CASES FROM THE COMMUNITY
Investigators Discuss the Role of Antibody-Drug Conjugates in the Management of Triple-Negative and HR-Positive Metastatic Breast Cancer

Part 1 of a 3-Part CME Satellite Symposium Series

Tuesday, December 9, 2025
7:00 PM – 8:30 PM CT

Faculty

Javier Cortés, MD, PhD
Professor Peter Schmid, FRCP, MD, PhD
Rita Nanda, MD
Priyanka Sharma, MD

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

Faculty

Javier Cortés, MD, PhD
Head, IBCC International Breast Cancer Center
Barcelona, Spain

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

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

Priyanka Sharma, MD
Frank B Tyler Professor in Cancer Research
Division of Medical Oncology
Department of Internal Medicine
Co-Program Leader
Drug Discovery, Delivery and Experimental Therapeutics Program
The University of Kansas Cancer Center
Westwood, Kansas

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

RTP
RESEARCH
TO PRACTICE

Dr Cortés — Disclosures
Faculty

Consulting Agreements	AbbVie Inc, AstraZeneca Pharmaceuticals LP, AvenCell Europe GmbH, Bioasis Technologies Inc, Biocon, BioInvent, BioNTech SE, Bliss Biopharmaceutical (Hangzhou) Co Ltd, Boehringer Ingelheim Pharmaceuticals Inc, BridgeBio, Circle Pharma, Daiichi Sankyo Inc, Delcath Systems Inc, Ellipses Pharma, ExpreS2ion Biotechnologies, Gilead Sciences Inc, Hexagon Bio, HiberCell, Jazz Pharmaceuticals Inc, Leuko-Labs, Lilly, Menarini Group, MSD, pharmaand GmbH, Reveal Genomics, Roche Laboratories Inc, Scorpion Therapeutics, Seagen Inc, Zymeworks Inc
Contracted Research Funding to Institution	AstraZeneca Pharmaceuticals LP, Baxalta GMBH/Servier Affaires, Bayer HealthCare Pharmaceuticals, Eisai Inc, F Hoffmann-La Roche Ltd, Guardant Health, IQVIA, MSD, Pfizer Inc, PIQUR Therapeutics AG, Roche Laboratories Inc, Takeda Pharmaceuticals USA Inc
Patents	US 2019/0338368 A1, WO 2014/199294 A
Speakers Bureaus	AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Eisai Inc, Gilead Sciences Inc, Lilly, MSD, Novartis, Pfizer Inc, Roche Laboratories Inc, Stemline Therapeutics Inc, Zuellig Pharma
Stock OPTIONS — Private Companies	MAJ3 Capital SL
Travel, Accommodation, Expenses	AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Eisai Inc, Gilead Sciences Inc, MSD, Novartis, Pfizer Inc, Roche Laboratories Inc, Stemline Therapeutics Inc
Nonrelevant Financial Relationships	Leuko-Labs (stock options, relative), Queen Mary University of London

RTP
RESEARCH
TO PRACTICE

Dr Nanda — Disclosures
Faculty

Advisory Committees	Arvinas, AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Exact Sciences Corporation, GE Healthcare, Gilead Sciences Inc, Guardant Health, Lilly, Mabwell Therapeutics Inc, Merck, Moderna, Novartis, Pfizer Inc, Stemline Therapeutics Inc, Summit Therapeutics
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

RTP
RESEARCH
TO PRACTICE

Prof Schmid — Disclosures
Faculty

Advisory Committees and Consulting Agreements	AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, Celgene Corporation, Eisai Inc, Merck, Novartis, Pfizer Inc, Puma Biotechnology Inc, Roche Laboratories Inc
Contracted Research	Astellas, AstraZeneca Pharmaceuticals LP, Genentech, a member of the Roche Group, Medivation Inc, a Pfizer Company, Merck, Novartis, OncoGenex Pharmaceuticals Inc, Roche Laboratories Inc

RTP
RESEARCH
TO PRACTICE

Dr Sharma — Disclosures
Faculty

Advisory Committees	AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Gilead Sciences Inc, Menarini Group, Merck, Novartis, Pfizer Inc, Stemline Therapeutics Inc
Contracted Research	Bristol Myers Squibb, Gilead Sciences Inc, Novartis
Data and Safety Monitoring Boards/Committees	Jazz Pharmaceuticals Inc

RTP
RESEARCH
TO PRACTICE

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: Aadi Bioscience, AbbVie Inc, ADC Therapeutics, Agendia Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Arvinas, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeOne, Biotheranostics Inc, A Hologic Company, Black Diamond Therapeutics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Celcuity, Clovis Oncology, Coherus BioSciences, Corcept Therapeutics Inc, CTI BioPharma, a Sobi Company, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, Exact Sciences Corporation, Exelixis Inc, Genentech, a member of the Roche Group, Genmab US Inc, Geron Corporation, Gilead Sciences Inc, GSK, Helsinn Therapeutics (US) Inc, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Jazz Pharmaceuticals Inc, Johnson & Johnson, Karyopharm Therapeutics, Kite, A Gilead Company, Kura Oncology, Legend Biotech, Lilly, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Mural Oncology Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Nuvalent, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Rigel Pharmaceuticals Inc, R-Pharm US, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Sumitomo Pharma America, Syndax Pharmaceuticals, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, and Tesaro, A GSK Company.

RTP
RESEARCH
TO PRACTICE

Commercial Support

This activity is supported by educational grants from Gilead Sciences Inc and Helsinn Therapeutics (US) Inc.

Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

RTP
RESEARCH
TO PRACTICE

CASES FROM THE COMMUNITY
Investigators Discuss the Optimal Management of HER2-Positive Breast Cancer

Part 2 of a 3-Part CME Satellite Symposium Series

Wednesday, December 10, 2025

7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Professor Giuseppe Curigliano, MD, PhD
Nadia Harbeck, MD, PhD
Ian E Krop, MD, PhD
Nancy U Lin, MD
Joyce O'Shaughnessy, MD

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

CASES FROM THE COMMUNITY
Investigators Discuss the Optimal Role of Endocrine-Based and Other Strategies in the Management of HR-Positive Breast Cancer

Part 3 of a 3-Part CME Satellite Symposium Series

Thursday, December 11, 2025

7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Angela DeMichele, MD, MSCE
Komal Jhaveri, MD, FACP, FASCO
Erica Mayer, MD, MPH, FASCO
Hope S Rugo, MD
Seth Wander, MD, PhD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Cases from the Community: Investigators Discuss Available Research Guiding the Management of Relapsed/Refractory Multiple Myeloma — What Happened at ASH 2025?

A CME/MOC-Accredited Live Webinar

Monday, December 15, 2025

5:00 PM – 6:00 PM ET

Faculty

Sagar Lonial, MD, FACP, FASCO

María-Victoria Mateos, MD, PhD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Practical Perspectives on the Current and Future Management of Immune Thrombocytopenia — What Happened at ASH 2025?

A CME/MOC-Accredited Live Webinar

Tuesday, December 16, 2025

5:00 PM – 6:30 PM ET

Faculty

Hanny Al-Samkari, MD
Cindy Neunert, MD, MSCS
Francesco Zaja, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Practical Perspectives on the Current Role of Bispecific Antibodies in the Management of Lymphoma — What Happened at ASH 2025?

A CME/MOC-Accredited Live Webinar

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

Faculty

Michael Dickinson, MD
Laurie H Sehn, MD, MPH

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Expert Second Opinion: Investigators Discuss the Optimal Management of Gastrointestinal Cancers

A CME Symposium Series Held in Conjunction with the 2026 ASCO® Gastrointestinal Cancers Symposium

HER2-Positive Gastrointestinal Cancers

Thursday, January 8, 2026

7:15 PM – 8:45 PM PT
(10:15 PM – 11:45 PM ET)

Advanced Gastroesophageal Cancers

Friday, January 9, 2026

6:00 PM – 8:00 PM PT
(9:00 PM – 11:00 PM ET)

RTP
RESEARCH TO PRACTICE

Grand Rounds

CME/MOC-Accredited Interactive Series

Through 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

Host a 1-hour session at your institution:
Email Meetings@ResearchToPractice.com
or call (800) 233-6153

RTP
RESEARCH
TO PRACTICE

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

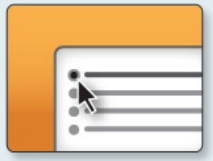
The Ritz-Carlton Orlando, Grande Lakes | Orlando, Florida

Moderated by Neil Love, MD

Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.



Answer Survey Questions: Complete the pre- and postmeeting surveys.

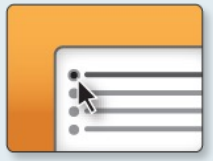
Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

RTP RESEARCH TO PRACTICE

Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.



Answer Survey Questions: Complete the pre- and postmeeting surveys.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get CME Credit: A credit link will be provided in the chat room at the conclusion of the program.

RTP
RESEARCH
TO PRACTICE

About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based program.
  An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

RTP
RESEARCH
TO PRACTICE

RTP Content Distribution Platform

250 Hours Annually		
Interviews	Panels	Meetings
110 hours	45 hours	95 hours

Podcast

Website/ App

Email

Streaming Platforms

Social Media

QR Code Cards

RTP Playlist with Neil Love, MD

BREAST CANCER

Dr Hope Rugo: Interview (28 min)

SMALL CELL LUNG CANCER

Drs Stephen Liu and Charles Rudin: Cases (58 min)

GASTROESOPHAGEAL CANCER

Drs Geoffrey Ku and Zev Wainberg: Cases (61 min)

PROSTATE CANCER

Drs Emmanuel Antonarakis and Karim Fizazi: Year in Review (60 min)

ENDOMETRIAL AND OVARIAN CANCER

Dr Shannon Westin: Interview (52 min)

NEUROENDOCRINE TUMORS

Drs Simron Singh and Jonathan Strosberg: Meeting (50 min)

NON-HODGKIN LYMPHOMA

Drs Jeremy Abramson, Joshua Brody, Christopher Flowers, Ann LaCasce and Tycel Phillips: Meeting, cases (59 min)

CHRONIC LYMPHOCYTIC LEUKEMIA

Drs Jennifer Brown and Paolo Ghia: Year in Review (59 min)

ACUTE MYELOID LEUKEMIA

Dr Jorge Cortes: Interview (43 min)

MULTIPLE MYELOMA

Drs Natalie Callander and Sagar Lonial: Patient videos (59 min)

IMMUNE THROMBOCYTOPENIA

Drs Hanny Al-Samkari, James Bussel and Nichola Cooper: Think Tank (117 min)

OCULAR TOXICITES IN ONCOLOGY

Dr Neel Pasricha: Interview (54 min)

Feedback (Please!)
DrNeilLove@ResearchToPractice.com

RTP Playlist with Neil Love, MD

Webinar for patients and families on relapsed multiple myeloma with Drs Natalie Callander and Sagar Lonial.

Relapsed Multiple Myeloma: Where We Were, Where We Are (4 min)

Common Questions from the Beginning (5 min)

Choosing Treatment Options (4 min)

Clinical Research Trials (6 min)

Neuropathy (5 min)

Chimeric Antigen Receptor (CAR) T-Cell Therapy (6 min)

Bispecific Antibodies (8 min)

Antibody-Drug Conjugates: Belantamab Mafadotin (8 min)

Interacting with the Oncology Team (5 min)

Other Questions (4 min)

Recording of Entire Webinar (62 min)

Feedback (Please!)
DrNeilLove@ResearchToPractice.com

ASH and SABCS RTP Video Participants

ASH and SABCS RTP Participating Faculty

RTP
RESEARCH
TO PRACTICE

CASES FROM THE COMMUNITY
Investigators Discuss the Role of Antibody-Drug Conjugates in the Management of Triple-Negative and HR-Positive Metastatic Breast Cancer

Part 1 of a 3-Part CME Satellite Symposium Series

Tuesday, December 9, 2025
7:00 PM – 8:30 PM CT

Faculty

Javier Cortés, MD, PhD
Professor Peter Schmid, FRCP, MD, PhD
Rita Nanda, MD
Priyanka Sharma, MD

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

Contributing General Medical Oncologists

Laila Agrawal, MD
Norton Cancer Institute
Louisville, Kentucky

Justin Favaro, MD, PhD
Oncology Specialists of Charlotte
Charlotte, North Carolina

Alan B Astrow, MD
Weill Cornell Medicine
Brooklyn, New York

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

Gigi Chen, MD
John Muir Health Cancer
Medical Group
Walnut Creek, California

Atif M Hussein, MD, MMM
Florida International University
Herbert Wertheim College of Medicine
Hollywood, Florida

RTP
RESEARCH
TO PRACTICE

Contributing General Medical Oncologists (Continued)

Yanjun Ma, MD, PhD
Tennessee Oncology
Murfreesboro, Tennessee

Jennifer Yannucci, MD
Low Country Cancer Care
Savannah, Georgia

Agenda

Module 1: Previously Untreated Metastatic Triple-Negative Breast Cancer (mTNBC) — Prof Schmid

Module 2: Integrating Antibody-Drug Conjugates (ADCs) into the Management of Endocrine-Resistant Hormone Receptor-Positive Metastatic Breast Cancer (mBC) — Dr Sharma

Module 3: Selection and Sequencing of Therapy for Relapsed/Refractory mTNBC — Dr Nanda

Module 4: Tolerability and Other Practical Considerations with ADCs and Other Cytotoxic Agents for mBC — Dr Cortés

Agenda

Module 1: Previously Untreated Metastatic Triple-Negative Breast Cancer (mTNBC) — Prof Schmid

Module 2: Integrating Antibody-Drug Conjugates (ADCs) into the Management of Endocrine-Resistant Hormone Receptor-Positive Metastatic Breast Cancer (mBC) — Dr Sharma

Module 3: Selection and Sequencing of Therapy for Relapsed/Refractory mTNBC — Dr Nanda

Module 4: Tolerability and Other Practical Considerations with ADCs and Other Cytotoxic Agents for mBC — Dr Cortés

Case Presentation: 82-year-old woman s/p MI, CVA, and active smoker with multiple comorbidities and TNBC develops bone-only metastases 4 months after declining capecitabine for post-neoadjuvant residual disease; PD-L1 assay is pending

Dr Justin Favaro (Charlotte, North Carolina)

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

Does active smoking put this patient at higher risk for pneumonitis with antibody-drug conjugates and/or immunotherapy?

Would you recommend first-line sacituzumab govitecan/pembrolizumab if this patient's tumor is PD-L1-positive? Would you reduce the starting dose of sacituzumab govitecan?

If this patient's tumor were PD-L1-negative, how would you decide between first-line sacituzumab govitecan and datopotamab deruxtecan (Dato-DXd)?

Case Presentation: 74-year-old woman has recurrent ER-negative, HER2-low (IHC 1+), PIK3CA-mutated, PD-L1-positive mBC 18 months after receiving 3 cycles of neoadjuvant paclitaxel/carboplatin/pembrolizumab, which was discontinued because of rash, diverticular abscess and DVT

Dr Alan Astrow (Brooklyn, New York)

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

How would you think through the use of first-line sacituzumab govitecan/pembrolizumab for patients who have already received pembrolizumab in the (neo)adjuvant setting?

For patients with diarrhea while receiving sacituzumab govitecan/pembrolizumab, how would you determine which agent is the cause?

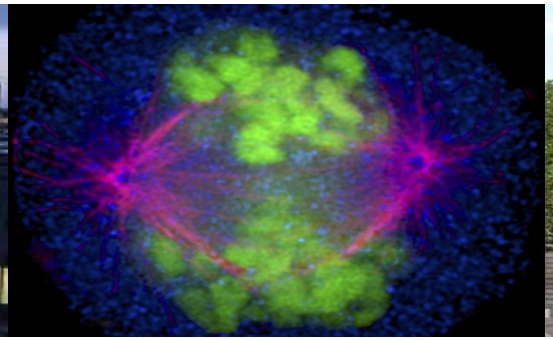
For a patient with triple-negative, PIK3CA-mutated mBC, is there any role for capivasertib?

First line treatment of metastatic Triple-negative breast cancer

Professor Peter Schmid, MD PhD FRCP

Lead, Centre for Experimental Cancer Medicine

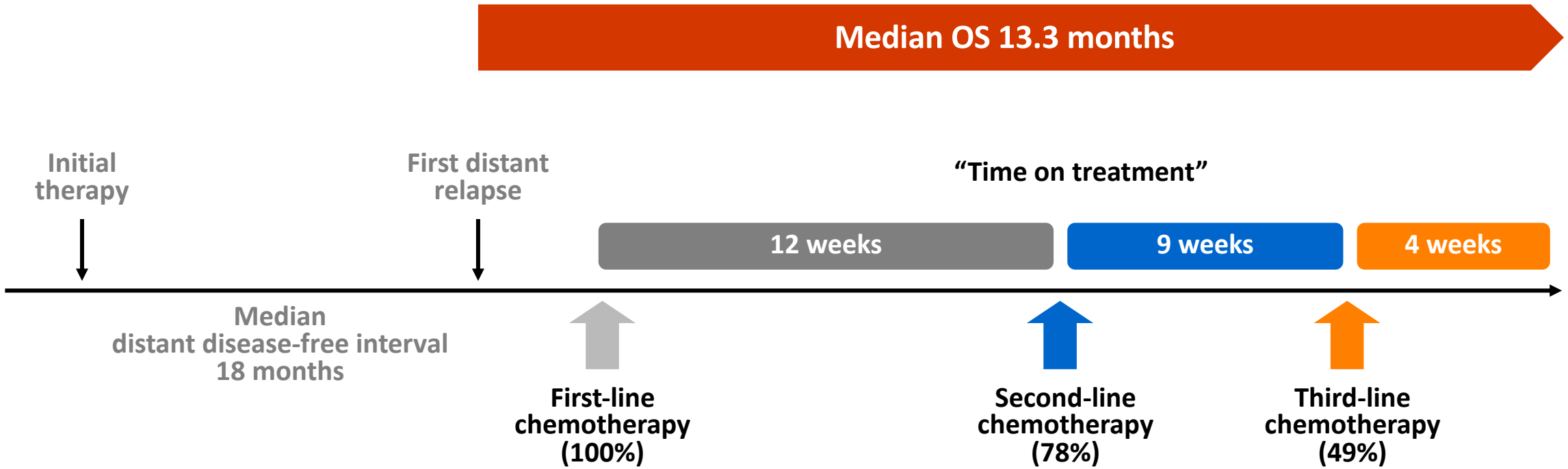
Barts Cancer Institute, St Bartholomew's Hospital
Queen Mary University of London


Queen Mary University of London

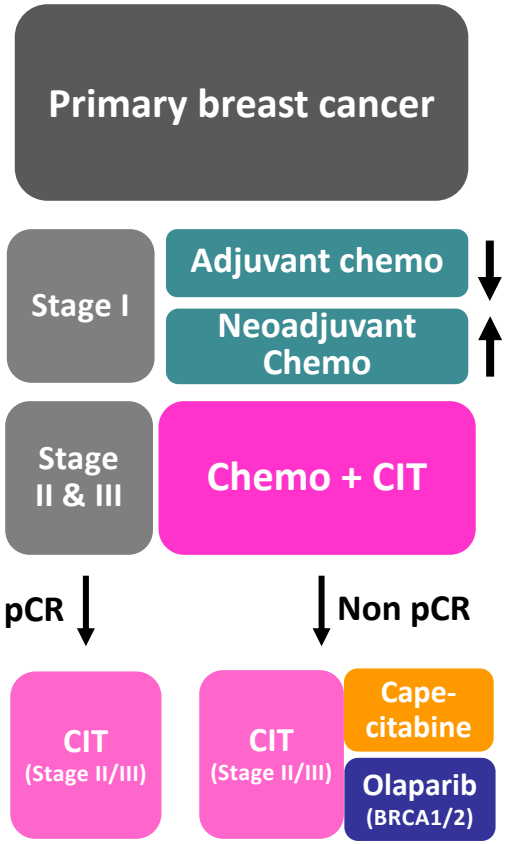
Barts Health NHS Trust

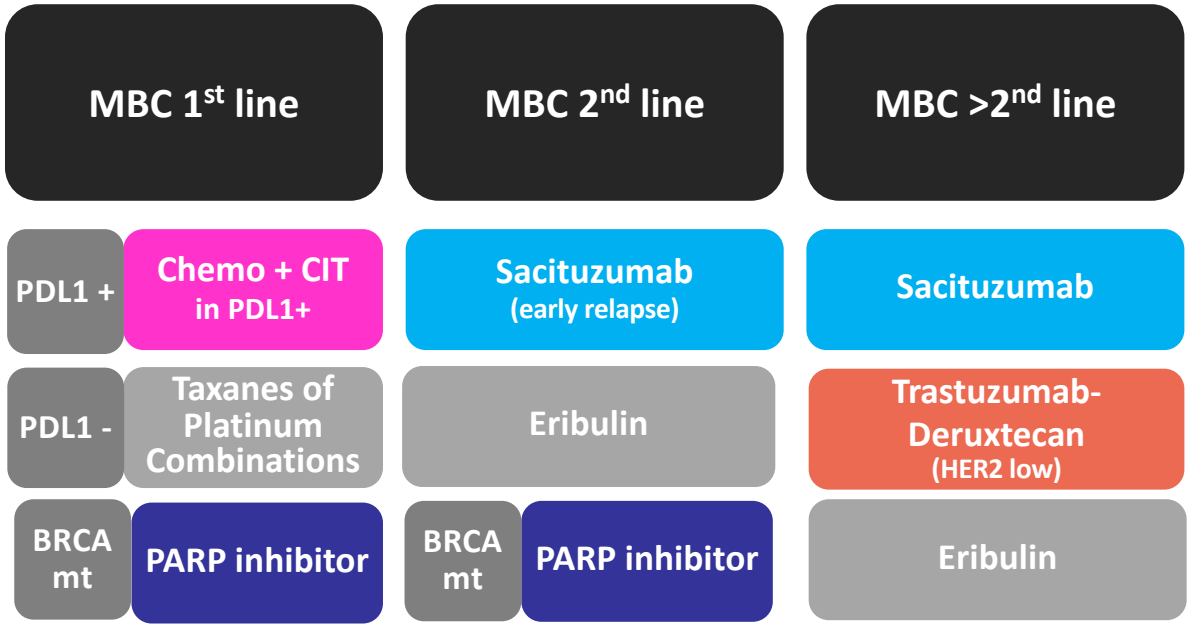
Poor outcome of metastatic TNBC



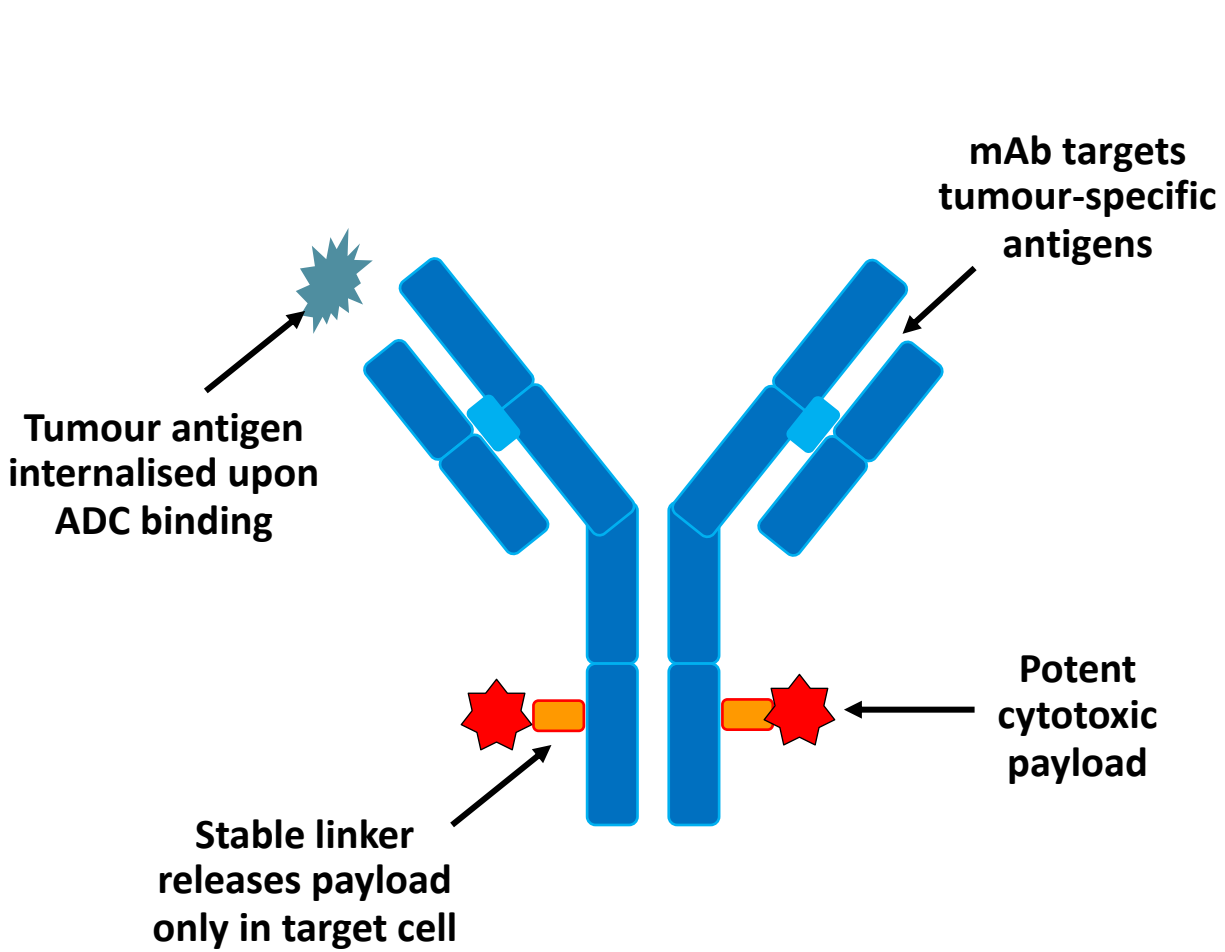
Kassam, et al. Clin Breast Cancer 2009

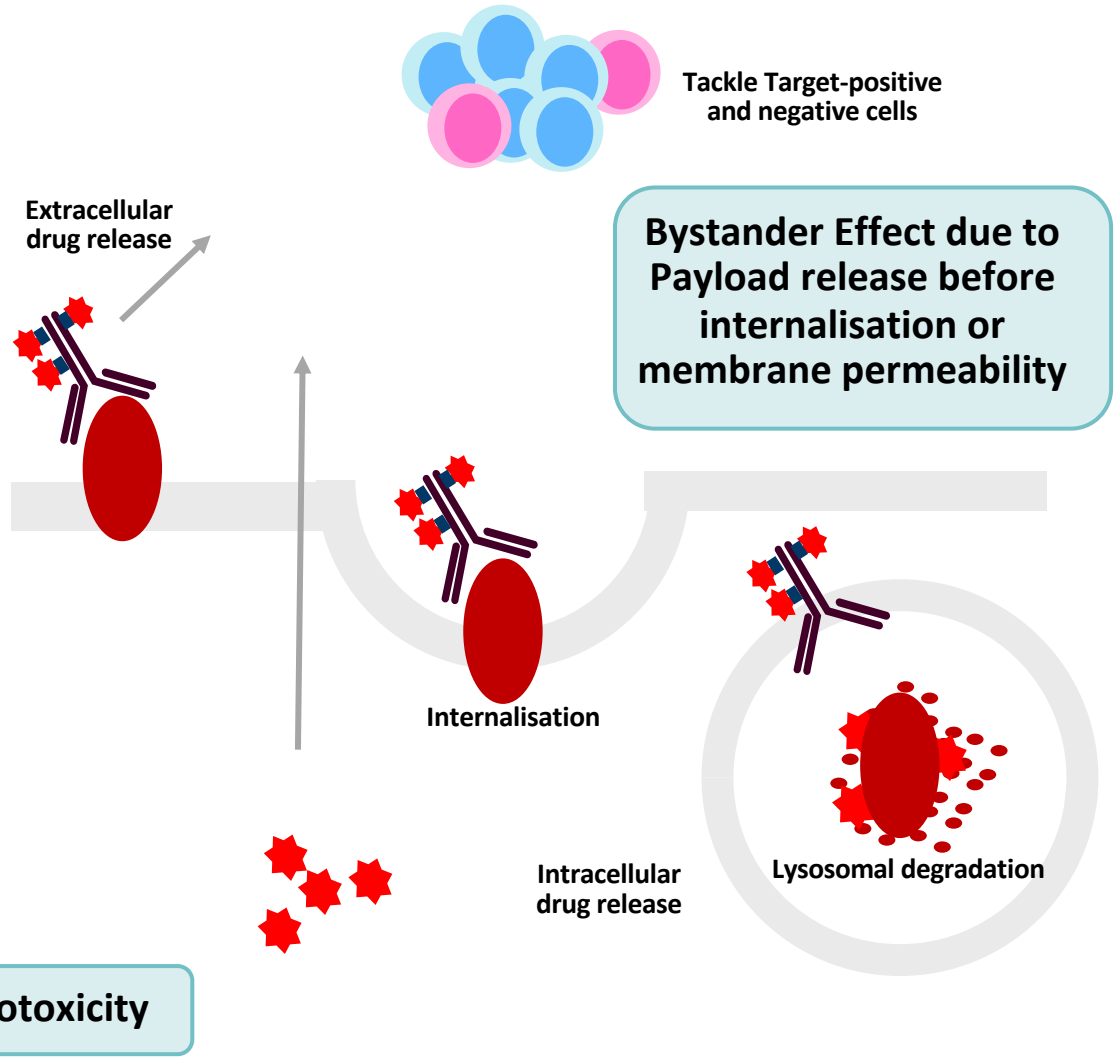
Triple Negative Breast Cancer – Management in 2024





New antibody–drug conjugates

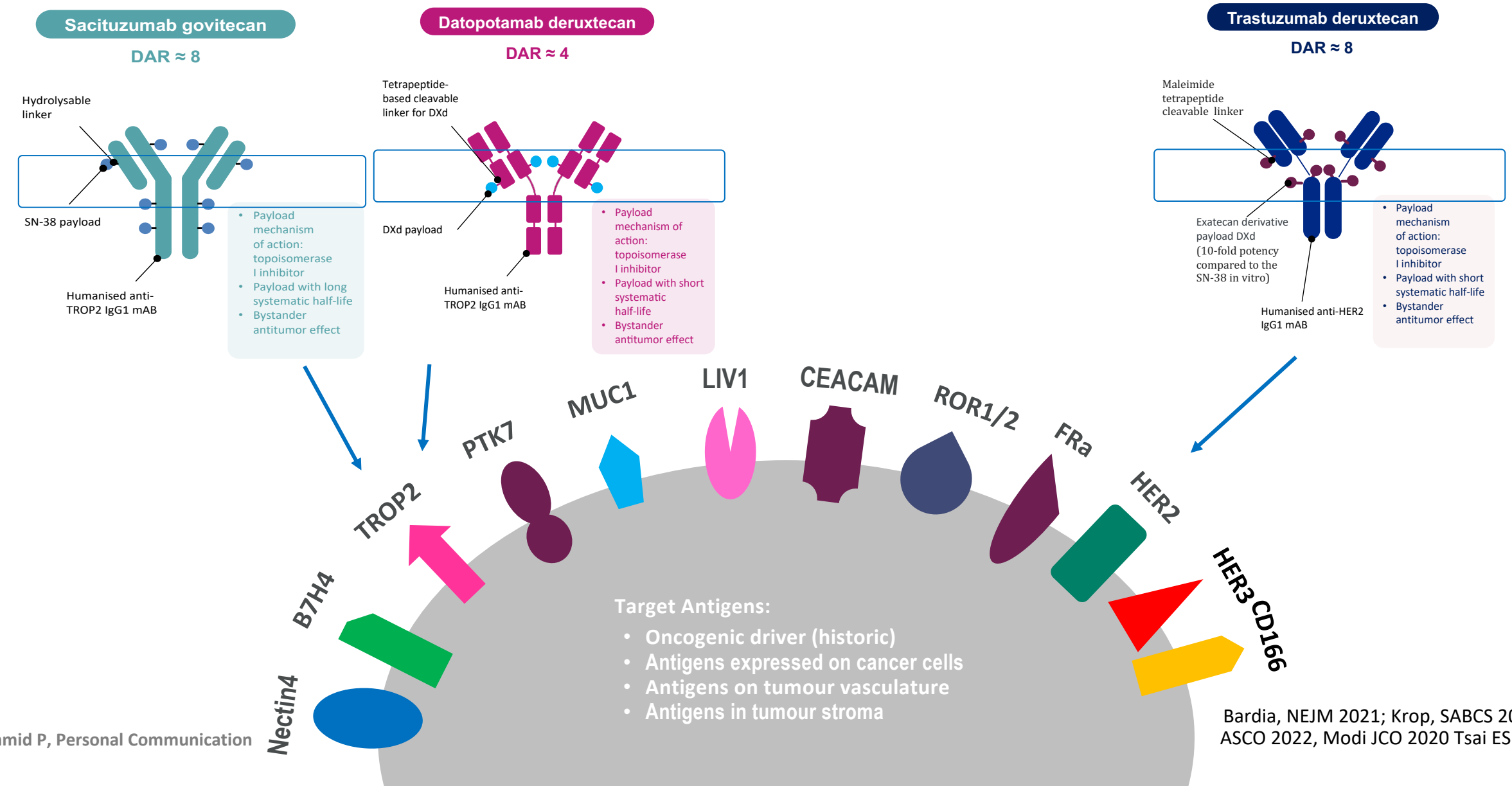




Schmid P, Personal Communication

ADC, antibody–drug conjugates; DCR, disease control rate
Modi S, et al. Presented at SABCS 2017. Abstract PD3-07.

Targets for Antibody-Drug Conjugates in Breast Cancer



Schmid P, Personal Communication

Bardia, NEJM 2021; Krop, SABCS 2021, Krop ASCO 2022, Modi JCO 2020 Tsai ESMO 2021

Sacituzumab Govitecan plus Pembro in PDL1+ 1L TNBC

ASCENT-04 Trial[1]

Study Population:

- US/Canada/EU: 38%
- DFI: de novo mTNBC 34%, 6-12m 18%, >12m 48%
- PDL1 positive: 100%
- Brain mets 4%
- Prior ICI 4%

- Metastatic TNBC
- No prior chemotherapy
- PDL1 positive CPS10+
- DFI >6 months
- Treated & stable brain mets allowed

Stratification factors:

- Region: US/Canada/Europe vs Rest
- DFI: de novo vs 6-12m vs >12m

R 1:1

Median follow-up 14.0 months

n = 221

Sacituzumab-Govitecan + Pembrolizumab

n = 222

Chemo + Pembrolizumab
Paclitaxel, Nab-Paclitaxel
Gemcitabine/Carboplatin

Taxane 55%, Carboplatin 45%

Primary endpoint: PFS

Key Secondary endpoint: OS, ORR, DOR, Safety

Eligible patients offered crossover to 2L SG provided through the study

81% of pts with subsequent Tx received SG

Tolaney S, et al. ASCO 2025

Sacituzumab Govitecan plus Pembro in PDL1+ 1L TNBC

ASCENT-04 Trial[1]

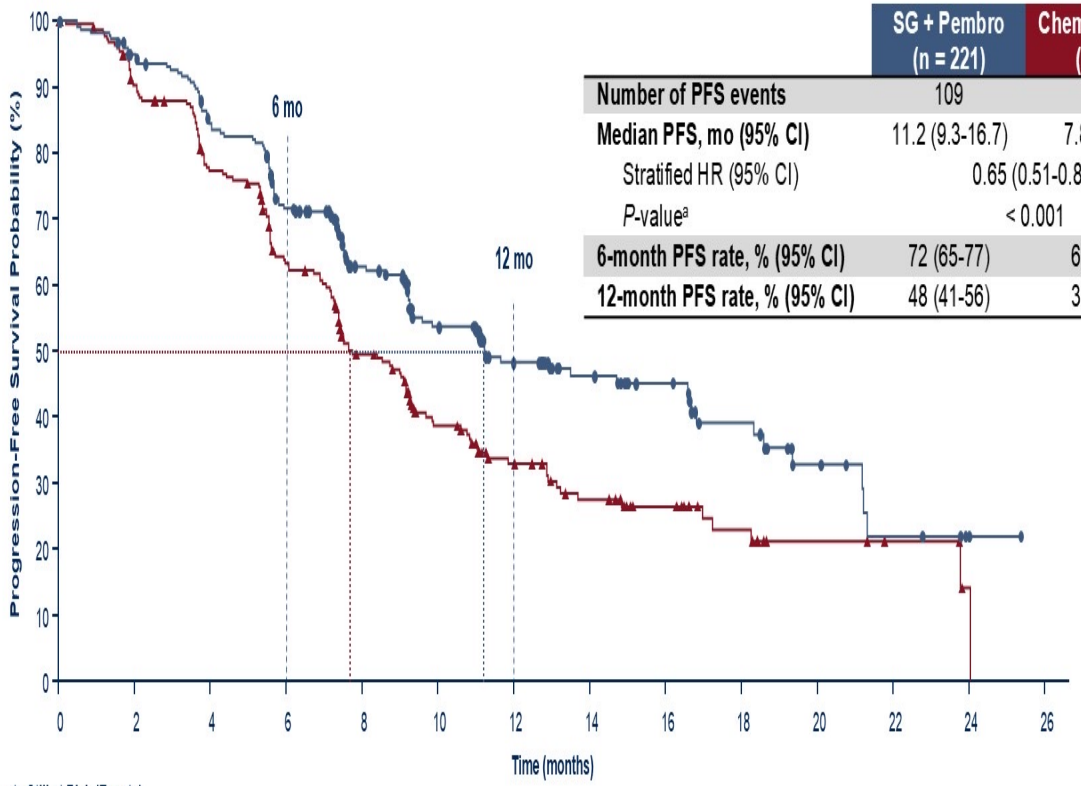
- Metastatic TNBC
- No prior chemotherapy
- PDL1 positive CPS10+
- DFI >6 months
- Treated & stable brain mets allowed

R 1:1

- Sacituzumab-Govitecan + Pembrolizumab
- Chemo + Pembrolizumab
  Paclitaxel, Nab-Paclitaxel
  Gemcitabine/Carboplatin

Stratification factors:
- Region: US/Canada/Europe vs Rest
- DFI: de novo vs 6-12m vs >12m

Progression-free Survival



	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)

	SG + Pembro n	SG + Pembro Median PFS, mo (95% CI)	Chemo + Pembro n	Chemo + Pembro Median PFS, mo (95% CI)	Unstratified HR (95% CI)
ITT population	221	**11.2** (9.3-16.7)	222	**7.8** (7.3-9.3)	0.66 (0.51-0.85)
Age group					
< 65 yr	163	**11.3** (9.3-16.8)	165	**7.5** (7.0-9.2)	0.61 (0.45-0.82)
≥ 65 yr	58	**11.1** (7.5-NR)	57	**9.3** (7.3-13.2)	0.85 (0.52-1.39)
ECOG PS					
0	156	**12.9** (9.3-16.8)	154	**8.7** (7.3-9.9)	0.65 (0.48-0.88)
≥ 1	65	**9.2** (7.5-18.3)	67	**7.5** (5.6-9.3)	0.66 (0.43-1.03)
Geographic region					
US/Canada/Western Europe	85	**11.7** (7.5-19.4)	85	**7.4** (5.7-9.9)	0.65 (0.43-0.98)
Rest of the world	136	**11.2** (9.3-16.7)	137	**8.4** (7.4-9.3)	0.66 (0.48-0.91)
Curative treatment-free interval					
De novo	75	**8.1** (7.3-18.6)	75	**7.7** (6.1-11.9)	0.89 (0.59-1.34)
Recurrent 6-12 mo	40	**9.9** (5.7-16.8)	40	**7.2** (4.4-9.1)	0.62 (0.36-1.08)
Recurrent > 12 mo	106	**16.6** (11.0-NR)	107	**8.7** (7.3-10.8)	0.52 (0.35-0.76)
Prior (neo)adjuvant anti-PD-(L)1 therapy					
Yes	9	**7.5** (0.9-NR)	11	**6.6** (2.1-NR)	1.08 (0.31-3.75)
No	212	**11.7** (9.3-16.8)	211	**7.8** (7.4-9.3)	0.65 (0.50-0.84)
Chemo selected prior to randomization					
Taxane	116	**11.1** (8.6-16.7)	114	**9.2** (7.2-12.9)	0.82 (0.58-1.17)
Gemcitabine/Carboplatin	105	**11.3** (9.2-21.2)	108	**7.4** (6.9-9.0)	0.52 (0.36-0.75)

Tolaney S, et al. ASCO 2025

Sacituzumab Govitecan plus Pembro in PDL1+ 1L TNBC

- Metastatic TNBC
- No prior chemotherapy
- PDL1 positive CPS10+
- DFI >6 months
- Treated & stable brain mets allowed

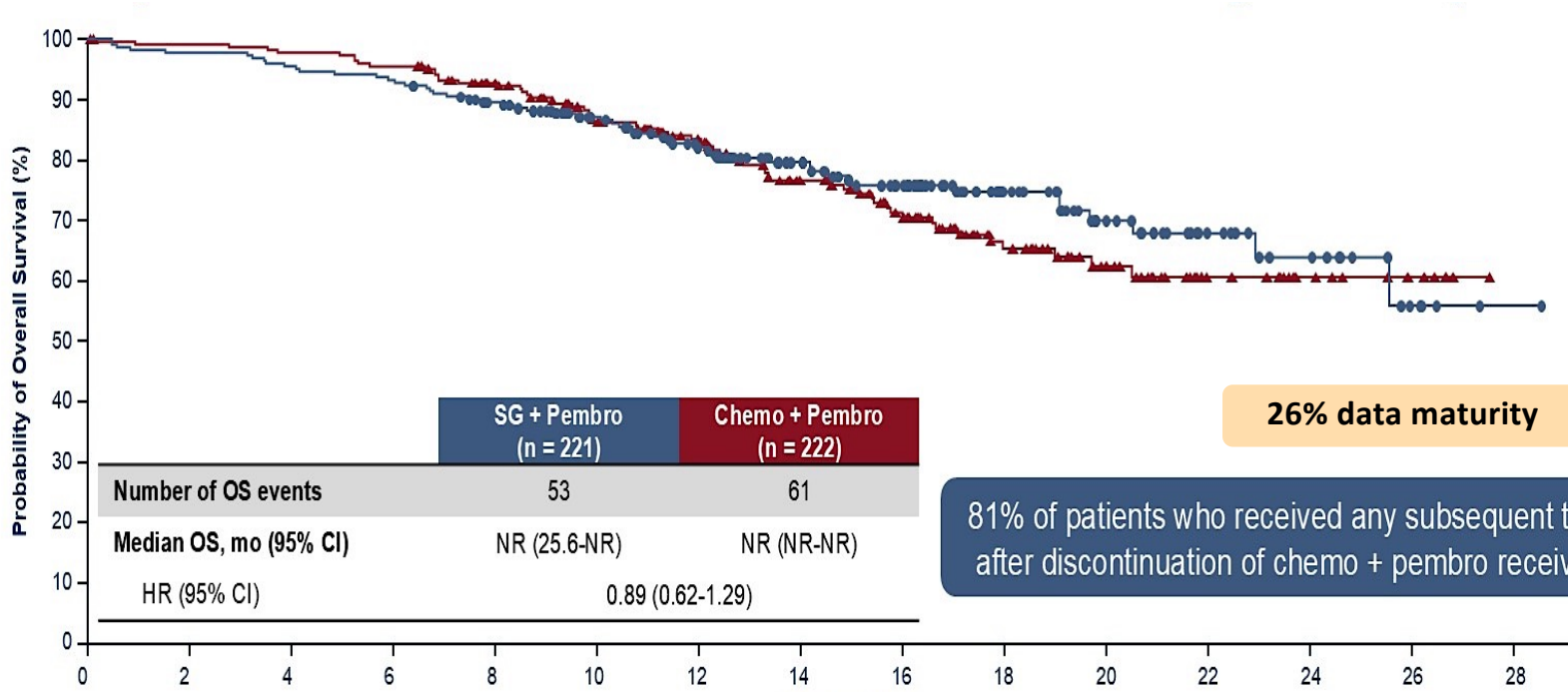
R 1:1

Sacituzumab-Govitecan + Pembrolizumab

Chemo + Pembrolizumab
Paclitaxel, Nab-Paclitaxel
Gemcitabine/Carboplatin

Stratification factors:
- Region: US/Canada/Europe vs Rest
- DFI: de novo vs 6-12m vs >12m

Descriptive Overall Survival Analysis



	SG + Pembro (n = 221)	Chemo + Pembro (n = 222)
Number of OS events	53	61
Median OS, mo (95% CI)	NR (25.6-NR)	NR (NR-NR)
HR (95% CI)	0.89 (0.62-1.29)	

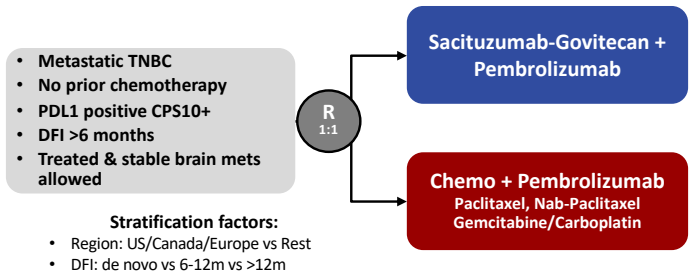
26% data maturity

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

No. of Patients Still at Risk (Events)																
SG + Pembro	221 (0)	216 (5)	211 (10)	206 (15)	190 (23)	162 (28)	138 (37)	111 (41)	88 (46)	55 (47)	36 (50)	21 (51)	14 (52)	5 (53)	1 (53)	0 (53)
Chemo + Pembro	222 (0)	218 (2)	215 (5)	210 (10)	193 (16)	166 (29)	142 (34)	111 (45)	87 (53)	56 (58)	38 (60)	19 (61)	11 (61)	6 (61)	0 (61)	

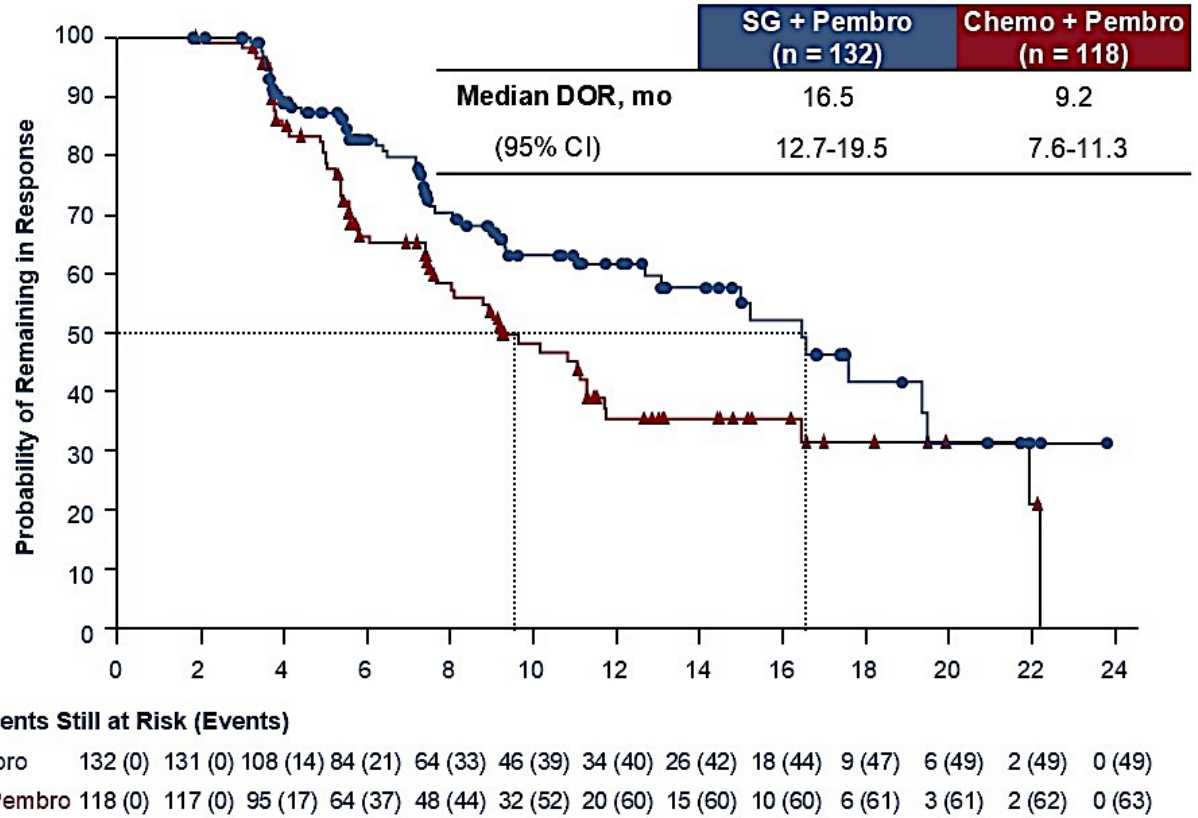
Tolaney S, et al. ASCO 2025

Sacituzumab Govitecan plus Pembro in PDL1+ 1L TNBC



Objective Response and Duration of Response

Variable	SG + Pembro (n = 221)	Chemo + Pembro (n = 222)
Objective response rate[a] (95% CI), %	60 (52.9-66.3)	53 (46.4-59.9)
Stratified odds ratio (95% CI)	1.3 (0.9-1.9)	
Best overall response, n (%)		
Complete response	28 (13)	18 (8)
Partial response	104 (47)	100 (45)
Stable disease	70 (32)	70 (32)
Stable disease ≥ 6 months	23 (10)	29 (13)
Progressive disease	9 (4)	26 (12)
Not evaluable	10 (5)	8 (4)
Time to response,[b] median (range), months	1.9 (1.0-9.3)	1.9 (1.1-11.4)



Tolaney S, et al. ASCO 2025

Exposure and Safety Summary

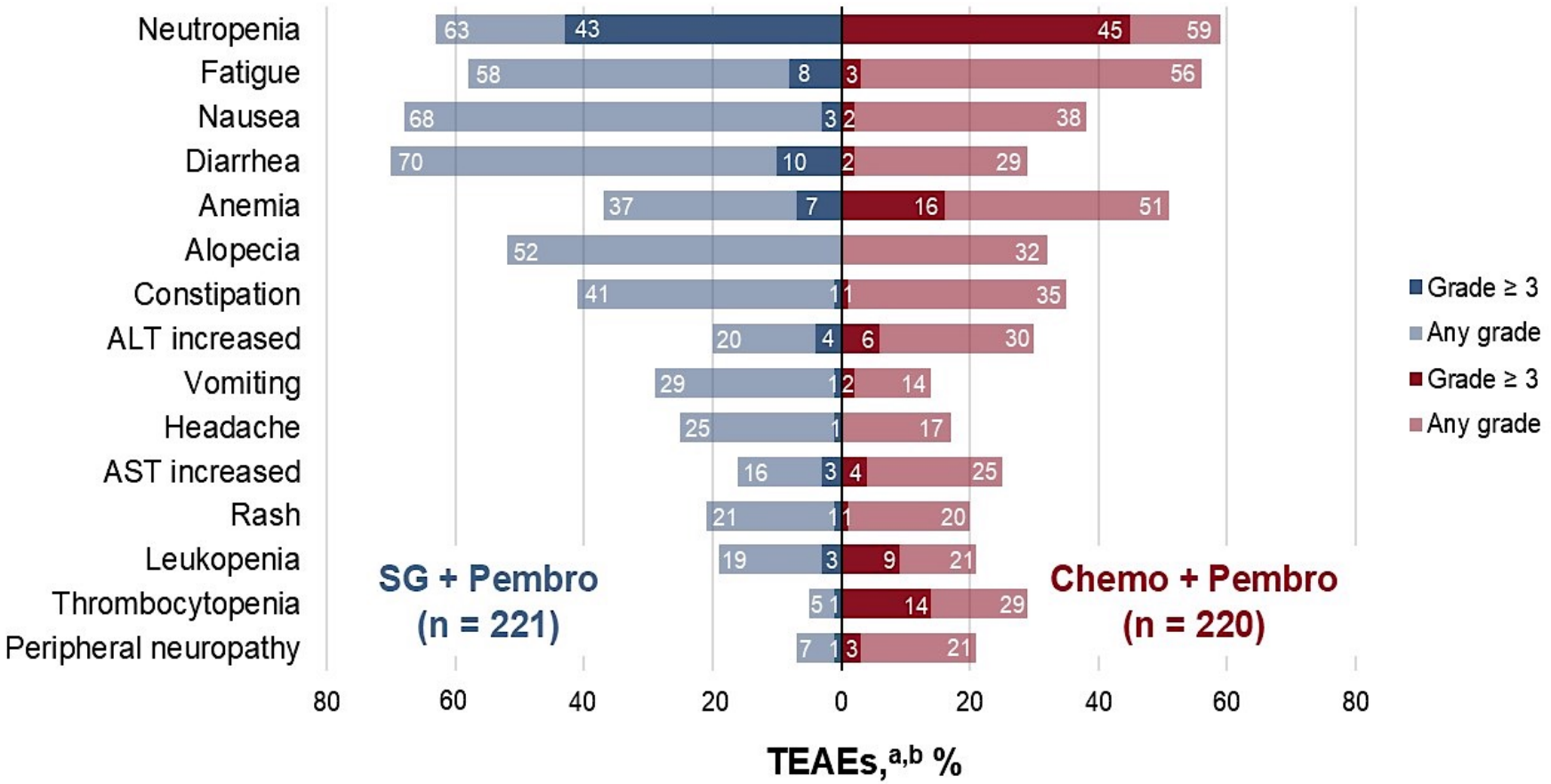
ITT population	SG + Pembro (n = 221)		Chemo + Pembro (n = 222)	
Treatment component	**SG**	**Pembro**	**Chemo**	**Pembro**
All treated patients, n	221	221	220	220
Median duration of treatment, mo (range)	8.9 (0.0-27.1)	8.5 (0.0-26.8)	6.2 (0.0-26.3)	6.4 (0.0-25.6)

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

Tolaney S, et al. ASCO 2025

Safety Summary: Most Common Adverse Events



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

Tolaney S, et al. ASCO 2025

Datopotamab-Deruxtecan (Dato-DXd) in 1L TNBC

TROPION-Breast02 Trial[1]

Study Population:

- US/Canada/EU: 37%
- DFI: de novo mTNBC 34%, 0-6m 15%, 0-12m 21%, >12m 45%
- PDL1 high: 10%
- Brain mets 10%
- Prior Taxanes 57%, Capecitabine 27%, Platinum 16%, ICI 5%

- Metastatic TNBC
- No prior chemotherapy
- Immunotherapy not an option
- Any DFI allowed
- Stable brain mets allowed

Stratification factors:

- PDL1 (positive vs negative)
- Region: US/Canada/Europe vs Rest
- DFI: de novo vs 0-12m vs >12m

R 1:1

Median follow-up 27.5 months

n = 323

Dato-DXd
6 mg/kg Q3W

n = 321

TPC
Paclitaxel, Nab-Paclitaxel
(if DFI >12/12),
Eribulin, Carboplatin, Capecitabine
(if taxane and DFI <6/12)

Taxane 82%, Carboplatin 4%, Eribulin 12%, Capecitabine 2%

Dual Primary endpoint: PFS, OS

Key Secondary endpoint: PFS (investigator), ORR, DOR, Safety

No crossover offered. Use of 2L SG NOT provided through the study

42% of pts with subsequent Tx received SG

30% of all TPC pts with SG (72% had 2L+)

PD-L1+ (capped at 10%) eligible if relapsed after PD-(L)1 inhibitor for eBC, or ineligible for PD-(L)1 inhibitor due to comorbidity, or No regulatory access to PD-(L)1 inhibitor

Dent R, et al. ESMO 2025

Datopotamab-Deruxtecan (Dato-DXd) in 1L TNBC

TROPION-Breast02 Trial[1]

- Metastatic TNBC
- No prior chemotherapy
- Immunotherapy not an option
- Any DFI allowed
- Stable brain mets allowed

R 1:1

n = 323 → **Dato-DXd** 6 mg/kg Q3W

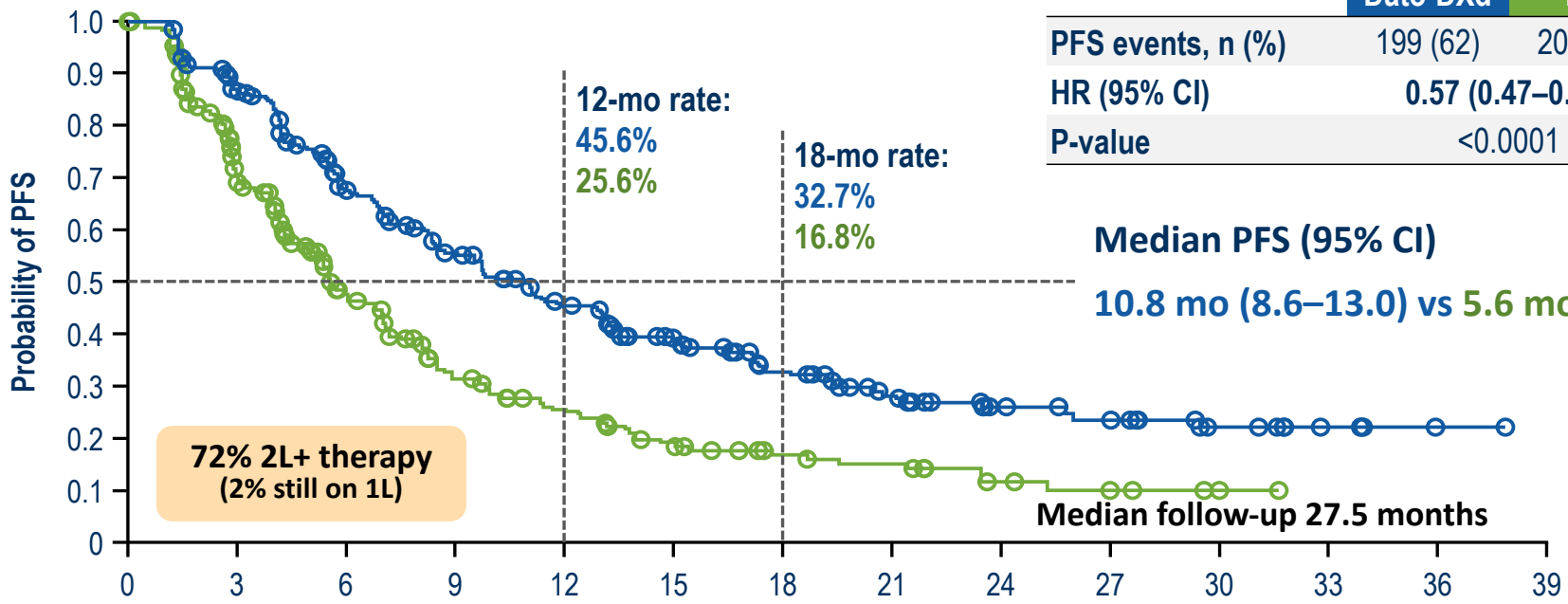
n = 321 → **TPC** Paclitaxel, Nab-Paclitaxel (if DFI >12/12), Eribulin, Carboplatin, Capecitabine (if taxane and DFI <6/12)

Stratification factors:

- PDL1 (positive vs negative)
- Region: US/Canada/Europe vs Rest
- DFI: de novo vs 0-12m vs >12m

Progression-free Survival

	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) vs 5.6 mo (5.0–7.0)

Number at risk													
Dato-DXd 323	265	191	150	116	84	56	41	24	20	10	5	1	0
ICC 321	191	107	64	46	29	19	16	8	6	1	0	0	0

Dent R, et al. ESMO 2025

Datopotamab-Deruxtecan (Dato-DXd) in 1L TNBC

TROPION-Breast02 Trial[1]

- Metastatic TNBC
- No prior chemotherapy
- Immunotherapy not an option
- Any DFI allowed
- Stable brain mets allowed

R 1:1

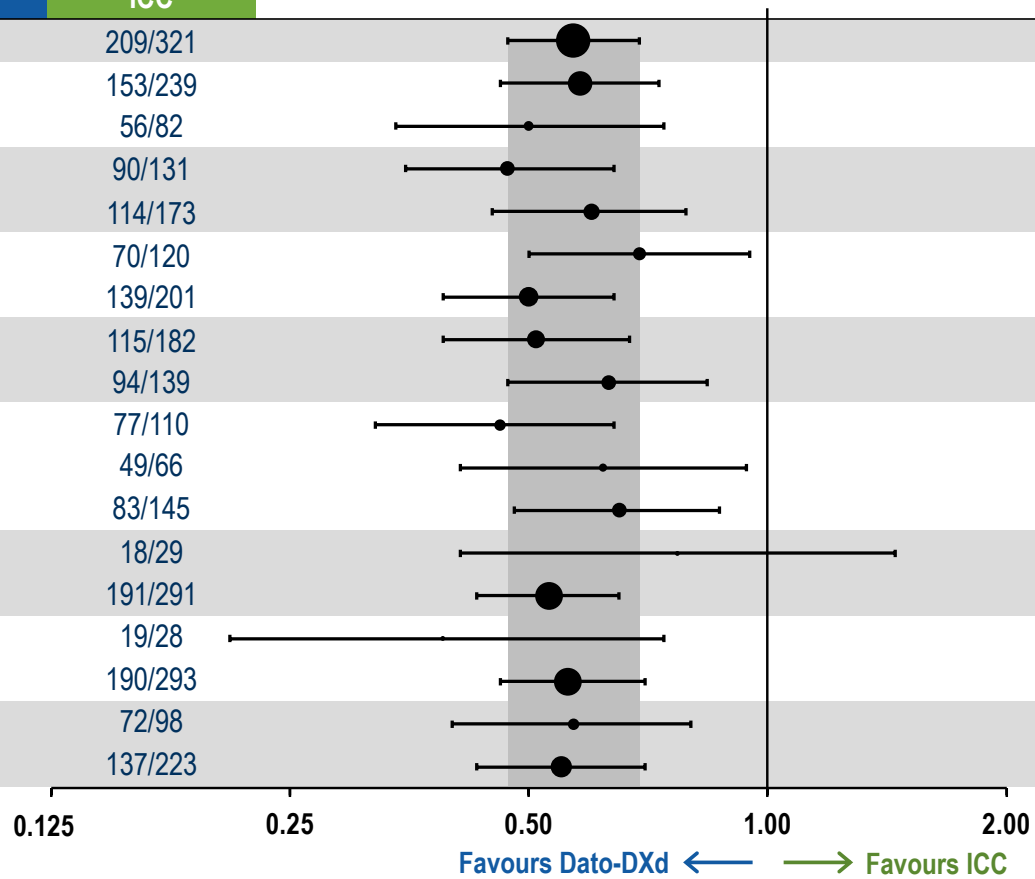
n = 323 → **Dato-DXd** 6 mg/kg Q3W

n = 321 → **TPC** Paclitaxel, Nab-Paclitaxel (if DFI >12/12), Eribulin, Carboplatin, Capecitabine (if taxane and DFI <6/12)

Stratification factors:
- PDL1 (positive vs negative)
- Region: US/Canada/Europe vs Rest
- DFI: de novo vs 0-12m vs >12m

PFS in Subgroups

		Events/patients, n		Hazard ratio (95% CI)
		Dato-DXd	ICC	
All patients		199/323	209/321	**0.57** (0.47–0.69)
Age at randomisation	<65 years	153/245	153/239	**0.58** (0.46–0.73)
	≥65 years	46/78	56/82	**0.50** (0.34–0.74)
Race	Asian	91/151	90/131	**0.47** (0.35–0.64)
	Non-Asian	94/151	114/173	**0.60** (0.45–0.79)
Geographic region	US, Canada, Europe	79/120	70/120	**0.69** (0.50–0.95)
	Other geographic regions	120/203	139/201	**0.50** (0.39–0.64)
ECOG PS	0	107/195	115/182	**0.51** (0.39–0.67)
	1	92/128	94/139	**0.63** (0.47–0.84)
DFI history	*De novo*	63/109	77/110	**0.46** (0.32–0.64)
	Prior DFI 0–12 months	44/67	49/66	**0.62** (0.41–0.94)
	Prior DFI >12 months	92/147	83/145	**0.65** (0.48–0.87)
PD-L1 status	High (CPS ≥10)	22/34	18/29	**0.77** (0.41–1.45)
	Low (CPS <10)	176/287	191/291	**0.53** (0.43–0.65)
Brain metastases*	Yes	26/36	19/28	**0.39** (0.21–0.74)
	No	173/287	190/293	**0.56** (0.46–0.70)
Liver metastases	Yes	70/93	72/98	**0.57** (0.40–0.80)
	No	129/230	137/223	**0.55** (0.43–0.70)



*Patients with asymptomatic, stable brain metastases were permitted in the study.

Dent R, et al. ESMO 2025

Datopotamab-Deruxtecan (Dato-DXd) in 1L TNBC

TROPION-Breast02 Trial[1]

- Metastatic TNBC
- No prior chemotherapy
- Immunotherapy not an option
- Any DFI allowed
- Stable brain mets allowed

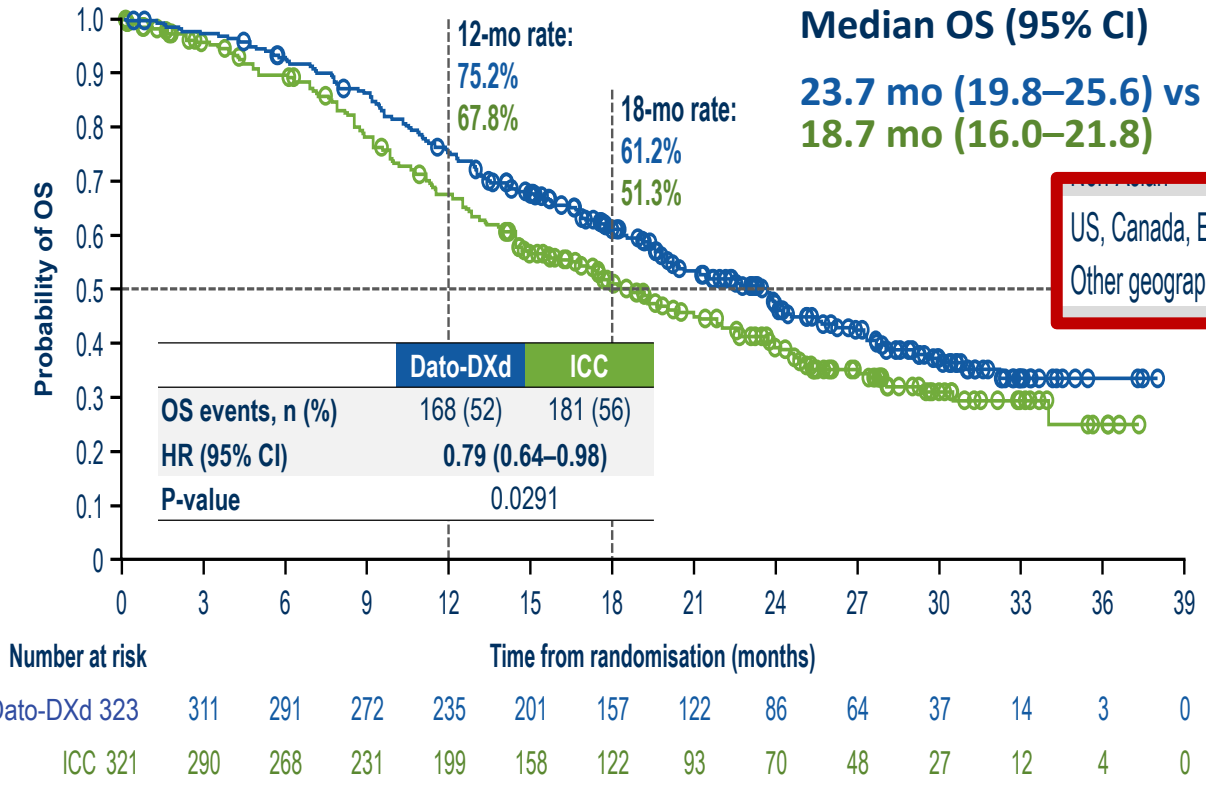
R 1:1

n = 323 → Dato-DXd 6 mg/kg Q3W

n = 321 → TPC: Paclitaxel, Nab-Paclitaxel (if DFI >12/12), Eribulin, Carboplatin, Capecitabine (if taxane and DFI <6/12)

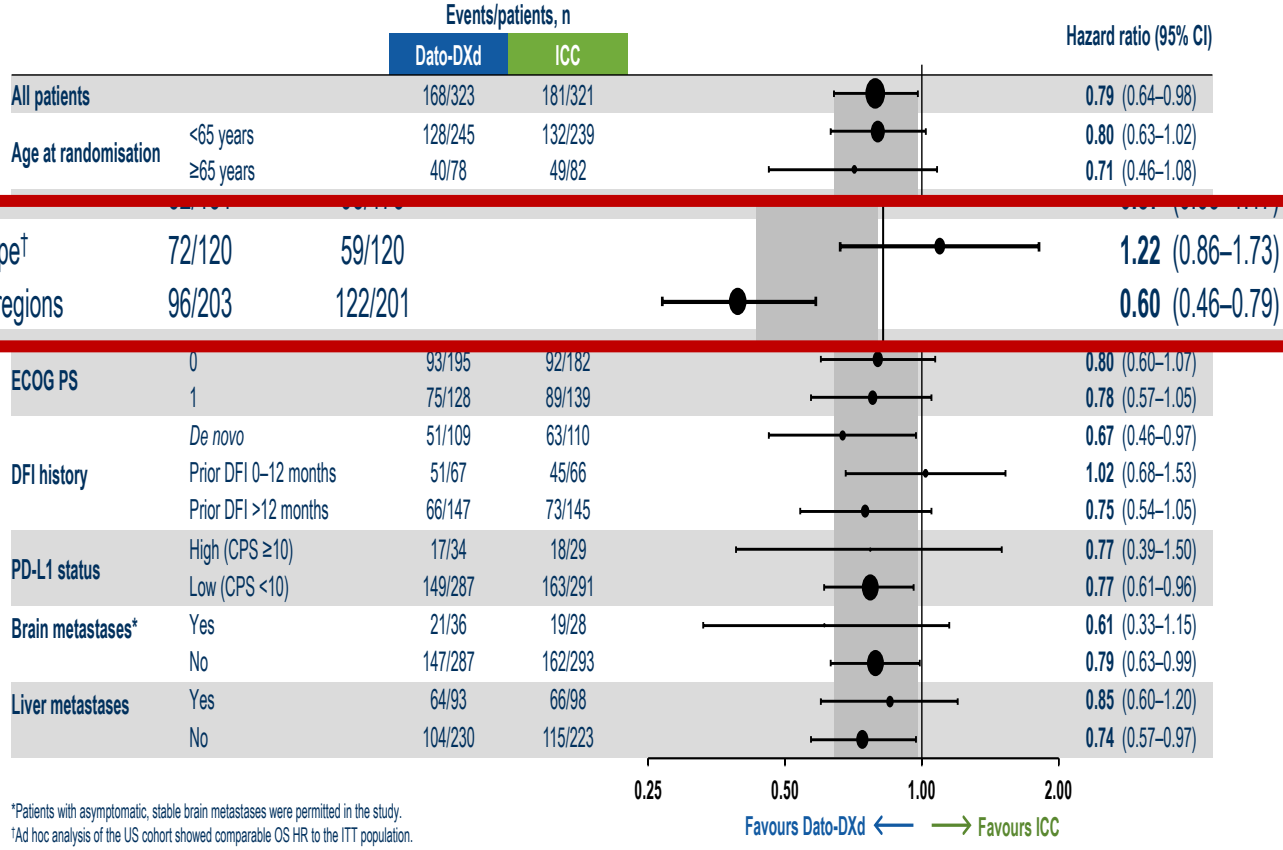
Stratification factors:
- PDL1 (positive vs negative)
- Region: US/Canada/Europe vs Rest
- DFI: de novo vs 0-12m vs >12m

Overall Survival



Median OS (95% CI)

23.7 mo (19.8–25.6) vs 18.7 mo (16.0–21.8)



*Patients with asymptomatic, stable brain metastases were permitted in the study.
†Ad hoc analysis of the US cohort showed comparable OS HR to the ITT population.

Dent R, et al. ESMO 2025

Tropion-Breast02: Overall Safety Summary

- **Median total treatment duration:**
  - **Dato-DXd: 8.5 mths** (range 0.7–38.0)
  - **ICC: 4.1 mths** (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

Most Common Treatment-Related AEs (≥15% of Patients)

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

Treatment-Related AESIs for 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
Adjudicat. 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

Sacituzumab Govitecan (SG) in 1L TNBC

ASCENT-03 Trial[1]

Study Population:

- US/Canada/EU: 32%
- DFI: de novo mTNBC 32%, 0-6m 0%, 6-12m 20%, >12m 48%
- PDL1 high: <1%
- Brain mets 5%
- Prior Taxanes 58%, Capecitabine 19%, Platinum 18%, ICI 4%

- Metastatic TNBC
- No prior chemotherapy
- Immunotherapy not an option
- DFI >6 months
- Treated & stable brain mets allowed

Stratification factors:

- Region: US/Canada/Europe vs Rest
- DFI: de novo vs 6-12m vs >12m

R 1:1

Median follow-up 13.2 months

n = 279

Sacituzumab-Govitecan
10 mg/kg d1&8 Q3W

n = 279

TPC
Paclitaxel, Nab-Paclitaxel
Gemcitabine/Carboplatin

Taxane 55%, Carboplatin 45%

Primary endpoint: PFS

Key Secondary endpoint: OS, ORR, DOR, Safety

Eligible patients offered crossover to 2L SG provided through the study

82% of pts with subsequent Tx received SG

53% of all TPC pts with SG (62% had 2L+)

PD-L1+ (capped at 10%) eligible if previously treated with a PD-(L)1 inhibitor in curative setting or Ineligible for a PD-(L)1 inhibitor due to a comorbidity

Cortes J, et al. ESMO 2025

Sacituzumab Govitecan (SG) in 1L TNBC

ASCENT-03 Trial[1]

- Metastatic TNBC
- No prior chemotherapy
- Immunotherapy not an option
- DFI >6 months
- Treated & stable brain mets allowed

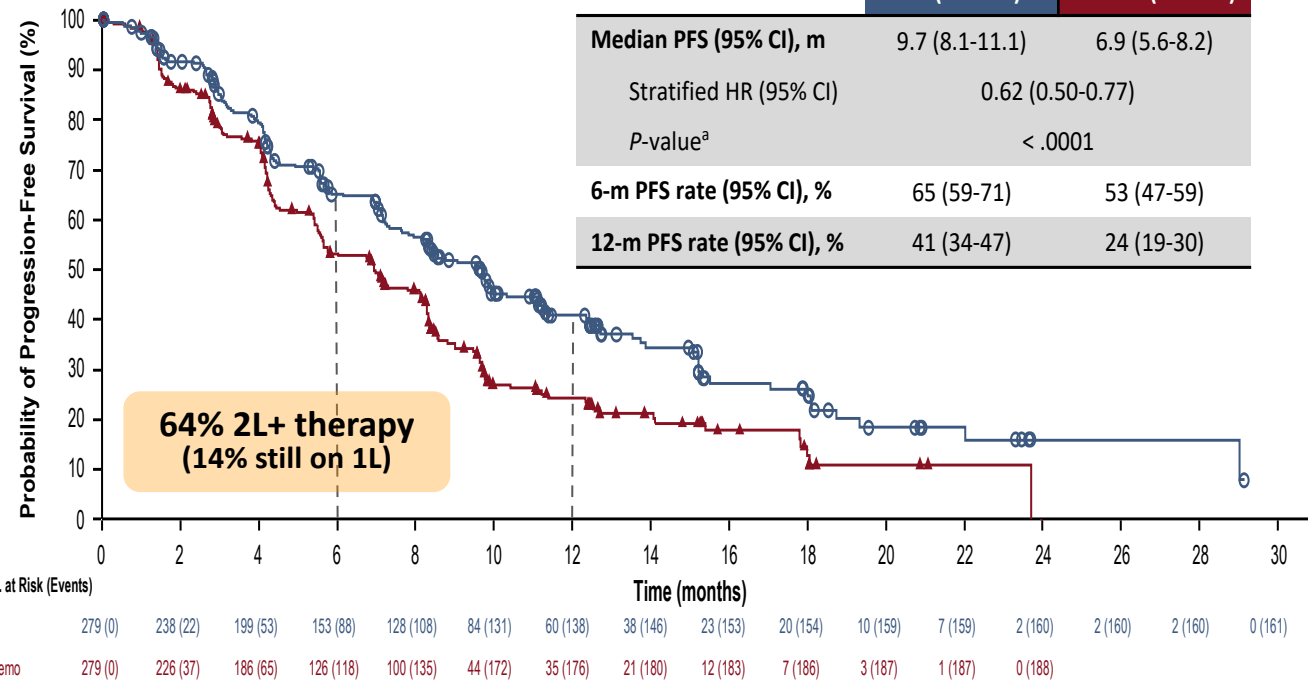
R 1:1

n = 279 → **Sacituzumab-Govitecan 10 mg/kg d1&8 Q3W**

n = 279 → **TPC**
Paclitaxel, Nab-Paclitaxel
Gemcitabine/Carboplatin

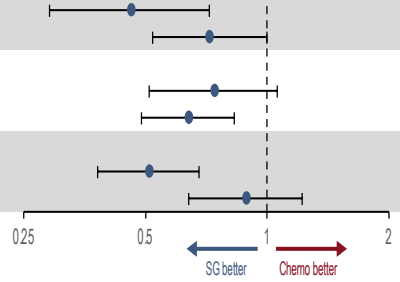
Stratification factors:
- Region: US/Canada/Europe vs Rest
- DFI: de novo vs 6-12m vs >12m

Progression-free Survival



	SG (n = 279)	Chemo (n = 279)
Median PFS (95% CI), m	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-m PFS rate (95% CI), %	65 (59-71)	53 (47-59)
12-m PFS rate (95% CI), %	41 (34-47)	24 (19-30)

	SG n	SG Median PFS, mo (95% CI)	Chemo n	Chemo Median PFS, mo (95% CI)	Unstratified HR (95% CI)
ITT population	279	9.7 (8.1-11.1)	279	6.9 (5.6-8.2)	0.66 (0.53-0.82)
Age group					
< 65 years	214	9.6 (7.6-10.3)	201	5.7 (4.4-7.0)	0.58 (0.45-0.74)
≥ 65 years	65	11.1 (7.3-13.9)	78	9.0 (8.3-10.0)	0.91 (0.58-1.44)
ECOG PS					
0	183	11.2 (9.7-13.5)	187	7.3 (6.0-8.3)	0.61 (0.47-0.80)
1	96	7.1 (5.4-8.5)	92	5.5 (4.2-7.2)	0.74 (0.52-1.05)
Geographic region					
United States/Canada/Western Europe	89	9.9 (7.8-13.9)	89	7.1 (5.4-8.3)	0.54 (0.36-0.79)
Rest of the world	190	9.6 (7.2-11.1)	190	6.9 (5.5-8.3)	0.72 (0.55-0.92)
Disease Status					
De novo	87	8.3 (5.6-12.4)	88	5.5 (4.2-7.3)	0.65 (0.45-0.94)
Recurrent 6-12 mo	58	8.3 (5.6-9.9)	57	5.6 (4.2-6.7)	0.46 (0.29-0.72)
Recurrent > 12 mo	134	11.1 (8.4-13.5)	134	8.4 (7.2-9.8)	0.72 (0.52-1.00)
PD-L1 status					
CPS < 1	102	8.5 (7.2-12.5)	98	8.3 (5.4-9.6)	0.74 (0.51-1.06)
1 ≤ CPS < 10	175	9.8 (7.6-11.3)	180	6.9 (5.5-8.1)	0.64 (0.49-0.83)
Chemo selected prior to randomization					
Taxane	154	11.1 (8.1-12.7)	155	5.7 (4.3-8.1)	0.51 (0.38-0.68)
Gemcitabine/carboplatin	125	8.5 (6.9-9.9)	124	8.1 (5.7-8.3)	0.89 (0.64-1.22)

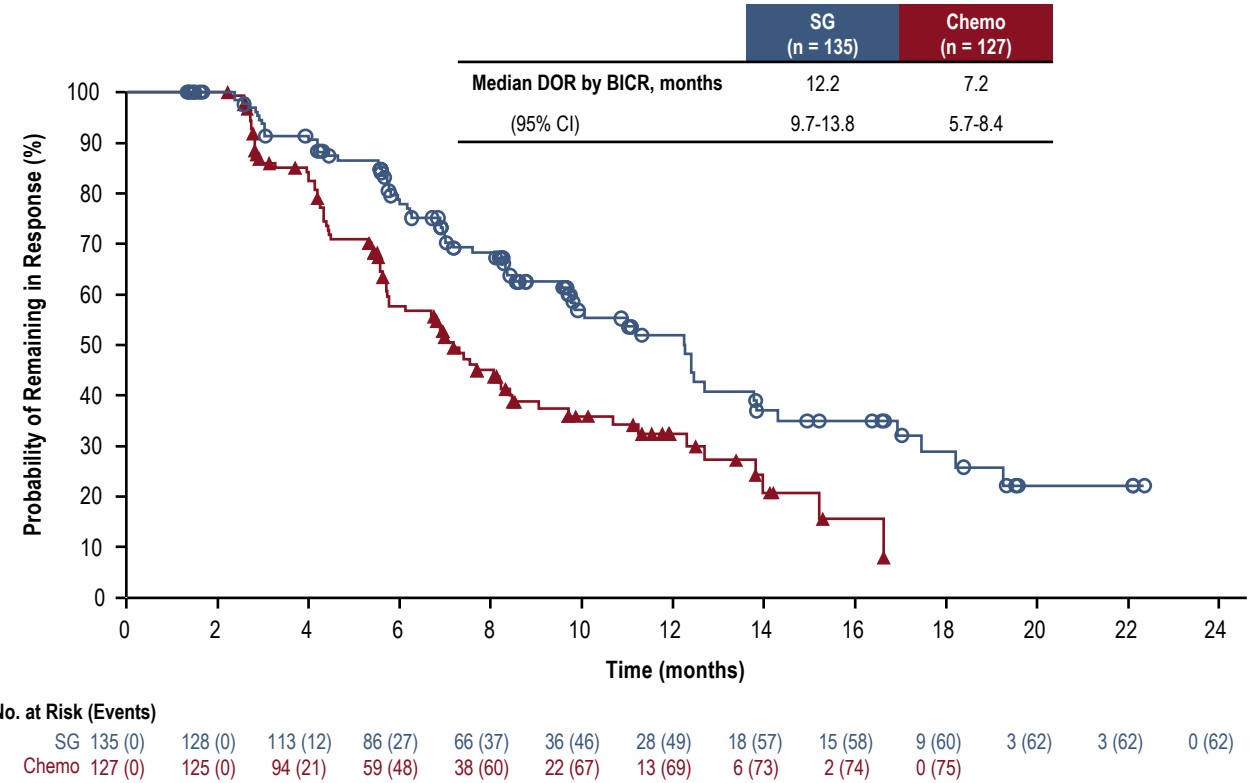


Cortes J, et al. ESMO 2025; Cortes J et al. N Engl J Med 2025

Sacituzumab Govitecan (SG) in 1L TNBC

Objective Response and Duration of Response

Variable	SG (n = 279)	Chemo (n = 279)
Objective response rate by BICR[a] (95% CI), %	48 (42-54)	46 (40-52)
Stratified odds ratio (95% CI)	1.1 (0.8-1.6)	
Best overall response (BICR), n (%)		
Complete response	20 (7)	15 (5)
Partial response	115 (41)	112 (40)
Stable disease	113 (41)	101 (36)
Stable disease ≥ 6 months	37 (13)	32 (11)
Progressive disease	14 (5)	36 (13)
Not evaluable	17 (6)	15 (5)
Time to response by BICR,[b] median (range), months	1.6 (0.7-16.7)	1.6 (0.9-6.8)



Data cutoff date: April 2, 2025. [a]Objective response rate is defined as the proportion of patients who achieved a best overall response of complete response/partial response. [b]Time to response (months) = (date of first documented confirmed complete or partial response - date of randomization + 1)/30.4375.
Chemo, chemotherapy; **BICR**, blinded independent central review; **DOR**, duration of response; **SG**, sacituzumab govitecan.

Cortes J, et al. ESMO 2025; Cortes J et al. N Engl J Med 2025

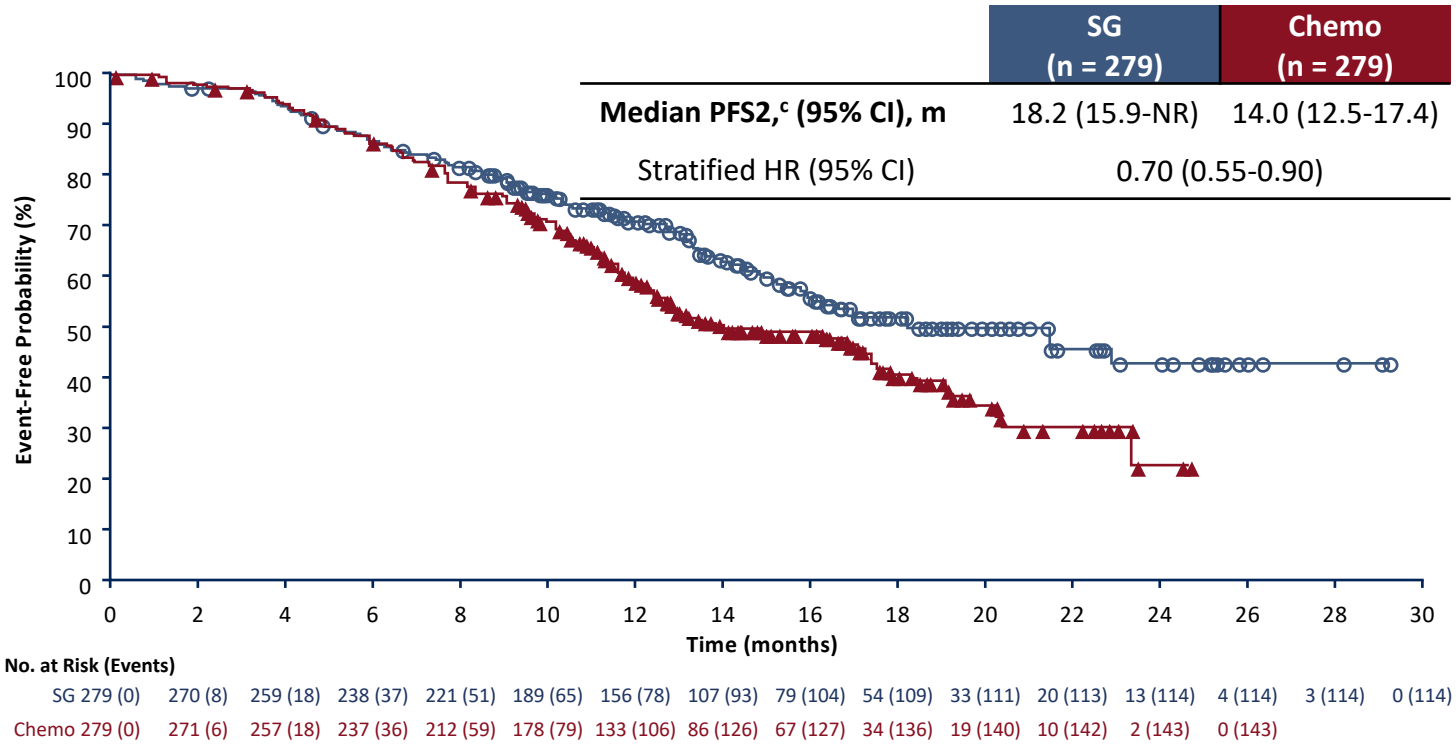
Sacituzumab Govitecan (SG) in 1L TNBC

Descriptive Overall Survival

- **Overall survival not yet mature[a]**
- Study continues to first formal OS analysis
- Of 179 patients who initiated subsequent treatment, 147 (82%) received SG

Overall survival	SG (n = 279)	Chemo (n = 279)
Number of events, %	103 (37)	103 (37)
Median (95% CI) , months	21.5 (17.7-NR)	20.2 (18.2-NR)
Stratified HR (95% CI)	0.98 (0.75-1.30)	
OS rate (95% CI), %		
12-month	75 (70-80)	73 (67-78)
24-month	46 (36-56)	42 (29-54)

Progression-Free Survival 2[b]



At the time of primary analysis, overall survival was immature and PFS2 was longer with SG vs chemo by investigator assessment

Data cutoff date: April 2, 2025. [a]At the time of this analysis, OS data maturity was 37%. [b]PFS2 is defined as the time from date of randomization to the first documented progression on next-line therapy based on investigator assessment of progressive disease or death due to any cause, whichever occurs first. [c]By investigator assessment.
2L, second line; **chemo**, chemotherapy; **HR**, hazard ratio; **NR**, not reached; **OS**, overall survival; **PFS2**, progression-free survival 2; **SG**, sacituzumab govitecan.

Cortes J, et al. ESMO 2025; Cortes J et al. N Engl J Med 2025

Exposure and 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, m (range)	8.3 (< 0.1-28.7)	6.3 (< 0.1-24.2)	5.8 (< 0.1-23.1)

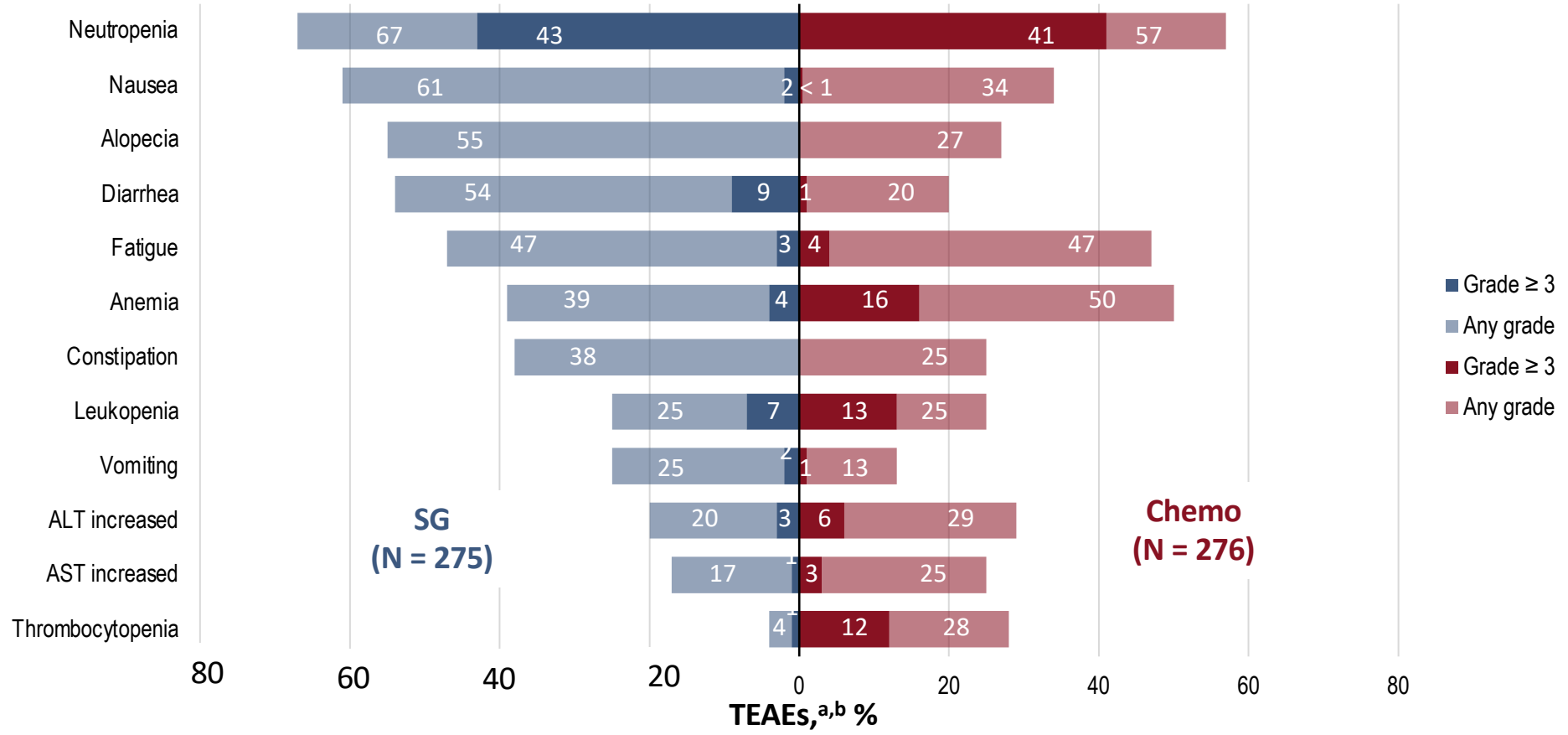
	SG (n = 275)	Chemo (n = 276)
Any TEAE	273 (99)	269 (97)
Grade ≥ 3 TEAEs	181 (66)	171 (62)
Treatment-related	167 (61)	147 (53)
Treatment-emergent SAE	71 (26)	67 (24)
Treatment-related	46 (17)	37 (13)
TEAEs leading to treatment discontinuation	10 (4)	33 (12)
TEAEs leading to dose interruption	181 (66)	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-CSFqw

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.

Safety Summary: Most Common Adverse Events



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.

Cortes J, et al. ESMO 2025;
Cortes J et al. N Engl J Med 2025

Patient-reported outcomes (PROs) with sacituzumab govitecan (SG) vs chemotherapy in patients with previously untreated advanced triple-negative breast cancer (TNBC) who are not candidates for PD-(L)1 inhibitors in the phase 3 ASCENT-03 study

Punie K et al. SABCS 2025;Abstract RF6-05.

December 10, 2025

1:00 PM–2:15 PM CST

Abstract Conclusions: The key secondary endpoints of LS mean changes from baseline to week 25 in physical functioning favored SG vs chemotherapy, while TTD in fatigue was similar in both treatment arms. These data, along with additional exploratory results reported here, suggest that SG was associated with more favorable and sustained benefits in QOL vs chemotherapy. The known gastrointestinal side effects of SG did not negatively impact global health status/QoL or functional domain scores in this analysis. Along with ASCENT-03 efficacy data, these data support SG as a potential new standard of care for patients with previously untreated advanced TNBC who are not candidates for PD-(L)1 inhibitors.

Tropion Breast02 and ASCENT-03 in 1L TNBC

TROPION-Breast02 Trial[1]

15% DFI 0-6mths

42% SG use in 2L+ treated TPC pts

72% 2L+ Tx

- Metastatic TNBC
- No prior chemotherapy
- Immunotherapy not an option
- Any DFI allowed
- Stable brain mets allowed

R 1:1

n = 323 → Dato-DXd 6 mg/kg Q3W

n = 321 → TPC: Paclitaxel, Nab-Paclitaxel (if DFI >12/12), Eribulin, Carboplatin, Capecitabine (if taxane and DFI <6/12)

Stratification factors:
- PDL1 (positive vs negative)
- Region: US/Canada/Europe vs Rest
- DFI: de novo vs 0-12m vs >12m

ASCENT-03 Trial[1]

- Metastatic TNBC
- No prior chemotherapy
- Immunotherapy not an option
- DFI >6 months
- Treated & stable brain mets allowed

R 1:1

n = 279 → Sacituzumab-Govitecan 10 mg/kg d1&8 Q3W

n = 279 → TPC: Paclitaxel, Nab-Paclitaxel Gemcitabine/Carboplatin

Stratification factors:
- Region: US/Canada/Europe vs Rest
- DFI: de novo vs 6-12m vs >12m

0% DFI 0-6mths

82% SG use in 2L+ treated TPC pts

64% 2L+ Tx

	Dato DXd	TPC		SG	TPC	
PFS	10.8	5.6	0.57	9.7	6.9	0.62
12m PFS rate	46%	26%		41%	24%	
RR	63%	29%		48%	46%	
PD	8%	16%		5%	13%	
DoR	12.3	7.1		12.2	7.2	
OS	23.7	18.7	0.79	21.5	20.2	0.98
12m OS rate	75%	68%		75%	73%	
Cross Over		42%			82%	
PFS2				18.2	14.0	0.70

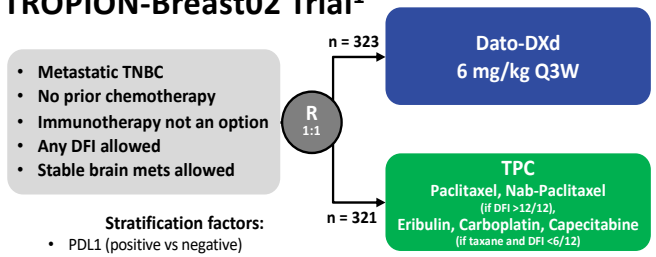
37% data maturity

FU 27.5 vs 13.2m

Dent R, et al. ESMO 2025;
Cortes J, et al. ESMO 2025;
Cortes J, et al. N Engl J Med 2025

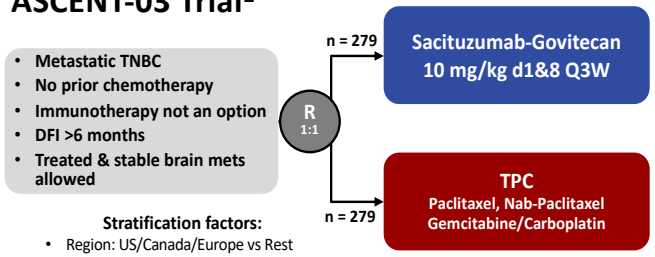
Tropion Breast02, ASCENT-03 and ASCENT-04 in 1L TNBC

TROPION-Breast02 Trial[1]



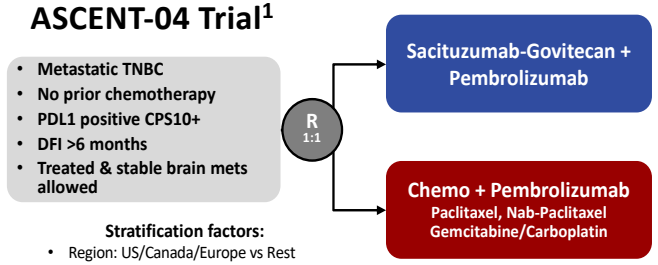
Stratification factors:
- PDL1 (positive vs negative)
- Region: US/Canada/Europe vs Rest
- DFI: de novo vs 0-12m vs >12m

ASCENT-03 Trial[1]



Stratification factors:
- Region: US/Canada/Europe vs Rest
- DFI: de novo vs 6-12m vs >12m

ASCENT-04 Trial[1]



Stratification factors:
- Region: US/Canada/Europe vs Rest
- DFI: de novo vs 6-12m vs >12m

	Dato DXd	TPC	
PFS	10.8	5.6	0.57
12m PFS rate	46%	26%	
RR	63%	29%	
PD	8%	16%	
DoR	12.3	7.1	
OS	23.7	18.7	0.79
12m OS rate	75%	68%	
Cross Over		42%	
PFS2	-	-	-

	SG	TPC	
PFS	9.7	6.9	0.62
12m PFS rate	41%	24%	
RR	48%	46%	
PD	5%	13%	
DoR	12.2	7.2	
OS	21.5	20.2	0.98
12m OS rate	75%	73%	
Cross Over		82%	
PFS2	18.2	14.0	0.70

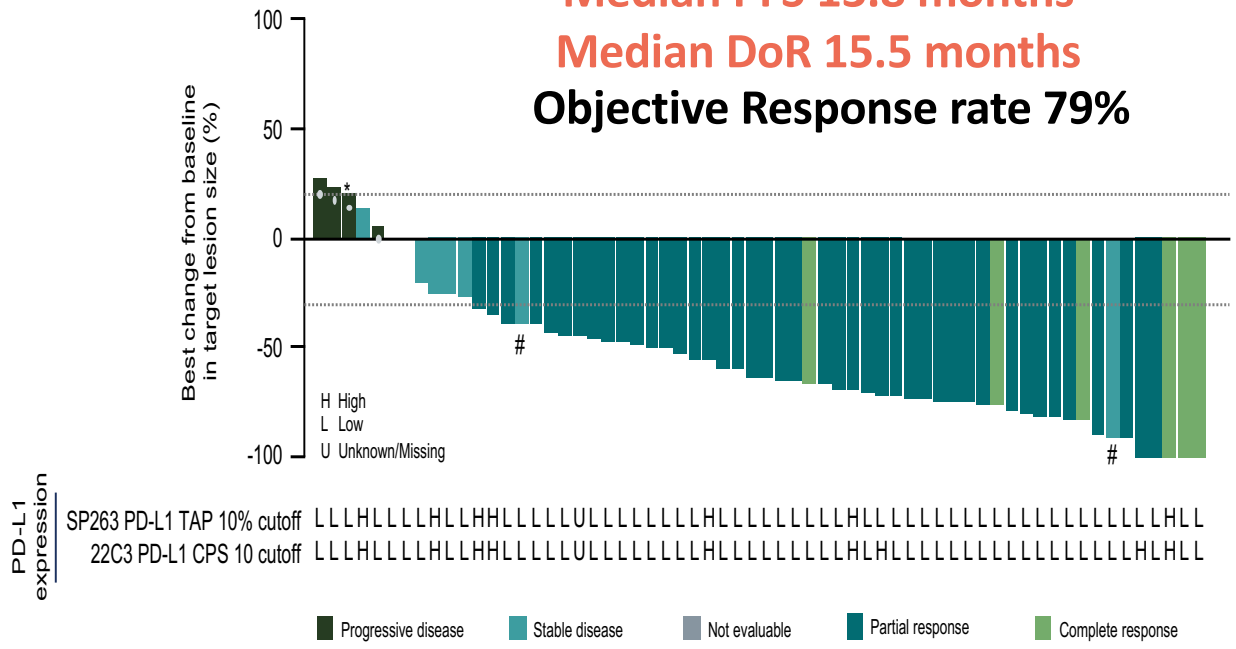
	SG + P	TPC + P	
PFS	11.2	7.8	0.65
12m PFS rate	48%	33%	
RR	60%	53%	
PD	4%	12%	
DoR	16.5	9.2	
OS	NR	NR	0.89
12m OS rate	75%	73%	
Cross Over		81%	
PFS2	-	-	-

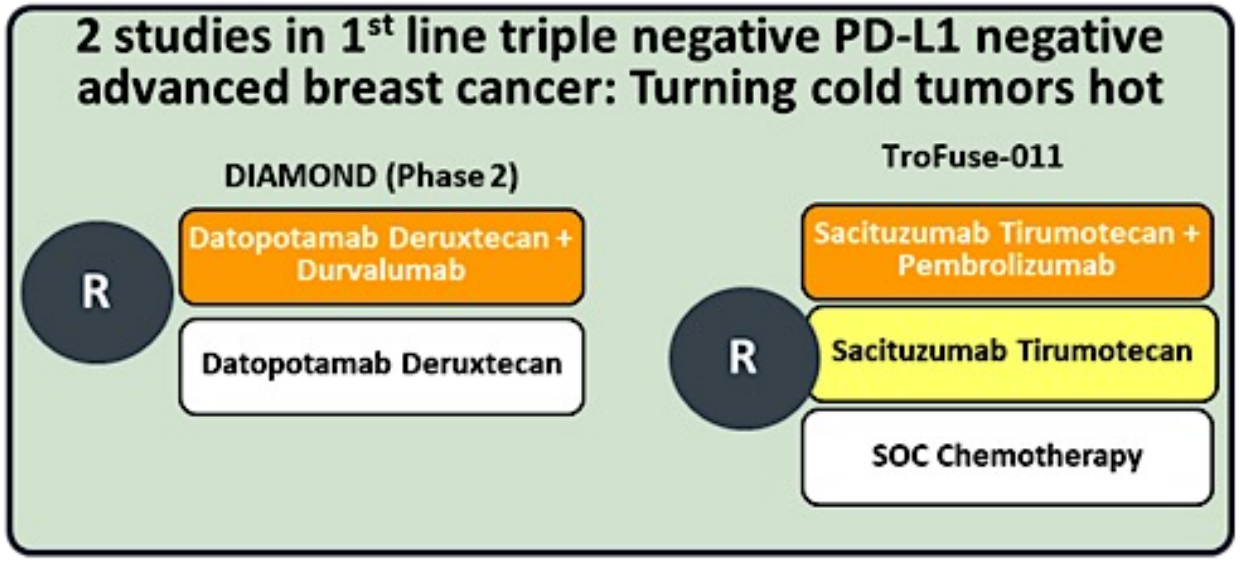
Dent R, et al. ESMO 2025; Cortes J, et al. ESMO 2025, Cortes J et al, N Engl J Med 2025; Tolaney S, et al, ASCO 2025

Is there a role for ICI in PDL1-neg when combined with ADC?

Dato-DXd plus Durvalumab in 1st line mTNBC (87% PDL1-negative)

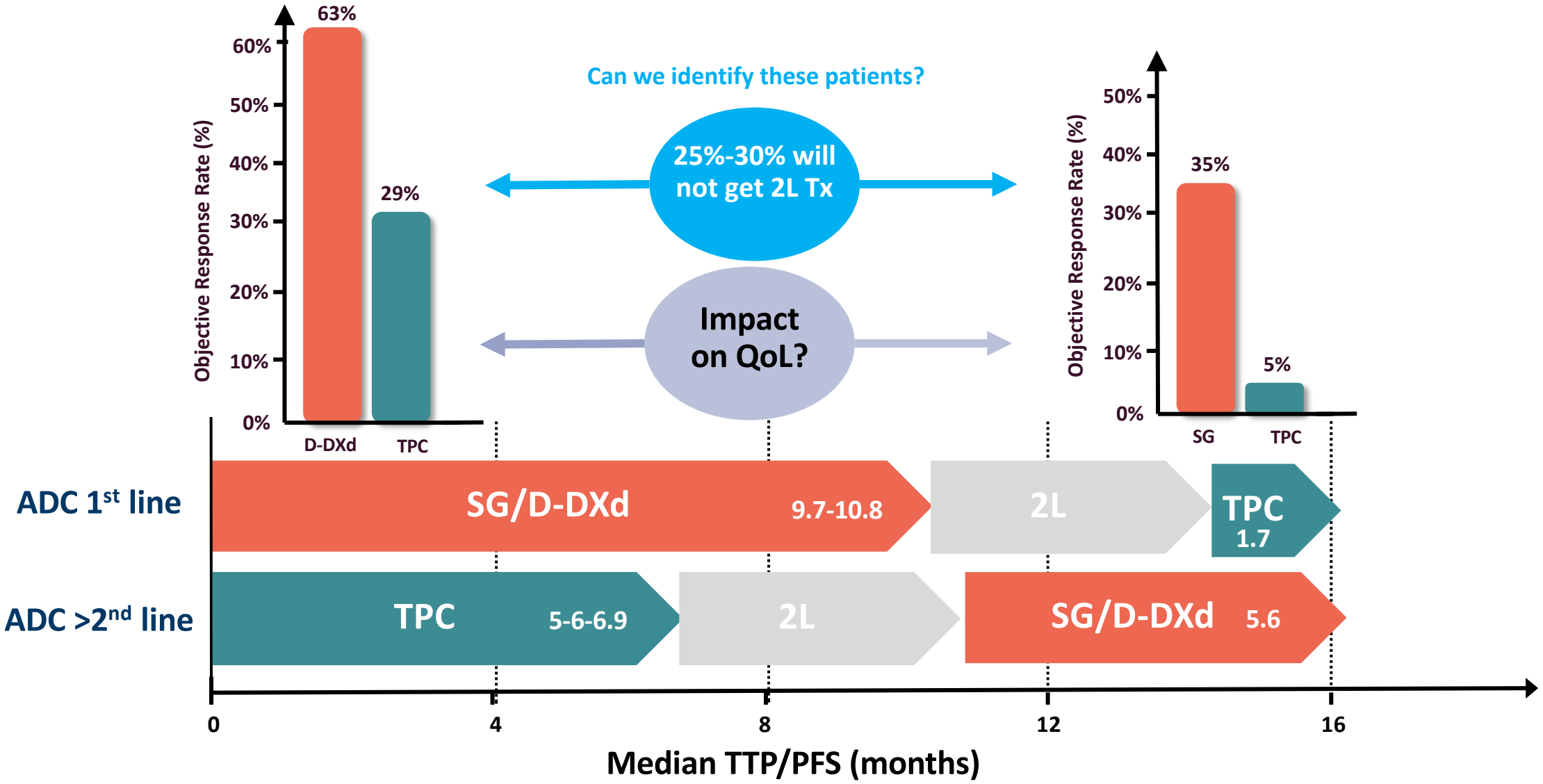
Median PFS 13.8 months
Median DoR 15.5 months
Objective Response rate 79%





Schmid, et al. ESMO 2025

ADCs in mTNBC: What is the best sequence?



Agenda

Module 1: Previously Untreated Metastatic Triple-Negative Breast Cancer (mTNBC) — Prof Schmid

Module 2: Integrating Antibody-Drug Conjugates (ADCs) into the Management of Endocrine-Resistant Hormone Receptor-Positive Metastatic Breast Cancer (mBC) — Dr Sharma

Module 3: Selection and Sequencing of Therapy for Relapsed/Refractory mTNBC — Dr Nanda

Module 4: Tolerability and Other Practical Considerations with ADCs and Other Cytotoxic Agents for mBC — Dr Cortés

Case Presentation: 80-year-old woman with multiregimen-recurrent ER-positive, HER2-low (IHC 1+) ESR1-mutant mBC receives sacituzumab govitecan

Dr Jennifer Yannucci (Savannah, Georgia)

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

Regulatory and accessibility issues aside, how would you sequence systemic therapy for patients with HR-positive, HER2-negative (IHC 0) mBC who are no longer eligible for endocrine treatment? Does this vary based on tumor status (visceral versus nonvisceral, tumor bulk, tumor-related symptomatology)?

Regulatory and accessibility issues aside, how would you sequence systemic therapy for patients with HR-positive, HER2-low or HER2-ultralow mBC who are no longer eligible for endocrine treatment? Does this vary based on tumor status (visceral versus nonvisceral, tumor bulk, tumor-related symptomatology)?

QUESTIONS FOR THE FACULTY

How do you choose between sacituzumab govitecan and Dato-DXd for patients with relapsed/refractory HR-positive, HER2-negative or HER2-low mBC?

Dr Ranju Gupta
(Bethlehem, Pennsylvania)

Role of Dato-DXd for patients with ER-positive, HER2-low mBC and progression on prior T-DXd

Dr Yanjun Ma
(Murfreesboro, Tennessee)

Case Presentation: 78-year-old woman with bilateral recurrence in the lungs of ER-negative, HER2-low (IHC 1+) breast cancer (PD-L1 TPS 20%) receives Dato-DXD with durvalumab on protocol

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

Would you employ Dato-DXd for a patient who has previously experienced disease progression on sacituzumab govitecan and vice versa?

Would you employ Dato-DXd for a patient who has previously experienced disease progression on trastuzumab deruxtecan (T-DXd) and vice versa?

What are the common toxicities of Dato-DXd, and how can these — including mucositis and ocular toxicity — be prevented and managed?

QUESTIONS FOR THE FACULTY

Should patients receiving Dato-DXd undergo an ophthalmologic or optometric evaluation if asymptomatic?

How important is the preemptive use of corticosteroid mouthwash?

How does the risk of ILD with Dato-DXd compare to that with T-DXd? Is screening imaging necessary? How should Grade 1 or 2 ILD be managed?

Integrating ADCs into the Management of Endocrine-Resistant Hormone Receptor (HR) Positive Metastatic Breast Cancer (mBC)

Priyanka Sharma, MD

Professor of Medicine

University of Kansas Medical Center

NCI Comprehensive Cancer Center

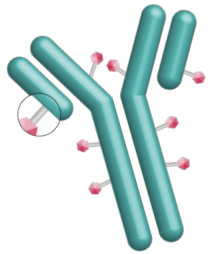
A Cancer Center Designated by the National Cancer Institute

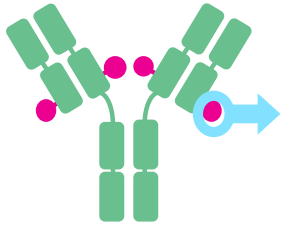
The University of Kansas Cancer Center

ADCs in Endocrine resistant HR+ mBC

- **TROP 2 directed ADC**
- **HER-2 directed ADC**

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

TROPiCS-02: A Phase 3 Study of SG in HR+/HER2- Locally Recurrent Inoperable or Metastatic Breast Cancer

NCT03901339

Metastatic or locally recurrent inoperable HR+/HER2− breast cancer that progressed after[a]:

- At least 1 endocrine therapy, taxane, and CDK4/6i in any setting
- At least 2, but no more than 4, lines of chemotherapy for metastatic disease
  - (Neo)adjuvant therapy for early-stage disease qualified as a prior line of chemotherapy if disease recurred within 12 months
- Measurable disease by RECIST 1.1

N=543

R 1:1

Treatment was continued until progression or unacceptable toxicity

Sacituzumab govitecan
10 mg/kg IV
days 1 and 8, every 21 days
n=272

Treatment of physician's choice[b]
(capecitabine, vinorelbine, gemcitabine or eribulin)
n=271

Stratification:
- Visceral metastases (yes/no)
- Endocrine therapy in metastatic setting ≥6 months (yes/no)
- Prior lines of chemotherapies (2 vs 3/4)

Endpoints

Primary
- PFS by BICR

Secondary
- OS
- ORR, DOR, CBR by LIR and BICR
- PRO
- Safety

[a]Disease histology based on the ASCO/CAP criteria. [b]Single-agent standard-of-care treatment of physician's choice was specified prior to randomization by the investigator.
ASCO/CAP, American Society of Clinical Oncology/College of American Pathologists; BICR, blinded independent central review; CBR, clinical benefit rate; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; DOR, duration of response; HER2-, human epidermal growth factor receptor 2-negative; HR+, hormonal receptor-positive; IV, intravenously; LIR, local investigator review; (Neo)adjuvant, neoadjuvant or adjuvant; ORR, objective response rate; OS, overall survival; PFS, progression-free survival, PRO, patient-reported outcomes; R, randomized; RECIST, Response Evaluation Criteria in Solid Tumors.

Rugo HS et al. J Clin Oncol. 2022;40:3365-3376

TROPiCS-02: Demographics and Baseline Characteristics

	SG (n = 272)	TPC (n = 271)
Female, %	99	99
Median age, (range) y	57 (29-86)	55 (27-78)
< 65 y, %	73	75
≥ 65 y, %	27	25
Race or ethnic group, %		
White	68	66
Black	3	5
Asian	4	2
Other[a]/Not reported[b]	25	28
Geographic region, %		
North America	42	42
Europe	58	58
ECOG PS, %		
0	43	46
1	57	54
Visceral metastases at baseline, %	**95**	**95**
Liver metastases,[c] %	84	87
De novo metastatic breast cancer, %	**29**	**22**

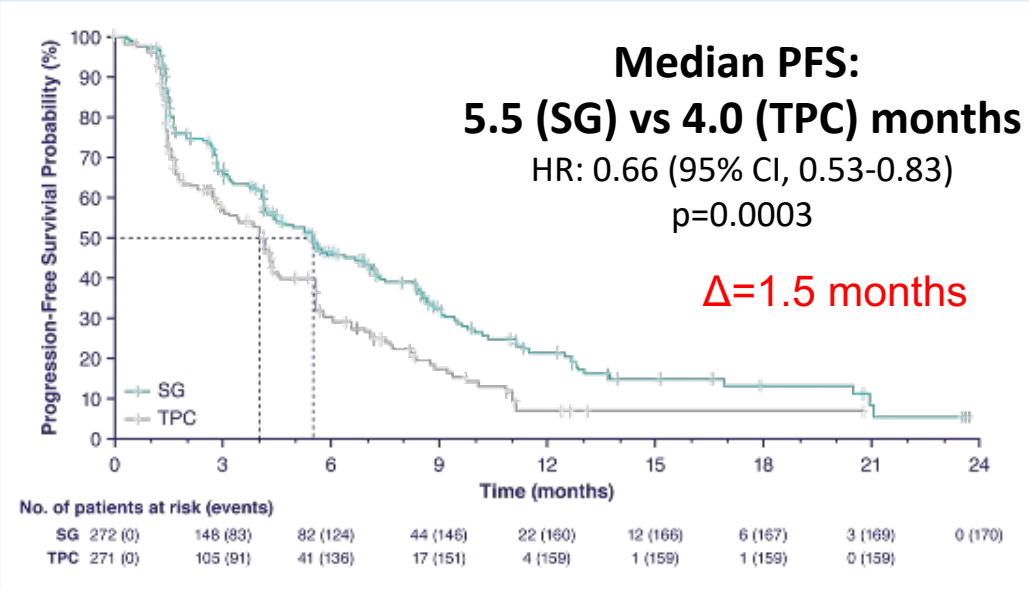
	SG (n = 272)	TPC (n = 271)
Median time from initial metastatic diagnosis to randomization, (range) mo	48.5 (1.2-243.8)	46.6 (3.0-248.8)
Prior chemotherapy in (neo)adjuvant setting, %	64	68
DFI < 12 mo, %	8	8
Prior endocrine therapy use in the metastatic setting ≥ 6 mo, %	86	86
Prior CDK4/6 inhibitor use, %		
≤ 12 months	59	61
> 12 months	39	38
Unknown	2	1
Number of prior lines of chemotherapy, %		
≤ 2	42	44
≥ 3	58	56
Median prior chemotherapy regimens in the metastatic setting, n (range)[d]	**3 (0-8)**	**3 (1-5)**

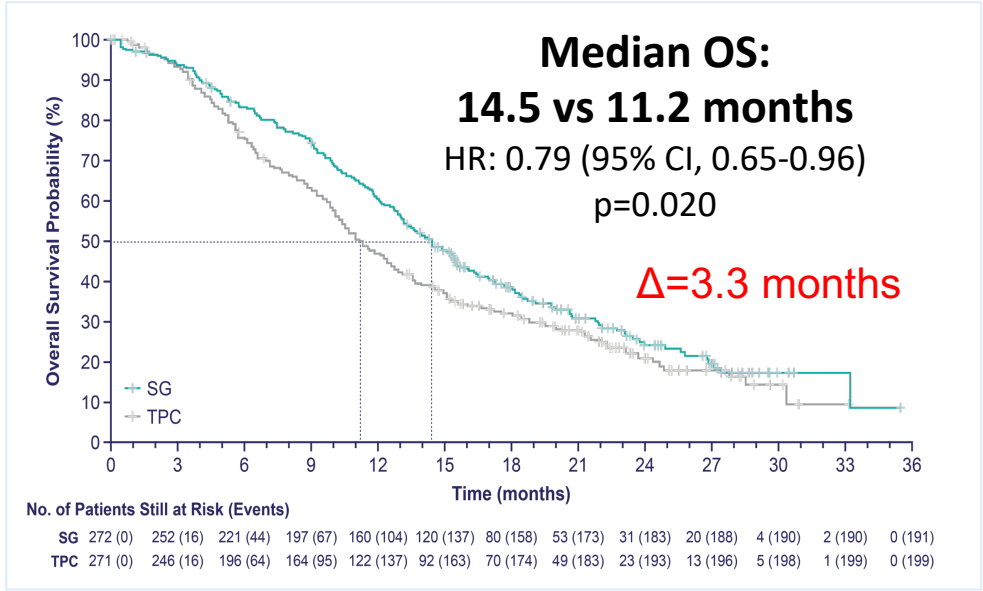
CDK, cyclin-dependent kinase; DFI, disease-free interval; ECOG PS, Eastern Cooperative Oncology Group performance status, (neo)adjuvant, neoadjuvant or adjuvant; RECIST, Response Evaluation Criteria In Solid Tumors; SG, sacituzumab govitecan; TPC, treatment of physician's choice.

[a]Includes American Indian or Alaska native, native Hawaiian or other Pacific Islander. [b]Not reported indicates local regulators did not allow collection of race or ethnicity information. [c]Presence of baseline target/non-target liver metastases per RECIST 1.1 by local investigator review. [d]The reported number of prior therapies was miscounted at screening for some patients; 9 patients received prior chemotherapy regimens in the metastatic setting outside the per-protocol range for inclusion criteria and were included in the intent-to-treat population.

Rugo HS et al. J Clin Oncol. 2022;40:3365-3376

TROPiCS-02: Results

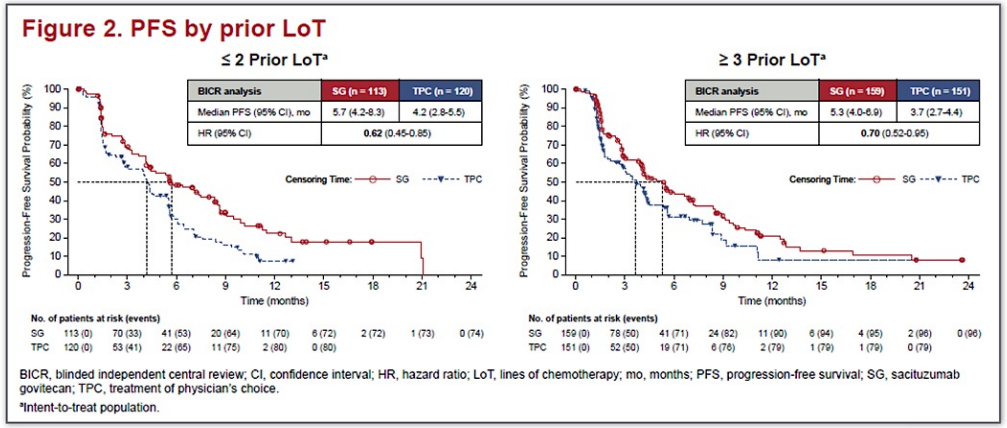




ORR: 21% vs. 14%. p=0.03

Efficacy by prior LoT in the metastatic setting

- PFS favored SG over TPC regardless of number of prior LoT **(Figure 2)**



In February 2023, FDA approved Sacituzumab govitecan for patients with unresectable locally advanced or metastatic HR+ HER2 negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting

Rugo HS et al. J Clin Oncol. 2022;40:3365-3376, Rugo HS et al ESMO 2022, Tolaney SM et al ASCO 2023, Cortes et al ESMO 2023

TROPION-Breast01 Study Design

Randomised, phase 3, open-label, global study (NCT05104866)

Key inclusion criteria:

- Patients with HR+/HER2– breast cancer* (HER2– defined as IHC 0/1+/2+; FISH negative)
- Previously treated **with 1–2 lines of chemotherapy (inoperable/metastatic setting)**
- Experienced progression on ET and for whom ET was unsuitable
- ECOG PS 0 or 1

1:1

(n=732)

Dato-DXd
6 mg/kg IV Day 1 Q3W
(n=365)

Investigator's choice of chemotherapy (ICC)
as per protocol directions†
(eribulin mesylate D1,8 Q3W; vinorelbine D1,8 Q3W; gemcitabine D1,8 Q3W; capecitabine D1–14 Q3W)
(n=367)

Endpoints:

- **Dual primary:** PFS by BICR per RECIST v1.1, and OS
- **Secondary:** included PFS (investigator assessed) PFS2, TFST, TSST, ORR, DCR at 12 weeks, DoR, PROs, and safety

Randomisation stratified by:

- **Lines of chemotherapy** in inoperable/metastatic setting (1 vs 2)
- **Geographic location** (USA/Canada/Europe vs other geographic regions)
- **Previous CDK4/6 inhibitor** (yes vs no)

- Treatment continued until PD, unacceptable tolerability, or other discontinuation criteria

Statistical considerations: Study deemed positive if either of the dual primary endpoints (PFS by BICR or OS) were statistically significant

Detailed description of the statistical methods published previously.[1] *Per American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines.
†ICC was administered as follows: eribulin mesylate, 1.4 mg/m^2 IV on Days 1 and 8, Q3W; capecitabine, 1000 or 1250 mg/m^2 orally twice daily on Days 1 to 14, Q3W (dose per standard institutional practice); vinorelbine, 25 mg/m^2 IV on Days 1 and 8, Q3W; or gemcitabine, 1000 mg/m^2 IV on Days 1 and 8, Q3W.
CDK4/6, cyclin-dependent kinase 4/6; D, day; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; FISH, fluorescent in-situ hybridisation; IHC, immunohistochemistry; IV, intravenous; PD, progressive disease; PFS2, time to second progression or death; PRO, patient-reported outcome; RECIST, Response Evaluation Criteria in Solid Tumors; TFST, time to first subsequent therapy; TSST, time to second subsequent therapy.

1. Bardia A, et al. JCO 2024

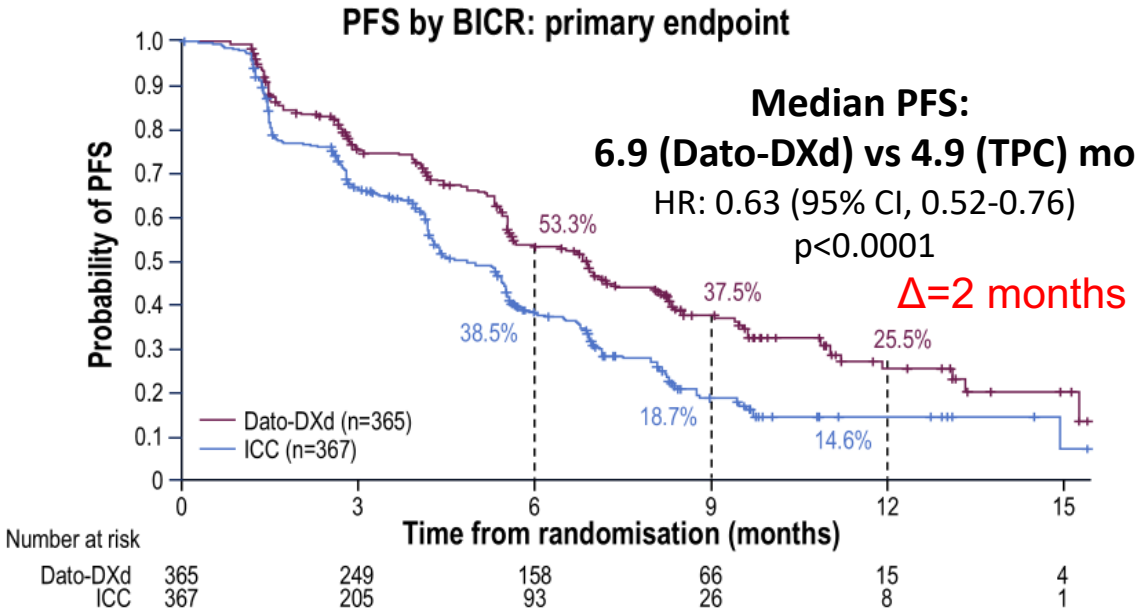
Demographics and Baseline Characteristics

		Dato-DXd (n=365)	ICC (n=367)
Age, median (range), years		56 (29–86)	54 (28–86)
Female, n (%)		360 (99)	363 (99)
Race, n (%)	Black or African American / Asian / White / Other*	4 (1) / 146 (40) / 180 (49) / 35 (10)	7 (2) / 152 (41) / 170 (46) / 38 (10)
Ethnicity, n (%)	Hispanic or Latino / Not Hispanic or Latino†	40 (11) / 322 (88)	43 (12) / 318 (87)
Prior lines of chemotherapy,‡ n (%)	1 / 2	229 **(63)** / 135 (37)	225 **(61)** / 141 (38)
Prior CDK4/6 inhibitor, n (%)	Yes / No	304 **(83)** / 61 (17)	300 **(82)** / 67 (18)
Prior taxanes and anthracyclines, n (%)	Taxane / Anthracycline	295 (81) / 228 (62)	296 (81) / 239 (65)
HER2 status at baseline by local testing,¶ n (%)	HER2 IHC 0	113 (31)	101 (28)
	HER2 IHC 1+, 2+ & FISH–	153 (42)	150 (41)

Median lines of prior chemotherapy =1

Bardia A, et al. JCO 2024, Pristilli B. et al. ESMO Virtual Plenary 2025

TROPION-Breast01: Results



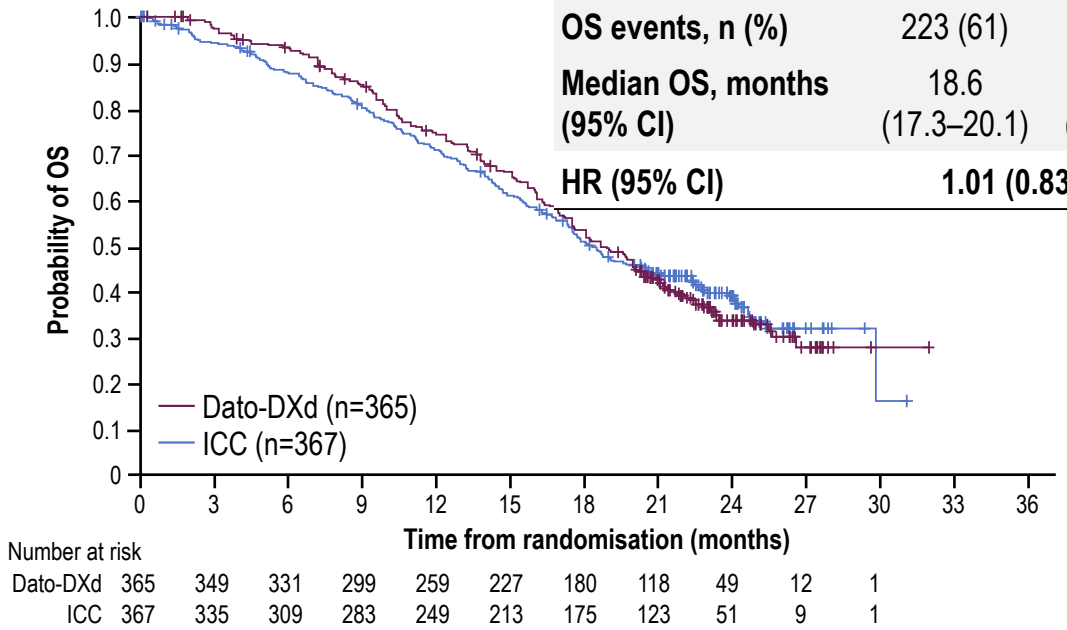
PFS by investigator assessment

Median 6.9 vs 4.5 months; HR 0.64 (95% CI 0.53–0.76)

ORR: 36.4% vs 22.9%

Final OS Analysis (Dual Primary Endpoint)

	Dato-DXd	ICC
OS events, n (%)	223 (61)	213 (58)
Median OS, months (95% CI)	18.6 (17.3–20.1)	18.3 (17.3–20.5)
HR (95% CI)	1.01 (0.83–1.22)	



Data cutoff: 24 July 2024. Pre-specified P-value boundary for OS analysis: α=0.0427.

24% in TPC arm received ADC after study therapy vs 12% in Dato-DXd arm

On January 17, 2025, the FDA approved datopotamab deruxtecan-dlnk for the treatment of adults with unresectable or metastatic, HR+, HER2-negative (IHC 0, IHC1+ or IHC2+/ISH-) breast cancer who have received prior endocrine-based therapy and chemotherapy for unresectable or metastatic disease.

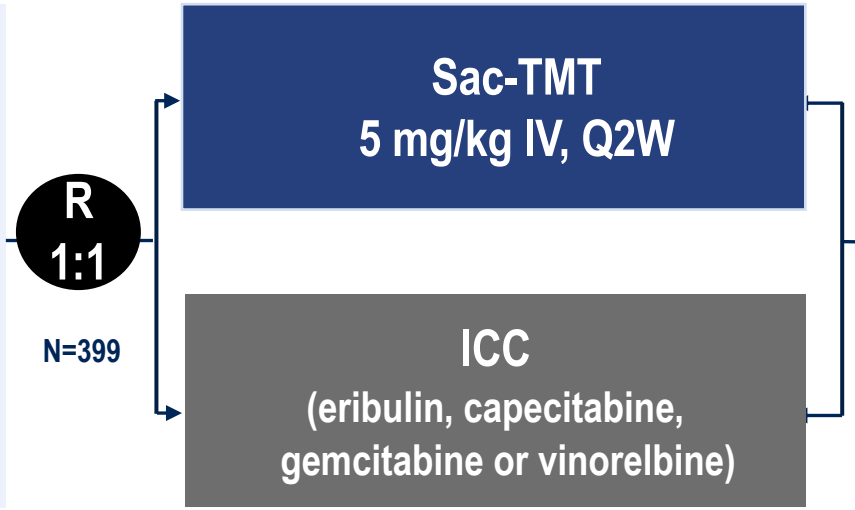
Bardia A, et al. JCO 2024, Pristilli B. et al. ESMO Virtual Plenary 2025

OptiTROP-Breast02 Study Design

Randomized, multi-center, open-label trial (NCT06081959)

Key Eligibility

- Previously treated with 1-4 lines of chemotherapy
- Received at least one endocrine, CDK 4/6 inhibitor, and taxane in any setting
- ECOG PS 0 or 1



Primary endpoints

- PFS by BICR per RECIST v1.1

Secondary endpoints

- PFS (investigator assessed)
- OS
- ORR, DCR
- DOR

Stratification Factors:

1. Lines of chemotherapy (1 vs >1)
2. HER2 status (zero vs low) [a]
3. Endocrine therapy ≥ 6 months (yes vs no)[b]

Statistical considerations:

- **Pre-specified interim analysis for PFS:** all randomized subjects who had the opportunity to complete 1 post-baseline tumor assessment and at least 188 PFS events occurred.
- **Pre-specified interim analysis for OS:** approximately 165 OS events occurred.
- O`Brien-Fleming α-spending as implemented by the Lan-DeMets method.

[a] HER2-zero: No staining, or barely perceptible staining with a proportion > 0% but ≤ 10%; HER2-low defined as IHC1+, or IHC2+ and ISH-negative. [b] If no prior endocrine therapy in advanced setting, assess if (neo)adjuvant endocrine therapy duration ≥ 2 years.

BICR, blinded independent central review; CDK 4/6, cyclin dependent kinase 4/6; DCR, disease control rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; ICC, investigator's choice of chemotherapy; IHC, immunohistochemistry; OS, overall survival; Q2W, every 2 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

PRESENTED BY : Ying Fan, MD

Fan Y et al ESMO 2025

OptiTROP-Breast02

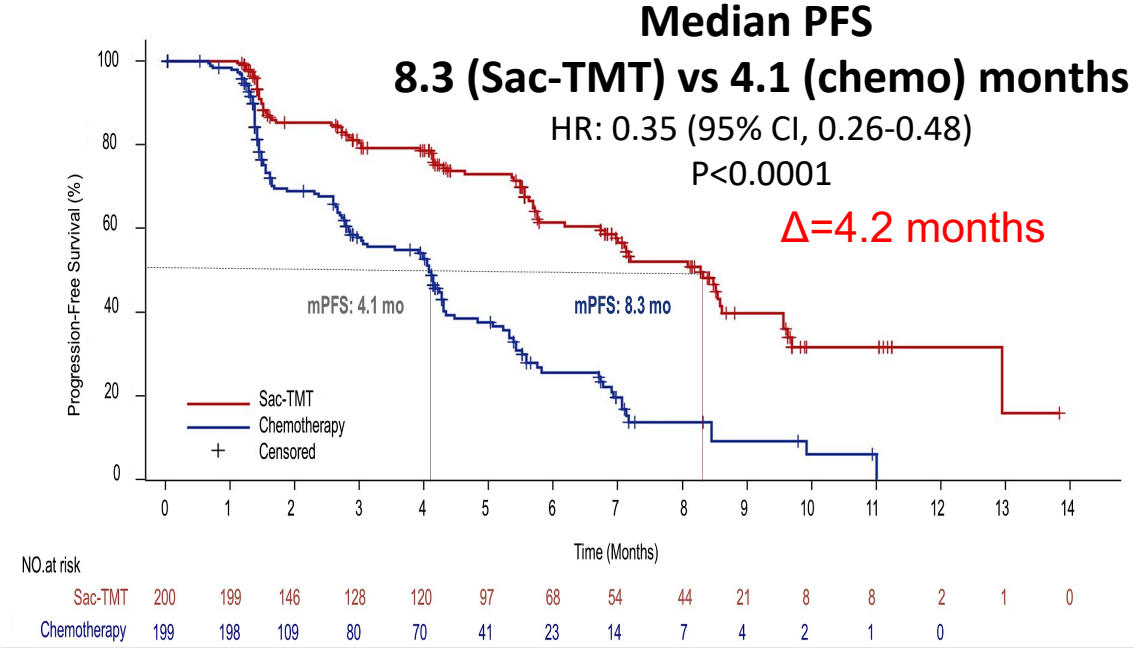
Characteristic	Sac-TMT (n = 200)	Chemotherapy (n = 199)
Median age, y (range)	53.5 (31, 74)	54.0 (33, 70)
≥ 65 y, n(%)	25 (12.5)	25 (12.6)
Female, n (%)	199 (99.5)	198 (99.5)
ECOG PS 1, n (%)	122 (61.0)	128 (64.3)
HER2 status (IHC) at baseline, n (%)		
Zero	108 (54.0)	103 (51.8)
Low	92 (46.0)	96 (48.2)
Median time from initial metastatic diagnosis to consent, mo (range)	84.9 (8.6, 384.3)	73.0 (12.6, 438.7)
Number of metastatic sites ≥3, n(%)	114 (57.0)	111 (55.8)
Visceral metastases, n (%)	193 (96.5)	189 (95.0)
Liver metastases, n (%)	157 (78.5)	146 (73.4)

Characteristic	Sac-TMT (n = 200)	Chemotherapy (n = 199)
Prior chemotherapy in (neo)adjuvant setting, n (%)	146 (73.0)	147 (73.9)
Prior taxane, n (%)	200 (100)	199 (100)
Prior endocrine therapy, n (%)	200 (100)	199 (100)
Prior CDK 4/6 inhibitor, n (%)	200 (100)	199 (100)
≤ 12 months	140 (70.0)	130 (65.3)
> 12 months	60 (30.0)	69 (34.7)
Lines of prior chemotherapy in the advanced/metastatic setting, n (%)		
1	87 (43.5)	86 (43.2)
2	79 (39.5)	83 (41.7)
≥ 3	34 (17.0)	30 (15.1)
Primary endocrine resistance[a], n (%)		
YES	53 (26.5)	54 (27.1)
NO	147 (73.5)	145 (72.9)

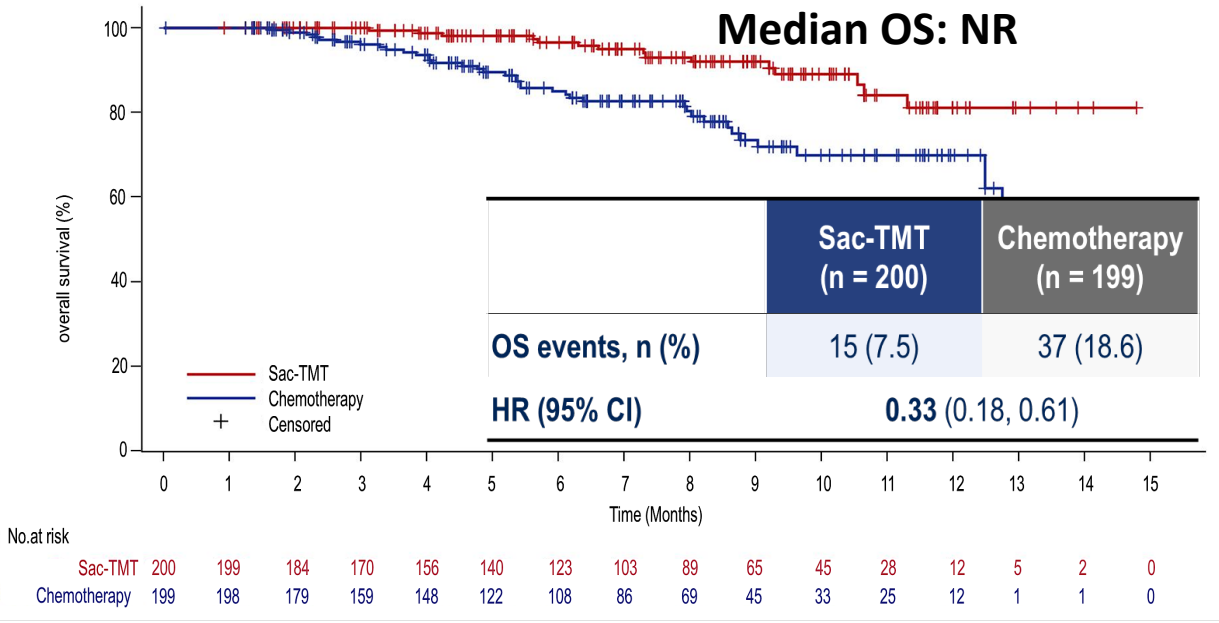
Fan Y et al ESMO 2025

OptiTROP-Breast02: Results

PFS



OS (descriptive)



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

ORR: 41.5% vs. 24.1%.

Fan Y et al ESMO 2025

1st Line TROP2 directed ADC vs chemotherapy in HR+/HER2 negative mBC

ASCENT-07: Sacituzumab govitecan vs TPC in HR+/HER2- mBC after ET

Key Eligibility Criteria
- **Advanced or metastatic breast cancer:**
  - **Progression on ≥2 prior lines of endocrine therapy* or progression within 6m of 1st line ET for mBC**
  - **No prior chemotherapy for metastatic disease**
- **HR+ (per ASCO/CAP; local assessment), HER2 0 or HER2-low (1+ or 2+/ISH-)**

R 1:1

Sacituzumab govitecan

Primary endpoint: PFS

TPC
Capecitabine, paclitaxel, or nab-paclitaxel

*Progression within 24 months of starting adjuvant endocrine therapy counted as one prior line.

NCT05840211

TroFuse-010: Sacituzumab tirumotecan ± Pembrolizumab vs TPC in HR+/HER2- mBC after ET

Key inclusion criteria:
- Unresectable locally advanced or metastatic centrally-confirmed **HR+/HER2-** breast cancer
- Disease recurrence on/after **CDK4/6i** (in the early or metastatic setting)

Key exclusion criteria:
- Previously treated with **chemotherapy** in metastatic setting
- Disease **recurrence** within **6 months** after completion of adjuvant/neoadjuvant chemotherapy

Stratification Factors:
1) PD-L1 status (CPS<1 vs CPS 1-9 vs CPS≥10)
2) TROP2 expression (low+medium vs high)
3) Geographical Region (WE vs NA vs ROW)

R 3:3:2

Arm A: MK-2870

Arm B: MK-2870 + Pembrolizumab

Arm C: TPC*

***Treatment of Physician's Choice:**
Paclitaxel/ Nab-Paclitaxel/ Capecitabine/ Liposomal Doxorubicin

Primary Endpoints:
PFS (by BICR) for Arm A vs Arm C
PFS (by BICR) for Arm B vs Arm C

Progressive Disease / Discontinuation from Study Intervention

Protocol-specified Follow-up

Key Secondary Endpoints:
OS for Arm A vs. Arm C
OS for Arm B vs. Arm C
PFS (by BICR) for Arm B vs. Arm A

NCT06312176

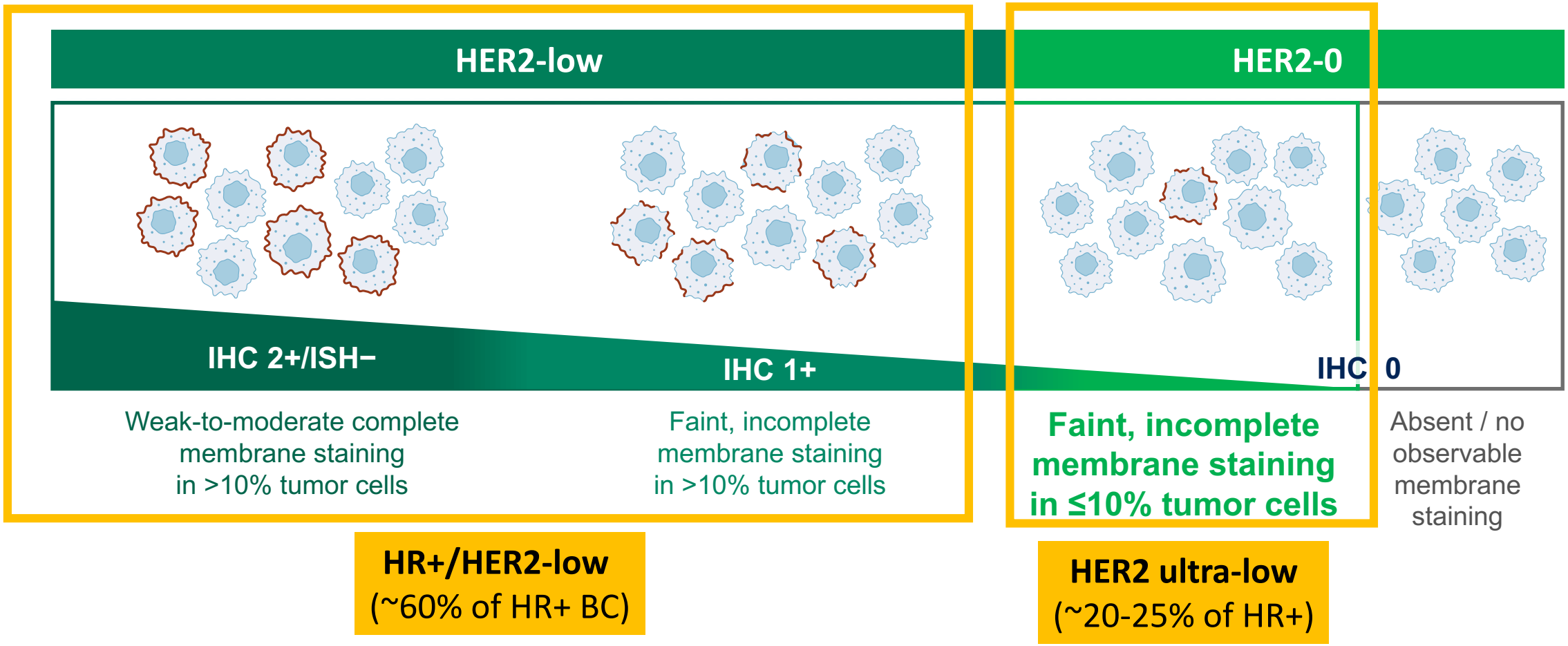
Nov 7, 2025 Press release: The Phase 3 ASCENT-07 study investigating sacituzumab govitecan-hziy versus chemotherapy as a first-line treatment post-endocrine therapy in HR+/HER2-negative metastatic breast cancer patients did not meet the primary endpoint of PFS as assessed by BICR. Overall survival is a key secondary endpoint and was not mature at the time of the primary analysis; however, an early trend was observed favoring patients treated with sacituzumab govitecan-hziy compared to chemotherapy.

Results to be presented on Wednesday General Session 1, SABCS 2025 (K Jhaveri et al)

TROP2-directed ADCs in mHR+, HER2 negative breast cancer

- TROP2-Directed ADC (SG, Dato-DXd, Sac-TMT) **>** Chemotherapy of physician's choice in chemotherapy pretreated metastatic disease
- SG and Dato-DXd FDA approved in United States for overlapping clinical scenarios
- ADCs differ in administration schedule and toxicities
- Awaiting results from 1st line trials

HER2-low breast cancer



Curigliano G et al. ASCO 2024.

DESTINY-Breast04: T-DXd vs TPC in HER2-low MBC (1-2 prior lines of chemotherapy)

Key Eligibility Criteria

- **Advanced or metastatic breast cancer:**
  - **≥1 prior endocrine therapy if HR+**
  - **1-2 prior chemotherapy regimens for metastatic disease or recurrence during or within 6 mo after adjuvant chemotherapy**
- **HER2 IHC 1+ or 2+/ISH- (as confirmed per central lab assessment) on archival or recent tumor biopsy**

R 2:1

T-DXd
5.4 mg/kg Q3W
(n = 373)

Primary endpoint: PFS in HR+ (BICR)

TPC
Capecitabine, eribulin, gemcitabine, paclitaxel, or nab-paclitaxel
(N=184)

Stratification factors:
- HER2 (1+ vs 2+/ISH-)
- N prior lines of chemotherapy (1 vs 2)
- HR status (positive [with vs without previous CDK4/6i] vs negative)

HR+ ≈ 480
HR– ≈ 60

Key secondary endpoints[d]
- PFS by BICR (all patients)
- OS (HR+ and all patients)

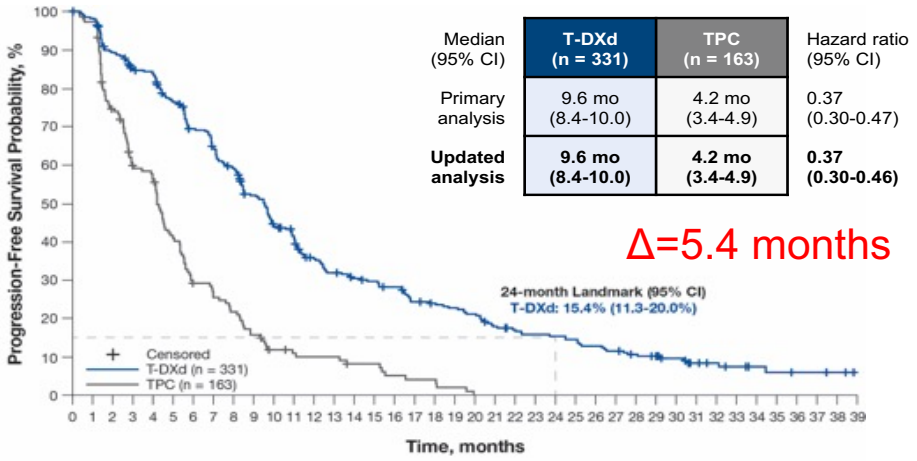
Secondary endpoints[d]
- PFS by investigator
- ORR by BICR and investigator
- DOR by BICR
- Safety
- Patient-reported outcomes (HR+)[e]

Modi S et al. ASCO 2022, Abstract LBA3; Modi S et al. N Engl J Med 2022;387(1):9-20.

DB04: T-DXd vs TPC for HER2-low MBC

Hormone Receptor-positive (n=494)

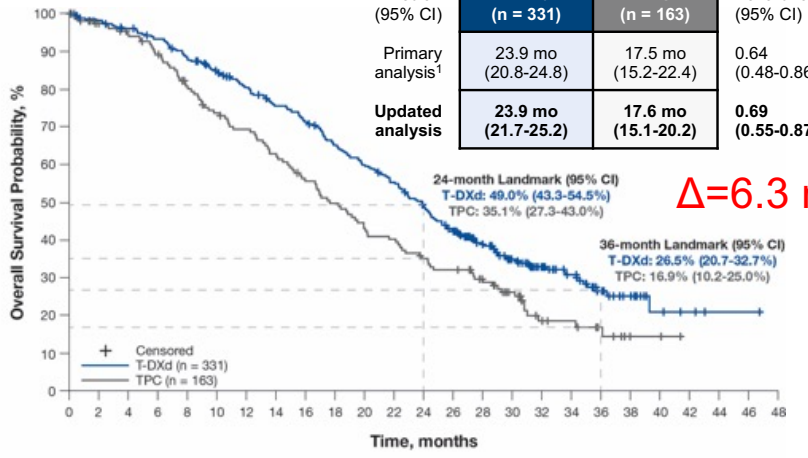
PFS



Median (95% CI)	T-DXd (n = 331)	TPC (n = 163)	Hazard ratio (95% CI)
Primary analysis	9.6 mo (8.4-10.0)	4.2 mo (3.4-4.9)	0.37 (0.30-0.47)
Updated analysis	**9.6 mo (8.4-10.0)**	**4.2 mo (3.4-4.9)**	**0.37 (0.30-0.46)**

Δ=5.4 months

OS

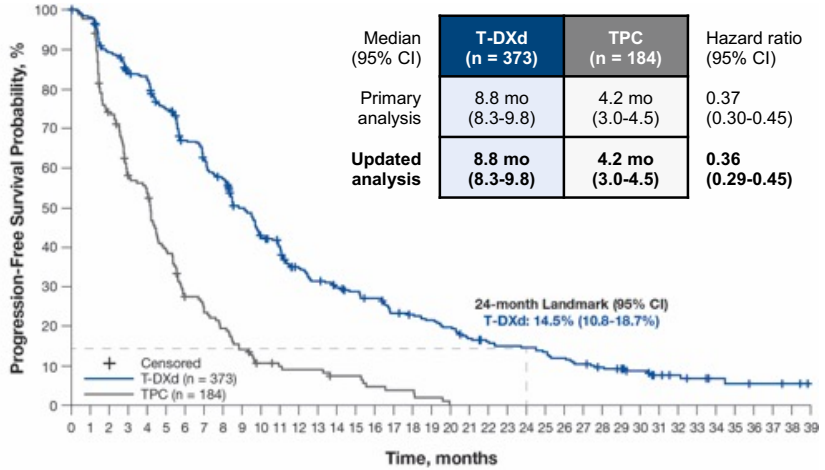


Median (95% CI)	T-DXd (n = 331)	TPC (n = 163)	Hazard ratio (95% CI)
Primary analysis[1]	23.9 mo (20.8-24.8)	17.5 mo (15.2-22.4)	0.64 (0.48-0.86)
Updated analysis	**23.9 mo (21.7-25.2)**	**17.6 mo (15.1-20.2)**	**0.69 (0.55-0.87)**

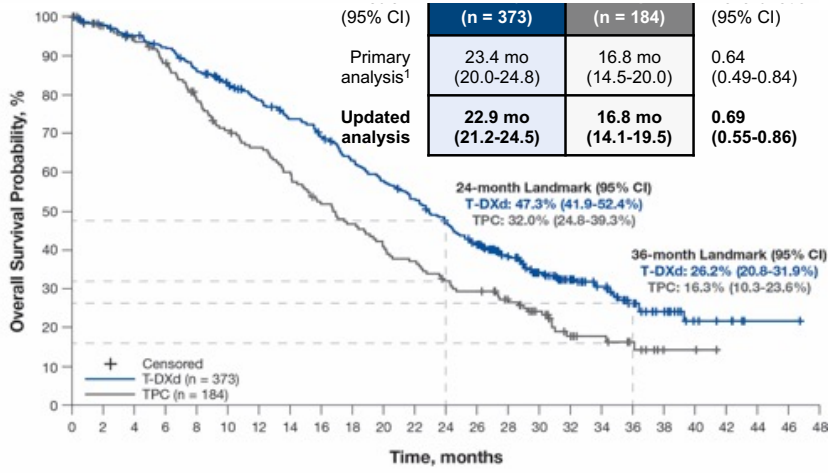
Δ=6.3 months

Median FU: 32.0 months

ALL Patients (n=557)



Median (95% CI)	T-DXd (n = 373)	TPC (n = 184)	Hazard ratio (95% CI)
Primary analysis	8.8 mo (8.3-9.8)	4.2 mo (3.0-4.5)	0.37 (0.30-0.45)
Updated analysis	**8.8 mo (8.3-9.8)**	**4.2 mo (3.0-4.5)**	**0.36 (0.29-0.45)**



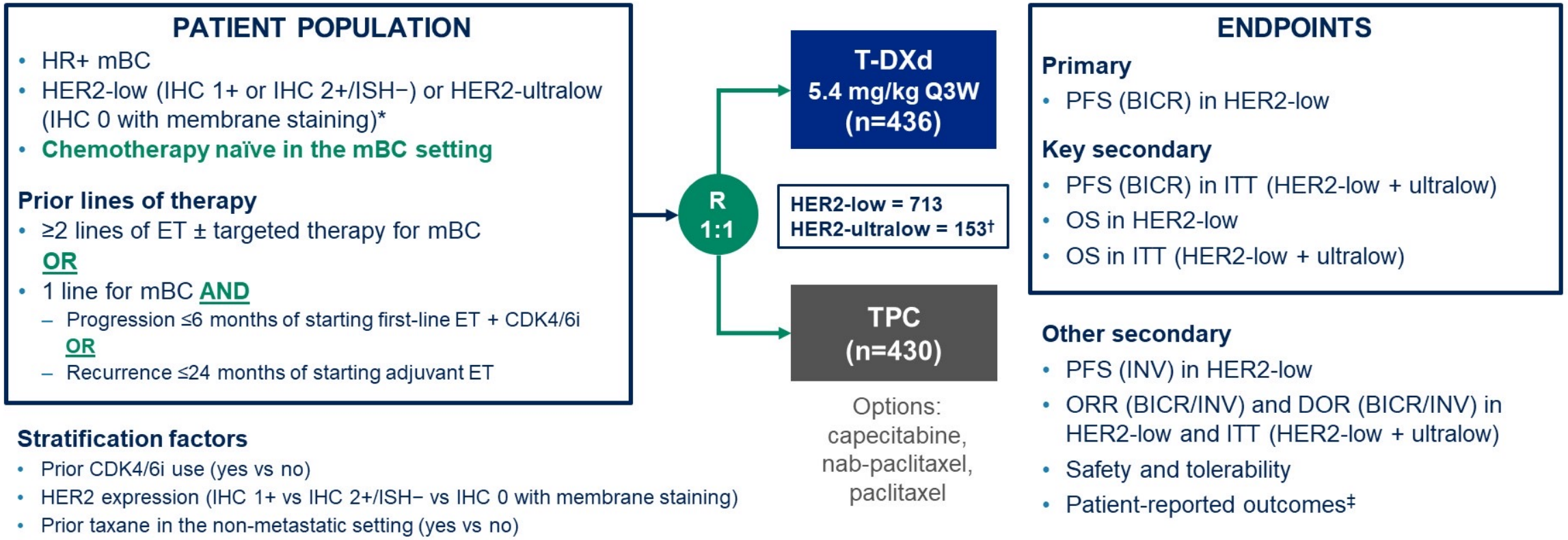
(95% CI)	(n = 373)	(n = 184)	(95% CI)
Primary analysis[1]	23.4 mo (20.0-24.8)	16.8 mo (14.5-20.0)	0.64 (0.49-0.84)
Updated analysis	**22.9 mo (21.2-24.5)**	**16.8 mo (14.1-19.5)**	**0.69 (0.55-0.86)**

ORR (HR+) : 52.6% vs. 16.3%.

With longer treatment duration, the overall safety profile of T-DXd was consistent with the primary analysis. Rates of ILD/pneumonitis remained unchanged with longer follow-up.

Modi S et al. ESMO 2023; Modi S Nat Med 2025.

DESTINY-Breast06: T-DXd vs TPC in HR+/HER2-low MBC After Progression on Endocrine Therapy



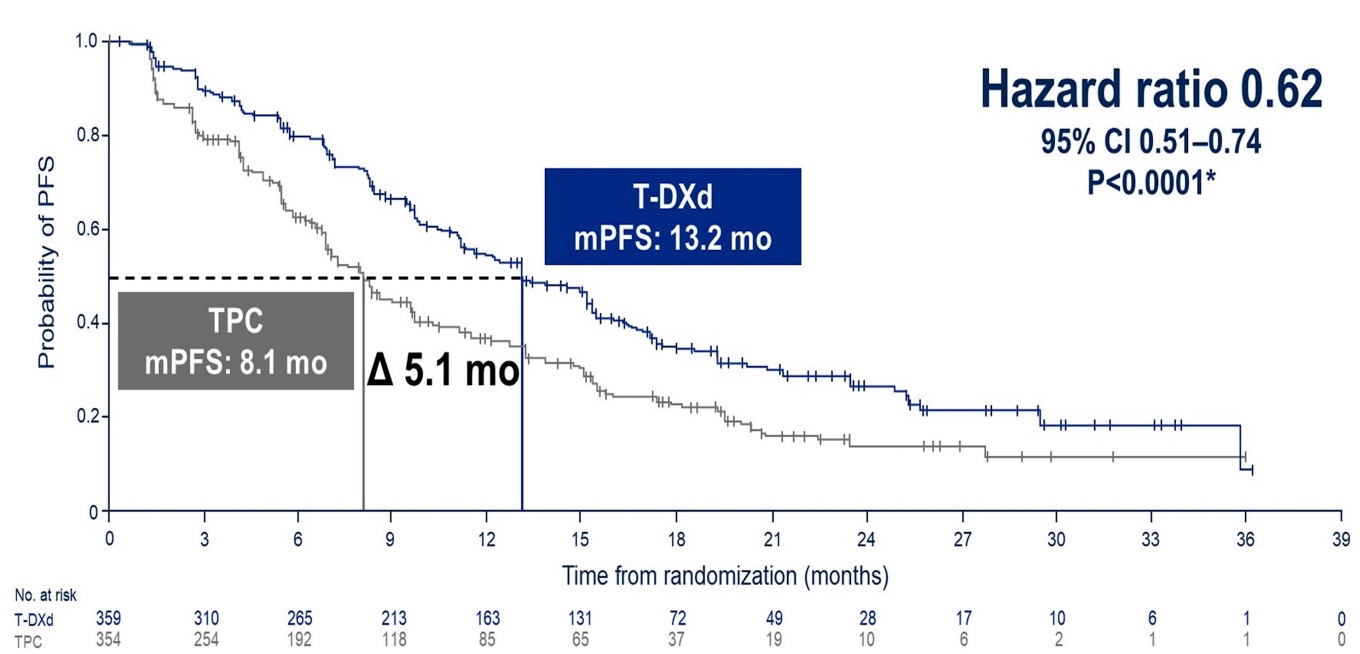
HER2 Ultra low: 17%
Bone only disease: 3%
Prior CDK4/6i: 89%

De novo mBC: 30%
Visceral disease 86%

Curigliano G et al. ASCO 2024; Bardia A et al. N Engl J Med. 2024;391:2110-22.

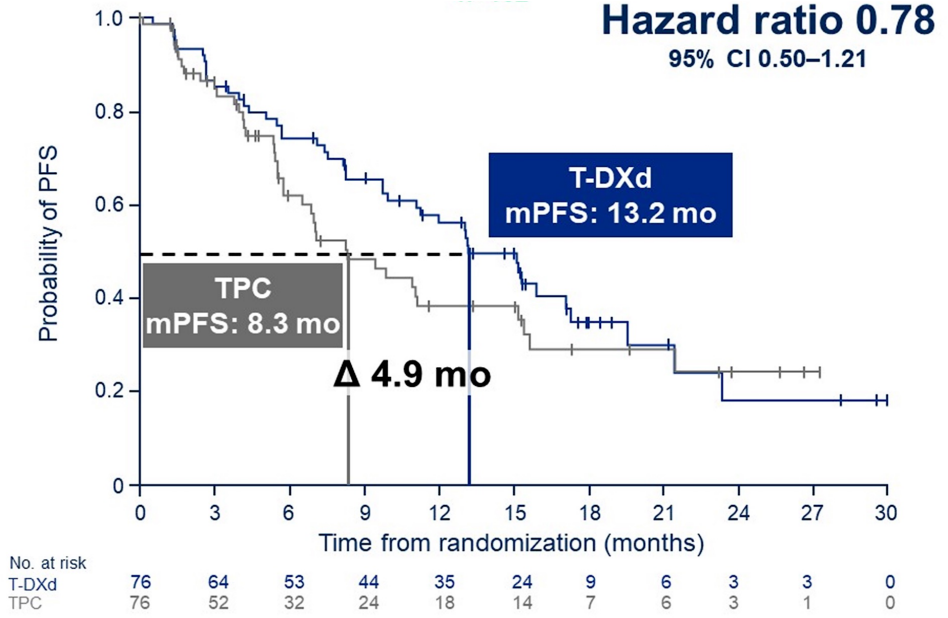
DB06: T-DXd Improved PFS vs TPC in HR+/HER2-low/ultra-low MBC

HER2-low (1+, 2+/ISH-)
(n=713)



ORR : 56.5% vs. 32.2%.

HER2 ultra-low (>0 <1+)
(n=152)

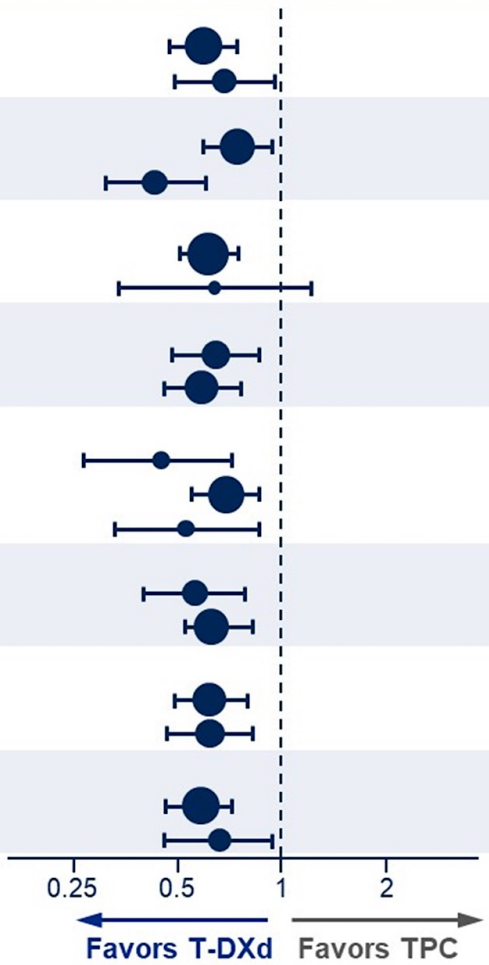


ORR: 61.8% vs. 26.3%.

Curigliano G et al. ASCO 2024; Bardia A et al. N Engl J Med. 2024;391:2110-22.

DB06 PFS subgroup analysis

	No. of events / no. of patients		mPFS (95% CI), months		Hazard ratio (95% CI)
	T-DXd	TPC	T-DXd	TPC	
Age					
<65 years	158/252	157/244	13.2 (11.2–15.2)	7.8 (6.9–8.6)	0.59 (0.47–0.74)
≥65 years	67/107	75/110	13.2 (9.7–17.0)	8.5 (6.9–11.5)	0.68 (0.49–0.95)
HER2 status*					
IHC 1+	157/238	150/234	12.9 (11.0–15.2)	8.2 (7.1–9.8)	0.74 (0.59–0.93)
IHC 2+/ISH−	65/117	80/118	15.2 (12.2–21.4)	7.0 (6.2–8.4)	0.43 (0.31–0.60)
Prior CDK4/6i					
Yes	206/324	212/320	13.1 (11.2–15.2)	7.9 (6.9–8.6)	0.61 (0.51–0.74)
No	19/35	20/34	16.1 (9.7–NE)	11.1 (6.9–20.6)	0.64 (0.34–1.21)
Prior taxane use (adjuvant/neoadjuvant setting)					
Yes	94/151	101/151	12.9 (9.7–14.0)	7.4 (6.3–9.3)	0.64 (0.48–0.85)
No	131/208	131/203	15.0 (11.3–16.5)	8.3 (7.0–9.7)	0.59 (0.46–0.76)
Number of prior lines of ET (metastatic setting)					
1	27/54	45/67	15.2 (9.7–19.1)	8.0 (5.7–8.5)	0.45 (0.27–0.72)
2	158/242	153/236	13.1 (11.2–15.2)	8.3 (6.9–10.0)	0.69 (0.55–0.86)
≥3	39/62	33/49	12.3 (8.3–18.5)	8.1 (5.4–9.7)	0.53 (0.33–0.86)
Endocrine resistance					
Primary	66/105	83/116	13.1 (10.0–15.2)	6.8 (5.3–8.1)	0.56 (0.40–0.78)
Secondary	159/254	148/236	13.2 (11.3–15.5)	9.0 (7.5–11.1)	0.65 (0.52–0.82)
Choice of chemotherapy†					
Capecitabine	131/220	134/208	13.5 (11.4–15.4)	8.5 (7.0–11.4)	0.62 (0.49–0.79)
Taxanes (Nab-paclitaxel + paclitaxel)	94/139	98/146	12.9 (9.6–15.4)	7.3 (6.4–8.3)	0.62 (0.46–0.82)
Liver metastases					
Yes	163/243	166/232	11.4 (9.8–13.2)	7.0 (6.4–8.1)	0.58 (0.46–0.72)
No	62/116	66/122	17.0 (15.0–19.4)	11.3 (8.2–14.8)	0.66 (0.46–0.93)

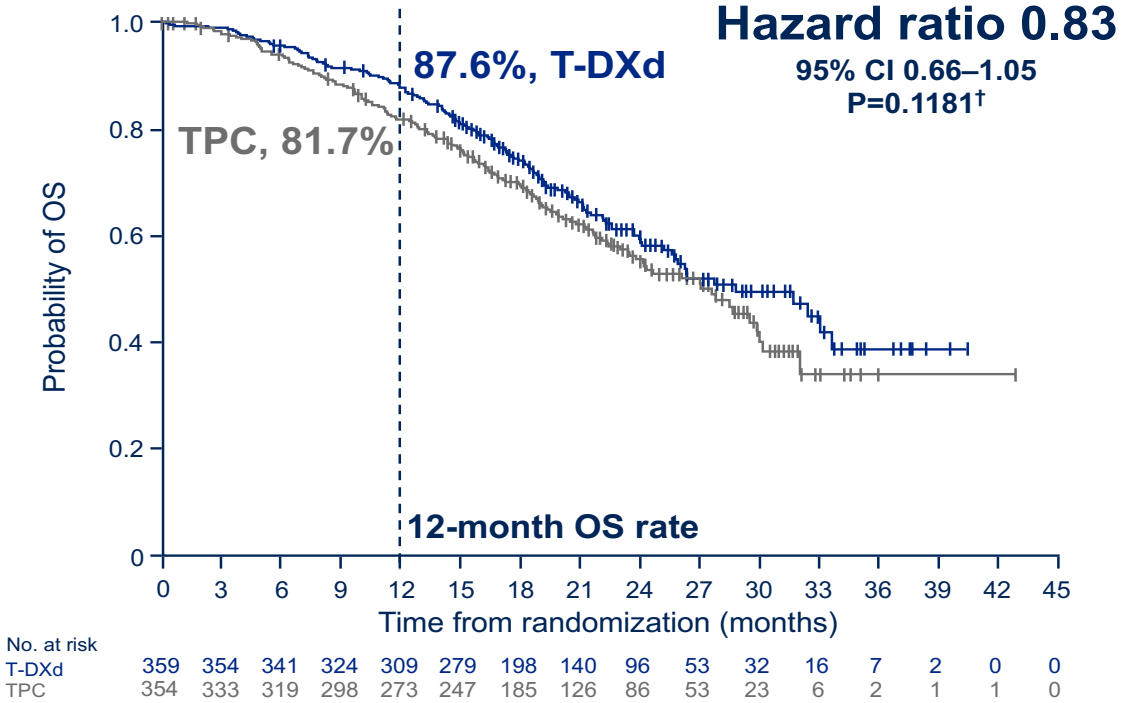


Size of circle is proportional to the number of events
*Based on central laboratory data (ie the HER2 result from the most recent evaluable sample prior to randomization); †specified by the investigator prior to randomization
BICR, blinded independent central review; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; CI, confidence interval; ET, endocrine therapy;
HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; (m)PFS, (median) progression-free survival;
NE, not evaluable; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice

Curigliano G et al. ASCO 2024; Bardia A et al. N Engl J Med. 2024;391:2110-22.

DB06: OS Analysis

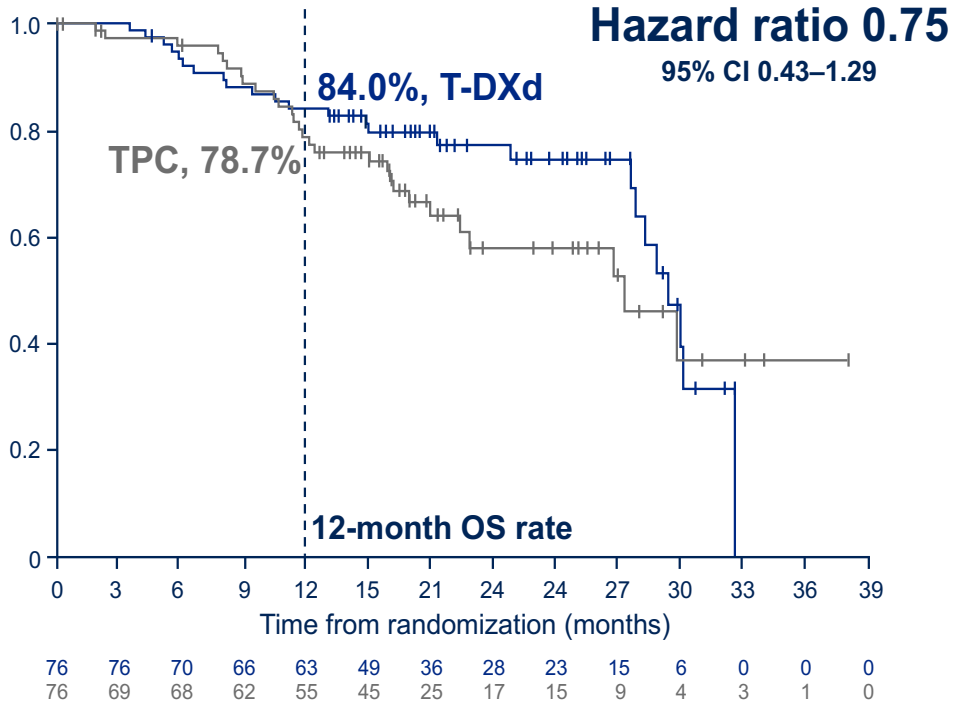
HER2-low (1+, 2+/ISH-)
(n=713)



Median FU: 18.6 months

20.1% in TPC arm received T-DXd after protocol therapy

HER2 ultralow (>0 <1+)
(n=152)



Median FU: 16.8 months

17.9% in TPC arm received T-DXd after protocol therapy

Will survival be same if T-DXd→ chemo vs chemo→T-DXd are compared in true cross over design?

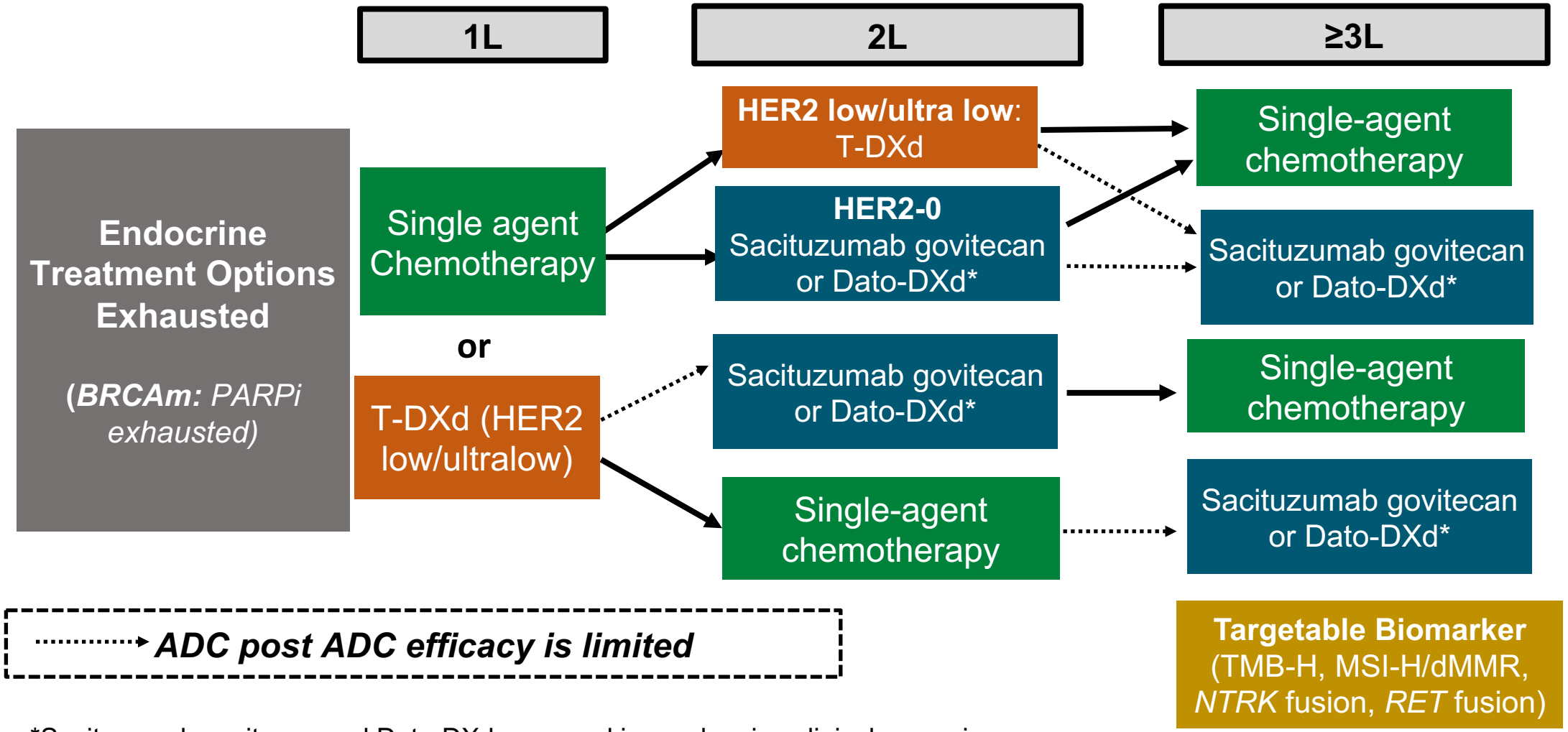
Curigliano G et al. ASCO 2024; Bardia A et al. N Engl J Med. 2024;391:2110-22.

T-DXd in HER2 low (ultra-low) ER+ breast cancer: First line or later after Endocrine therapy ?

- On August 5, 2022, the FDA approved fam-trastuzumab deruxtecan-nxki for adult patients with unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer who have received a prior chemotherapy in the metastatic setting or developed disease recurrence during or within six months of completing adjuvant chemotherapy.
- On January 27, 2025, the FDA approved fam-trastuzumab deruxtecan-nxki for unresectable or metastatic HR-positive, HER2-low (IHC 1+ or IHC 2+/ISH-) or HER2-ultralow (IHC 0 with membrane staining) breast cancer, as determined by an FDA-approved test, that has progressed on one or more endocrine therapies in the metastatic setting.
  - FDA also approved the PATHWAY anti-HER-2 (4B5) Rabbit Monoclonal Primary Antibody assay as a companion diagnostic device to identify patients with HER2-ultralow (IHC 0 with membrane staining) breast cancer

- For HR+ HER2 low/ultra low mBC: T-DXd as first cytotoxic therapy or chemotherapy as first cytotoxic therapy followed by T-DXd upon progression are reasonable options based on
  - Disease burden, sites of metastatic disease, patient preference and Performance status

Treatment algorithm HR+/HER2- MBC



*Sacituzumab govitecan and Dato-DXd approved in overlapping clinical scenarios
Dato-DXd approved with ≥1 prior CT; Sacituzumab govitecan approved with ≥2 prior CT

Agenda

Module 1: Previously Untreated Metastatic Triple-Negative Breast Cancer (mTNBC) — Prof Schmid

Module 2: Integrating Antibody-Drug Conjugates (ADCs) into the Management of Endocrine-Resistant Hormone Receptor-Positive Metastatic Breast Cancer (mBC) — Dr Sharma

Module 3: Selection and Sequencing of Therapy for Relapsed/Refractory mTNBC — Dr Nanda

Module 4: Tolerability and Other Practical Considerations with ADCs and Other Cytotoxic Agents for mBC — Dr Cortés

Dr Ranju Gupta
(Bethlehem, Pennsylvania)

Case Presentation: 73-year-old woman with recurrent ER-negative, HER2-low (IHC 2+) mBC receives sacituzumab govitecan and achieves complete remission

Dr Gigi Chen
(Walnut Creek, California)

Management of neutropenia associated with sacituzumab govitecan

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

Are there any predictors of treatment benefit with sacituzumab govitecan? Does level of TROP2 expression correlate with benefit?

Do you employ prophylactic antidiarrheals with sacituzumab govitecan?

Have you observed nausea and vomiting with sacituzumab govitecan?

Do you employ prophylactic growth factors with sacituzumab govitecan?

Dr Ranju Gupta
(Bethlehem, Pennsylvania)

Case Presentation: 69-year-old woman with recurrent ER-negative, HER2-low (IHC 1+) mBC (HER2 V697L mutation) receives T-DXd with complete response but develops Grade 1 ILD

Dr Laila Agrawal
(Louisville, Kentucky)

Management of T-DXd-related side effects

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

Does tumor involvement in the lung or pleura affect your decision to use T-DXd? What about preexisting cardiopulmonary conditions, including COPD?

What is your approach to screening for ILD with T-DXd?

How do you manage Grade 1 ILD with T-DXd? In what situations will you rechallenge? What about Grade 2 ILD?

QUESTIONS FOR THE FACULTY

How, if at all, does level of HER2 expression (IHC 2+ versus 1+ versus ultralow) affect your use of T-DXd?

In what situations, if any, would you use T-DXd for a patient with HR-negative, HER2-ultralow disease?

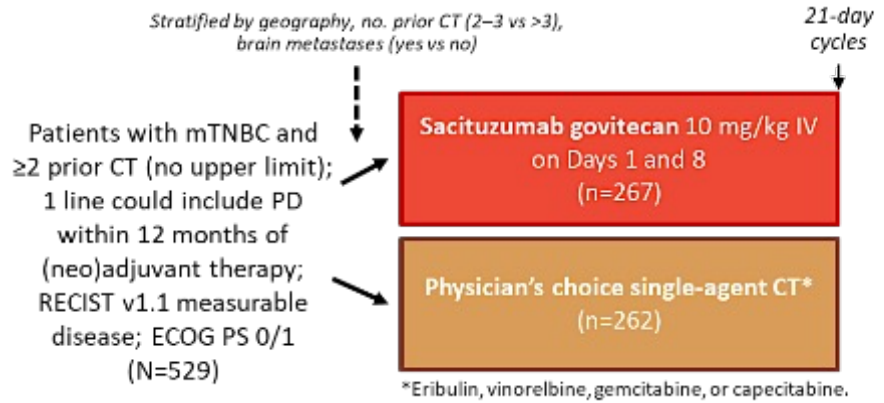
How do you generally sequence sacituzumab govitecan and T-DXd for patients with relapsed/refractory HR-negative, HER2-low mBC?

Have you encountered patients with mBC and HER2 TKD mutations, and would you consider zongertinib or sevabertinib for such patients?

Selection and Sequencing of Therapy for Relapsed/Refractory (R/R) mTNBC

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

ASCENT: Sacituzumab Govitecan Improves PFS/OS in Advanced Triple-Negative Breast Cancer

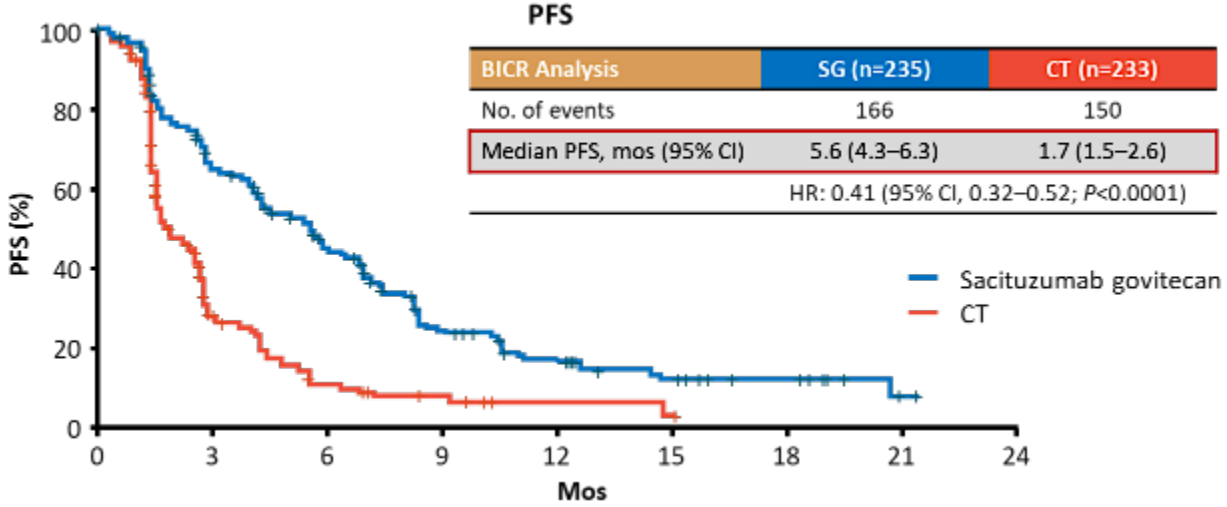


- Primary endpoint: PFS by IRC in patients without brain metastases
- Secondary endpoints: PFS (full population), OS, ORR, DoR, TTR, safety

- Sacituzumab govitecan is FDA approved for both TN (Apr 2021) and HR+/HER2- (Feb 2023) MBC
- Trop-2 expressed in most TN and HR+
- **Trop-2 expression not required for use**

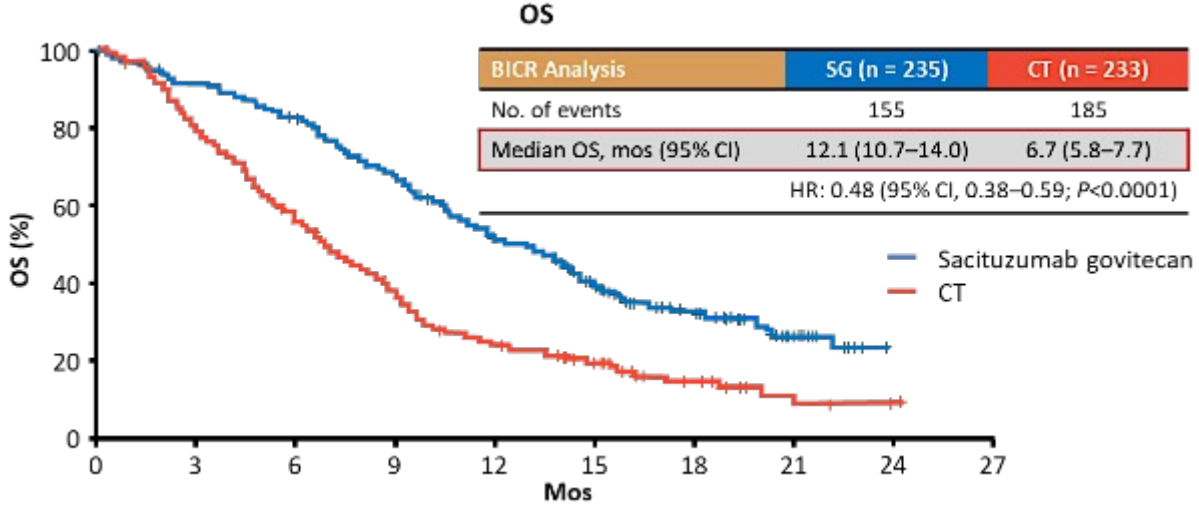
PFS

BICR Analysis	SG (n=235)	CT (n=233)
No. of events	166	150
Median PFS, mos (95% CI)	5.6 (4.3–6.3)	1.7 (1.5–2.6)
	HR: 0.41 (95% CI, 0.32–0.52; *P*<0.0001)	



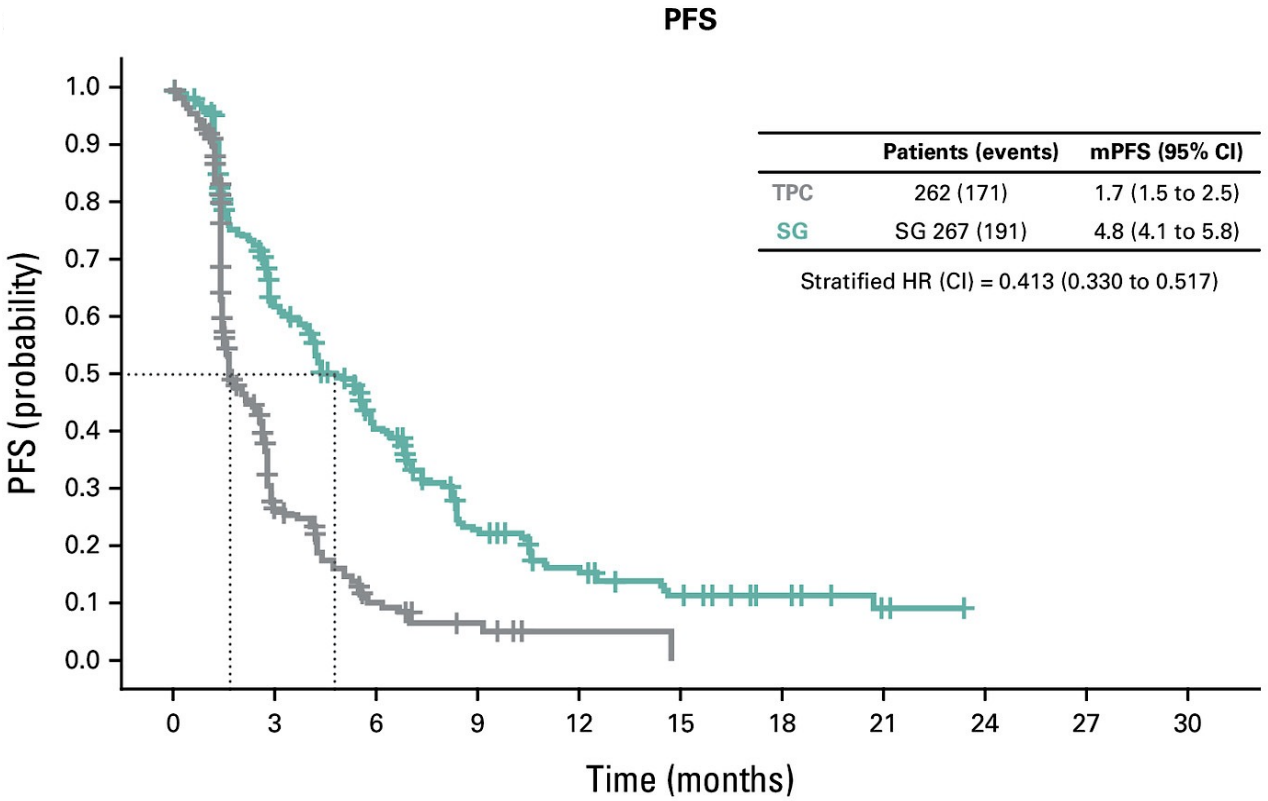
OS

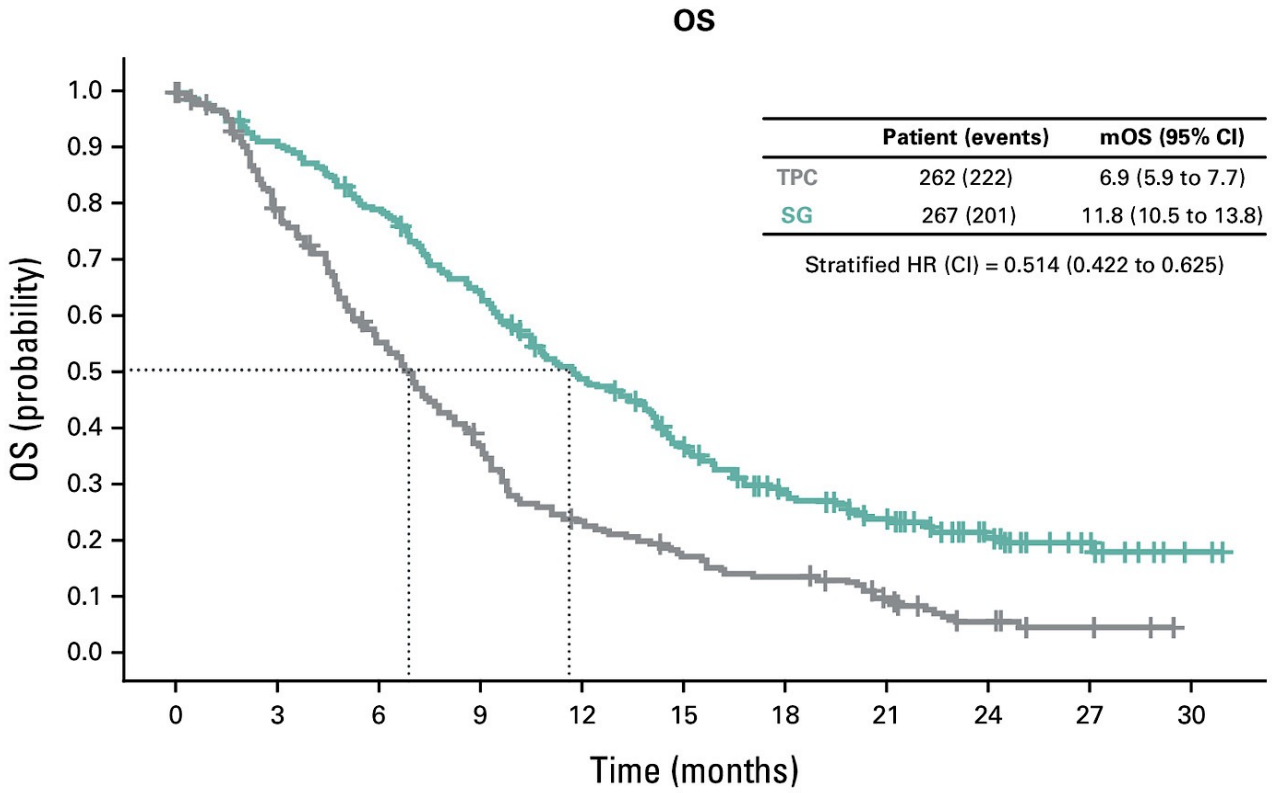
BICR Analysis	SG (n = 235)	CT (n = 233)
No. of events	155	185
Median OS, mos (95% CI)	12.1 (10.7–14.0)	6.7 (5.8–7.7)
	HR: 0.48 (95% CI, 0.38–0.59; *P*<0.0001)	



Bardia, et al. NEJM 2021.

Phase III ASCENT Trial: Final Survival Outcomes (ITT Population)



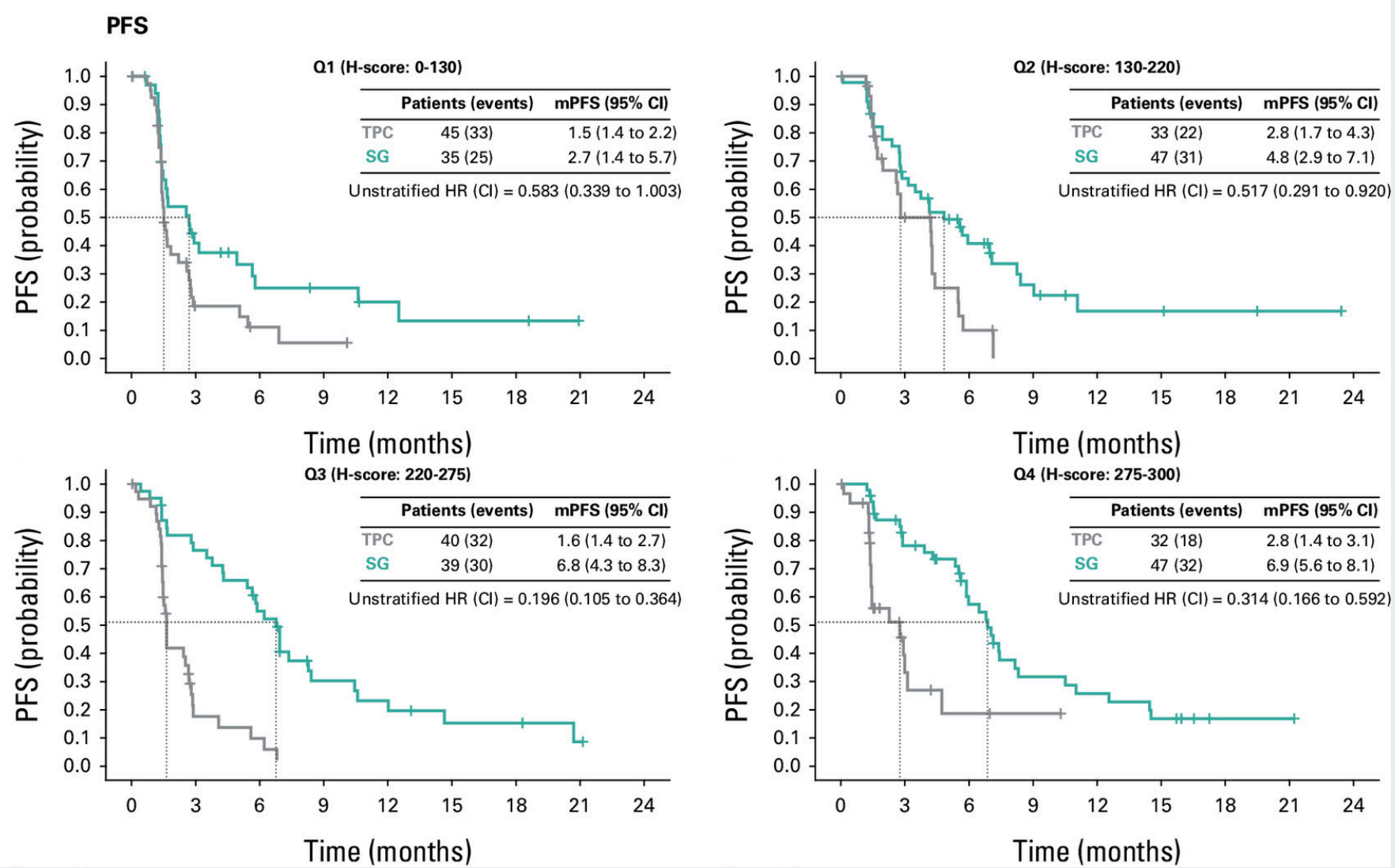


ITT = intention to treat; PFS = progression-free survival; TPC = treatment of physician's choice; SG = sacituzumab govitecan; OS = overall survival

Bardia A et al. *J Clin Oncol* 2024 May 20;42(15):1738-44.

RTP RESEARCH TO PRACTICE

Phase III ASCENT: Final PFS Outcomes by TROP2 Expression



PFS = progression-free survival; TPC = treatment of physician's choice

Bardia A et al. *J Clin Oncol* 2024 May 20;42(15):1738-44.

Phase III ASCENT: Adverse Events (Safety Population)

Adverse Event	Sacituzumab Govitecan (N=258)			Chemotherapy (N=224)		
	Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4
	number of patients (percent)					
Any adverse event	252 (98)	117 (45)	48 (19)	192 (86)	71 (32)	33 (15)
Hematologic event						
Neutropenia†	163 (63)	88 (34)	44 (17)	96 (43)	45 (20)	29 (13)
Anemia‡	89 (34)	20 (8)	0	54 (24)	11 (5)	0
Leukopenia§	41 (16)	23 (9)	3 (1)	25 (11)	10 (4)	2 (1)
Thrombocytopenia¶	14 (5)	2 (1)	2 (1)	25 (11)	3 (1)	0
Febrile neutropenia	15 (6)	12 (5)	3 (1)	5 (2)	4 (2)	1 (<1)
Gastrointestinal event						
Diarrhea	153 (59)	27 (10)	0	27 (12)	1 (<1)	0
Nausea	147 (57)	6 (2)	1 (<1)	59 (26)	1 (<1)	0
Vomiting	75 (29)	2 (1)	1 (<1)	23 (10)	1 (<1)	0
Constipation	44 (17)	0	0	32 (14)	0	0
Abdominal pain	29 (11)	3 (1)	0	9 (4)	1 (<1)	0
General disorders and administration-site conditions						
Fatigue	115 (45)	8 (3)	0	68 (30)	12 (5)	0
Asthenia	31 (12)	2 (1)	0	23 (10)	3 (1)	0
Skin and subcutaneous disorders: alopecia‖	119 (46)	0	0	35 (16)	0	0
Metabolism and nutrition disorders: decreased appetite	51 (20)	4 (2)	0	32 (14)	1 (<1)	0
Nervous system disorders**††	64 (25)	1 (<1)	0	53 (24)	5 (2)	0
Respiratory, thoracic, and mediastinal disorders††	41 (16)	5 (2)‡‡	0	17 (8)	1 (<1)	0
Musculoskeletal and connective-tissue disorders††	32 (12)	0	0	28 (12)	3 (1)	0
Infections and infestations††	30 (12)	6 (2)	1 (<1)	22 (10)	4 (2)	3 (1)

Bardia A et al. *N Engl J Med* 2021;384:1529-41.

T-DXd improves PFS/OS for advanced HR-negative/HER2-low Advanced Breast Cancer (Exploratory)

Patients[a]
- HER2-low (IHC 1+ vs IHC 2+/ISH−), unresectable, and/or mBC treated with 1-2 prior lines of chemotherapy in the metastatic setting
- HR+ disease considered endocrine refractory

R 2:1

T-DXd
5.4 mg/kg Q3W
(n = 373)

HR+ ≈ 480
HR− ≈ 60

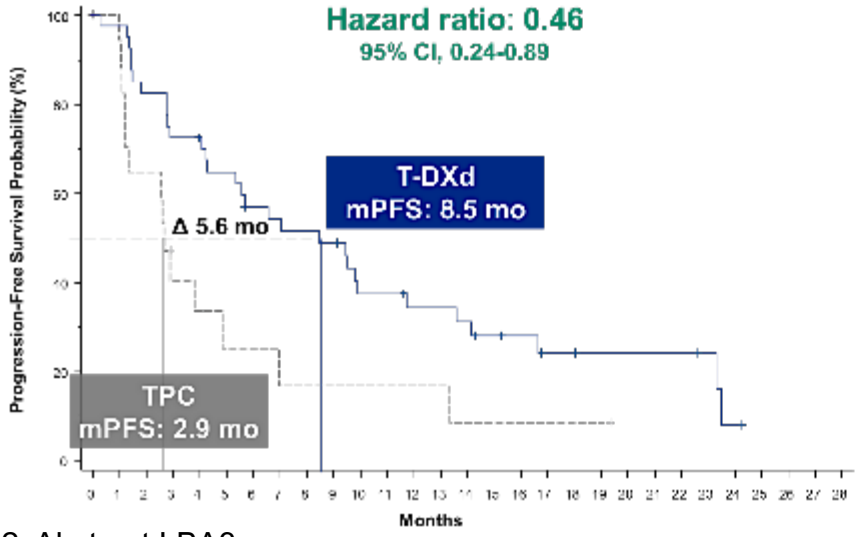
TPC
Capecitabine, eribulin, gemcitabine, paclitaxel, nab-paclitaxel[c]
(n = 184)

Primary endpoint
- PFS by BICR (HR+)

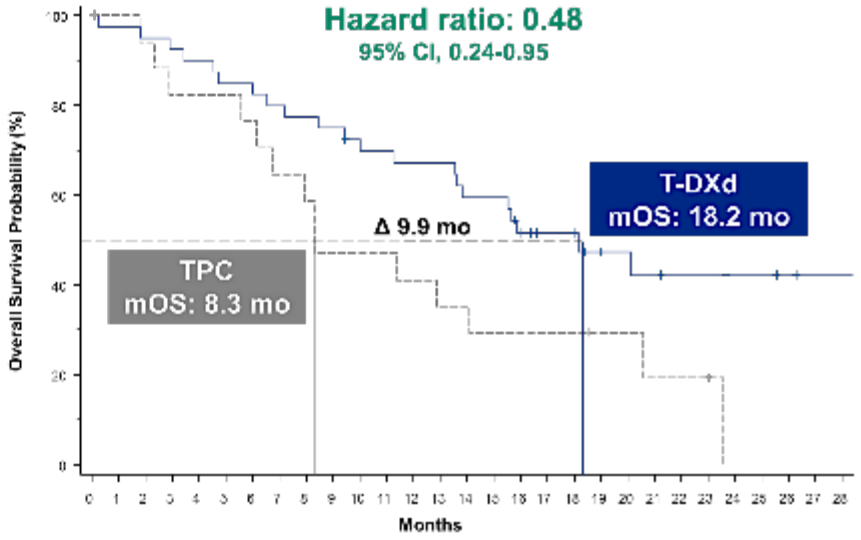
Key secondary endpoints[b]
- PFS by BICR (all patients)
- OS (HR+ and all patients)

Stratification factors
- Centrally assessed HER2 status[d] (IHC 1+ vs IHC 2+/ISH−)
- 1 versus 2 prior lines of chemotherapy
- HR+ (with vs without prior treatment with CDK4/6 inhibitor) versus HR−

PFS

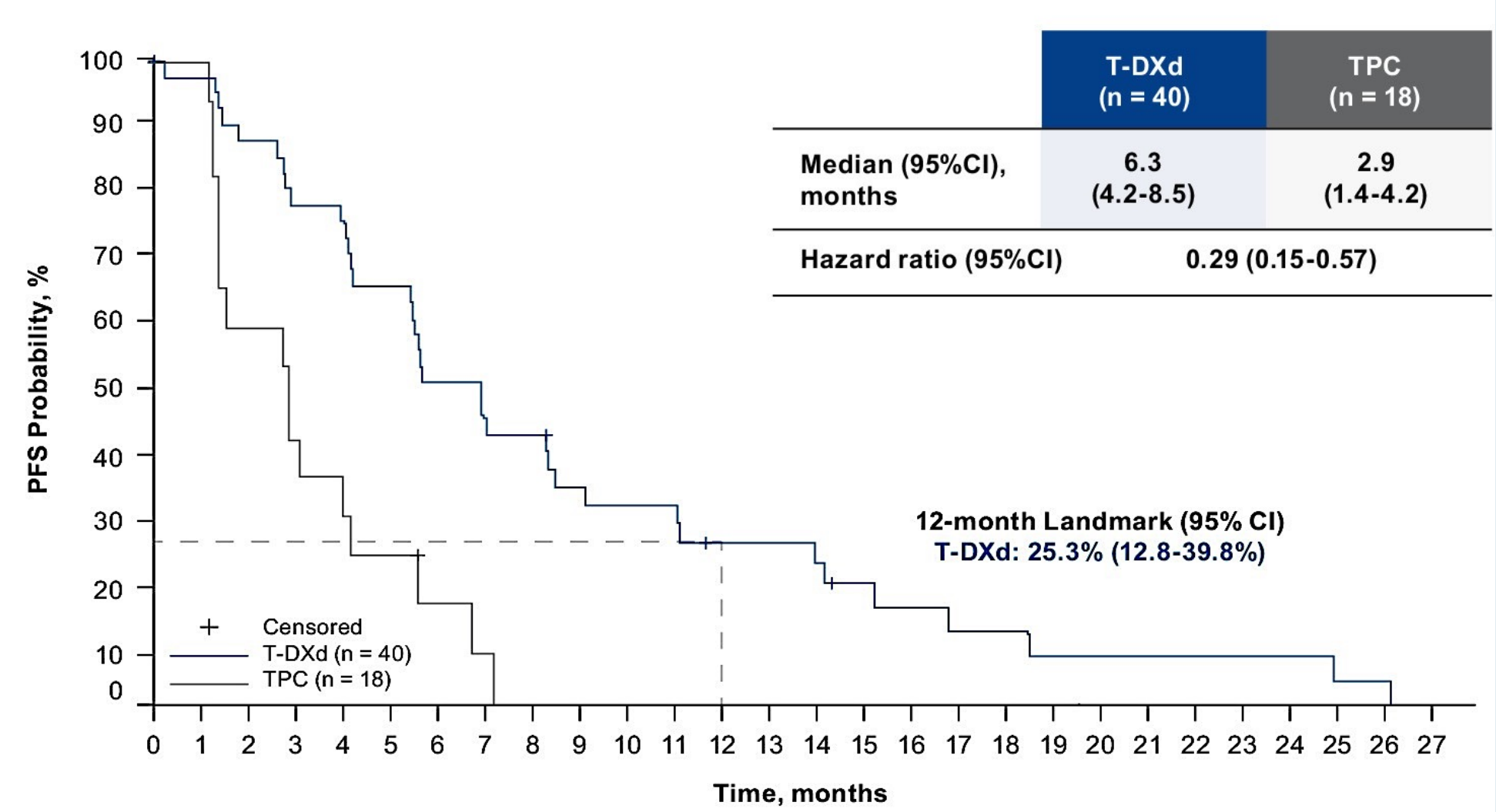


OS



Modi S, et al. ASCO. 2022. Abstract LBA3.

Phase III DESTINY-Breast04 Trial: Updated Progression-Free Survival (PFS) in the HR-Negative Population

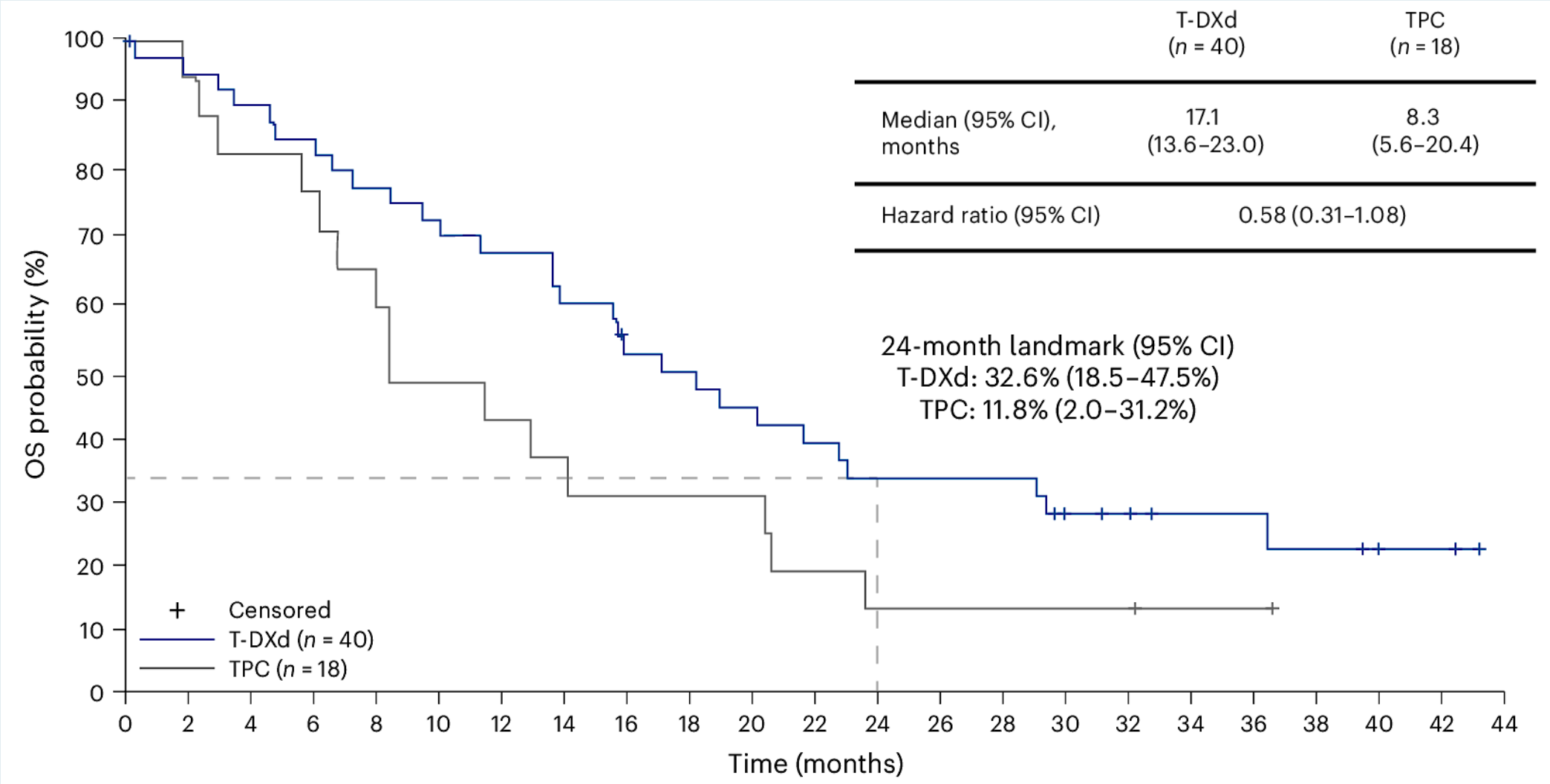


	T-DXd (n = 40)	TPC (n = 18)
Median (95%CI), months	6.3 (4.2-8.5)	2.9 (1.4-4.2)
Hazard ratio (95%CI)	0.29 (0.15-0.57)	

T-DXd = trastuzumab deruxtecan

Modi S et al. *Nat Med* 2025 October 8;[Online ahead of print].

Phase III DESTINY-Breast04: Updated Overall Survival (OS) in the HR-Negative Population



	T-DXd (*n* = 40)	TPC (*n* = 18)
Median (95% CI), months	17.1 (13.6–23.0)	8.3 (5.6–20.4)
Hazard ratio (95% CI)	0.58 (0.31–1.08)	

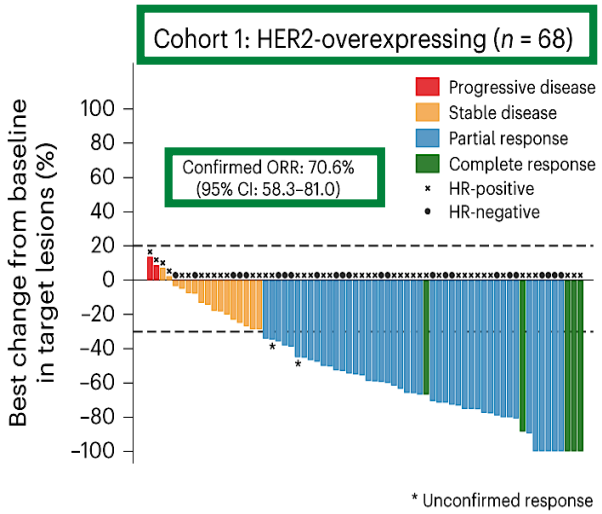
Modi S et al. *Nat Med* 2025 October 8;[Online ahead of print].

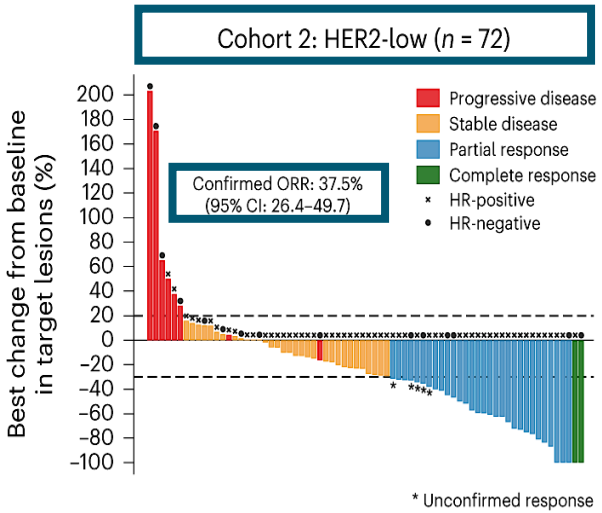
Daisy Trial: Benefit of T-DXd in HER2 0

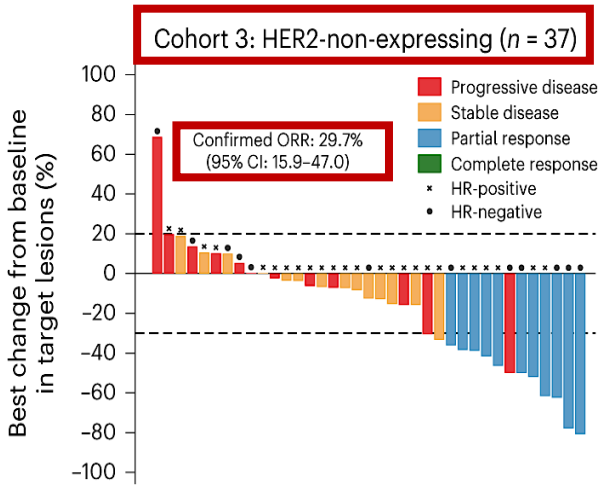
COHORT 1 HER2 overexpressing: HER2 IHC 3+ or IHC 2+/ISH+ (*n*=72)
- Previous taxanes
- Resistant to trastuzumab and T-DM1

COHORT 2 HER2-low: HER2 IHC 2+/ISH- or IHC 1+ (*n*=74)
- Previous anthracyclines and taxanes
- If HR+: resistant to CDK4/6 inhibitors plus HT

COHORT 3 HER2 non-expressing: HER2 IHC 0 (*n*=40)
- Previous anthracyclines and taxanes
- If HR+: resistant to CDK4/6 inhibitors plus HT







Data cut-off: Oct 19, 2021	Cohort 1 HER2 IHC 3+ or IHC 2+/ISH+ (n=68)	Cohort 2 HER2 IHC 2+/ISH- or IHC 1+ (n=72)	Cohort 3 HER2 IHC 0 (n=37)
Median PFS (mths) (95% CI)	11.1 (8.5–14.4)	6.7 (4.4-8.3)	4.2 (2-5.7)
HR (95% CI)	0.53 (0.34-0.84)	1.00	1.96 (1.21-3.15)
p-value	*p* <0.0001		

- Tumor heterogeneity
- HER2 > 0 and < 1+

Mosele et al, ESMO Breast 2022

TROPION-PanTumor01: Datopotamab DXd in Advanced TNBC

ORR by BICR:
- All patients: **32%**
- Topo I inhibitor-naive patients: **44%**

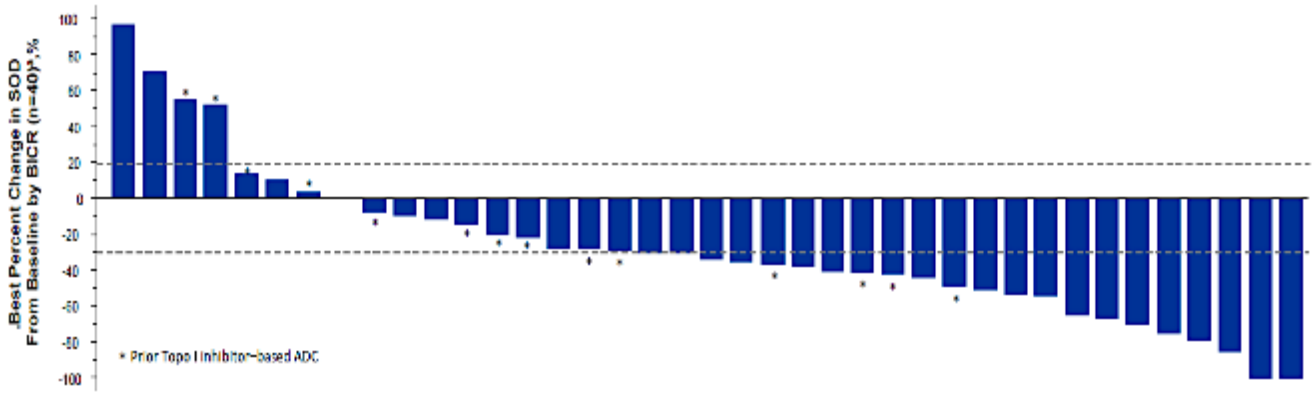
mDOR: 16.8 months in both groups

mPFS:
- All patients: 4.4 months
- Topo I inhibitor-naive patients: 7.3 months

mOS:
- All patients: 13.5 months
- Topo I inhibitor-naive patients: 14.3 months

AEs: Most common TEAEs: stomatitis (73%), nausea (66%), vomiting (39%)

Antitumor Tumor Responses by BICR



Bardia et al, SABCS 2022.

OptiTROP-Breast01: Randomized, Controlled, Open-Label Phase III Study (NCT05347134)

Patients with locally recurrent or metastatic TNBC

- Relapsed or refractory to 2 or more prior chemotherapy regimens for unresectable, locally advanced or metastatic disease
  - For prior therapy, 1 could be in the (neo)adjuvant setting, provided progression occurred during treatment or within 12 months after treatment discontinuation
- Received taxane(s) in any setting

R 1:1

- **Sac-TMT, 5 mg/kg IV, every 2 weeks**
- **Physician's choice of chemotherapy:** eribulin, capecitabine, gemcitabine, or vinorelbine

Treatment until disease progression, unacceptable toxicity or any other reason for discontinuation

Endpoints[a]

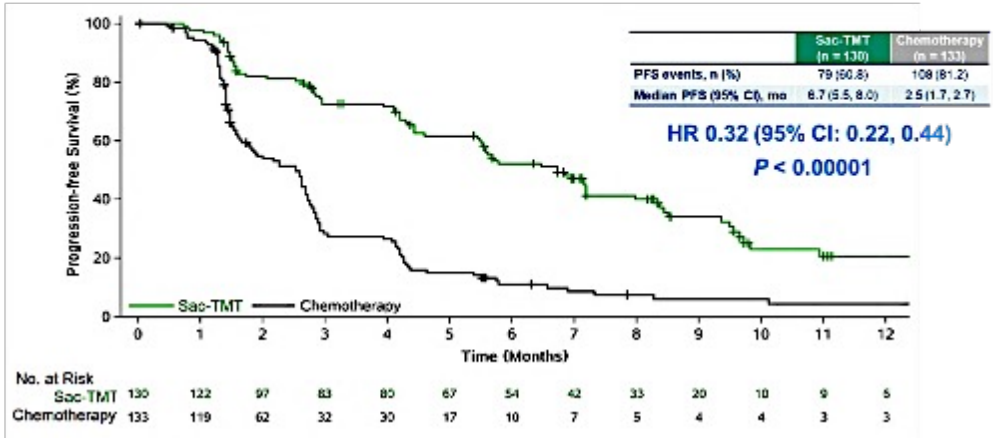
Primary
- PFS by BICR

Secondary
- OS
- PFS by investigator assessment
- ORR, DOR
- Safety

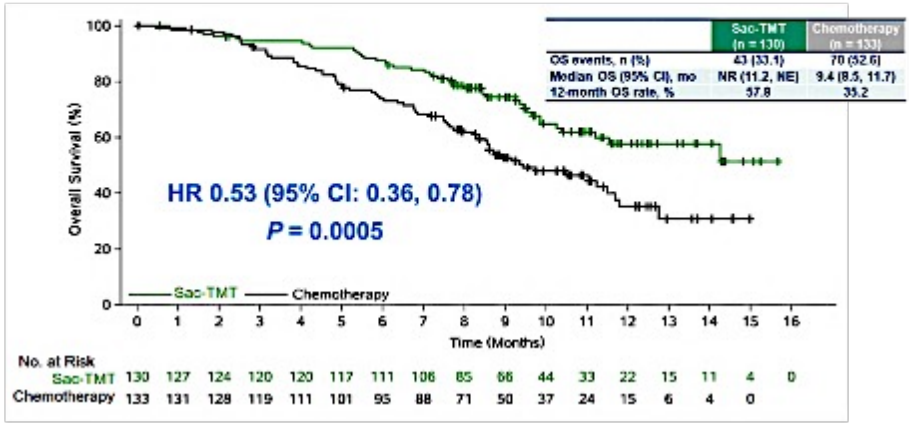
Stratification factors
- Line of prior therapy (2–3 vs >3)
- Presence of liver metastases (yes vs no)

Tumor assessment
- Every 6 weeks for the first year and every 12 weeks afterward.

PFS

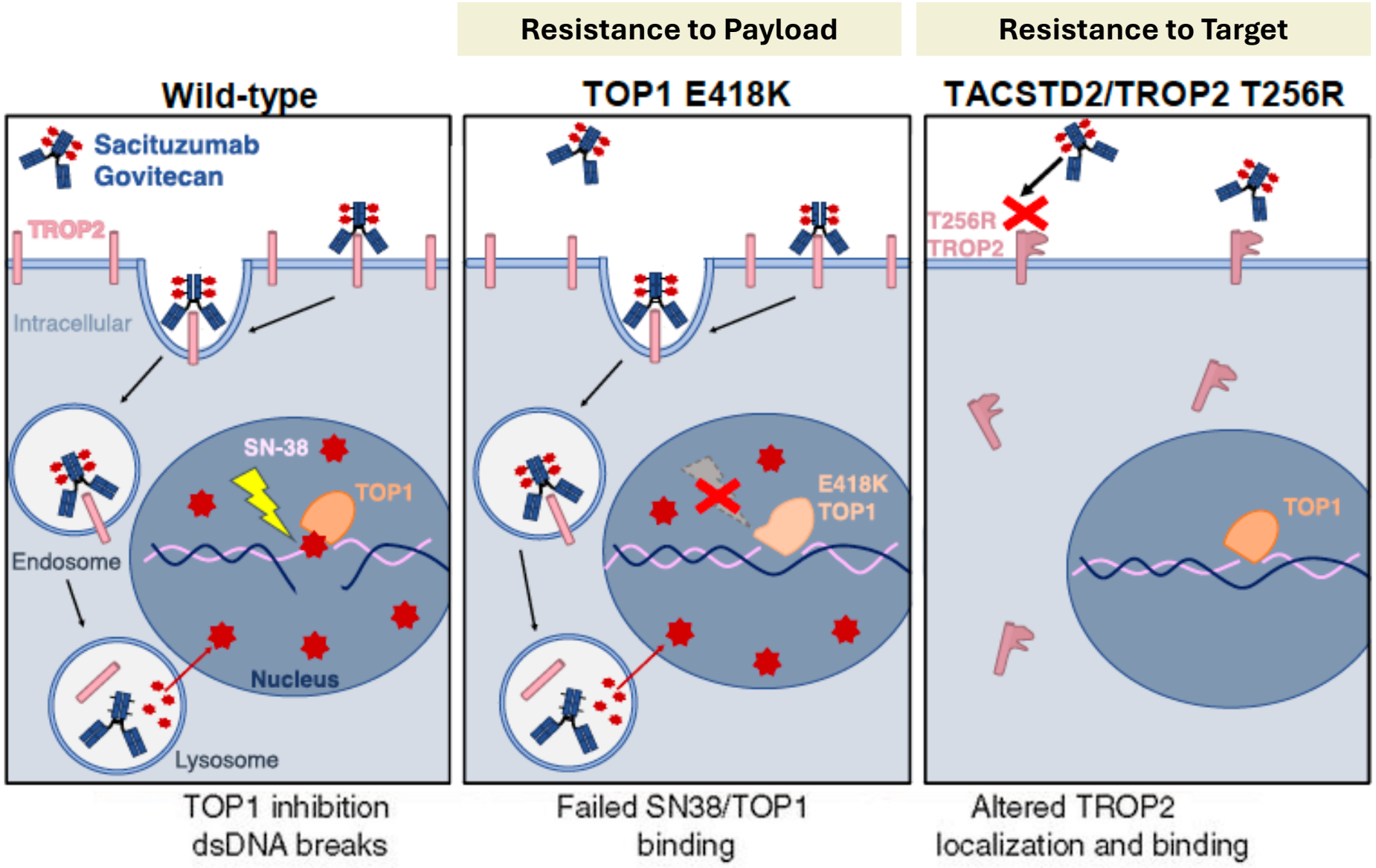


OS



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

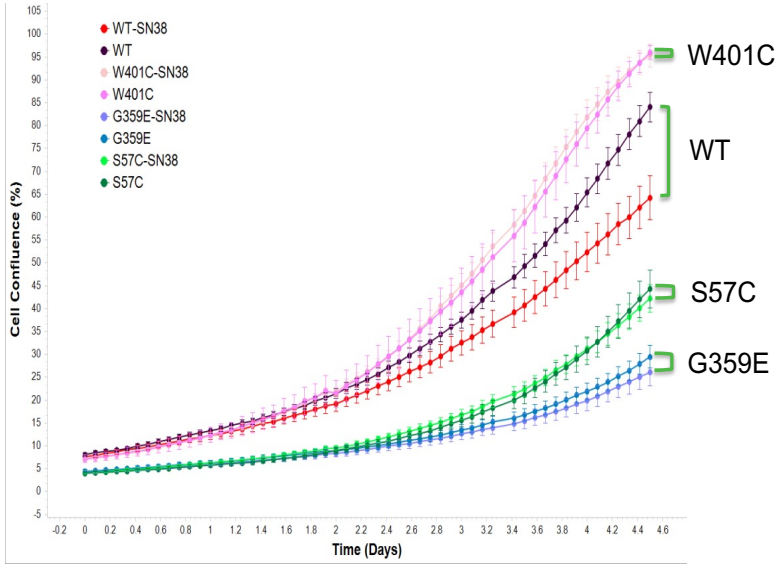
Mechanisms of Resistance to ADCs



Coates et al. *Cancer Discov* 2021

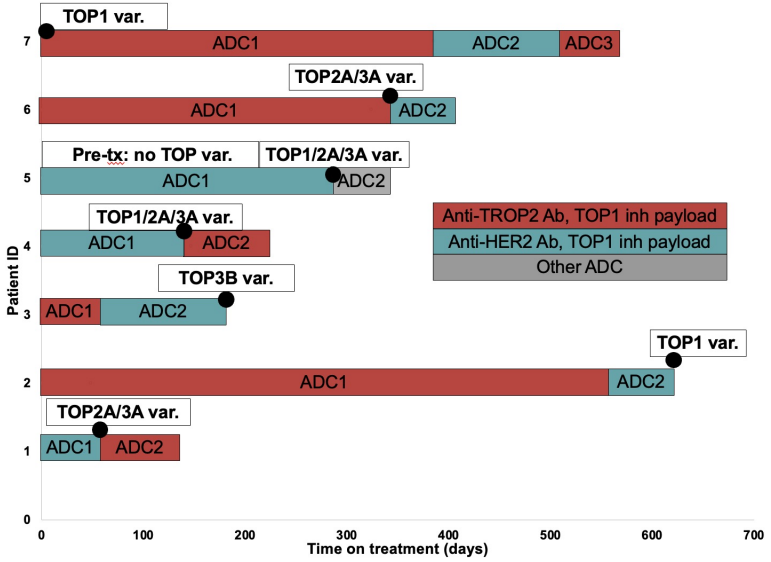
Mechanisms of ADC Resistance

TOP1 mutations in ctDNA post-Topo1i ADC[1]



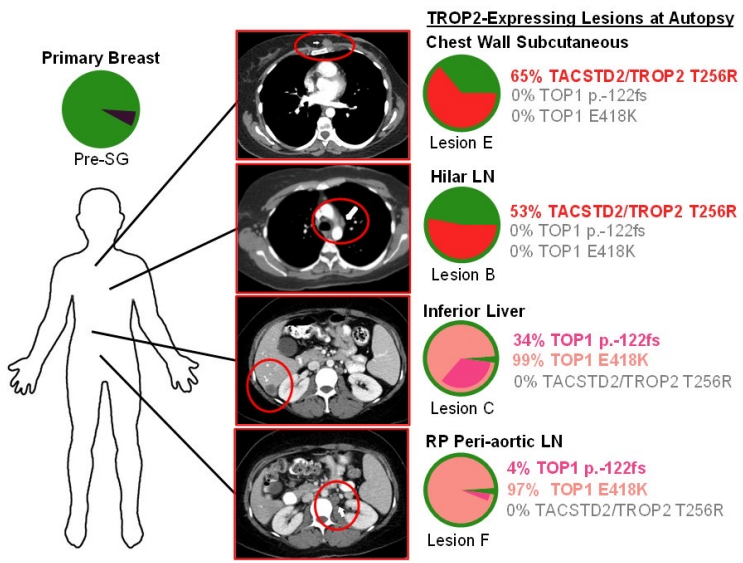
- TOP1 mutations are observed in ctDNA after treatment with Topo1i ADC

Clinical course of pts with TOP variants[2]



- N=20 pts with available tissue for WES
- TOP1 variants (resistance to payload) was associated with shorter response to ADC2

Rapid autopsy study post-SG[3]



- Modeling clonal evolution of resistance reveals emergence of TOP1 and Trop2 mutations in rapid autopsy study post-SG

1. Abelman et al. AACR 2024;Abstract 3888
2. Abelman et al. SABCS 2023;Abstract PS08-03
3. Coates et al. *Cancer Discovery* 2021

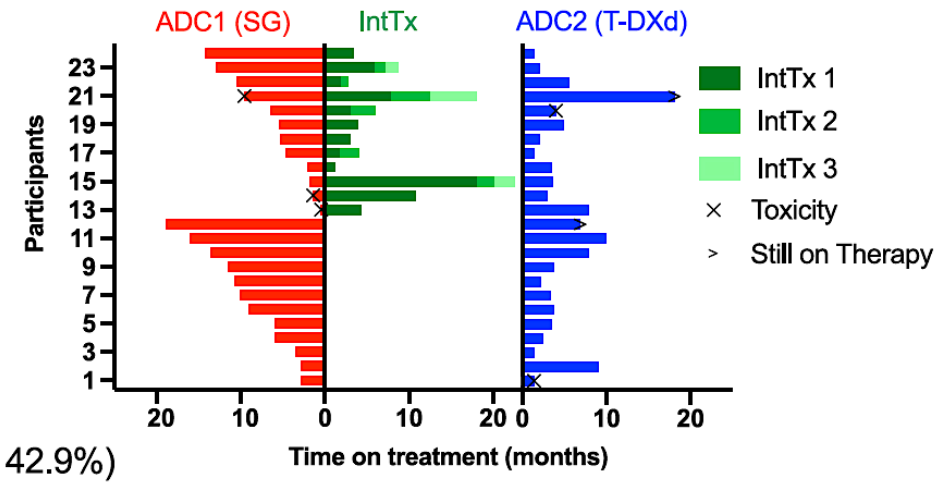
Retrospective Data about Sequential use of Topo1i ADCs

HR+/HER2-low MBC (n=56)

HR-/HER2-low MBC (n=28)

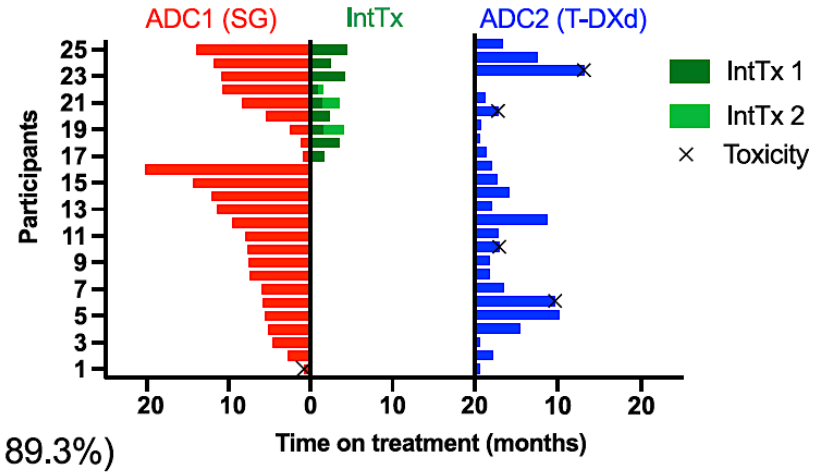
SG → T-DXd

A.



(n=24, 42.9%)

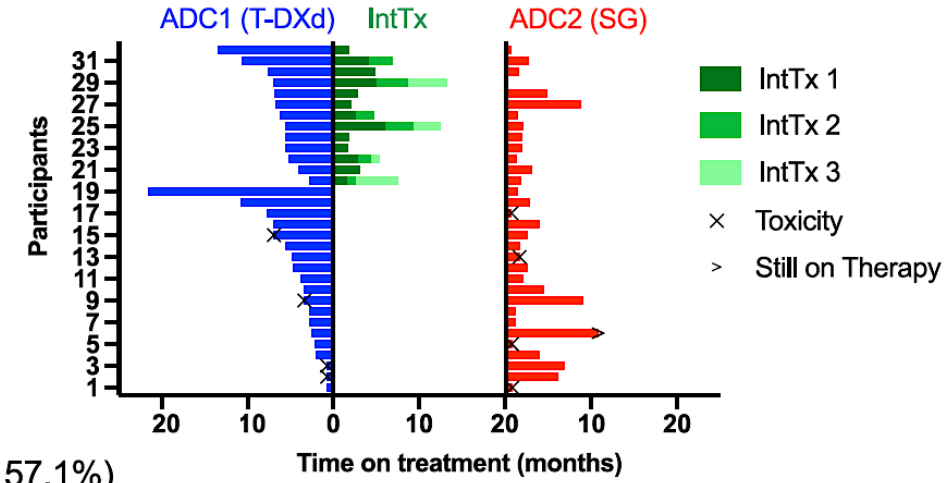
C.



(n=25, 89.3%)

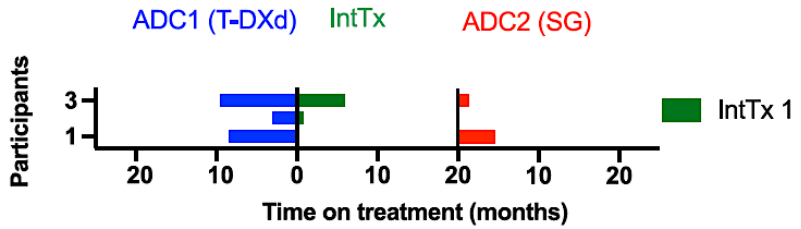
T-DXd → SG

B.



(n=32, 57.1%)

D.

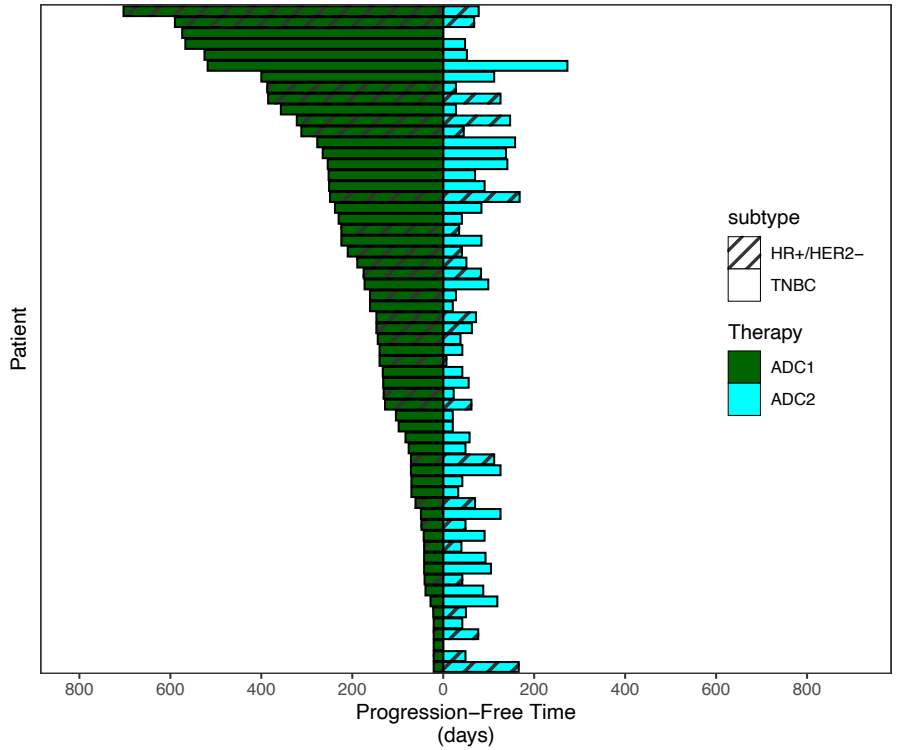


(n=3, 10.7%)

Huppert et al *NPJ Breast* 2025

Retrospective Data about Sequential use of Topo1i ADCs

- **Abelman et al. (n=68)[1]:**
  - Analyzed pts who had received two ADCs (including experimental ADCs)
  - Median time to progression ADC1= 161d, ADC2 = 77d
- **Mai et al. (n=85)[2]:**
  - Analyzed pts who had received SG and T-DXd for HER2-neg MBC
  - 64/85 patients (75.3%) had a longer PFS for ADC1 vs. ADC2
- **Poumeaud et al. (n=179)[3]:**
  - Analyzed pts who had received SG and T-DXd for HER2-neg MBC
  - Median PFS2 for ADC2: 2.7mo

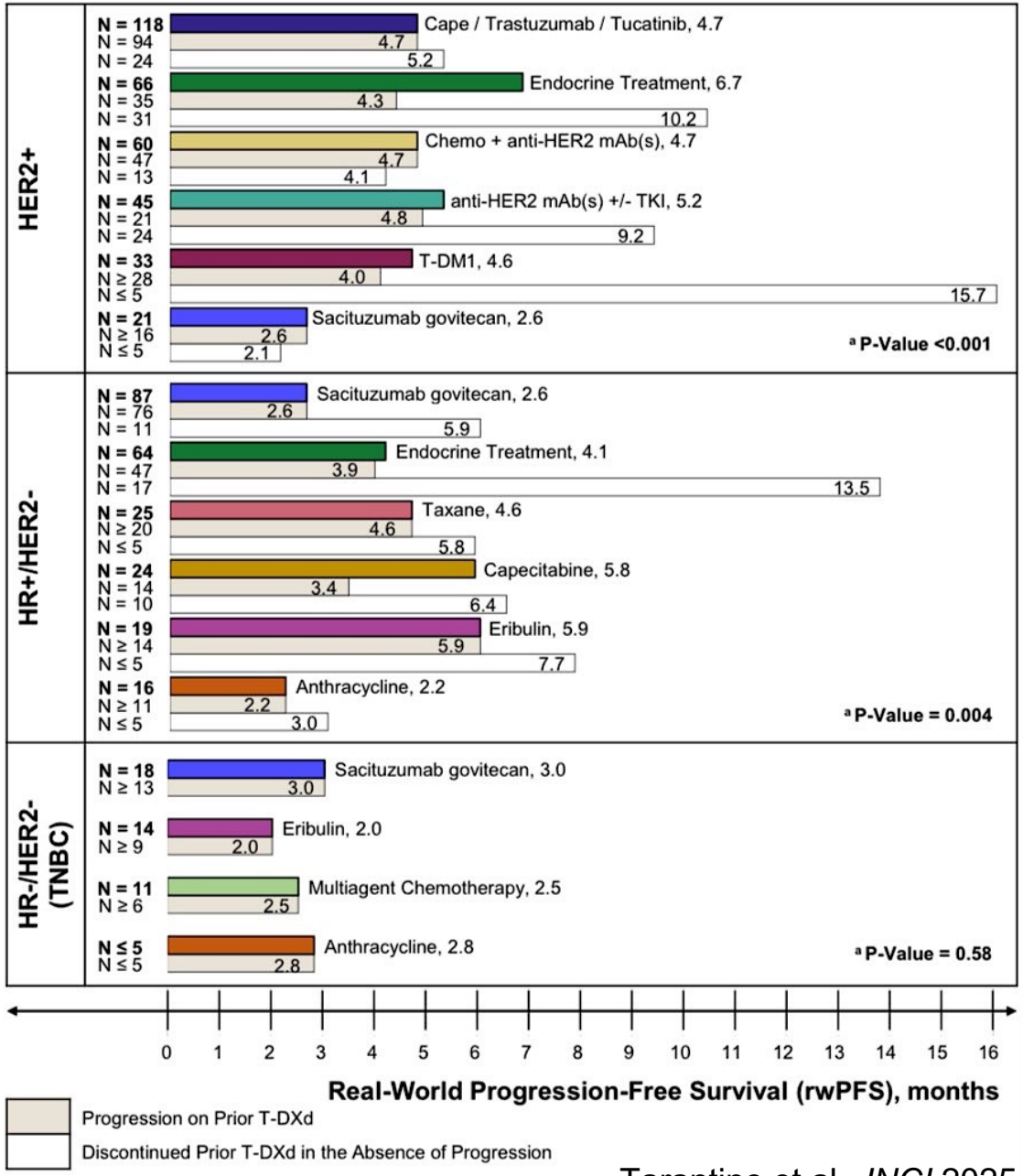


1. Abelman et al. SABCS 2023;Abstract PS08-03
2. Mai et al. ASCO 2024;Abstract 1085
3. Poumeaud et al. *Br J Cancer* 2024

Retrospective Data about Sequential use of Topo1i ADCs

- Using Flatiron registry data (n=**633**), evaluated real-world efficacy of **immediate subsequent therapy given after T-DXd**
- Short rwPFS (≤ 3mo) of SG post T-DXd suggests some degree of cross resistance among Topo1 ADCs

rwPFS by post-TDXd regimen



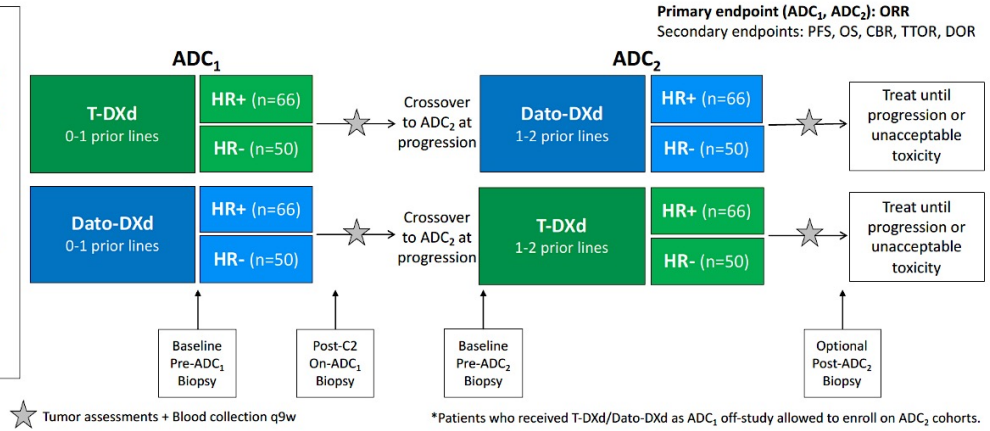
Tarantino et al. *JNCI* 2025

Prospective Trials of Sequential ADCs for HER2- MBC

TBCRC 064 TRADE-DXd: TReatment of ADC-Refractory Breast CancEr with Dato-DXd or T-DXd: TRADE-DXd
NCT06533826; PI: Garrido-Castro

Eligibility:
- Confirmed unresectable locally advanced or metastatic disease
- History of HER2-low BC: IHC 1+ or 2+/ISH- (any sample: primary or met)
- Measurable disease
- Prior endocrine therapy and CDK4/6 inhibitor for HR+ MBC
- Prior topo-I inhibitor allowed only in neo-/adjuvant setting(s) and if ≥12m elapsed since last dose to metastatic recurrence

*Randomization 1:1 to T-DXd or Dato-DXd as ADC_1 for allocation purposes.



SERIES: Phase II, single-arm, multi-center, open-label study of SG post-progression on T-DXd
NCT06263543; PI: Mahtani

N=75

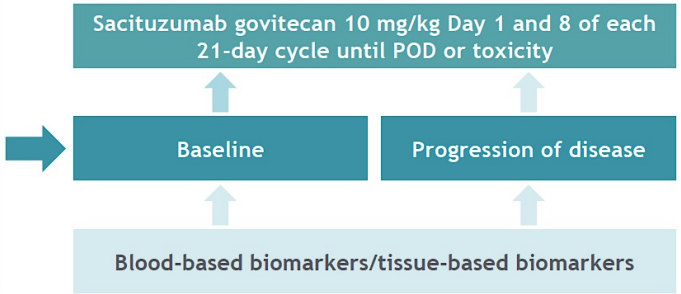
HR+/HER2 LOW (IHC 1+/2+ &ISH-) mBC

Refractory to at least one prior endocrine therapy

Received >1 ≤4 chemotherapies in the metastatic setting

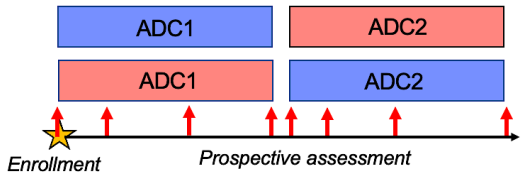
CDK4/6i (in adjuvant or metastatic setting)

Trastuzumab deruxtecan*



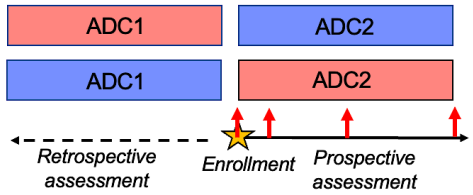
TBCRC 067 ENCORE: ProspectivE Registry of Sequential ANtibody Drug COnjugates in HER2 Negative Metastatic BREast Cancer
NCT06774027; PI: Huppert

Cohorts 1 & 2: Enrollment Prior to ADC1



- **Cohort 1:** HR+/HER2- MBC (~35 patients)
- **Cohort 2:** mTNBC (~25 patients)

Cohorts 3 & 4: Enrollment Prior to ADC2



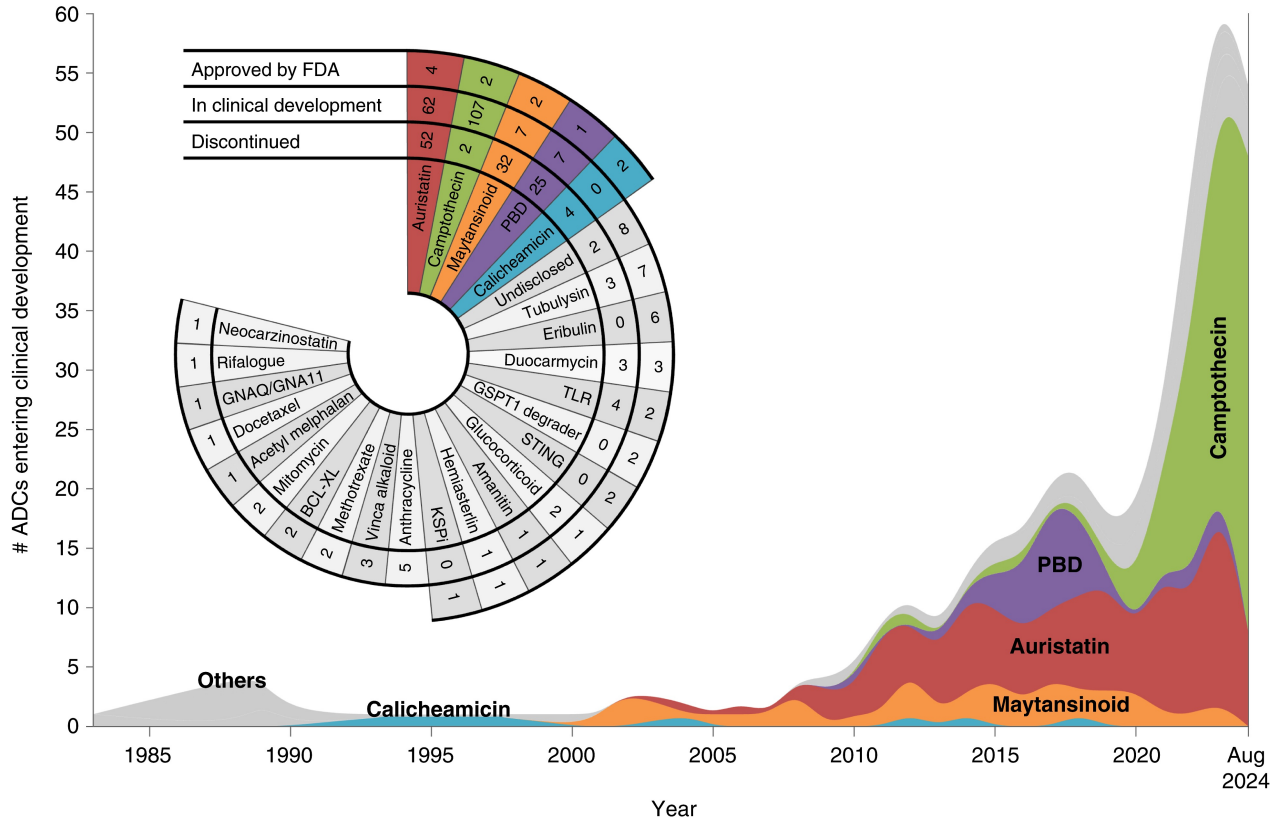
- **Cohort 3:** HR+/HER2- MBC (~25 patients)
- **Cohort 4:** mTNBC (~15 patients)

↑= Study Blood Draw (20ml)

For all cohorts:
- ADCs and imaging at least q12wk per SOC
- PRO data collection
- Research blood collection: Prior to C1D1, C2D1, C5D1, q4 cycles, end of treatment
- Archival tissue collection and research biopsy if SOC biopsy planned
- Intervening therapies between ADCs is allowed

ADC Future Directions

- Novel ADC targets
- Novel ADC payloads
  - Chemo, dual-payload ADCs, immunostimulatory agents, protein degraders, radioisotopes, others
- Combination strategies with ADCs
  - ADCs plus IO, targeted therapies, etc.
- ADCs moving earlier: (neo)adjuvant, 1L MBC
- Predictive biomarkers of ADC response/resistance
- Need prospective data on ADC sequencing
- Ongoing efforts to improve toxicity and management



Of the >200 ADCs in clinical development:
- ~110 have Topo1 payloads
- ~60 have auristatin payloads
- Some with novel payloads

Colombo et al. *Cancer Discovery* 2024

Agenda

Module 1: Previously Untreated Metastatic Triple-Negative Breast Cancer (mTNBC) — Prof Schmid

Module 2: Integrating Antibody-Drug Conjugates (ADCs) into the Management of Endocrine-Resistant Hormone Receptor-Positive Metastatic Breast Cancer (mBC) — Dr Sharma

Module 3: Selection and Sequencing of Therapy for Relapsed/Refractory mTNBC — Dr Nanda

Module 4: Tolerability and Other Practical Considerations with ADCs and Other Cytotoxic Agents for mBC — Dr Cortés

Case Presentation: 42-year-old woman with multiregimen-recurrent ER-positive, HER2-low mBC who has experienced severe nausea with past treatments is about to initiate T-DXd

Dr Atif Hussein (Hollywood, Florida)

RTP
RESEARCH
TO PRACTICE

Oncologists Who Utilize Trastuzumab Deruxtecan (T-DXd)

Tertiary centers

- Breast cancer clinical investigators
- GU cancers clinical investigators
- GI cancers clinical investigators
- Gynecologic cancers clinical investigators
- Pulmonary cancers clinical investigators

Community based practices

- General medical oncologists
- Gynecologic oncologists
- Urologic oncologists

Consensus or Controversy? Clinical Investigators Provide Perspectives on the Current and Future Management of Urothelial Bladder Cancer

Part 2 of a 2-Part CME Symposium Series Held in Conjunction with the 2024 ASCO Genitourinary Cancers Symposium

Friday, January 26, 2024

7:00 PM – 9:00 PM PT (10:00 PM – 12:00 AM ET)

Faculty

Matthew Milowsky, MD, FASCO

Peter H O'Donnell, MD

Jonathan E Rosenberg, MD

Arlene Siefker-Radtke, MD

Moderator

Evan Y Yu, MD

RTP RESEARCH TO PRACTICE


KU
MEDICAL
CENTER
University of Kansas

Data + Perspectives: Clinical Investigators Discuss the Emerging Role of AKT Inhibitors in the Care of Patients with Prostate Cancer

A CME Satellite Symposium Held in Conjunction with the American Urological Association Annual Meeting 2025 (AUA2025)

Saturday, April 26, 2025

8:00 AM – 9:30 AM PT (11:00 AM – 12:30 PM ET)

Faculty

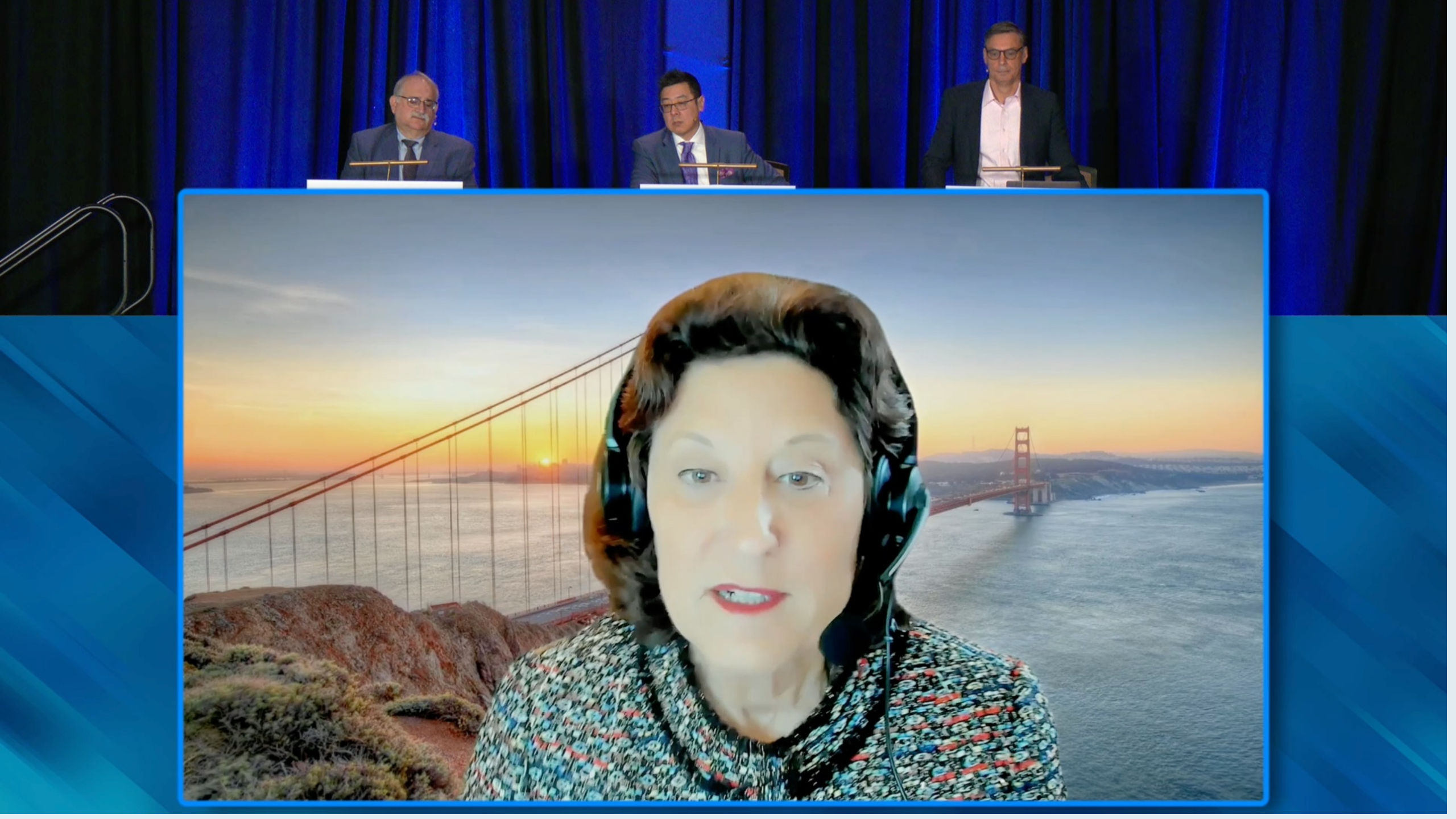
Leonard G Gomella, MD

Evan Y Yu, MD

Moderator

Daniel George, MD

RTP RESEARCH TO PRACTICE



Nausea and Vomiting with T-DXd

Table 1. Nausea and vomiting rates in patients receiving T-DXd in the DESTINY trials.[a]

Trial	Reference	Patient population	Nausea, %		Vomiting, %	
			Any grade	Grade ≥3[b]	Any grade	Grade ≥3[b]
Treatment-emergent adverse events reported						
DESTINY-Breast01	[26]	*N* = 184 HER2-positive metastatic breast cancer	78	8	46	4
DESTINY-Breast02	[27]	*N* = 404 HER2-positive metastatic breast cancer	73	7	38	4
DESTINY-Breast03	[28]	*N* = 261 HER2-positive unresectable or metastatic breast cancer	77	7	52	2
DESTINY-Lung02	[29]	*N* = 152 (*n* = 101 5.4 mg/kg; *n* = 50 6.4 mg/kg) Metastatic *HER2*-mutant non-small cell lung cancer	67 (5.4 mg/kg) 82 (6.4 mg/kg)	4 (5.4 mg/kg) 6 (6.4 mg/kg)	32 (5.4 mg/kg) 44 (6.4 mg/kg)	3 (5.4 mg/kg) 2 (6.4 mg/kg)
DESTINY-CRC01	[30]	*N* = 86 HER2-expressing metastatic colorectal cancer	62	6	31	1
DESTINY-Gastric01	[31]	*N* = 125 HER2-positive advanced gastric cancer	63	5	26	0
DESTINY-PanTumor02	[32]	*N* = 267 Locally advanced or metastatic HER2-expressing solid tumors	55	N/A	25	N/A
Treatment-related adverse events reported						
DESTINY-Breast04	[33]	*N* = 371 HER2-low metastatic breast cancer	73	5	34	1
DESTINY-Lung01	[34]	*N* = 91 Metastatic *HER2*-mutant non-small cell lung cancer	73	9	40	3

[a]The DESTINY trials did not include a consistent recommendation for the use of antiemetics. Many patients were treated with antiemetics after experiencing nausea and/or vomiting.
[b]Adverse events were graded per National Cancer Institute Common Terminology Criteria for Adverse Events.
HER2: human epidermal growth factor receptor 2; N/A: not available; T-DXd: trastuzumab deruxtecan.

Park YH et al. *Future Oncol* 2025;21:1261-72.

RTP RESEARCH TO PRACTICE

QUESTIONS FOR THE FACULTY

How do you approach the use of prophylactic antinausea/vomiting agents for patients about to receive their first dose of T-DXd? Does this change for a patient with prior nausea/vomiting from chemotherapy?

When and how do you use olanzapine for patients receiving T-DXd? If you use it, do you do so the night before or the morning of? For how long do you continue it? What dose do you use?

Have you experienced any pushback from patients, given that this is an antipsychotic drug? How did you address this?

QUESTIONS FOR THE FACULTY

How would you compare the effectiveness of (fos)netupitant/palonosetron (NEPA) to other available approaches to antiemetic prophylaxis? How do they compare in terms of practical considerations related to administration?

Would you be comfortable recommending NEPA as antiemetic prophylaxis for a patient who was about to start an ADC? Is there any reason to believe it would be any more or less effective that it would be with conventional cytotoxic chemotherapy?

QUESTIONS FOR THE FACULTY

What is your strategy to preventing delayed and long-delayed nausea and vomiting with emetogenic therapies, including ADCs? Is NEPA effective in this regard?

REVIEW

OPEN ACCESS

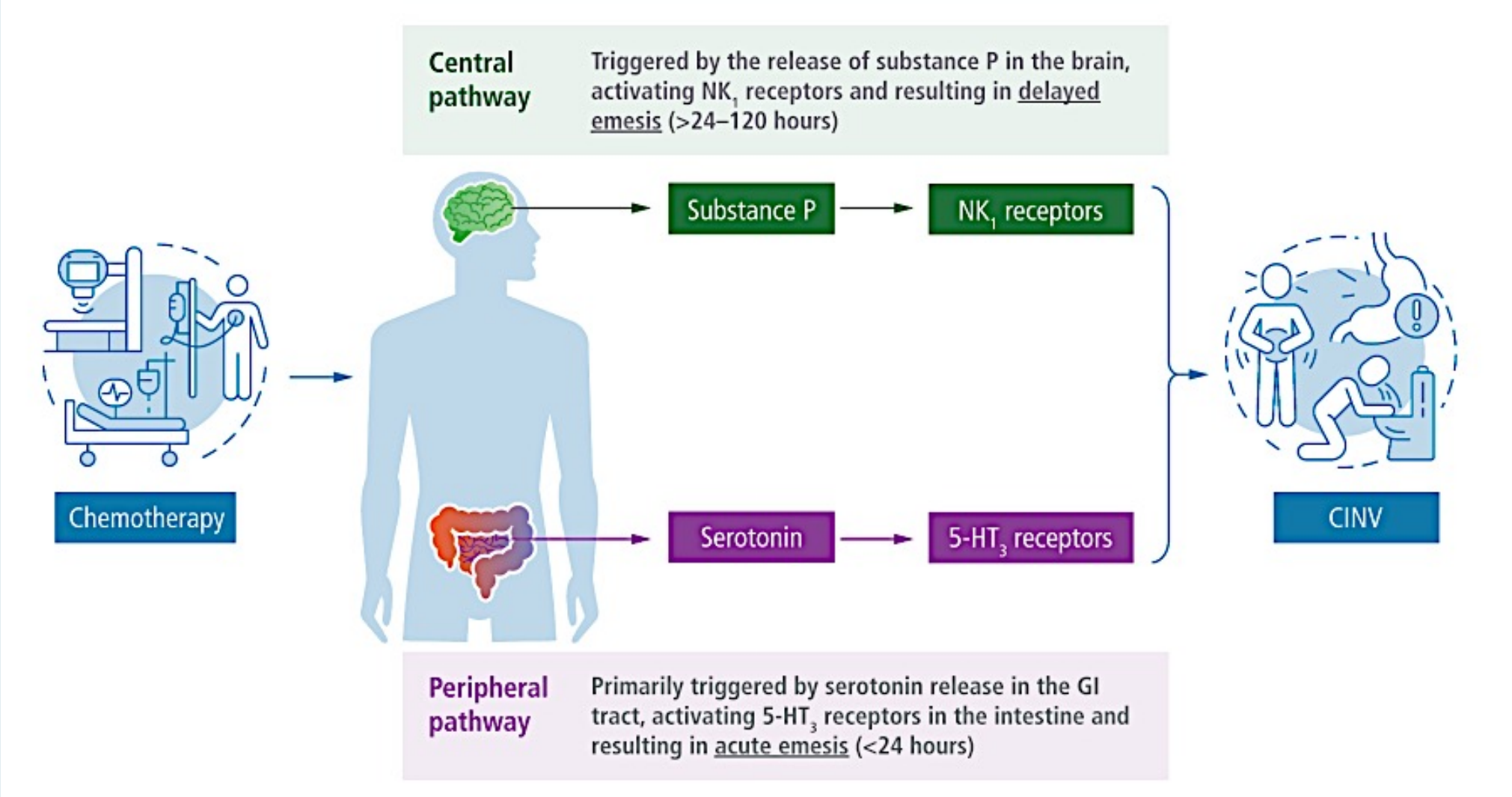
Nausea and vomiting in an evolving anticancer treatment landscape: long-delayed and emetogenic antibody-drug conjugates

Yeon Hee Park[a], Giampaolo Bianchini[b,c], Javier Cortés[d,e,f], Luca Licata[b], María Vidal[g,h], Hirotoshi Iihara[i], Eric J. Roeland[j], Karin Jordan[k,l], Florian Scotté[m], Lee Schwartzberg[n], Rudolph M. Navari[o], Matti Aapro[p] and Hope S. Rugo[q]

[a]Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [b]Department of Medical Oncology, IRCCS San Raffaele Hospital, Milan, Italy; [c]School of Medicine and Surgery, Vita-Salute San Raffaele University, Milan, Italy; [d]International Breast Cancer Center (IBCC), Pangaea Oncology, Quironsalud Group, Barcelona, Spain; [e]IOB Madrid, Hospital Beata María Ana, Madrid, Spain; [f]Faculty of Biomedical and Health Sciences, Department of Medicine, Universidad Europea de Madrid, Madrid, Spain; [g]Department of Medical Oncology, Hospital Clinic, Translational Genomics and Targeted Therapies in Solid Tumors, IDIBAPS, Barcelona, Spain; [h]Department of Medicine, University of Barcelona, Barcelona, Spain; [i]Department of Pharmacy, Gifu University Hospital, Gifu, Japan; [j]Knight Cancer Institute, Oregon Health and Science University, Portland, OR, USA; [k]Department of Hematology, Oncology and Palliative Medicine, Ernst von Bergmann Hospital, Potsdam, Germany; [l]Department of Medicine V, Hematology, Oncology and Rheumatology, University of Heidelberg, Heidelberg, Germany; [m]Interdisciplinary Cancer Course Department, Gustave Roussy Cancer Institute, Villejuif, France; [n]Renown Health-Pennington Cancer Institute, University of Nevada, Reno, NV, USA; [o]World Health Organization, Mount Olive, AL, USA; [p]Genolier Cancer Centre, Clinique de Genolier, Genolier, Switzerland; [q]University of California San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA

Park YH et al. *Future Oncol* 2025;21:1261-72.

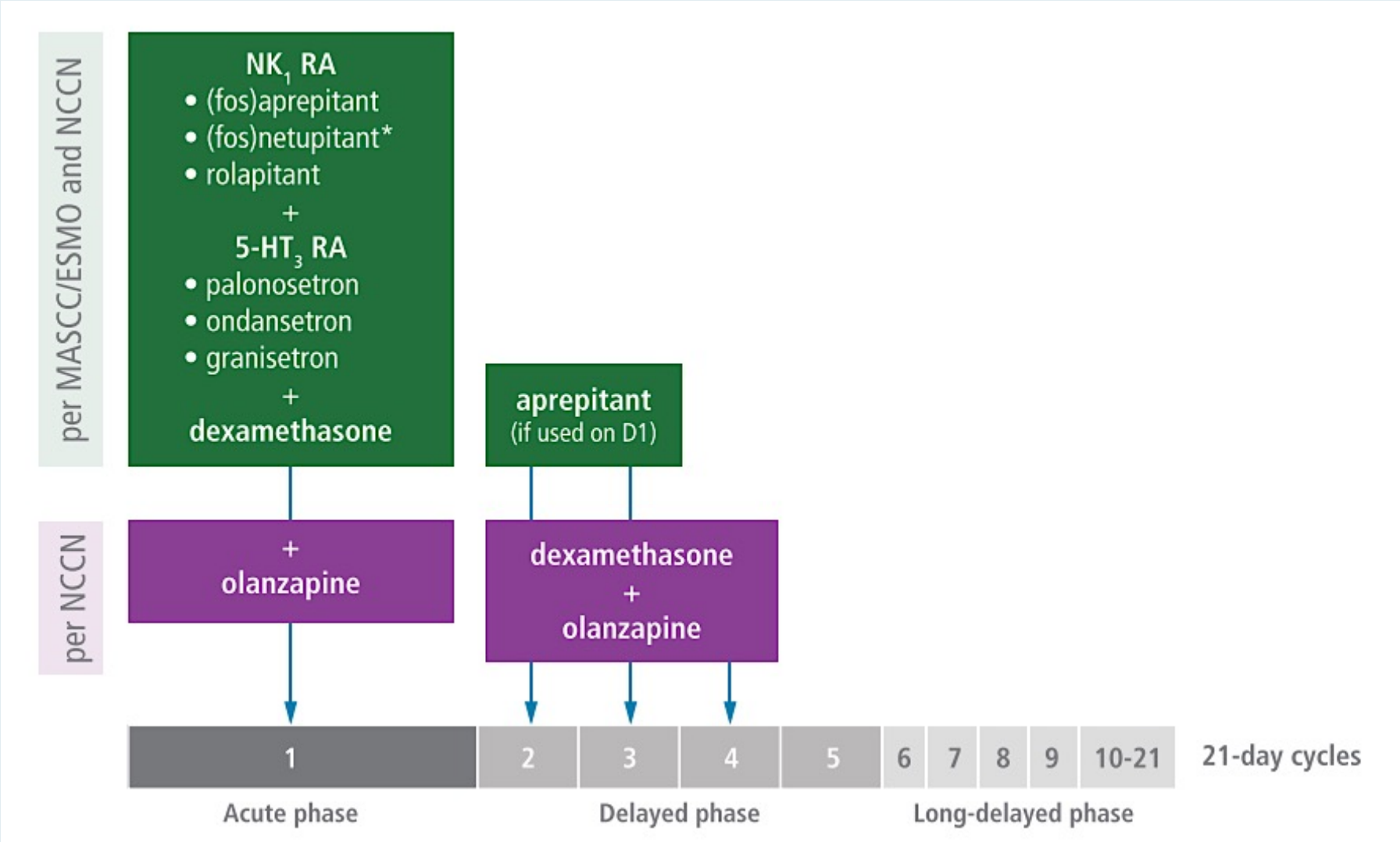
Pathophysiology of Chemotherapy-Induced Nausea and Vomiting (CINV)



Park YH et al. *Future Oncol* 2025;21:1261-72.

RTP RESEARCH TO PRACTICE

Antiemetic Management for T-DXd and Sacituzumab Govitecan: MASCC/ESMO Guidelines



Park YH et al. *Future Oncol* 2025;21:1261-72.

RTP RESEARCH TO PRACTICE

Nausea and Vomiting Beyond the Delayed Phase

- It has become clear that chemotherapy-induced nausea and vomiting (CINV) can persist beyond 120 hours, and this “long-delayed” CINV has been poorly characterized, highlighting an unmet need to continue assessing CINV beyond day 5 after chemotherapy initiation.
- Some ADCs are associated with long-delayed nausea and vomiting, and with the improved progression-free survival reported with ADC treatment, this risk is particularly relevant for patients because of the long treatment duration.

Park YH et al. *Future Oncol* 2025;21:1261-72.

RTP RESEARCH TO PRACTICE

Preventing Nausea and Vomiting in the Long-Delayed Phase

- The fixed-combination antiemetic netupitant and palonosetron (NEPA) has a long plasma elimination half-life and duration of receptor occupancy, characteristics that make it suitable for providing long-lasting antiemetic prophylaxis.
- NEPA demonstrated high efficacy in both the traditionally defined delayed phase and in multiple studies investigating its effect in the long-delayed phase.
- Limited studies on antiemetic prophylaxis for patients receiving ADCs have highlighted the need for early and adequate treatment and have produced promising results with NEPA.

Park YH et al. *Future Oncol* 2025;21:1261-72.

Cannabinoids for GI toxicity, anticipatory nausea and vomiting

Dr Atif Hussein (Hollywood, Florida)

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

Do you use cannabinoids to prevent or manage nausea/vomiting, and what type of preparation do you recommend? How do patients respond to this idea, and how effective is this strategy?

How often do you observe anticipatory nausea and vomiting in patients receiving ADCs or chemotherapy, and what strategies have you found effective for managing this?

Tolerability and Other Practical Considerations with the Use of ADCs and Other Cytotoxic Agents in mBC

Javier Cortés MD PhD

- International Breast Cancer Center (IBCC), Pangaea Oncology, Quironsalud Group, Barcelona, Spain
- IOB Madrid, Hospital Beata Maria Ana, Madrid Spain
- Universidad Europea de Madrid, Faculty of Biomedical and Health Sciences, Department of Medicine, Madrid, Spain
- Medica Scientia Innovation Research (MEDSIR) - Oncoclínicas&Co, Jersey City (New Jersey, USA), Sao Paulo (Brazil).

ADCs in chemo-pretreated HR+/HER2- MBC as an example: Safety

	OptiTROP-Breast 02	Destiny-Breast 04	Tropion-Breast 01	TROPiCS-02
ADC Payload (MoA)	Sacituzumab tirumotecan Topo I Inhibitor	Trastuzumab Deruxtecan Topo I Inhibitor	Datopotamab deruxtecan Topo I Inhibitor	Sacituzumab govitecan Topo I Inhibitor
TRAEs Grade ≥ 3 (%)	62	54	21	74
TRAEs associated with discontinuation (%)	0	17	3	6
Most frequent TEAEs (All grade (Grade ≥3)) (%)				
	Leuco / Neutropenia 86 (31)	**Nausea** 73 (5)	**Stomatitis** 59 (7)	**Neutropenia** 70 (51)
	Anemia 84 (13)	**Fatigue** 52 (8)	**Nausea** 51 (1)	**Diarrhea** 57 (9)
	Stomatitis 63 (10)	**Transaminitis** 42 (4)	**Ocular Events** 49 (1)	**Nausea** 55 (1)
	Nausea 39 (0)	**Neutropenia** 35 (14)	**Fatigue** 24 (2)	**Fatigue** 37 (6)

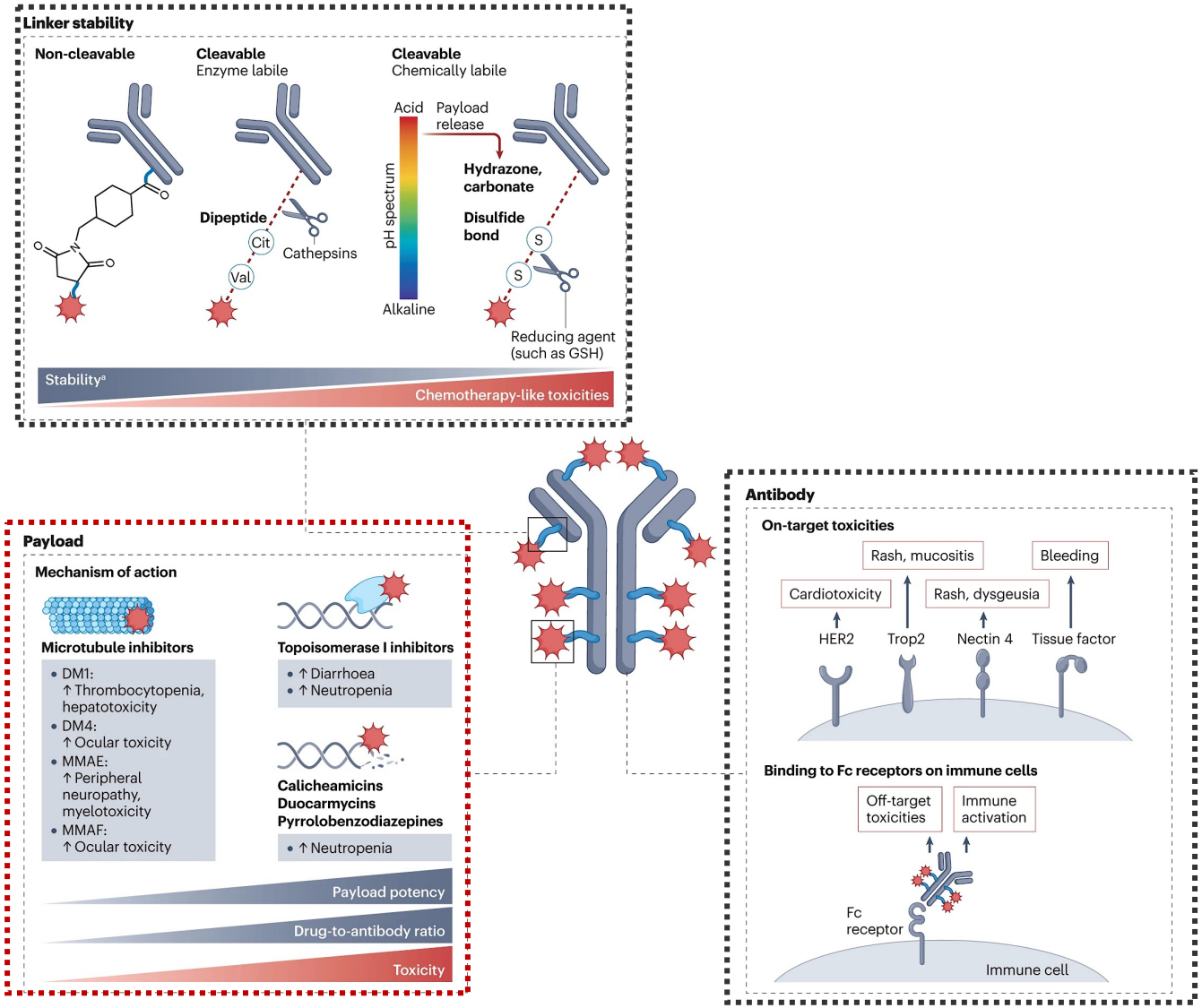
~12% ILD/pneumonitis

1. Li M, et al. ESMO 2025; 2. Modi S, et al. N Engl J Med 2022; 3. Pristilli B. et al. ESMO Virtual Plenary 2025; 4. Rugo H, et al. Lancet 2023; Table by Cortes J. ESMO 2025

Determinants of the toxicities of ADCs

More unstable linkers lead to more chemotherapy-related side effects.

Payload-related toxicities dominate the toxicity profile of most ADCs



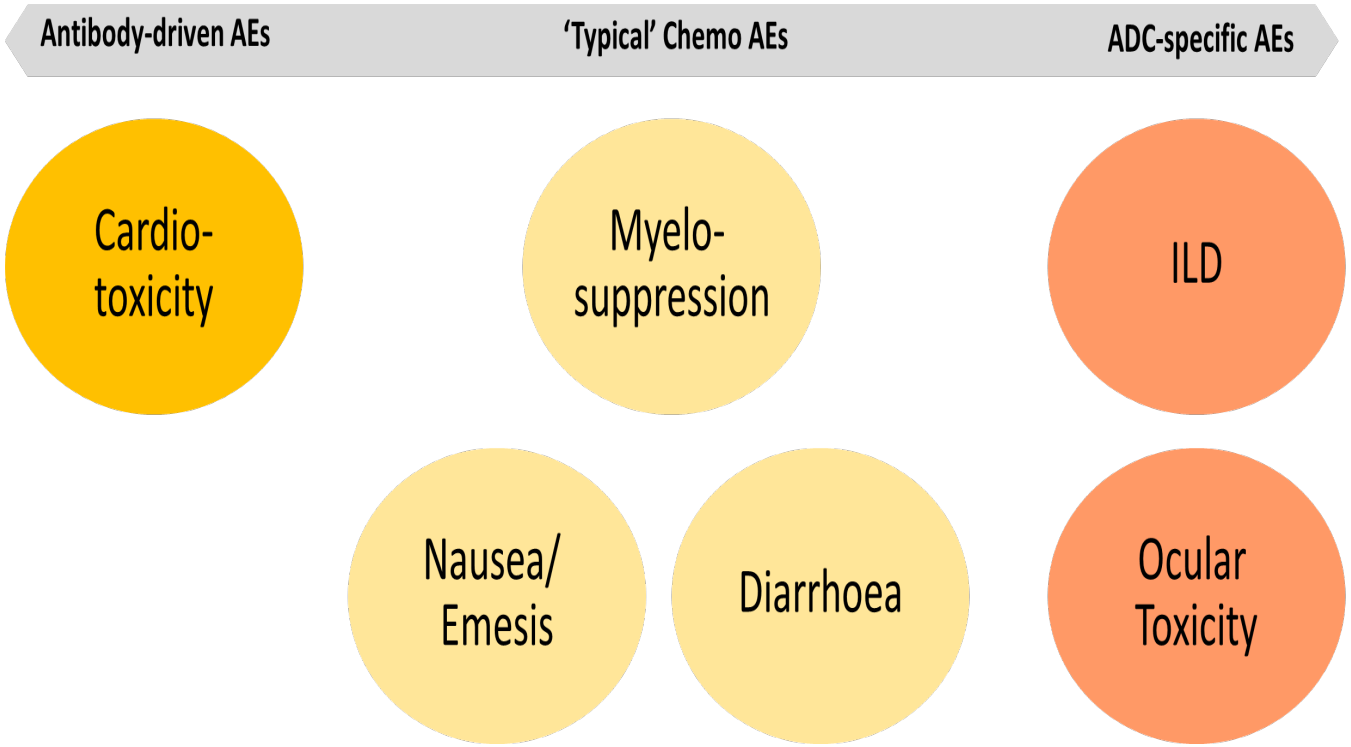
Antibody-related toxicities are common, but rarely limit the tolerable dose of the ADC

Examples:
- **Cardiotoxicity with T-DXd**
- **Mucositis with Dato-DXd**

Tarantino P Nature Rev Clin Onc 2023

Is ADC-related toxicity truly better than that of chemotherapy?

Toxicities Are Not Inherent to the Antibody-Drug Conjugate Class



ADC	ADC Description	Characteristic Toxicity
Trastuzumab emtansine	HER2 targeted ADC with DM1 payload	Thromobocytopenia Elevated LFTs
Sacituzumab govitecan	TROP2 targeted ADC with SN-38 payload	Neutropenia
Trastuzumab deruxtecan	HER2 targeted ADC with DXd payload	Interstitial lung disease Nausea
Datopotamab deruxtecan	TROP targeted ADC with DXd payload	Ocular toxicity
Sacituzumab tirumotecan	TROP2 targeted ADC with belotecan-derivative payload	Hematologic toxicities Stomatitis
Trastuzumab botidotin	HER2 targeted ADC with duostatin-5 payload	Ocular toxicity

While antibody–drug conjugates (ADCs) exhibit specific toxicity profiles, they do not invariably confer a reduction in systemic toxicity relative to conventional cytotoxic chemotherapy

Table, modified from Hamilton E. ASCO 2024

Types of nausea and vomiting[1]

Practitioners should consider the type of nausea and vomiting when choosing antiemetic medications

Anticipatory	A learned or conditioned response occurring before or during treatment, resulting from sights, sounds and smells of the treatment area
Acute	Occurs within minutes to hours after treatment, and usually within the first 24 hours. Common with IV infusion or oral administration
Delayed	Occurs >24 hours and lasts a few days after treatment
Breakthrough	Occurs despite preventative treatment, requiring more or different agents
Refractory	Occurs when agents fail to prevent or control nausea and vomiting, requiring more or different agents

Cancer. Treatments and side effects. https://www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/nausea-and-vomiting/managing.html. Accessed December 4, 2025; Natale JJ. Am J Manag Care. 2018;24(18_Suppl):S391-S397.

Guidelines* recommend three classes of antiemetics for patients undergoing emetogenic treatment[1-3]

1 5-HT3 receptor antagonists

- **Palonosetron:** 0.25 mg IV; 0.5 mg oral
- **Granisetron:** 1 mg IV; 2 mg oral
- **Dolasetron:** 100 mg oral
- **Tropisetron:** 5 mg IV; 5 mg oral
- **Ondansetron:** 8 mg IV; 16 mg oral

2 NK-1 receptor antagonists

- **Aprepitant:** 125 mg (acute); 80 mg daily for 2 days (delayed)
- **Fosaprepitant:** 150 mg IV
- **Netupitant:** 300 mg

3 Corticosteroids

Dexamethasone:

- Acute emesis: 8 mg once
- Delayed emesis: 8 mg daily / 4 mg twice a day for 2–3 days

*Includes ASCO and MASCC / ESMO guidelines

ASCO, American Society of Clinical Oncology; ESMO, European Society for Medical Oncology; MASCC, Multinational Association of Supportive Care in Cancer

1. WHO Collaborating Centre for Drug Statistics Methodology. ATC/DDD Index 2021. https://www.whocc.no/atc_ddd_index/?code. Accessed December 2025; 2. Hesketh PJ, et al. *J Clin Oncol* 2017;35:3240–3261; 3. Roila F, et al. *Ann Oncol*. 2016;27:v119–v133

Low dose olanzapine with optimized treatment duration for delayed nausea

Steering committee

Low dose olanzapine (5 mg) could be offered to patients who experience delayed nausea, but treatment duration might need to be proactively optimized to curtail side effects.

Rationale

- Delayed nausea is a particularly challenging adverse event to manage.[1]
- While its incidence may not have been reported in clinical trials, a few cases where delayed nausea posed an issue for patients on T-DXd have been reported from clinical experience.
- Based on clinical experience and in line with recommendations, olanzapine (5 mg) may benefit patients for whom delayed nausea is a concern.[2,3]

1. Rapoport BL. Front Pharmacol 2017;8:19; 2. Bardia A et al. Oncologist. 2022;27:637–45; 3. Rugo HS et al. ESMO Open 2022;7:100553.

SG: Management of Neutropenia

- Withhold drug for ANC <1500/mm^3 on Day 1 of any cycle, ANC <1000/mm^3 on Day 8 of any cycle, or neutropenic fever
  - Initiate anti-infective treatment in patients with febrile neutropenia without delay
- Dose modifications may be required
  - Do not re-escalate dose after dose reduction for adverse events has been made
- Administer G-CSF as clinically indicated or as indicated in the table for severe neutropenia

Severe Neutropenia	Occurrence	Dose Modification
Grade 4 neutropenia ≥7 days *OR* grade 3/4 febrile neutropenia *OR* at time of scheduled treatment, grade 3/4 neutropenia that delays dosing by 2-3 wk for recovery to grade ≤1	First	25% dose reduction and administer G-CSF
	Second	50% dose reduction and administer G-CSF
	Third	Discontinue treatment and administer G-CSF
At time of scheduled treatment, grade 3/4 neutropenia that delays dosing by >3 wk for recovery to grade ≤1	First	Discontinue treatment and administer G-CSF

SG: Management of Diarrhea

- At onset, rule out infectious causes and, if negative, initiate loperamide (4 mg initially, 2 mg with every episode, max 16 mg/day); discontinue loperamide 12 hr after resolution
- Use supportive measures (eg, fluid and electrolyte substitution) as clinically indicated
- Withhold drug for grade 3/4 diarrhea at time of scheduled administration; resume at reduced dose when resolved to grade ≤1; consider premedication for subsequent treatments

Severe Diarrhea	Occurrence	Dose Modification
Any grade 3/4 diarrhea due to treatment that is not controlled with antidiarrheal agents	First	25% dose reduction
	Second	50% dose reduction
	Third	Discontinue treatment
At time of scheduled treatment, grade 3/4 diarrhea that delays dosing by >3 wk for recovery to grade ≤1	First	Discontinue treatment

SG: PRIMED Strategy

Key Eligibility Criteria

- Patients ≥18 years old with <u>mTNBC or metastatic HR+/HER2- breast cancer</u>
- Received at least 1 and up to 2 prior SOC chemotherapy regimens for metastatic disease
- ECOG PS ≤1

Study Treatment

Sacituzumab govitecan
10 mg/kg IV D1 and D8

⊕

Loperamide
2 mg PO BID, or 4 mg QD on D2, D3, D4, and D9, D10, D11 (First two cycles*)

⊕

G-CSF
0.5 MU/kg/day SC QD on D3, D4, and D10, D11 (First two cycles*)

Study Endpoints

Primary endpoints

- Co-primary endpoints are incidence of grade ≥2 diarrhea and grade ≥3 neutropenia at cycle 2

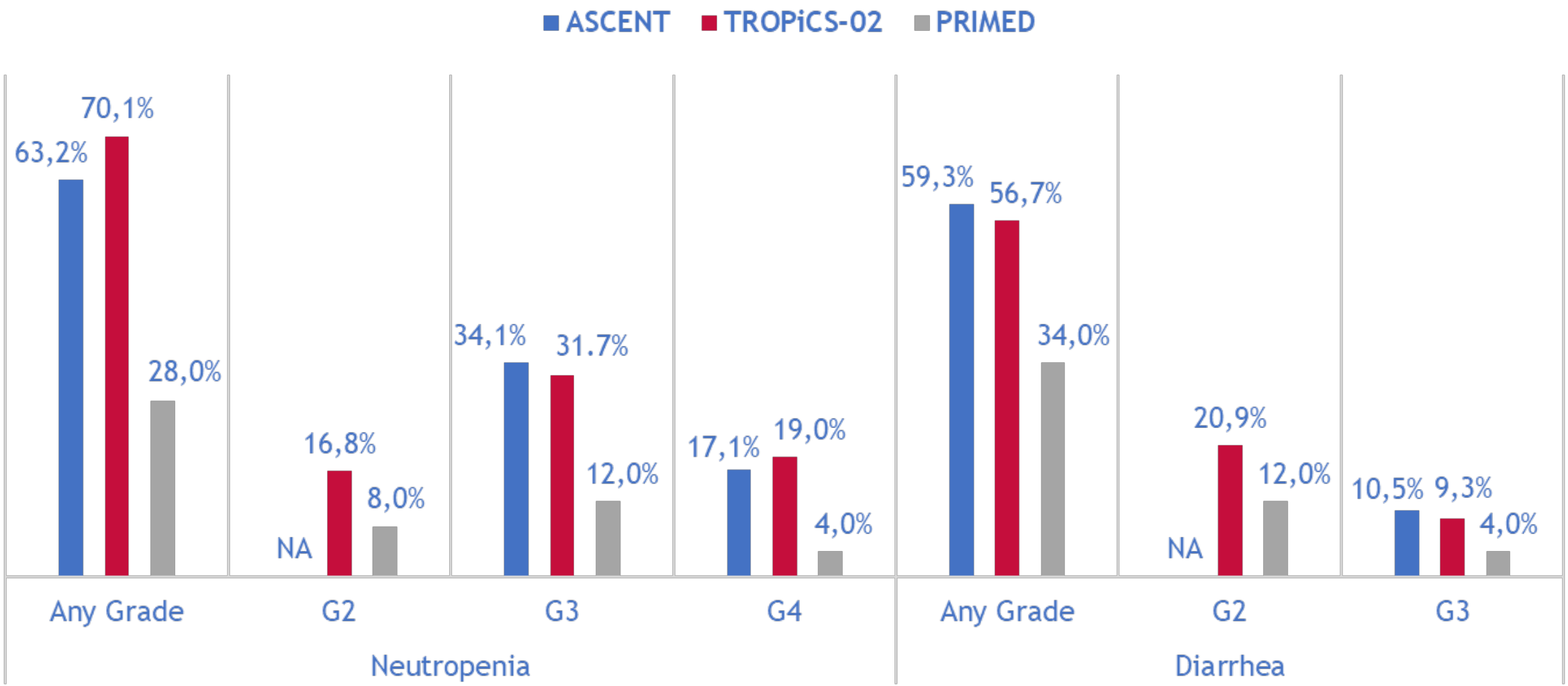
Secondary endpoints

- Tolerability and safety per NCI-CTCAE v5 at cycle 2
- Discontinuation and dose reductions
- Efficacy in terms of PFS, ORR, clinical benefit rate, time to response, DOR, and best percentage of change in tumor burden

Incidence in first 2 cycles, n (%)	Any grade	Grade 2	Grade 3	Grade 4
Neutropenia	14 (28.0)	4 (8.0)	6 (12.0)	2 (4.0)
Diarrhea	17 (34.0)	6 (12.0)	2 (4.0)	0

Perez-Garcia-J, et al EClinicalMedicine 2025

SG: PRIMED Strategy vs. ASCENT vs. TROPICS-02



Bardia A, et al. NEJM 2021; Rugo H, et al. JCO 2022; Perez-Garcia-J, et al EClinicalMedicine 2025

T-DXd: Management of LVEF changes

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 Cancer Annual Congress. 2024.

What is ILD?

ILD (Interstitial Lung Disease) is a broad term for a group of diffuse, parenchymal lung disorders including some types of pneumonitis

Symptoms

- Nonspecific cough[1,2]
- Fever[3]
- Shortness of breath (dyspnoea)[2]
- Pneumonitis and idiopathic pulmonary fibrosis[4]

Clinical signs

- Inflammation or scarring of the lung interstitium[2]
- Chest radiographic abnormalities[1]
- Changes in pulmonary function tests reflecting decreased lung volume[1]
- Microscopic patterns of inflammation and fibrosis[2]

Risk factors

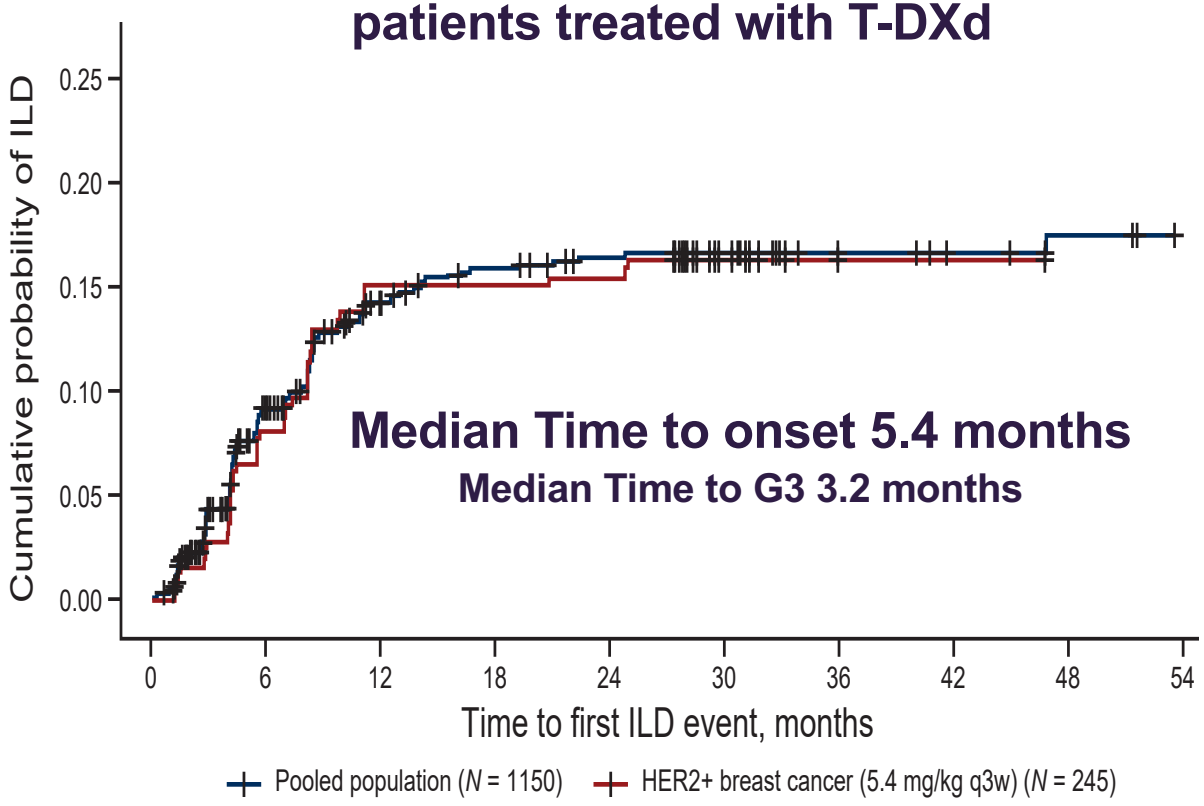
- Patient history of ILD/pneumonitis or lung disease[4,5]
- Smoking status[4,5]
- Age >70 years[5]
- Male[5]
- Use of anticancer agents
- Dose
- Geographic Region

ILD, interstitial lung disease.

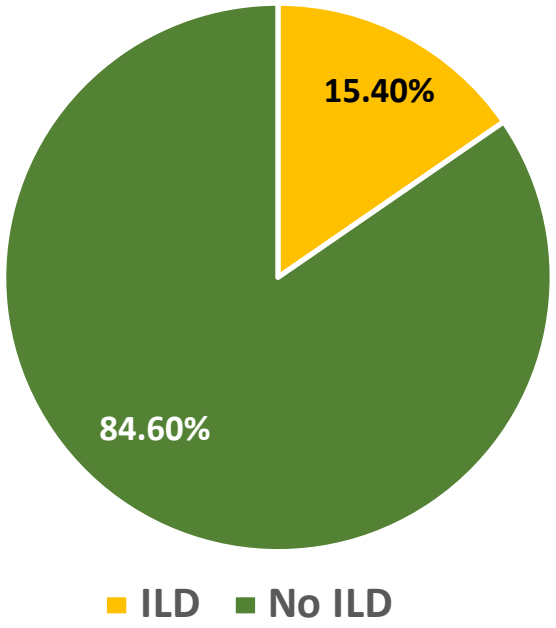
1. Wells AU et al. Thorax 2008; 2. Meyer KC. Transl Respir Med 2014; 3. Modi S et al. N Engl J Med 2020; 4. Kreuter M et al. Biomed Res Int 2015 5. Choi W et al. BMC Pulm Med. 2018

Incidence and time course of ILD with T-DXd

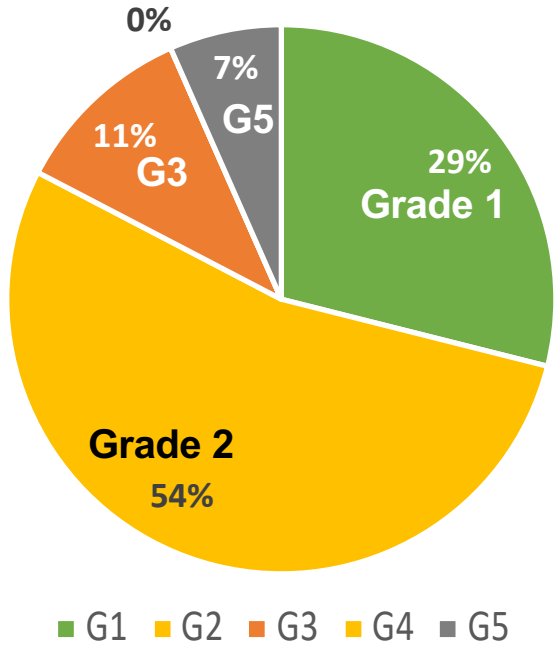
Cumulative probability of developing ILD for patients treated with T-DXd



Incidence of ILD



Severity of ILD



ILD does not appear to be directly associated with cumulative exposure to T-DXd

Powell CA, et al. ESMO OPEN 2022; Modi S, et al. N Engl J Med. 2022

T-DXd: 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

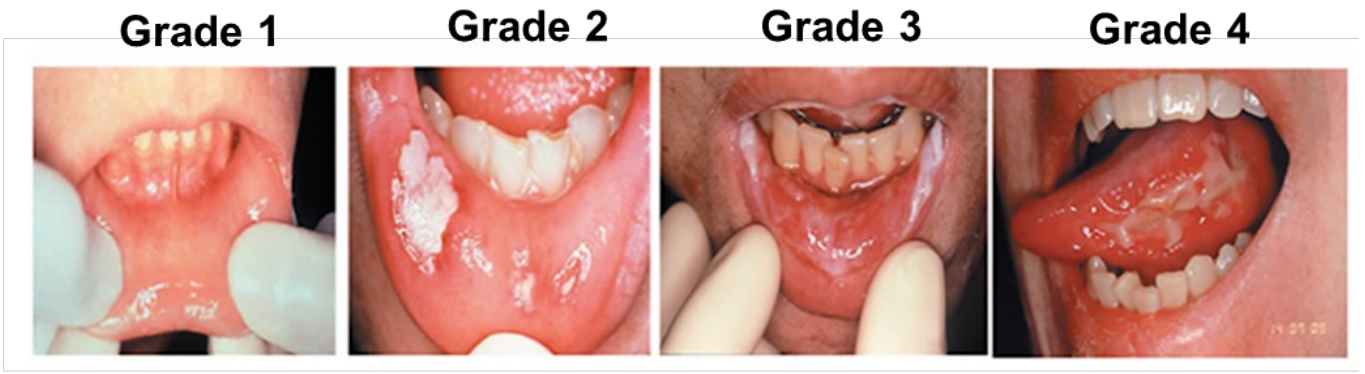
	Grade 1	Grade 2	Grade 3/4
Description	Asymptomatic (diagnostic observations only)	Symptomatic; limiting instrument. ADL	Severe symptoms; limiting self-care ADL; oxygen (G3); Life-threatening (G4)
T-DXd	Hold (restart if resolved within 49 days, otherwise discontinue)	Discontinue	Discontinue
Dose reduction	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 Cancer Annual Congress. 2024.

Dato-DXd: Identification of Mucositis/Stomatitis

What to look for:

- Lips and mucosa appear redder than usual
- Visible sores on oral mucosa
- Mouth pain, which may affect chewing and swallowing
- Changes in ability to taste



Stomatitis	Characteristics
Grade 1	Asymptomatic or mild symptoms
Grade 2	Moderate pain/ulceration not interfering with oral intake
Grade 3	Severe pain/ulceration interfering with oral intake
Grade 4	Oral intake not possible; life-threatening consequences

Dato-DXd: Prophylaxis of Mucositis/Stomatitis

Prophylaxis Use	Protocol Management Recommendations
Strongly suggested	▪ Steroid-containing mouth rinse (eg, dexamethasone) – Swish and spit 3-4 times daily for 1-2 min ▪ Oral hygiene: teeth brushing, flossing, and rinsing with water ▪ Patient education: stomatitis awareness, early signs and symptoms, and oral care routine
May be considered	▪ Cryotherapy: ice chips, ice water, or popsicles held in the mouth for a few min before infusion, during infusion, and for some time after the infusion ▪ Inert bland rinses (eg, alcohol-free bicarbonate) – Swish and spit 3-4 times daily for 1-2 min prior to steroid-containing mouth rinse or instead of steroid-containing mouth rinse (if unavailable)

Rugo H, et al. Support Care Cancer. 2025

Dato-DXd: Management of Mucositis/Stomatitis

Grade	Prophylaxis Status	Protocol Management Recommendations
1	With or without prophylaxis adherence	▪ Diet modification: avoid spicy, acidic and crunchy foods ▪ Topical steroid gel: use for spot therapy directly to mouth ulcers ▪ Steroid containing mouth rinse: 3-4 times daily for 1-2 min
2	With prophylaxis adherence	▪ Delay Dato-DXd treatment until symptom improvement to grade ≤1 ▪ Reinitiate Dato-DXd at a reduced dose: typically from 6 to 4 mg/kg ▪ Use steroid-containing mouth rinse: 3-4 times daily for 1-2 min
	Without prophylaxis adherence	▪ Delay Dato-DXd treatment until symptom improvement to grade ≤1 ▪ Use steroid-containing mouth rinse: 3-4 times daily for 1-2 min
3	With or without prophylaxis adherence	▪ Delay Dato-DXd treatment until symptom improvement to grade ≤1 ▪ Consider reinitiating Dato-DXd at a reduced dose: typically from 6 to 4 mg/kg ▪ Use steroid-containing mouth rinse: 3-4 times daily for 1-2 min
4	n/a	▪ Permanently discontinue drug

Rugo H, et al. Support Care Cancer. 2025

ADC-associated Ocular Surface Toxicity

Prevention/Diagnostic

1. **Use lubricating eyedrops daily**
2. **Avoid the use of contact lenses**
3. **Ophthalmological Assessment**

Dry Eye

- **Stinging**
- **Burning or scratchy sensation**
- **Eye redness**
- **Foreign body feeling**
- **Sensitivity to light**
- **Blurred vision**
- **Difficulty with contact lenses**

Keratitis

- Symptoms of Dry Eye
- **Eye pain**
- **Excess tears**
- **Other discharge**
- **Difficulty opening eyelid due to pain or irritation**
- **Decreased vision**
- **Ulceration**

Management

	G1	G2	G3	G4
ADC	Continue	Hold until <G2	Hold until <G2	Discontinue
Dose reduction	N/A	N/A	Reduce by 1 Level (if >7d)	Discontinue

1. **Lubricating eyedrops:** sodium hyaluronate **night gel 4/d, Hypromellose eyedrops 4-5/d,** carmellose sodium **4/d**
2. **Immune suppressive eyedrops: Ciclosporin eyedrops**

Schmid P. ESMO Breast Cancer Annual Congress. 2024.

Dose optimization strategies

DOSE CAPPING	**The dose of enfortumab vedotin (normally 1.25 mg/kg) was capped to 125 mg, after reports of fatal adverse events among patients with baseline body weight ≥100 kg**
CAPPING OF DURATION	**Polatuzumab vedotin is approved to be administered for a maximum of 6 cycles, to reduce the risk of permanent peripheral neuropathy**
RESPONSE-GUIDED DOSING	**After an initial induction, the dose of inotuzumab ozogamicin is reduced to a lower, maintenance dose, among those patients that achieve CR**
FRACTIONATED DOSING	**After being withdrawn from market for excessive toxicity (2010), gemtuzumab ozogamicin was reapproved in 2017 with a fractionated, less toxic dosing**

Courtesy Paolo Tarantino. SABCS 2024

Contributing General Medical Oncologists

Laila Agrawal, MD
Norton Cancer Institute
Louisville, Kentucky

Alan B Astrow, MD
Weill Cornell Medicine
Brooklyn, New York

Gigi Chen, MD
John Muir Health Cancer
Medical Group
Walnut Creek, California

Justin Favaro, MD, PhD
Oncology Specialists of Charlotte
Charlotte, North Carolina

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

Atif M Hussein, MD, MMM
Florida International University
Herbert Wertheim College of Medicine
Hollywood, Florida

RTP
RESEARCH
TO PRACTICE

Contributing General Medical Oncologists (Continued)

Yanjun Ma, MD, PhD
Tennessee Oncology
Murfreesboro, Tennessee

Jennifer Yannucci, MD
Low Country Cancer Care
Savannah, Georgia

CASES FROM THE COMMUNITY
Investigators Discuss the Optimal Management of HER2-Positive Breast Cancer

Part 2 of a 3-Part CME Satellite Symposium Series

Wednesday, December 10, 2025

7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Professor Giuseppe Curigliano, MD, PhD
Nadia Harbeck, MD, PhD
Ian E Krop, MD, PhD
Nancy U Lin, MD
Joyce O'Shaughnessy, MD

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

Thank you for joining us!
Your feedback is very important to us.

Please complete the survey currently up on the iPads for attendees in the room and on Zoom for those attending virtually. The survey will remain open up to 5 minutes after the meeting ends.

How to Obtain CME Credit

In-person attendees: Please refer to the program syllabus for the CME credit link or QR code. Online/Zoom attendees: The CME credit link is posted in the chat room.

RTP
RESEARCH
TO PRACTICE