineligible to receive immunotherapy.

The safety profile of sacituzumab govitecan-hziy in the ASCENT-03 study was consistent with prior studies, and no new safety signals were identified in this patient population. Overall survival (OS) is a key secondary endpoint and was not mature at the time of PFS primary analysis. No OS detriment was observed."

https://www.gilead.com/news/news-details/2025/ascent-03-trodelvy-demonstrates-highly-statistically-significant--clinically-meaningful-improvement-in-progression-free-survival-in-patients-with-first-line-metastatic-triple-negative-breast

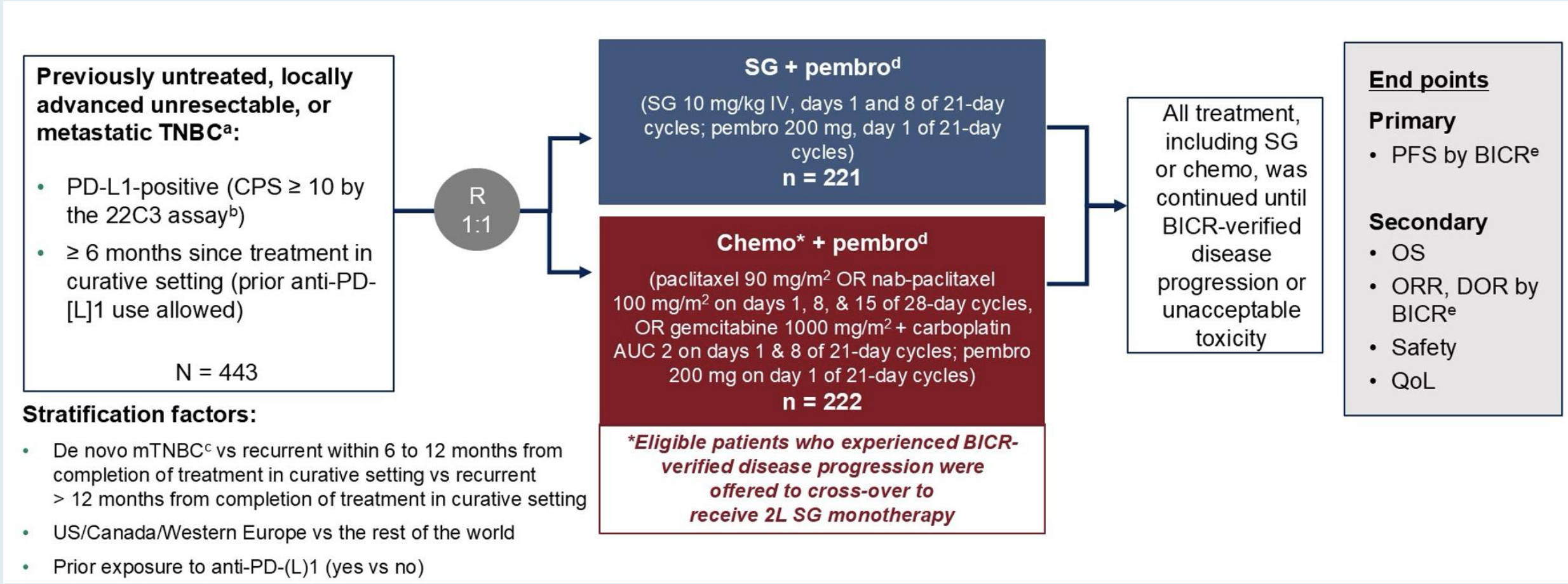
RTP RESEARCH TO PRACTICE

Sacituzumab Govitecan Plus Pembrolizumab vs Chemotherapy Plus Pembrolizumab in Patients With Previously Untreated, PD-L1 Positive, Advanced or Metastatic Triple-Negative Breast Cancer: Primary Results From the Randomized, Phase 3 ASCENT-04/KEYNOTE-D19 Study

Sara M Tolaney[1], Evandro de Azambuja[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 Banuelas[14], Ruffo Freitas-Junior[15], Javier Salvador Bofill[16], Maryam Afshari[17], Dianna Gary[17], Lu Wang[17], Catherine Lai[17], Peter Schmid[18]

ASCO 2025;Abstract LBA109.

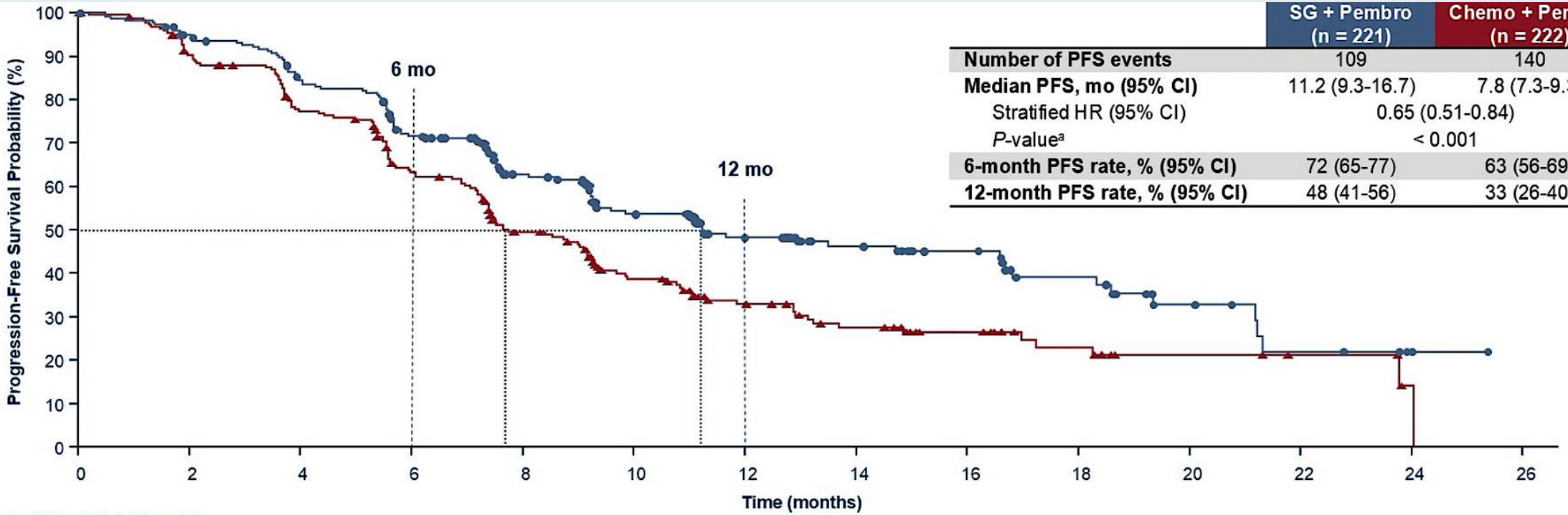
Phase III ASCENT-04/KEYNOTE-D19 Study Design



SG = sacituzumb govitecan; pembro = pembrolizumab

Tolaney SM et al. ASCO 2025;Abstract LBA109.

Phase III ASCENT-04/KEYNOTE-D19: Progression-Free Survival by BICR



	SG + Pembro (n = 221)	Chemo + Pembro (n = 222)
Number of PFS events	109	140
Median PFS, mo (95% CI)	11.2 (9.3-16.7)	7.8 (7.3-9.3)
Stratified HR (95% CI)	0.65 (0.51-0.84)	
P-value[a]	< 0.001	
6-month PFS rate, % (95% CI)	72 (65-77)	63 (56-69)
12-month PFS rate, % (95% CI)	48 (41-56)	33 (26-40)

No. of Patients Still at Risk (Events)

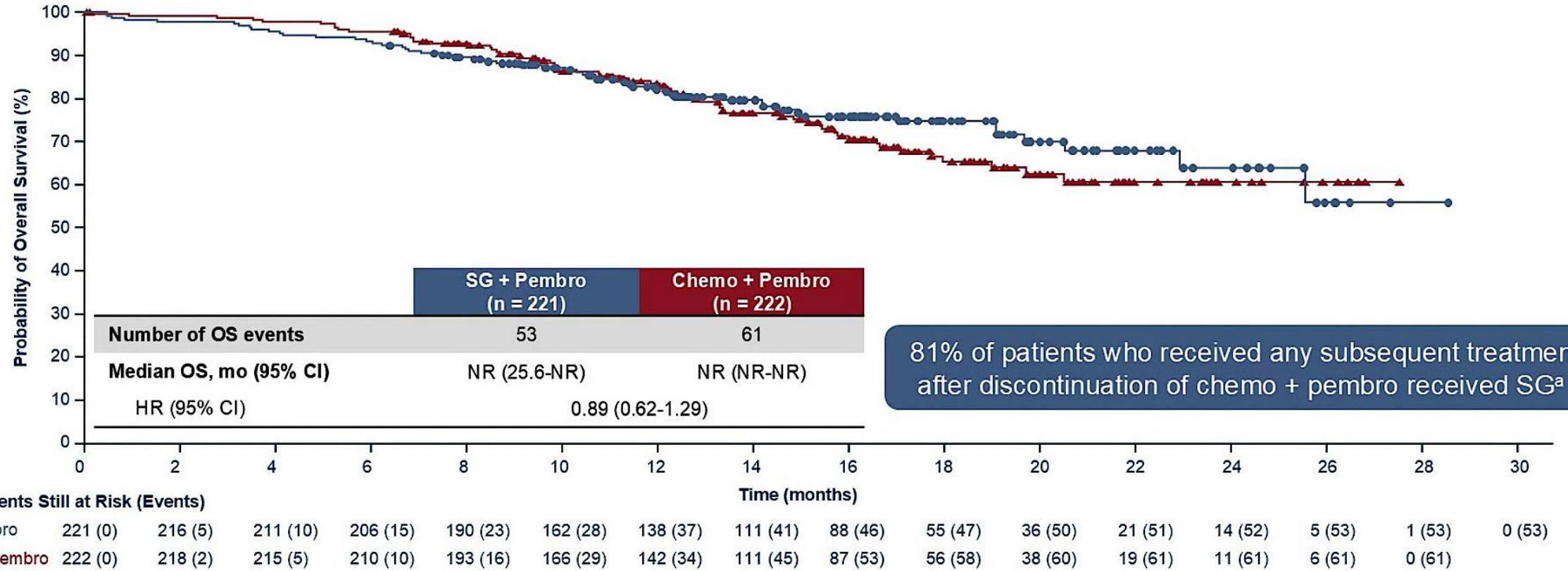
SG + Pembro	221 (0)	202 (11)	174 (33)	142 (59)	105 (75)	78 (89)	58 (96)	42 (98)	34 (99)	22 (103)	11 (106)	6 (109)	2 (109)	0 (109)
Chemo + Pembro	222 (0)	191 (21)	159 (48)	123 (76)	88 (102)	59 (120)	40 (128)	29 (134)	21 (135)	13 (137)	7 (138)	4 (138)	1 (139)	0 (140)

SG + pembro demonstrated statistically significant and clinically meaningful improvement in PFS vs chemo + pembro by BICR analysis, with a 35% reduction in risk of disease progression or death

BICR = blinded independent central review

Tolaney SM et al. ASCO 2025;Abstract LBA109.

Phase III ASCENT-04/KEYNOTE-D19: Descriptive Overall Survival at Primary Analysis



81% of patients who received any subsequent treatment after discontinuation of chemo + pembro received SG[a]

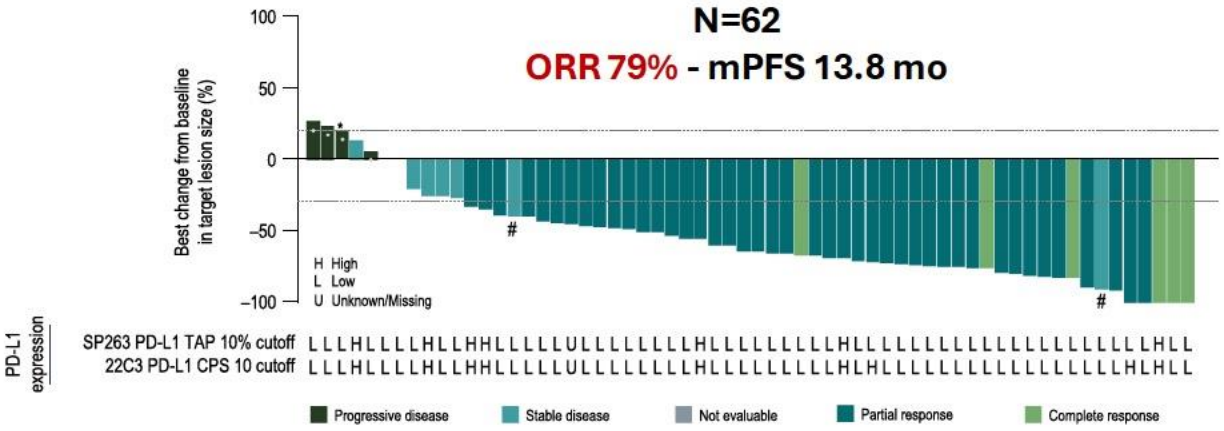
OS data were immature (maturity rate, 26%), however, a positive trend in improvement was observed for SG + pembro vs chemo + pembro

Tolaney SM et al. ASCO 2025;Abstract LBA109.

ADCs in metastatic triple-negative breast cancer

- Combining ADCs and immune-checkpoint inhibitors

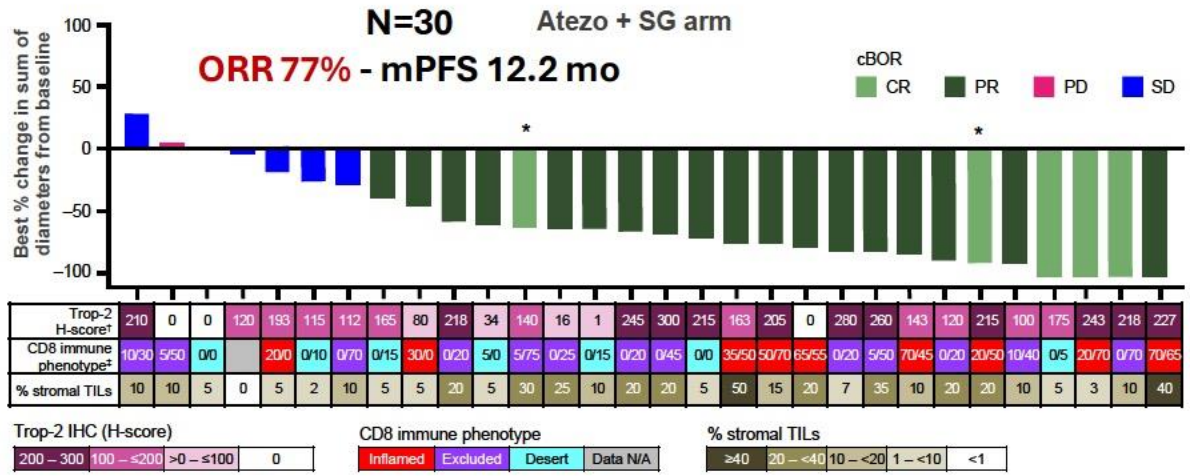
BEGONIA Trial
Dato-DXd + Durvalumab
in 1st line mTNBC



Antitumour responses were observed **regardless of PD-L1 expression** level as assessed by 2 separate PD-L1 assays and scoring methods

Schmid et al, ESMO 2023

Morpheus-PAN BC Trial
Sacituzumab Govitecan + Atezolizumab
in PD-L1+ 1st line mTNBC



Schmid et al, ESMO Breast 2024

Courtesy of Rebecca A Dent, MD, MSc

Agenda

Introduction: Legendary Figures in Breast Cancer Research

Case 1: Dr Favaro – 82-year-old woman, a current smoker with PMH of myocardial infarction and stroke, develops recurrent TNBC

Case 2: Dr Rudolph – 67-year-old woman with mTNBC (PD-L1 20%) receives chemotherapy/ pembrolizumab followed by sacituzumab govitecan

Case 3: Dr Zelkowitz – 68-year-old woman with localized TNBC develops myocarditis during neoadjuvant chemotherapy/pembrolizumab

Case 4: Dr Gupta – 64-year-old woman with recurrent ER-negative, HER2-low, PI3K-mutant mTNBC

Case 5: Dr Lee – 63-year-old woman with recurrent TNBC confined to contralateral neck nodes

Case 6: Dr Rodriguez – 43-year-old woman with mTNBC s/p multiple lines of chemotherapy receives sacituzumab govitecan

Case 7: Dr Gupta – 76-year-old woman with ER-negative, HER2-low breast cancer develops an isolated brain metastasis

Case 8: Dr Rudolph – 68-year-old woman with mTNBC experiences severe diarrhea with sacituzumab govitecan

RTP RESEARCH TO PRACTICE

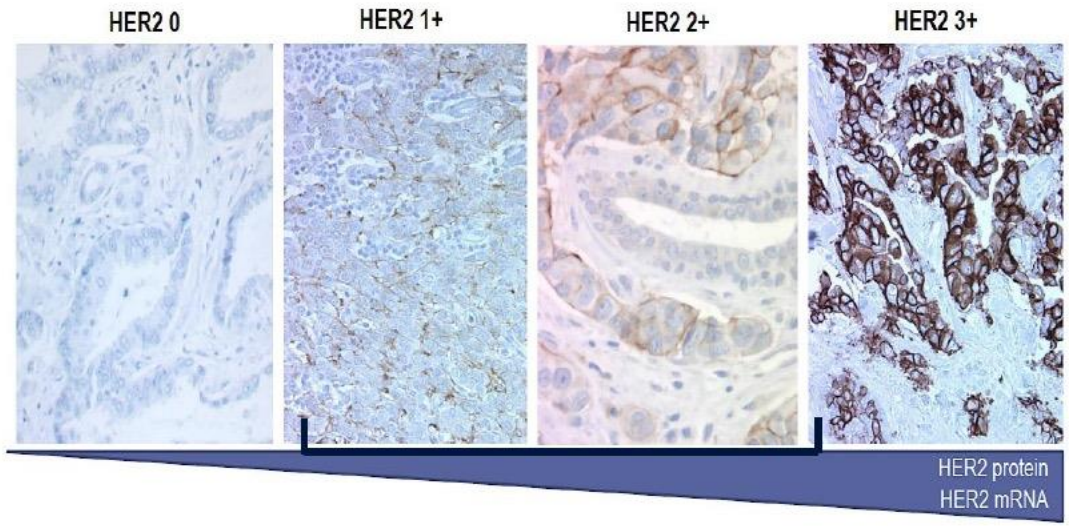
Case Presentation: 67-year-old woman with mTNBC (PD-L1 20%) receives chemotherapy/pembrolizumab followed by sacituzumab govitecan

Dr Priya Rudolph (Athens, Georgia)

RTP
RESEARCH
TO PRACTICE

Trastuzumab Deruxtecan active in HER2-low MBC

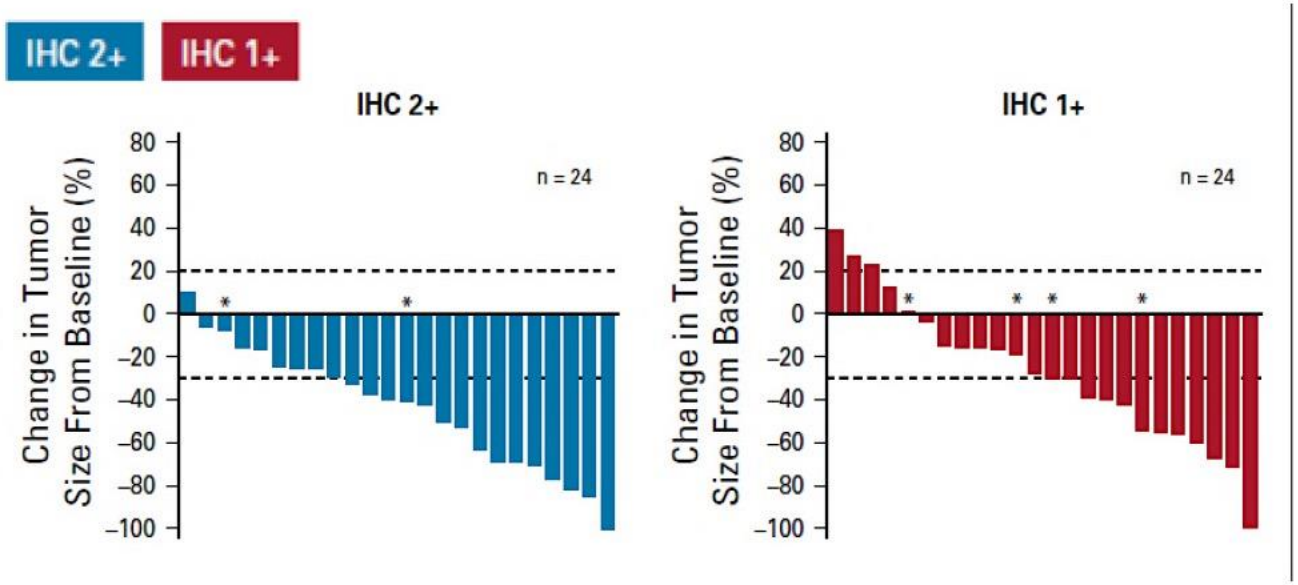
HER2: Continuum of expression in breast cancer



HER2-low
HER2 IHC 2+/ISH- OR IHC 1+/ISH – or untested

Of ~6100 breast cancer cases by IHC
~ 75% of cases of HR+ BC were considered HER2-low
~ 49% of cases of TNBC were considered HER2-low

T-DXd: Best percent change in tumor size in HER2-low MBC



Confirmed ORR: 37%
Confirmed DCR: 87%
Median DoR: 10.4 months
Median PFS: 11.1 months

- T-DXD demonstrated significant anti-tumor activity in HER2 IHC 2+ and 1+ tumors

Penault-Llorca F. ESMO E-learning module
Modi S et al. JCO 2020

Courtesy of Joyce O'Shaughnessy, MD

2022 ASCO ANNUAL MEETING

DESTINY-Breast04

Trastuzumab deruxtecan (T-DXd) vs treatment of physician's choice in patients with HER2-low unresectable and/or metastatic breast cancer: Results of DESTINY-Breast04, a randomized, phase 3 study

Shanu Modi Memorial Sloan Kettering Cancer Center, Memorial Hospital, New York, NY, USA

June 5, 2022

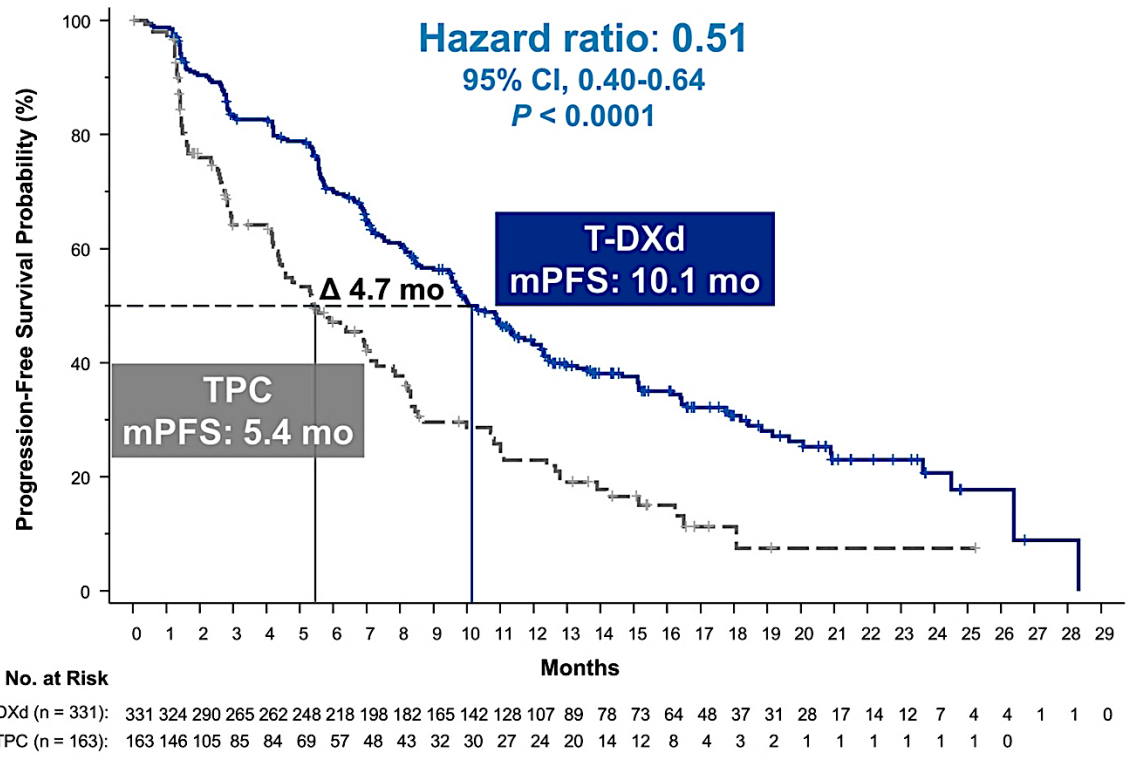
Additional authors: William Jacot, Toshinari Yamashita, Joo Hyuk Sohn, Maria Vidal, Eriko Tokunaga, Junji Tsurutani, Naoto Ueno, Yee Soo Chae, Keun Seok Lee, Naoki Niikura, Yeon Hee Park, Xiaojia Wang, Binghe Xu, Dhiraj Gambhire, Lotus Yung, Gerold Meinhardt, Yibin Wang, Nadia Harbeck, David Cameron

On behalf of the DESTINY-Breast04 investigators

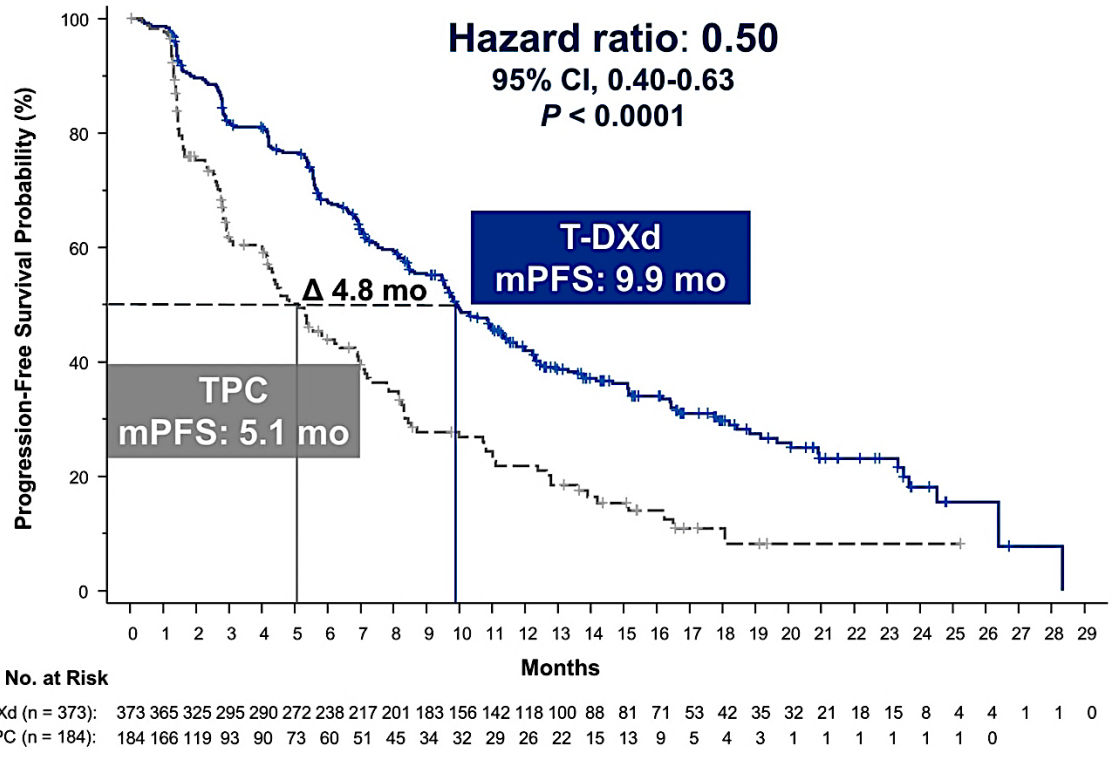
Abstract LBA3

Phase III DESTINY-Breast04: PFS

Hormone receptor–positive



All patients

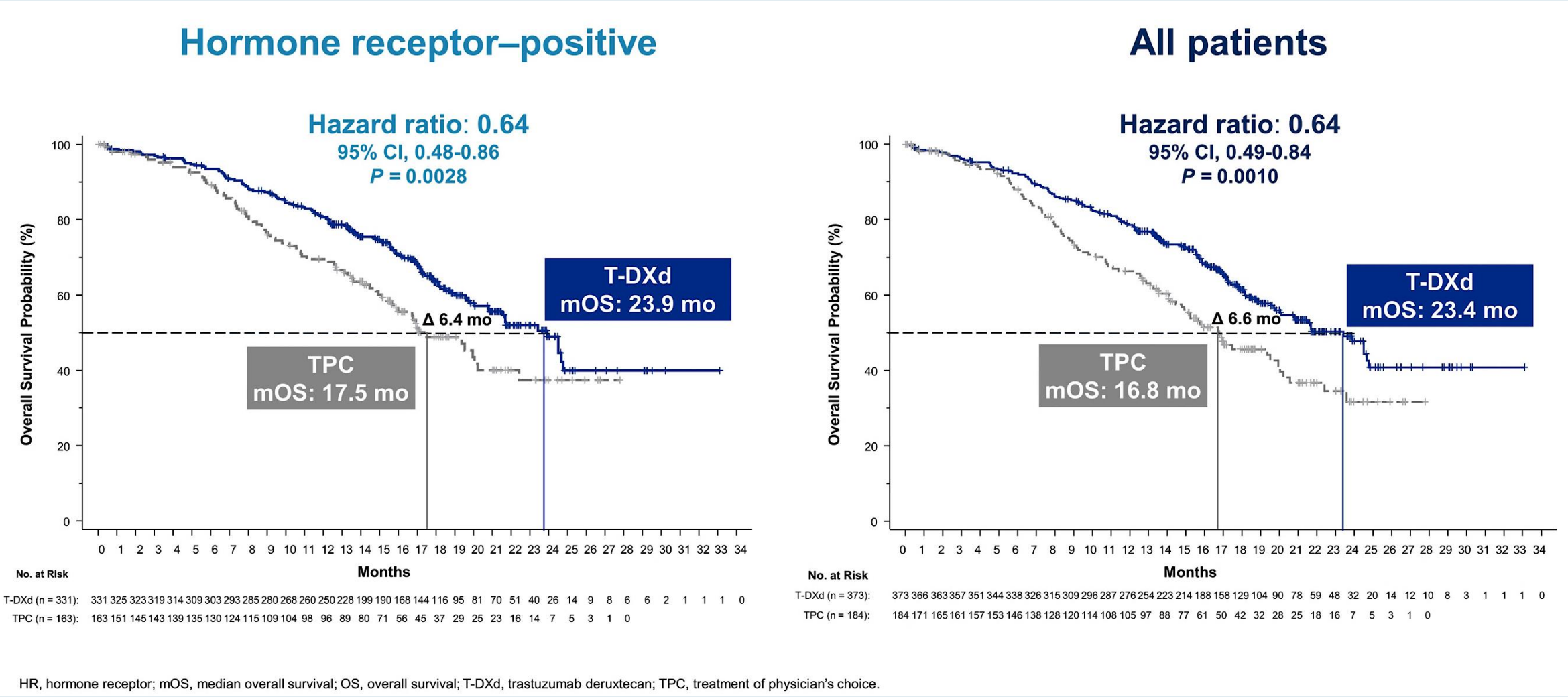


PFS by blinded independent central review.

HR, hormone receptor; mPFS, median progression-free survival; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

Modi S et al. ASCO 2022;Abstract LBA3.

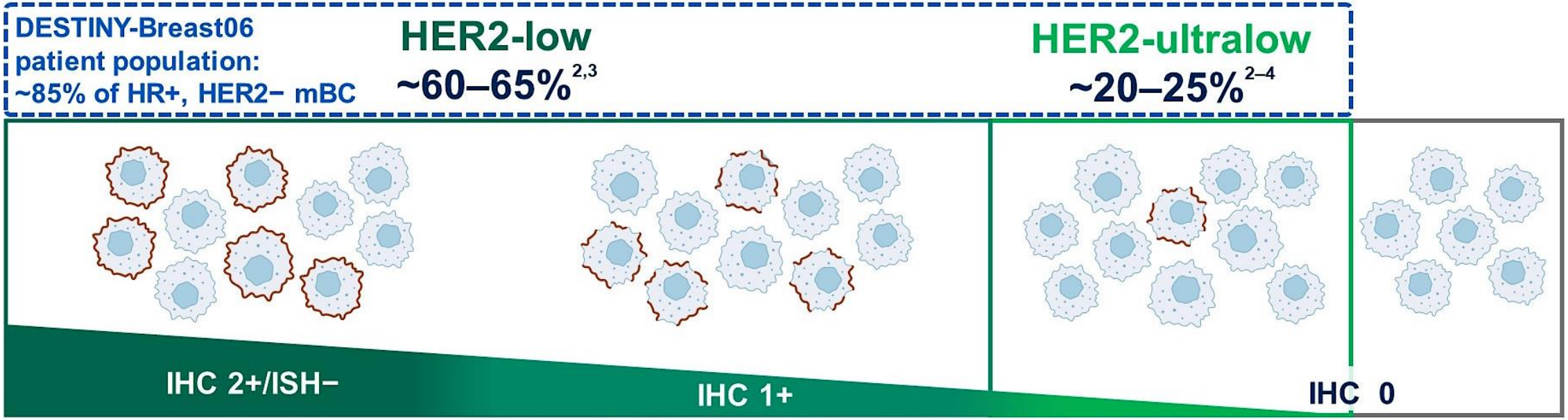
Phase III DESTINY-Breast04: OS



HR, hormone receptor; mOS, median overall survival; OS, overall survival; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

Modi S et al. ASCO 2022;Abstract LBA3.

HER2-Ultralow Disease



ASCO/CAP, American Society of Clinical Oncology / College of American Pathologists; HER2, human epidermal growth factor receptor 2; HR+, hormone receptor–positive; IHC, immunohistochemistry; ISH, in situ hybridization; mBC, metastatic breast cancer; T-DXd, trastuzumab deruxtecan

Images adapted from Venetis K, et al. *Front Mol Biosci*. 2022;9:834651. CC BY 4.0 license available from: https://creativecommons.org/licenses/by/4.0/

1. Wolff AC, et al. *J Clin Oncol*. 2023;41:3867–3872; 2. Denkert C, et al. *Lancet Oncol*. 2021;22:1151–1161; 3. Chen Z, et al. *Breast Cancer Res Treat*. 2023;202:313–323; 4. Mehta S, et al. *J Clin Oncol*. 2024;42(Suppl. 16):Abstract e13156

Curigliano G et al. ASCO 2024;Abstract LBA1000.

2024 ASCO ANNUAL MEETING

DESTINY BREAST06

Trastuzumab deruxtecan vs physician's choice of chemotherapy in patients with hormone receptor–positive, human epidermal growth factor receptor 2 (HER2)–low or HER2-ultralow metastatic breast cancer with prior endocrine therapy: primary results from DESTINY-Breast06

Giuseppe Curigliano
European Institute of Oncology, IRCCS, Milan, Italy;
Department of Oncology and Hematology-Oncology, University of Milan, Italy

Sunday, June 2, 2024

Additional authors: Xichun Hu, Rebecca Dent, Kan Yonemori, Carlos H Barrios, Joyce A O'Shaughnessy, Hans Wildiers, Qingyuan Zhang, Seock-Ah Im, Cristina Saura, Laura Biganzoli, Joohyuk Sohn, Christelle Lévy, William Jacot, Natasha Begbie, Jun Ke, Gargi Patel, Aditya Bardia

On behalf of the DESTINY-Breast06 investigators

Abstract LBA1000

RTP RESEARCH TO PRACTICE

Phase III DESTINY-Breast06 Study Design

DESTINY-Breast06: a Phase 3, randomized, multicenter, open-label study (NCT04494425)

PATIENT POPULATION

- HR+ mBC
- HER2-low (IHC 1+ or IHC 2+/ISH−) or HER2-ultralow (IHC 0 with membrane staining)*
- **Chemotherapy naïve in the mBC setting**

Prior lines of therapy

- ≥2 lines of ET ± targeted therapy for mBC
  OR
- 1 line for mBC **AND**
  - Progression ≤6 months of starting first-line ET + CDK4/6i
    OR
  - Recurrence ≤24 months of starting adjuvant ET

R 1:1

T-DXd
5.4 mg/kg Q3W
(n=436)

HER2-low = 713
HER2-ultralow = 153†

TPC
(n=430)

Options:
capecitabine,
nab-paclitaxel,
paclitaxel

ENDPOINTS

Primary

- PFS (BICR) in HER2-low

Key secondary

- PFS (BICR) in ITT (HER2-low + ultralow)
- OS in HER2-low
- OS in ITT (HER2-low + ultralow)

Other secondary

- PFS (INV) in HER2-low
- ORR (BICR/INV) and DOR (BICR/INV) in HER2-low and ITT (HER2-low + ultralow)
- Safety and tolerability
- Patient-reported outcomes‡

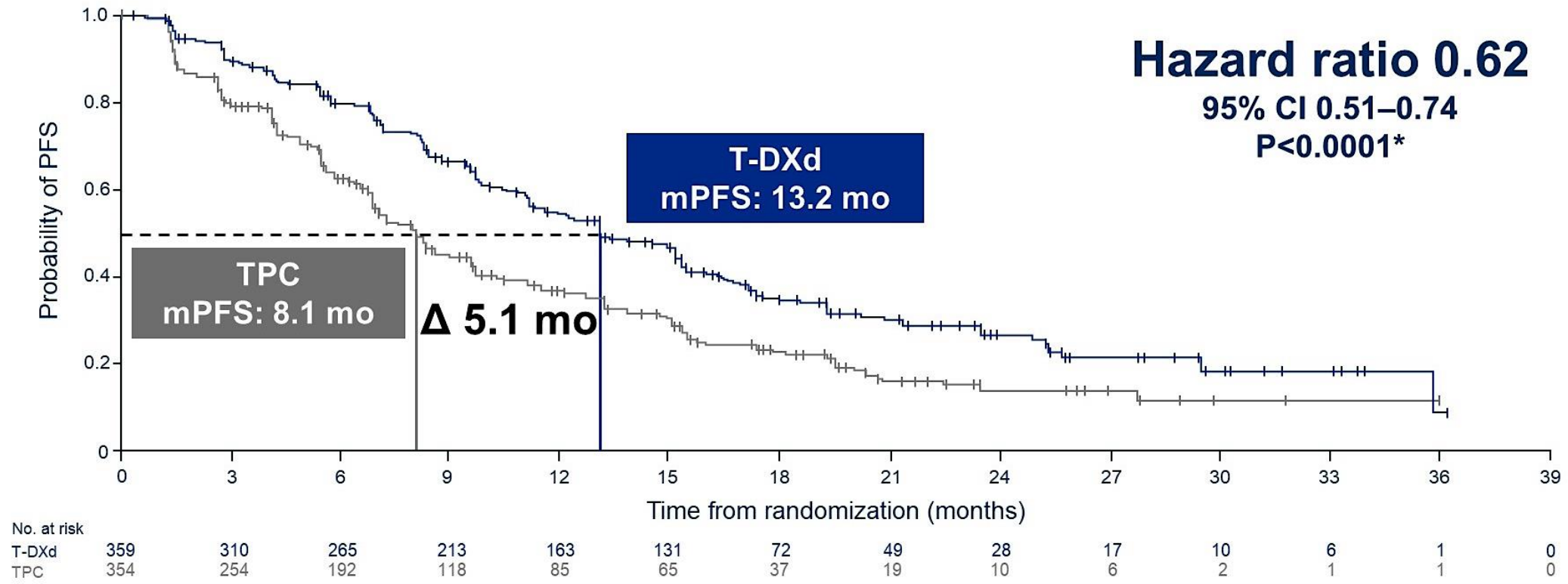
Stratification factors

- Prior CDK4/6i use (yes vs no)
- HER2 expression (IHC 1+ vs IHC 2+/ISH− vs IHC 0 with membrane staining)
- Prior taxane in the non-metastatic setting (yes vs no)

*Study enrollment was based on central HER2 testing. HER2 status was determined based on the most recent evaluable HER2 IHC sample prior to randomization. HER2-ultralow was defined as faint, partial membrane staining in ≤10% of tumor cells (also known as IHC >0<1+); †HER2-ultralow status as determined per IRT data (note: efficacy analyses in the HER2-ultralow subgroup were based on n=152 as determined per central laboratory testing data); ‡to be presented separately
BICR, blinded independent central review; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; DOR, duration of response; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR+, hormone receptor–positive; IHC, immunohistochemistry; INV, investigator assessed; IRT, interactive response technology; ISH, in situ hybridization; ITT, intent-to-treat; mBC, metastatic breast cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice
NCT04494425. Updated. April 12, 2024. Available from: https://clinicaltrials.gov/study/NCT04494425 (Accessed May 13, 2024)

Curigliano G et al. ASCO 2024;Abstract LBA1000.

Phase III DESTINY-Breast06: PFS in HER2-Low Disease (Primary Endpoint)

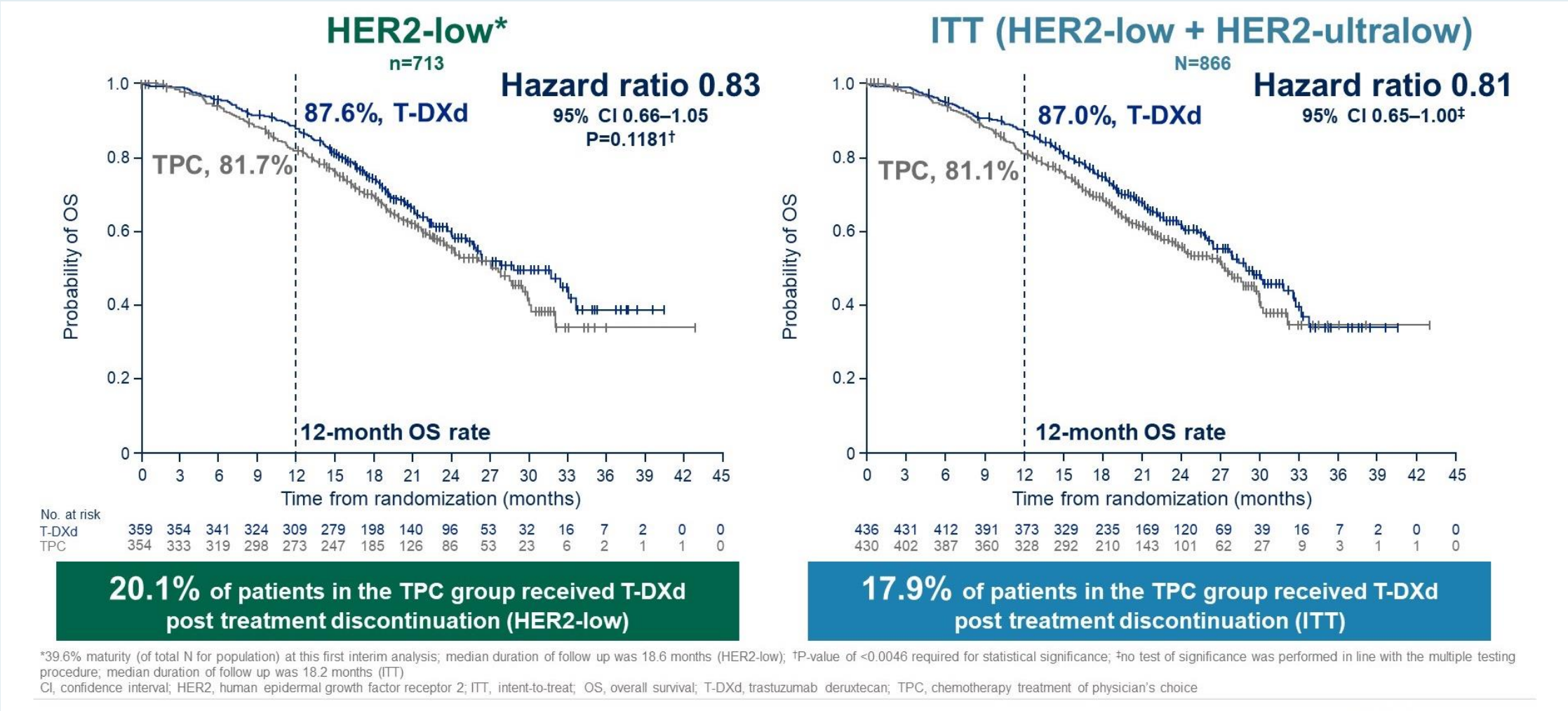


T-DXd demonstrated a statistically significant and clinically meaningful improvement in PFS compared with standard-of-care chemotherapy in HER2-low

*P-value of <0.05 required for statistical significance
BICR, blinded independent central review; CI, confidence interval; HER2, human epidermal growth factor receptor 2; mo, months; (m)PFS, (median) progression-free survival; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice

Curigliano G et al. ASCO 2024;Abstract LBA1000.

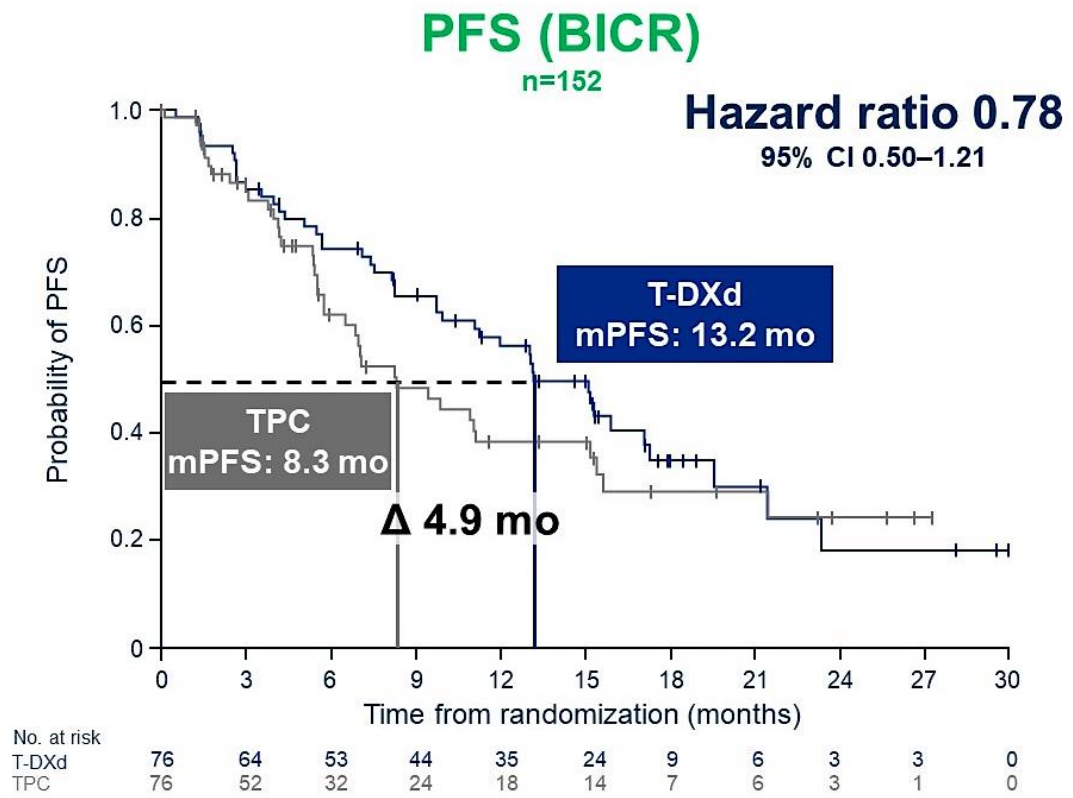
Phase III DESTINY-Breast06: Overall Survival (~40% Maturity)

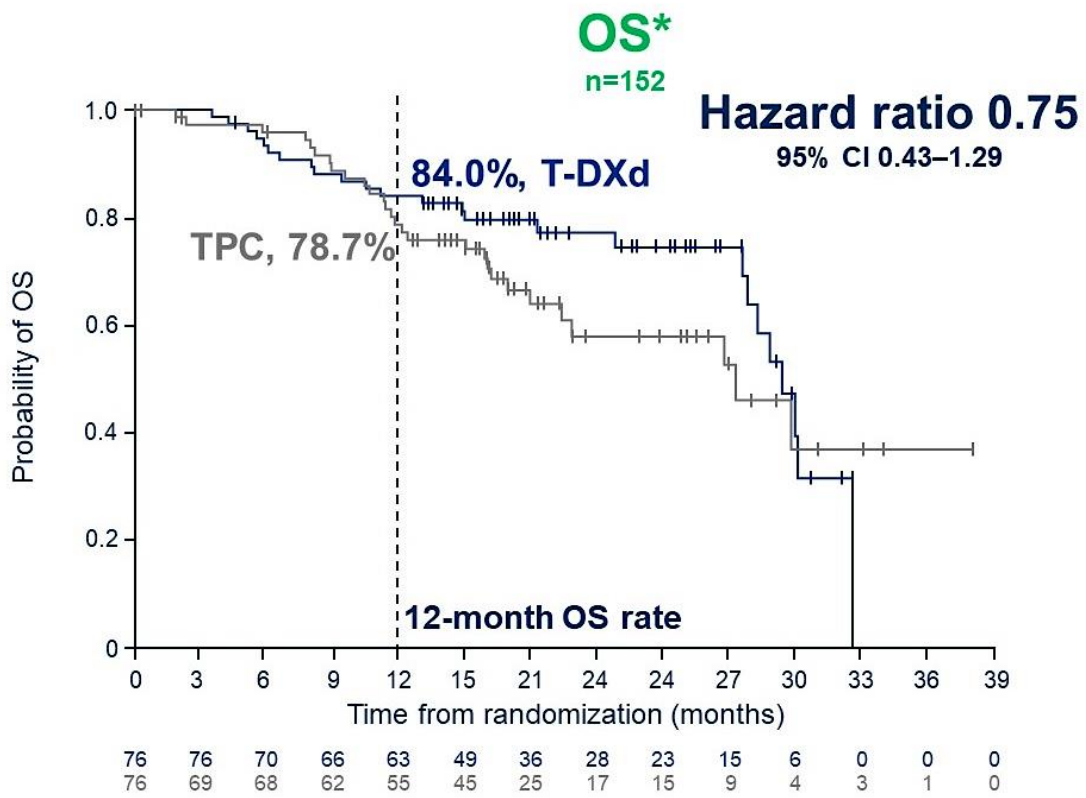


*39.6% maturity (of total N for population) at this first interim analysis; median duration of follow up was 18.6 months (HER2-low); †P-value of <0.0046 required for statistical significance; ‡no test of significance was performed in line with the multiple testing procedure; median duration of follow up was 18.2 months (ITT)
CI, confidence interval; HER2, human epidermal growth factor receptor 2; ITT, intent-to-treat; OS, overall survival; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice

Curigliano G et al. ASCO 2024;Abstract LBA1000.

Phase III DESTINY-Breast06: Survival in HER2-Ultralow Disease



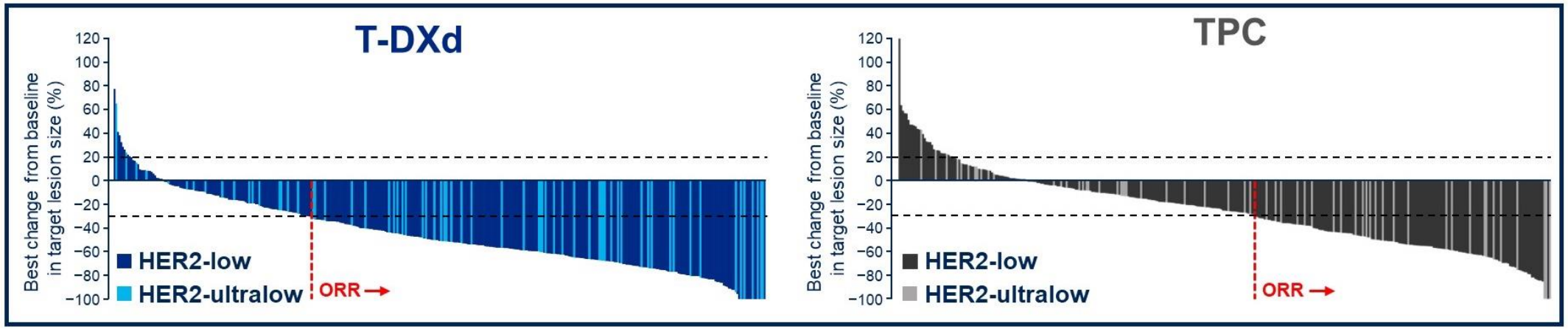


PFS improvement with T-DXd vs TPC in HER2-ultralow was consistent with results in HER2-low

*34.9% maturity (of total N for population) at this first interim analysis; median duration of follow up was 16.8 months
BICR, blinded independent central review; CI, confidence interval; HER2, human epidermal growth factor receptor 2; OS, overall survival; mo, months; (m)PFS, (median) progression-free survival; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice

Curigliano G et al. ASCO 2024;Abstract LBA1000.

Phase III DESTINY-Breast06: Activity by HER2 Expression



	HER2-low*		ITT		HER2-ultralow*	
	T-DXd (n=359)	TPC (n=354)	T-DXd (n=436)	TPC (n=430)	T-DXd (n=76)	TPC (n=76)
Confirmed ORR, n (%)	**203 (56.5)**	**114 (32.2)**	**250 (57.3)**	**134 (31.2)**	**47 (61.8)**	**20 (26.3)**
Best overall response, n (%)						
Complete response	9 (2.5)	0	13 (3.0)	0	4 (5.3)	0
Partial response	194 (54.0)	114 (32.2)	237 (54.4)	134 (31.2)	43 (56.6)	20 (26.3)
Stable disease	125 (34.8)	170 (48.0)	148 (33.9)	212 (49.3)	22 (28.9)	42 (55.3)
Clinical benefit rate, n (%)†	275 (76.6)	190 (53.7)	334 (76.6)	223 (51.9)	58 (76.3)	33 (43.4)
Median duration of response, mo	14.1	8.6	14.3	8.6	14.3	14.1

ORR based on RECIST v1.1; response required confirmation after 4 weeks
*HER2-low status defined at randomization per IRT data, and HER2-ultralow status defined by central laboratory testing data; †defined as complete response + partial response + stable disease at Week 24, by blinded independent central review
HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; IRT, interactive response technology; ITT, intent-to-treat; mo, months; ORR, objective response rate; RECIST, Response Evaluation Criteria in Solid Tumors; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice

Curigliano G et al. ASCO 2024;Abstract LBA1000.

Agenda

Introduction: Legendary Figures in Breast Cancer Research

Case 1: Dr Favaro – 82-year-old woman, a current smoker with PMH of myocardial infarction and stroke, develops recurrent TNBC

Case 2: Dr Rudolph – 67-year-old woman with mTNBC (PD-L1 20%) receives chemotherapy/ pembrolizumab followed by sacituzumab govitecan

Case 3: Dr Zelkowitz – 68-year-old woman with localized TNBC develops myocarditis during neoadjuvant chemotherapy/pembrolizumab

Case 4: Dr Gupta – 64-year-old woman with recurrent ER-negative, HER2-low, PI3K-mutant mTNBC

Case 5: Dr Lee – 63-year-old woman with recurrent TNBC confined to contralateral neck nodes

Case 6: Dr Rodriguez – 43-year-old woman with mTNBC s/p multiple lines of chemotherapy receives sacituzumab govitecan

Case 7: Dr Gupta – 76-year-old woman with ER-negative, HER2-low breast cancer develops an isolated brain metastasis

Case 8: Dr Rudolph – 68-year-old woman with mTNBC experiences severe diarrhea with sacituzumab govitecan

RTP RESEARCH TO PRACTICE

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

Dr Richard Zelkowitz (Bridgeport, Connecticut)

RTP RESEARCH TO PRACTICE

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RTP RESEARCH TO PRACTICE

Case Presentation: 64-year-old woman with recurrent ER-negative, HER2-low, PI3K-mutant mTNBC

Dr Ranju Gupta (Bethlehem, Pennsylvania)

RTP RESEARCH TO PRACTICE

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RTP RESEARCH TO PRACTICE

Case Presentation: 63-year-old woman with recurrent TNBC confined to contralateral neck nodes

Dr Eric Lee (Fountain Valley, California)

RTP
RESEARCH
TO PRACTICE

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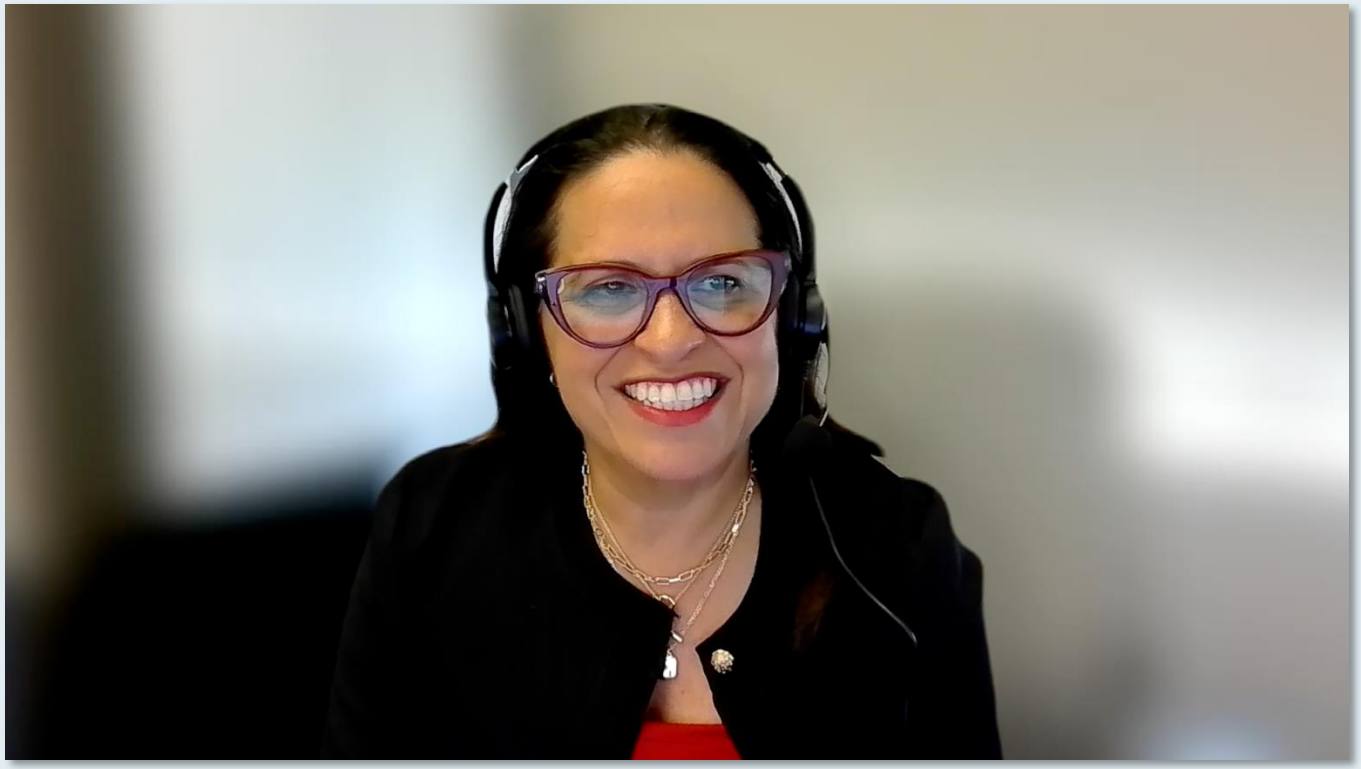
RTP RESEARCH TO PRACTICE

Case Presentation: 43-year-old woman with mTNBC s/p multiple lines of chemotherapy receives sacituzumab govitecan



Dr Estelamari Rodriguez (Miami, Florida)

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. Published 2025 June 18.

Phase II PRIMED: Patients Experiencing Neutropenia and Diarrhea During the First 2 Treatment Cycles

Neutropenia				
Any grade	Grade 2	Grade 3	Grade 4	Primary endpoint: ≥ grade 3 neutropenia
14 (28.0%)	4 (8.0%)	6 (12.0%)	2 (4.0%)	8 (16.0%); p = 0.00023
Diarrhea				
Any Grade	Grade 2	Grade 3	Grade 4	Primary endpoint: ≥ grade 2 diarrhea
17 (34.0%)	6 (12.0%)	2 (4.0%)	0 (0.0%)	8 (16.0%); p = 0.084

***Table 2*: Primary endpoints: Number of patients experiencing neutropenia and diarrhea during the first two treatment cycles.**

Pérez-García JM et al. *EClinicalMedicine* 2025;85:103309. Published 2025 June 18.

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RTP RESEARCH TO PRACTICE

Case Presentation: 76-year-old woman with ER-negative, HER2-low breast cancer develops an isolated brain metastasis

Dr Ranju Gupta (Bethlehem, Pennsylvania)

RTP RESEARCH TO PRACTICE

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RTP RESEARCH TO PRACTICE

Case Presentation: 68-year-old woman with PD-L1-negative mTNBC experiences severe diarrhea with second-line sacituzumab govitecan

Dr Priya Rudolph (Athens, Georgia)

RTP
RESEARCH
TO PRACTICE

FDA Approves Datopotamab Deruxtecan-dlnk for Unresectable or Metastatic HR-Positive, HER2-Negative Breast Cancer

Press Release: January 17, 2025

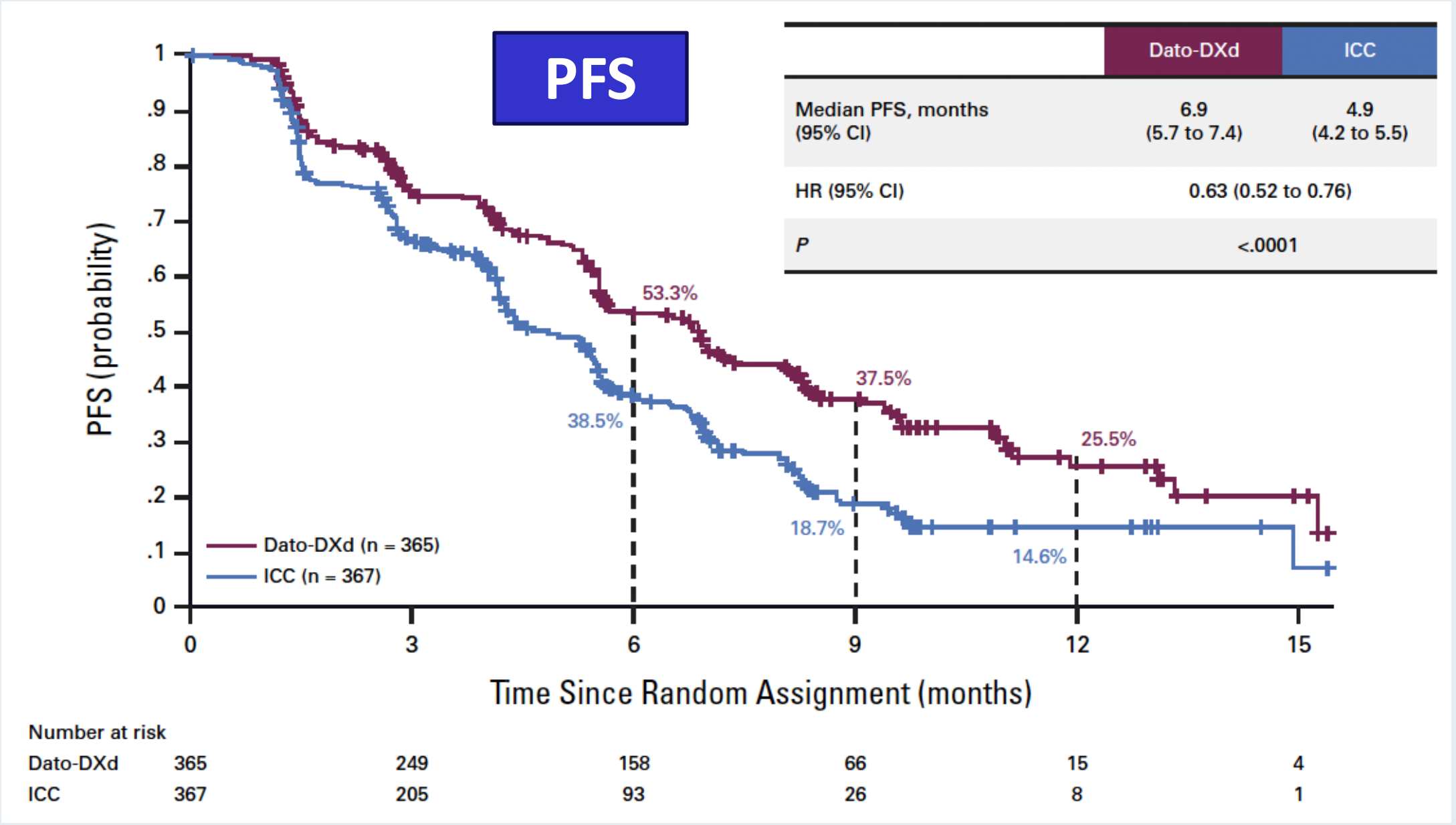
"On January 17, 2025, the Food and Drug Administration approved datopotamab deruxtecan-dlnk, a Trop-2-directed antibody and topoisomerase inhibitor conjugate, for adult patients with unresectable or metastatic, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC1+ or IHC2+/ISH-) breast cancer who have received prior endocrine-based therapy and chemotherapy for unresectable or metastatic disease.

Efficacy was evaluated in TROPION-Breast01 (NCT05104866), a multicenter, open-label, randomized trial. Patients must have experienced disease progression, been deemed unsuitable for further endocrine therapy, and have received one or two lines of prior chemotherapy for unresectable or metastatic disease. Patients were excluded for a history of ILD/pneumonitis requiring steroids, ongoing ILD/pneumonitis, clinically active brain metastases, or clinically significant corneal disease. Patients also were excluded for ECOG performance status >1."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-datopotamab-deruxtecan-dlnk-unresectable-or-metastatic-hr-positive-her2-negative-breast

RTP RESEARCH TO PRACTICE

Phase III TROPION-Breast01 Trial: Progression-Free Survival (PFS)



	Dato-DXd	ICC
Median PFS, months (95% CI)	6.9 (5.7 to 7.4)	4.9 (4.2 to 5.5)
HR (95% CI)	0.63 (0.52 to 0.76)	
P	<.0001	

Bardia A et al. *J Clin Oncol* 2025;43(3):285-96.

ICC = investigator's choice of chemotherapy

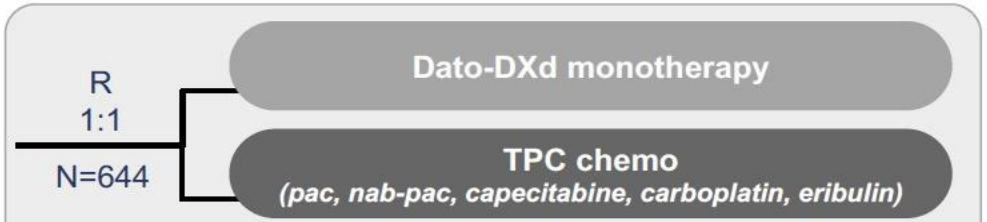
TROPION-Breast02 + TROPION-Breast05 Study Design

TROPION-Breast02[1,2]

Patient Population

- Untreated, inoperable/locally advanced or metastatic TNBC
- **PD-L1− (CPS <10) OR PD-L1+ (CPS ≥10)** if treated with an anti-PD-(L)1 agent for eBC or if they cannot be treated with an anti-PD-(L)1 agent due to a comorbidity, or if no regulatory access to an anti-PD-(L)1 agent
- **No minimum DFI since completion of Tx in curative setting** (DFI ≤12 months capped at 20%)
- History of ILD/pneumonitis and clinically significant corneal disease excluded

Study Design



Stratification Factors

- Geographic region
- PD-L1 status
- De novo vs prior DFI ≤12 months vs prior DFI >12 months

Key Endpoints[a]

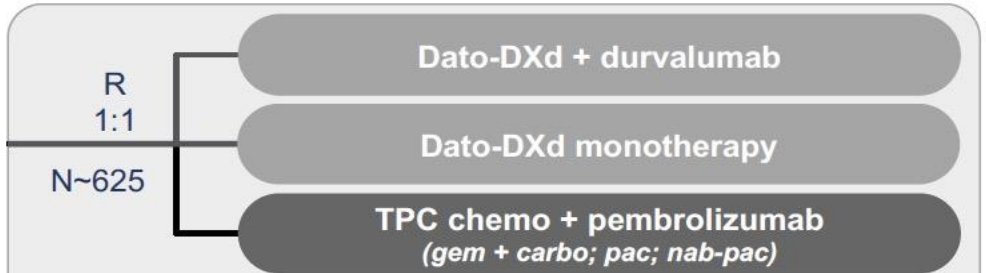
- Primary: PFS by BICR, OS
- Secondary: ORR, DOR, PFS (investigator), safety, PROs

TROPION-Breast05[3]

Patient Population

- **PD-L1+ (CPS ≥10)** untreated, inoperable/locally advanced or metastatic TNBC
- **DFI ≥6 months since Tx in curative setting** (DFI 6–12 months capped at 20%)
- Prior PD-(L)1 use allowed in this setting
- History of ILD/pneumonitis and clinically significant corneal disease excluded

Study Design



Stratification Factors

- Geographic region
- Prior PD-(L)1
- De novo vs prior DFI 6–12 months vs prior DFI >12 months

Key Endpoints[a]

- Primary: PFS by BICR
- Secondary: OS, PFS (investigator), ORR, safety, PROs

[a]Secondary endpoints not exhaustive.

1L, first line; BICR, blinded independent central review; carbo, carboplatin; chemo, chemotherapy; CPS, combined positive score; Dato-DXd, datopotamab deruxtecan; DFI, disease-free interval; eBC, early-stage breast cancer; gem, gemcitabine; nab-pac, nab-paclitaxel; ORR, objective response rate; OS, overall survival; pac, paclitaxel; PD-1, programmed death protein 1; PD-L1, programmed death ligand 1; PD-L1−, programmed death ligand 1-negative; PD-L1+, programmed death ligand 1-positive; PFS, progression-free survival; PROs, patient-reported outcomes; R, randomization; TNBC, metastatic triple-negative breast cancer; TPC, treatment of physician's choice; Tx, therapy.

1. Dent RA, et al. *Future Oncol*. 2023;19(35):2349–2359; 2. https://clinicaltrials.gov/study/NCT05374512; 3. Schmid P, et al. *Ther Adv Med Oncol*. 2025;17:17588359251327992.

Courtesy of Sara M Tolaney, MD, MPH

Sacituzumab Tirumotecan (sac-TMT)

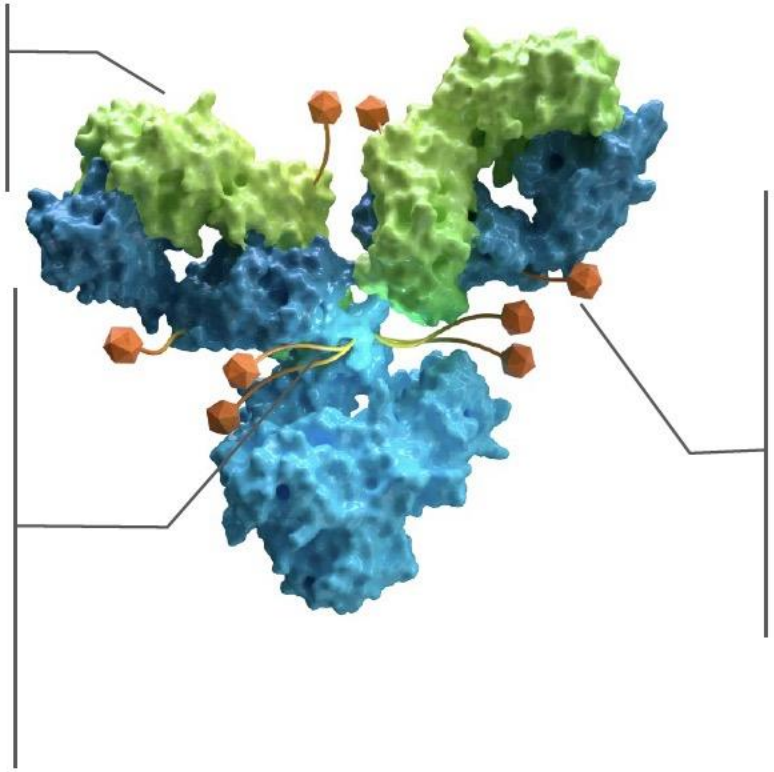
Sac-TMT is a TROP2 ADC developed with a proprietary Kthiol (pyrimidine-thiol) linker conjugated to a novel topoisomerase I inhibitor at DAR 7.4. The features of sac-TMT lead to release of the payload both in the tumor microenvironment (TME) and inside tumor cells, achieving a balance between the safety and efficacy of the ADC.

Antibody

- hRS7, a recombinant humanized anti-TROP2 antibody with high affinity

Linker

- **Kthiol conjugation:** irreversible coupling to improve stability of ADC
- **Payload release:** intracellular enzymatic cleavage and extracellular hydrolysis in TME
- **Balanced stability:** balance between efficacy and safety to expand therapeutic window



Payload

- **Novel topo I inhibitor** (belotecan derivative named T030), highly active
- Average **DAR: 7.4** (range:7–8)
- **Bystander effect**
- Methylsulfonyl derivatization enhances linker stability and toxin permeability

Courtesy of Sara M Tolaney, MD, MPH

ADC, antibody-drug conjugate; DAR, drug-to-antibody ratio; TME, tumor microenvironment; TROP2, trophoblast cell surface antigen 2.

nature medicine

Article

https://doi.org/10.1038/s41591-025-03630-w

Sacituzumab tirumotecan in previously treated metastatic triple-negative breast cancer: a randomized phase 3 trial

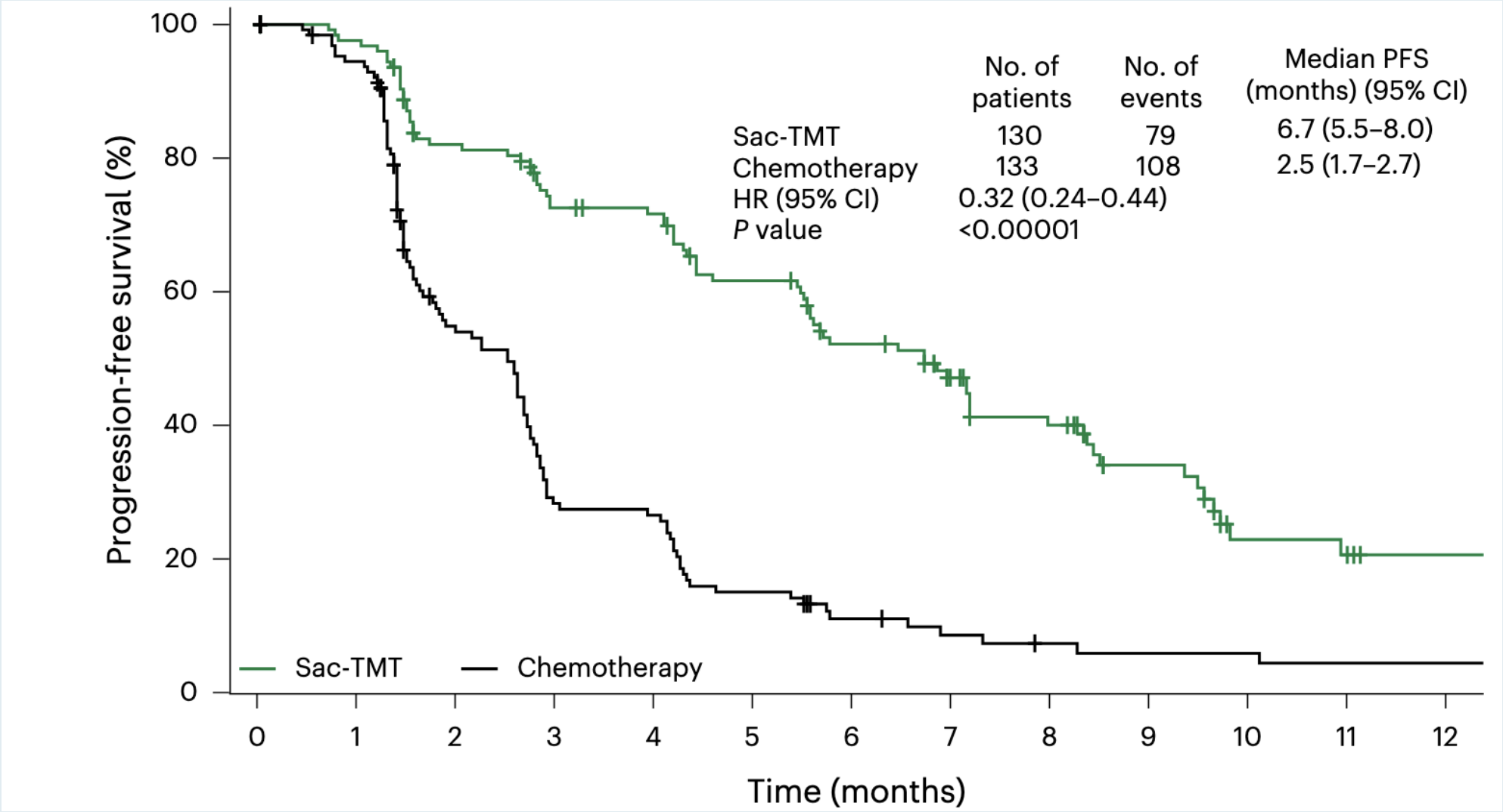
Received: 27 October 2024

Accepted: 4 March 2025

Published online: 11 April 2025

Yongmei Yin[1,17], Ying Fan[2,17], Quchang Ouyang[3,17], Lihua Song[4], Xiaojia Wang[5], Wei Li[6], Man Li[7], Xi Yan[8], Shusen Wang[9], Tao Sun[10], Yuee Teng[11], Xianjun Tang[12], Zhongsheng Tong[13], Zhengkui Sun[14], Junyou Ge[15,16], Xiaoping Jin[15], Yina Diao[15], Gesha Liu[15] & Binghe Xu[2]

Phase III OptiTROP-Breast01: Final PFS Analysis (by BICR)



Yin Y et al. *Nat Med* 2025;31(6):1969-75.

Sacituzumab Tirumotecan (Sac-TMT) as First-line Treatment for Unresectable Locally Advanced/Metastatic Triple-negative Breast Cancer (a/m TNBC): Initial Results From the Phase II OptiTROP-Breast05 Study

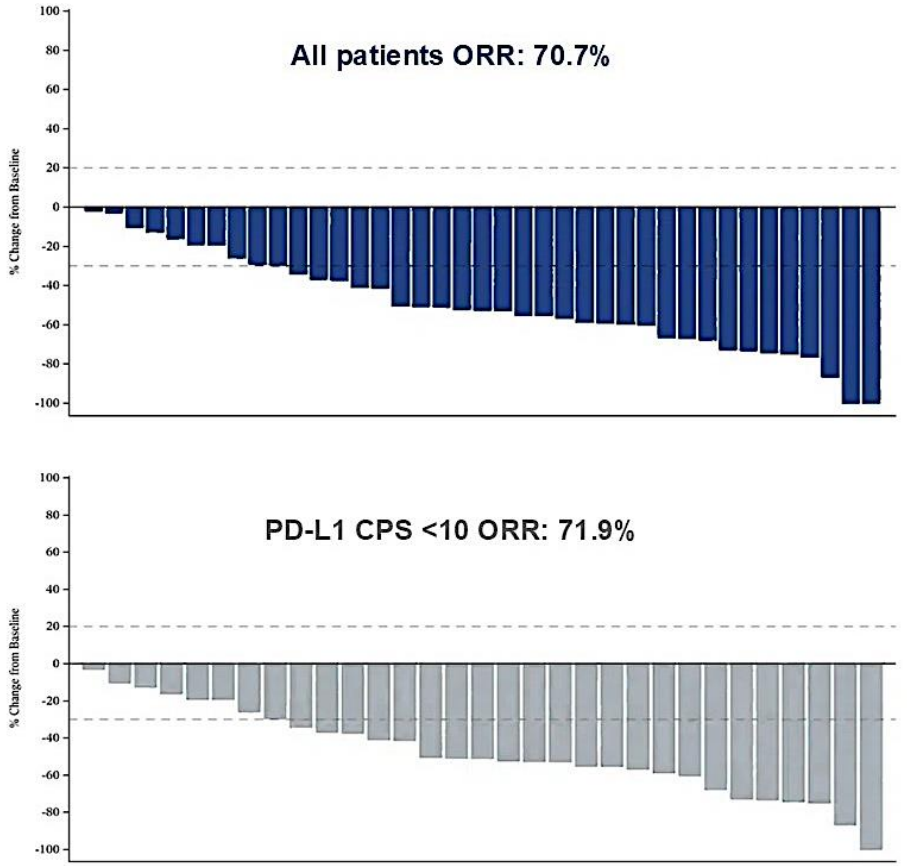
Yongmei Yin[1], Quchang Ouyang[2], Min Yan[3], Jian Zhang[4], Lihua Song[5], Wei Li[6], Yuanting Gu[7], Xiaoyu Liu[8], Jingfen Wang[9], Xiaojia Wang[10], Xi Yan[11], Jin Yang[12], Weipeng Zhao[13], Yuee Teng[14], Tingjing Yao[15], Zhengkui Sun[16], Xiaoping Jin[17], Yina Diao[17], Gesha Liu[17], Junyou Ge[17]

ASCO 2025;Abstract 1019.

Phase II OptiTROP-Breast05: Responses

Antitumor Responses were observed regardless of PD-L1 expression.

	All patients (N = 41)	PD-L1 CPS <10[c] (N = 32)
ORR[a], n (%)	29 (**70.7**)	23 (**71.9**)
(95% CI)	(54.5, 83.9)	(53.3, 86.3)
CR[b], n (%)	2 (4.9)	1 (3.1)
PR, n (%)	27 (65.9)	22 (68.8)
Confirmed PR, n (%)	24 (58.5)	19 (59.4)
SD, n (%)	9 (22.0)	7 (21.9)
DCR, n (%)	38 (**92.7**)	30 (**93.8**)
(95% CI)	(80.1, 98.5)	(79.2, 99.2)



Data cutoff: Nov 18, 2024. **Median follow-up was 18.6 months.**
[a] Including confirmed PR/CR or response pending confirmation.
[b] All CRs were confirmed by investigators.
[c] PD-L1 expression was assessed at a central lab with PD-L1 IHC 22C3 pharmDx.
CR: complete response; PR: partial response; SD: stable disease.

ORR = objective response rate; DCR = disease control rate

Yin Y et al. ASCO 2025;Abstract 1019.

Contributing General Medical Oncologists

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Consensus or Controversy? Clinical Investigators Provide Perspectives on the Current and Future Care of Patients with Relapsed/Refractory Multiple Myeloma

Part 1 of a 2-Part CME/MOC-, NCPD- and ACPE-Accredited Satellite Symposium Series During the Society of Hematologic Oncology 2025 Annual Meeting

Thursday, September 4, 2025
6:42 PM – 7:42 PM CT

Faculty

Meletios-Athanasios (Thanos) C Dimopoulos, MD
Hans Lee, MD
Noopur Raje, MD

Moderator

Joseph Mikhael, MD, MEd

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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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