Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Antibody-Drug Conjugates for Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, February 18, 2026
5:00 PM – 6:00 PM ET

Faculty

Hope S Rugo, MD
Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

RTP Year in Review 2026

Faculty

Hope S Rugo, MD
Director, Women's Cancers Program
Division Chief, Breast Medical Oncology
Professor, Department of Medical Oncology and Therapeutics Research
City of Hope Comprehensive Cancer Center
Duarte, California
Professor Emeritus, UCSF

Sara M Tolaney, MD, MPH
Chief, Division of Breast Oncology
Dana-Farber Cancer Institute
Associate Professor of Medicine
Harvard Medical School
Boston, Massachusetts

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, and Gilead Sciences Inc.

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, 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, Nuvation Bio Inc, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Revolution Medicines 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.

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.

Dr Rugo — Disclosures

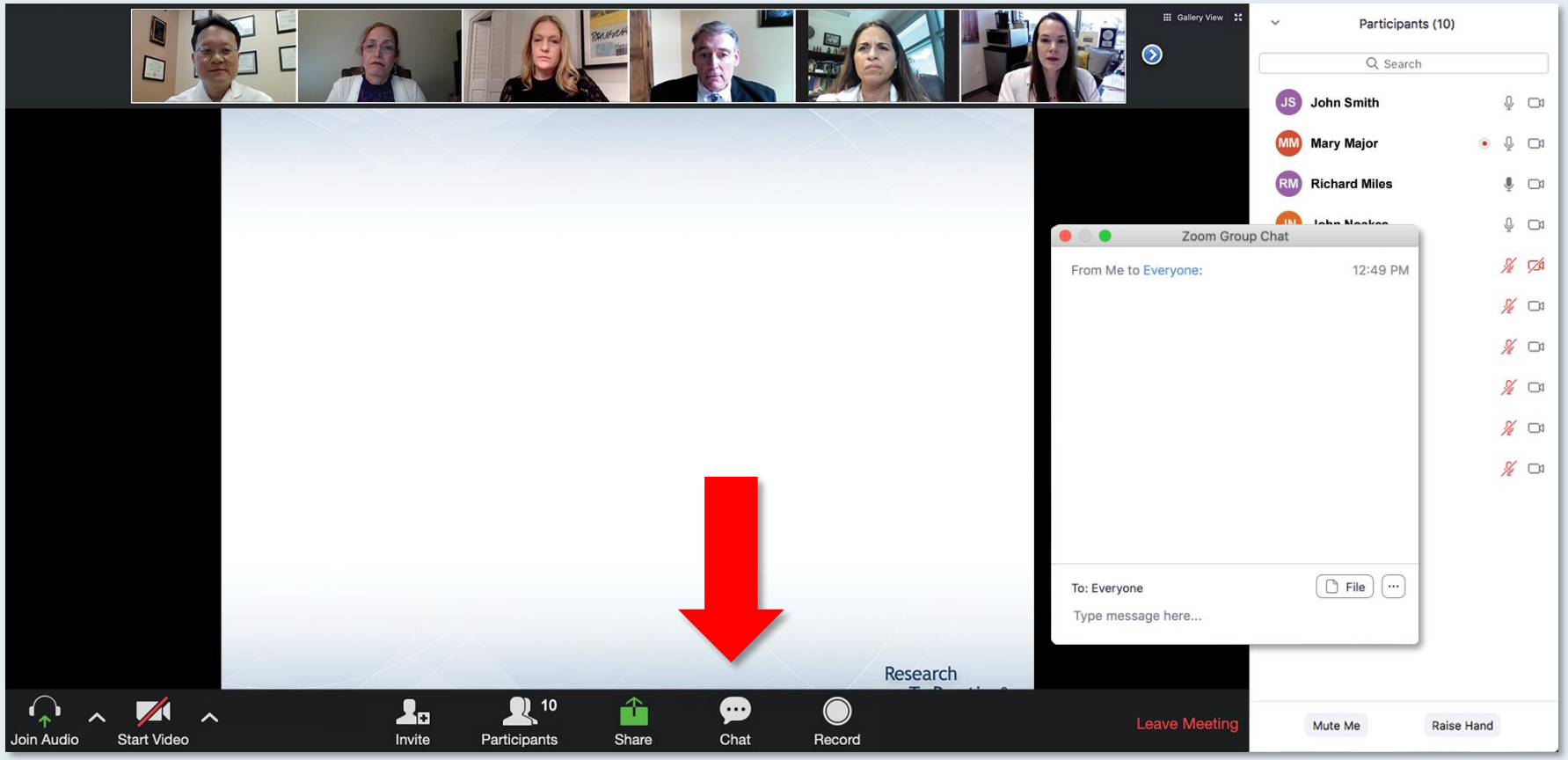
Advisory Committees and Consulting Agreements	BioNTech SE, Bristol Myers Squibb, Helsinn Therapeutics (US) Inc, Napo Pharmaceuticals
Contracted Research (Funding to City of Hope)	Bicycle Therapeutics, Genentech, a member of the Roche Group, Stemline Therapeutics Inc
Contracted Research (Funding to Prior Institution, UCSF)	Ambrx Inc, AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, Lilly, Merck, Novartis, Pfizer Inc, Stemline Therapeutics Inc

Dr Tolaney — Disclosures

Consulting Agreements	Aadi Bioscience, Aktis Oncology, Ambrx, Artios Pharma Limited, Arvinas, AstraZeneca Pharmaceuticals LP, Avenzo Therapeutics, Bayer HealthCare Pharmaceuticals, BeOne, Bicycle Therapeutics, BioNTech SE, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Celcuity, Circle Pharma, Cullinan Therapeutics, Daiichi Sankyo Inc, eFFECTOR Therapeutics Inc, Eisai Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, Hengrui Therapeutics Inc, Jazz Pharmaceuticals Inc, Johnson & Johnson, Launch Therapeutics, Lilly, Menarini Group, Merck, Mersana Therapeutics Inc, Natera Inc, Olema Oncology, Pfizer Inc, Reveal Genomics, Samsung Bioepis, Seagen Inc, Stemline Therapeutics Inc, Sumitovant Biopharma, Summit Therapeutics, SystImmune Inc, Tango Therapeutics, Tempus, Zuellig Pharma
Contracted Research	AstraZeneca Pharmaceuticals LP, Bristol Myers Squibb, Daiichi Sankyo Inc, Exelixis Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, Jazz Pharmaceuticals Inc, Lilly, Menarini Group, Merck, NanoString Technologies, Novartis, OncoPep, Pfizer Inc, Seagen Inc, Stemline Therapeutics Inc
Travel Support	Arvinas, AstraZeneca Pharmaceuticals LP, Gilead Sciences Inc, Jazz Pharmaceuticals Inc, Lilly, Pfizer Inc, Roche Laboratories Inc

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.

We Encourage Clinicians in Practice to Submit Questions

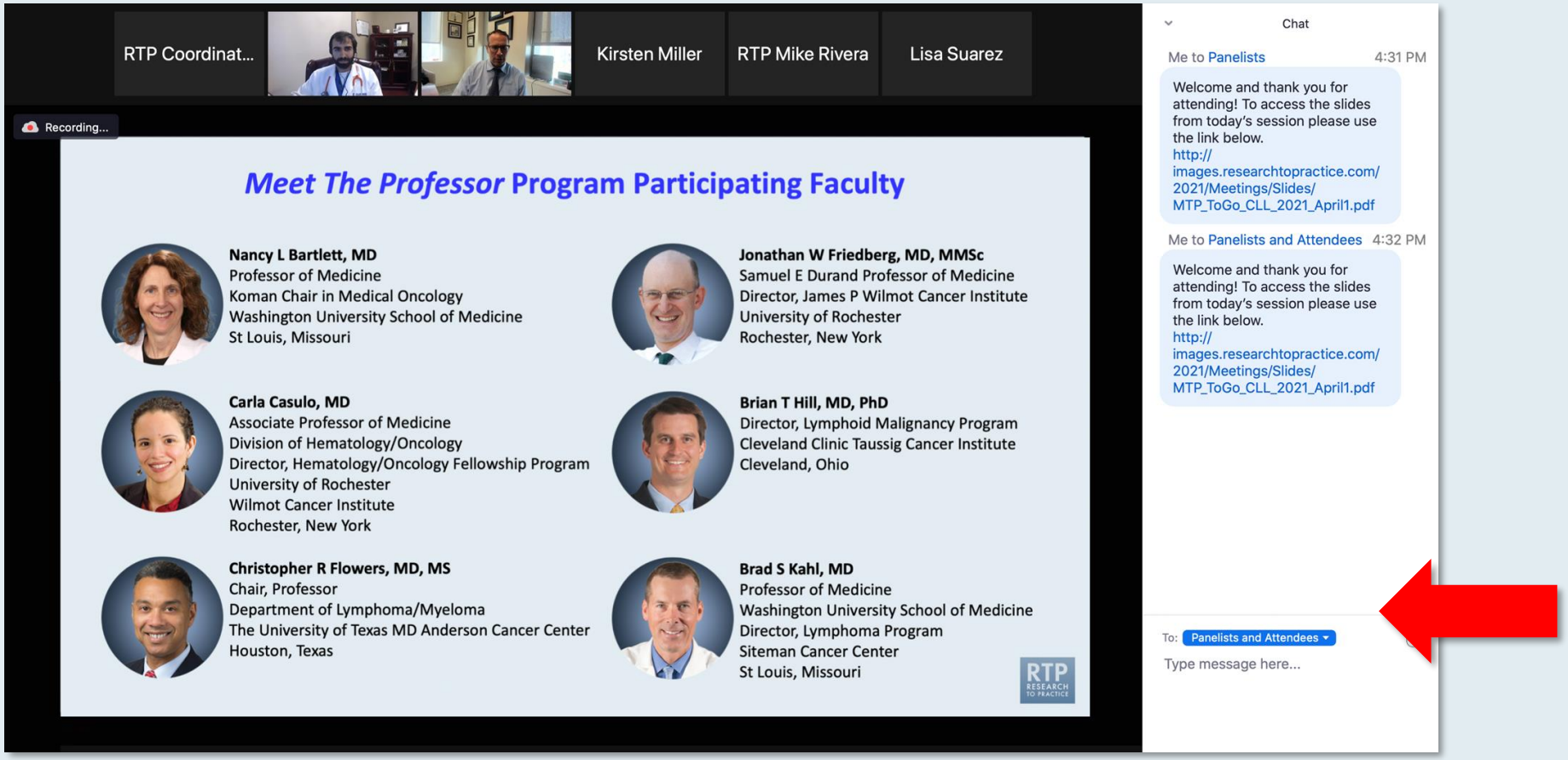


Feel free to submit questions now before the program begins and throughout the program.

RTP Year in Review 2026

Familiarizing Yourself with the Zoom Interface

Expand chat submission box

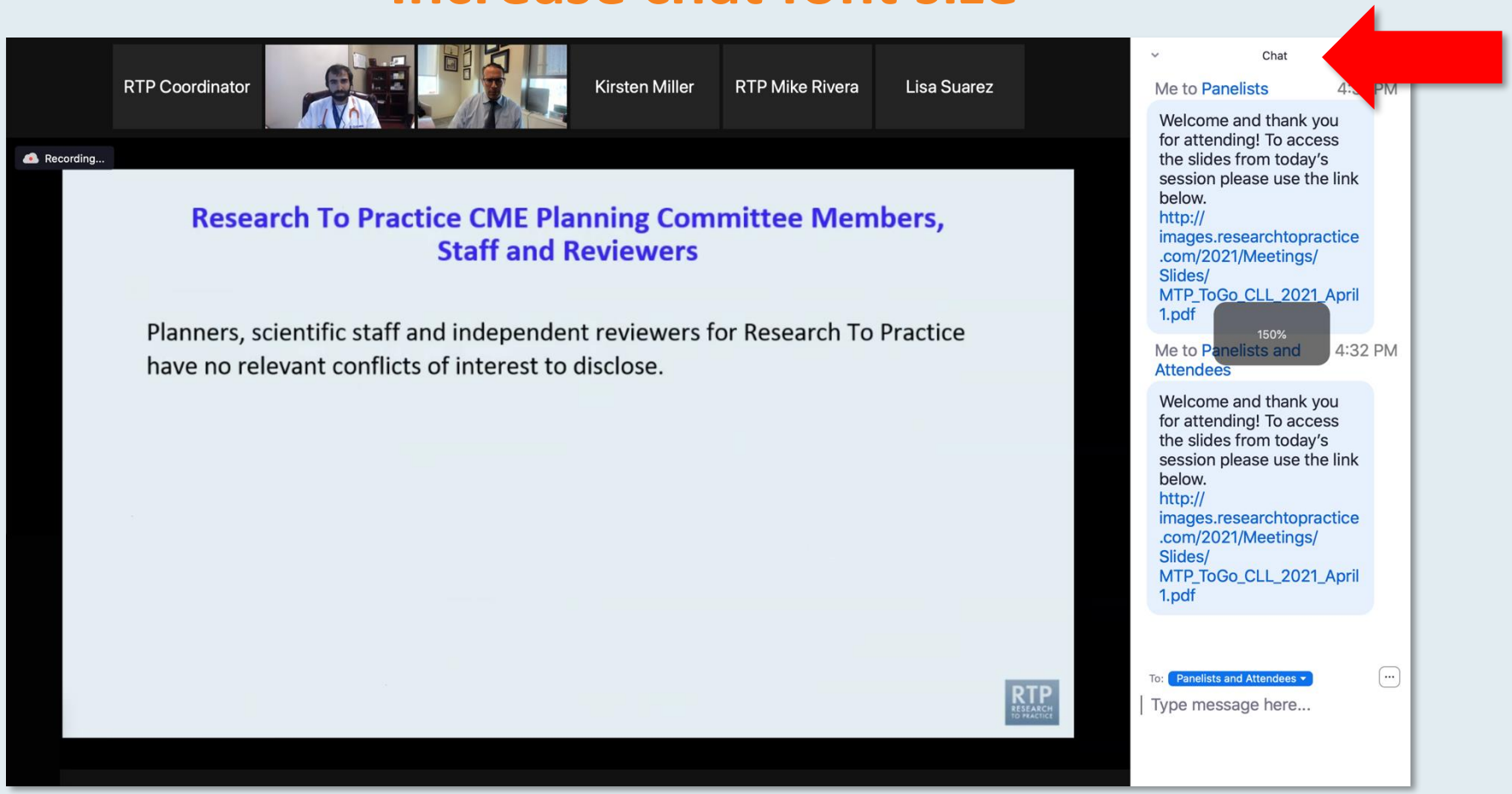


Drag the white line above the submission box up to create more space for your message.

RTP Year in Review 2026

Familiarizing Yourself with the Zoom Interface

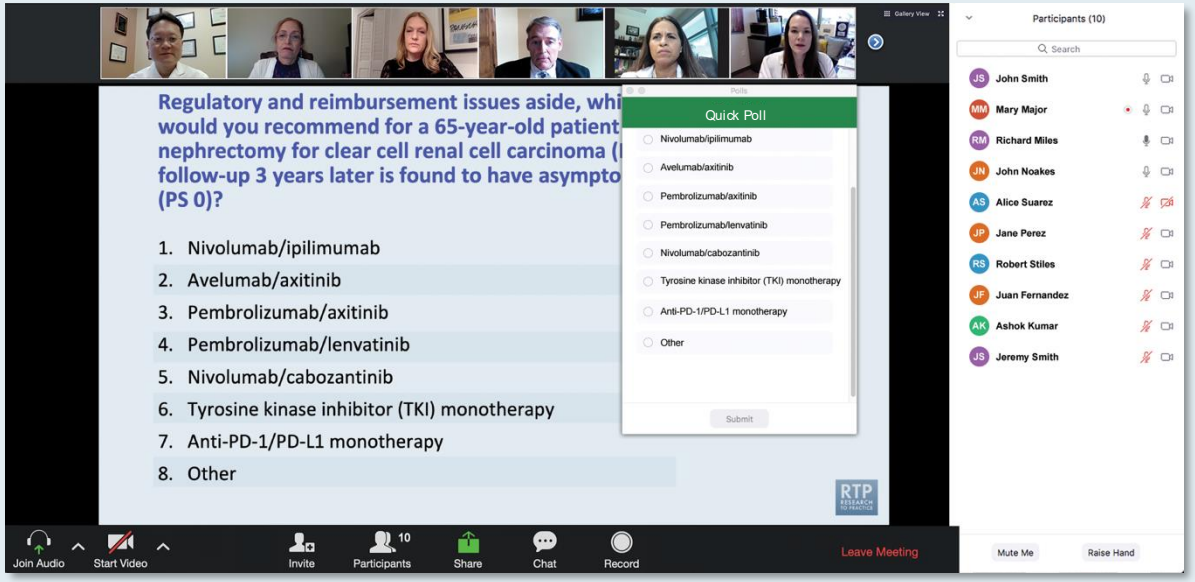
Increase chat font size



Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

RTP Year in Review 2026

Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys



Endocrine-Based Therapy for HR-Positive Breast Cancer — Proceedings from a San Antonio 2025 Symposium Series

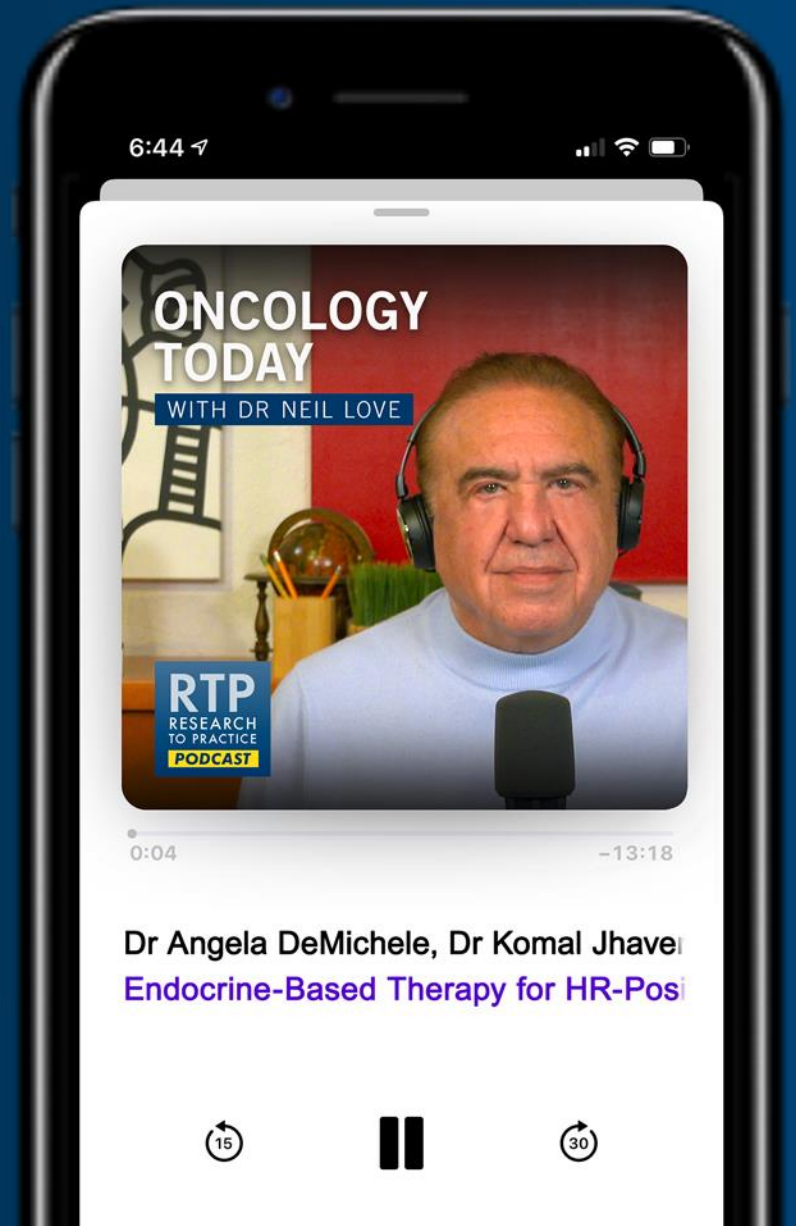
DR ANGELA DEMICHELE
ABRAMSON CANCER CENTER

DR HOPE S RUGO
CITY OF HOPE COMPREHENSIVE CANCER CENTER

DR KOMAL JHAVERI
MEMORIAL SLOAN KETTERING CANCER CENTER

DR SETH WANDER
MASSACHUSETTS GENERAL HOSPITAL

DR ERICA MAYER
DANA-FARBER CANCER INSTITUTE



Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Ovarian Cancer

A CME/MOC-Accredited Live Webinar

Thursday, February 19, 2026
5:00 PM – 6:00 PM ET

Faculty

Nicoletta Colombo, MD
Angeles Alvarez Secord, MD, MHSc

Moderator

Neil Love, MD

RTP Year in Review 2026

Second Opinion: Integrating Novel Approaches into the Management of Non-Muscle-Invasive and Muscle-Invasive Bladder Cancer

A CME Symposium Held Adjunct to the
2026 ASCO® Genitourinary Cancers Symposium

Thursday, February 26, 2026
7:00 PM – 9:00 PM PT (10:00 PM – 12:00 AM ET)

Faculty

Matthew D Galsky, MD
Shilpa Gupta, MD
Andrea Necchi, MD

Moderator

Terence Friedlander, MD

RTP RESEARCH TO PRACTICE

Second Opinion: Clinical Investigators Provide Perspectives on the Future Role of AKT Inhibition in the Management of Prostate Cancer

A CME Symposium Held Adjunct to the
2026 ASCO® Genitourinary Cancers Symposium

Friday, February 27, 2026
6:00 PM – 7:30 PM PT (9:00 PM – 10:30 PM ET)

Faculty

Professor Karim Fizazi, MD, PhD
Daniel George, MD

Moderator

Elisabeth I Heath, MD

RTP
RESEARCH TO PRACTICE

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Bruton Tyrosine Kinase Inhibitors for Chronic Lymphocytic Leukemia

A CME/MOC-Accredited Live Webinar

Wednesday, March 11, 2026

5:00 PM – 6:00 PM ET

Faculty

Jennifer R Brown, MD, PhD

Wojciech Jurczak, MD, PhD

Moderator

Neil Love, MD

RTP Year in Review 2026

Grand Rounds

CME/MOC-Accredited Interactive Series

Regional Activities

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

Year in Review:
Antibody-Drug Conjugates (ADCs) for Breast Cancer

INTRODUCTION: Long-Term Outcomes with ADCs

MODULE 1: HER2-Positive Breast Cancer

- First-line treatment for metastatic disease (current role of endocrine therapy?)
- Brain metastases
- Neoadjuvant and adjuvant therapy
- Olanzapine prophylaxis with T-DXd; rechallenge after ILD

MODULE 2: HER2-Negative Breast Cancer

- TROP2-targeted ADCs for triple-negative metastatic breast cancer (mBC)
- TROP2-targeted ADCs for HR-positive, HER2-negative mBC

RTP Year in Review 2026

Thank you for joining us!

Please take a moment to complete the survey currently up on Zoom.
Your feedback is very important to us.

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

RTP Year in Review 2025

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Antibody-Drug Conjugates for Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, February 18, 2026
5:00 PM – 6:00 PM ET

Faculty

Hope S Rugo, MD
Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

RTP Year in Review 2026

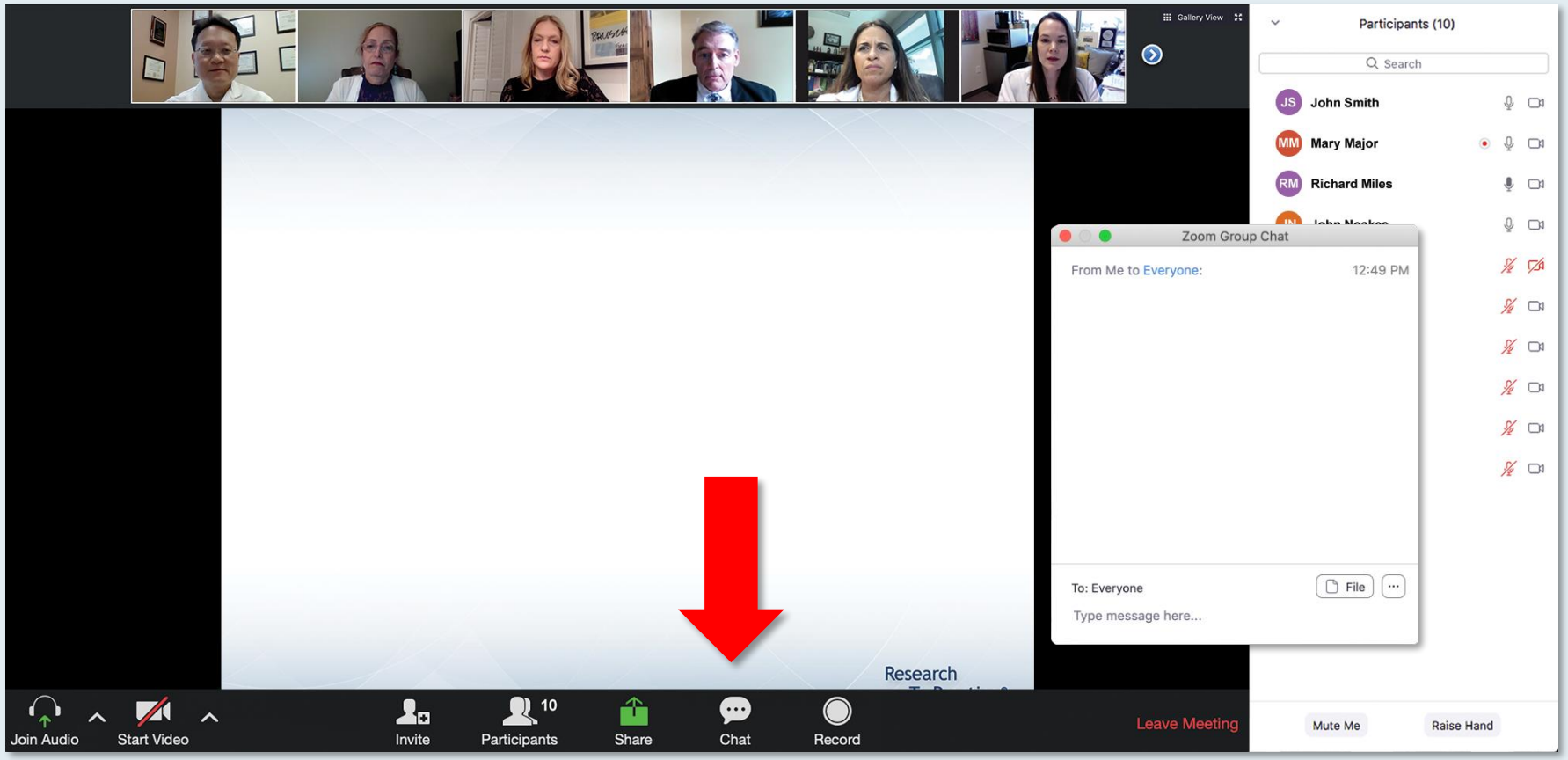
Faculty

Hope S Rugo, MD
Director, Women's Cancers Program
Division Chief, Breast Medical Oncology
Professor, Department of Medical Oncology and Therapeutics Research
City of Hope Comprehensive Cancer Center
Duarte, California
Professor Emeritus, UCSF

Sara M Tolaney, MD, MPH
Chief, Division of Breast Oncology
Dana-Farber Cancer Institute
Associate Professor of Medicine
Harvard Medical School
Boston, Massachusetts

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

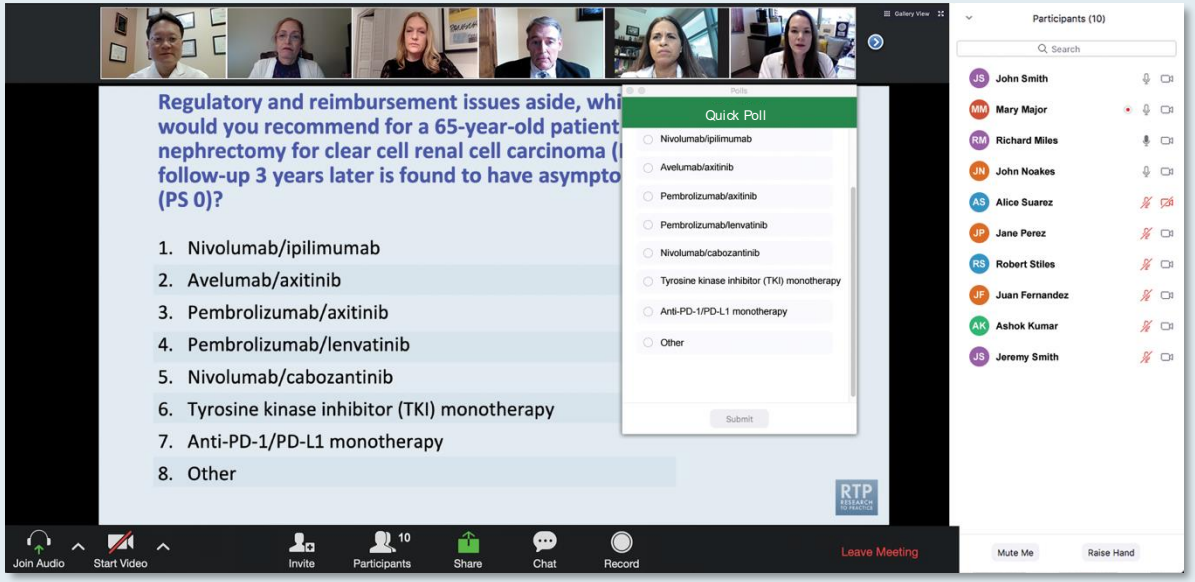
We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.

RTP Year in Review 2026

Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys



Endocrine-Based Therapy for HR-Positive Breast Cancer — Proceedings from a San Antonio 2025 Symposium Series

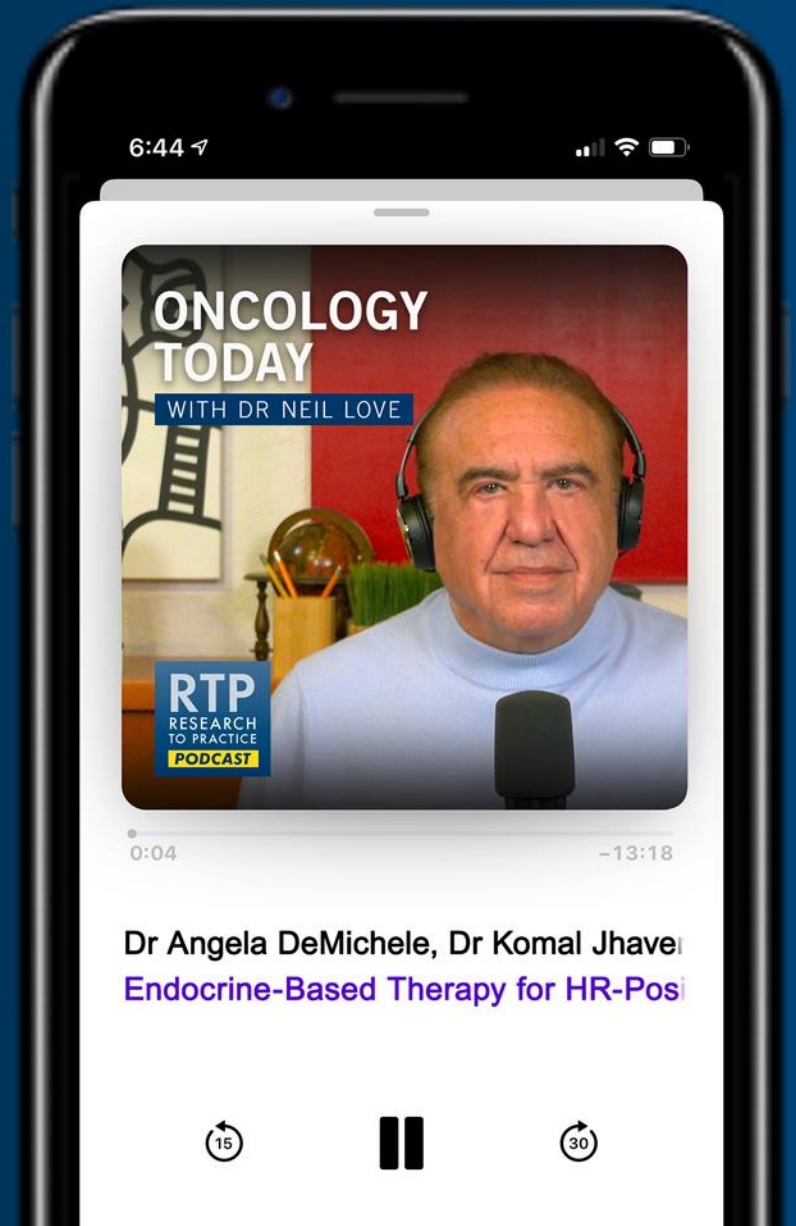
DR ANGELA DEMICHELE
ABRAMSON CANCER CENTER

DR HOPE S RUGO
CITY OF HOPE COMPREHENSIVE CANCER CENTER

DR KOMAL JHAVERI
MEMORIAL SLOAN KETTERING CANCER CENTER

DR SETH WANDER
MASSACHUSETTS GENERAL HOSPITAL

DR ERICA MAYER
DANA-FARBER CANCER INSTITUTE



Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Ovarian Cancer

A CME/MOC-Accredited Live Webinar

Thursday, February 19, 2026
5:00 PM – 6:00 PM ET

Faculty

Nicoletta Colombo, MD
Angeles Alvarez Secord, MD, MHSc

Moderator

Neil Love, MD

RTP Year in Review 2026

Second Opinion: Integrating Novel Approaches into the Management of Non-Muscle-Invasive and Muscle-Invasive Bladder Cancer

A CME Symposium Held Adjunct to the
2026 ASCO® Genitourinary Cancers Symposium

Thursday, February 26, 2026
7:00 PM – 9:00 PM PT (10:00 PM – 12:00 AM ET)

Faculty

Matthew D Galsky, MD
Shilpa Gupta, MD
Andrea Necchi, MD

Moderator

Terence Friedlander, MD

RTP RESEARCH TO PRACTICE

Second Opinion: Clinical Investigators Provide Perspectives on the Future Role of AKT Inhibition in the Management of Prostate Cancer

A CME Symposium Held Adjunct to the
2026 ASCO® Genitourinary Cancers Symposium

Friday, February 27, 2026
6:00 PM – 7:30 PM PT (9:00 PM – 10:30 PM ET)

Faculty

Professor Karim Fizazi, MD, PhD
Daniel George, MD

Moderator

Elisabeth I Heath, MD

RTP
RESEARCH TO PRACTICE

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Bruton Tyrosine Kinase Inhibitors for Chronic Lymphocytic Leukemia

A CME/MOC-Accredited Live Webinar

Wednesday, March 11, 2026

5:00 PM – 6:00 PM ET

Faculty

Jennifer R Brown, MD, PhD

Wojciech Jurczak, MD, PhD

Moderator

Neil Love, MD

RTP Year in Review 2026

Grand Rounds

CME/MOC-Accredited Interactive Series

Regional Activities

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

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Antibody-Drug Conjugates for Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, February 18, 2026
5:00 PM – 6:00 PM ET

Faculty

Hope S Rugo, MD
Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

RTP Year in Review 2026

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, and Gilead Sciences 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.

Dr Rugo — Disclosures

Advisory Committees and Consulting Agreements	BioNTech SE, Bristol Myers Squibb, Helsinn Therapeutics (US) Inc, Napo Pharmaceuticals
Contracted Research (Funding to City of Hope)	Bicycle Therapeutics, Genentech, a member of the Roche Group, Stemline Therapeutics Inc
Contracted Research (Funding to Prior Institution, UCSF)	Ambrx Inc, AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, Lilly, Merck, Novartis, Pfizer Inc, Stemline Therapeutics Inc

Dr Tolaney — Disclosures

Consulting Agreements	Aadi Bioscience, Aktis Oncology, Ambrx, Artios Pharma Limited, Arvinas, AstraZeneca Pharmaceuticals LP, Avenzo Therapeutics, Bayer HealthCare Pharmaceuticals, BeOne, Bicycle Therapeutics, BioNTech SE, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Celcuity, Circle Pharma, Cullinan Therapeutics, Daiichi Sankyo Inc, eFFECTOR Therapeutics Inc, Eisai Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, Hengrui Therapeutics Inc, Jazz Pharmaceuticals Inc, Johnson & Johnson, Launch Therapeutics, Lilly, Menarini Group, Merck, Mersana Therapeutics Inc, Natera Inc, Olema Oncology, Pfizer Inc, Reveal Genomics, Samsung Bioepis, Seagen Inc, Stemline Therapeutics Inc, Sumitovant Biopharma, Summit Therapeutics, SystImmune Inc, Tango Therapeutics, Tempus, Zuellig Pharma
Contracted Research	AstraZeneca Pharmaceuticals LP, Bristol Myers Squibb, Daiichi Sankyo Inc, Exelixis Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, Jazz Pharmaceuticals Inc, Lilly, Menarini Group, Merck, NanoString Technologies, Novartis, OncoPep, Pfizer Inc, Seagen Inc, Stemline Therapeutics Inc
Travel Support	Arvinas, AstraZeneca Pharmaceuticals LP, Gilead Sciences Inc, Jazz Pharmaceuticals Inc, Lilly, Pfizer Inc, Roche Laboratories Inc

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, 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, Nuvation Bio Inc, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Revolution Medicines 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.

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.

City of Hope

Year in Review: Current and Emerging Role of HER2 ADCs

Hope S. Rugo, MD
Director, Women's Cancers Program
Division Chief, Breast Medical Oncology
Professor, Department of Medical Oncology & Therapeutics Research
City of Hope Comprehensive Cancer Center
Professor Emeritus, UCSF

Year in Review: ADCs for Metastatic HER2- Breast Cancer

Sara M. Tolaney, MD, MPH
Division of Breast Oncology at Dana-Farber Cancer Institute

Dana-Farber Cancer Institute

RTP Year in Review 2026

Key Datasets

Hope S Rugo, MD

- Harbeck N et al. **Neoadjuvant trastuzumab deruxtecan** alone or followed by paclitaxel, trastuzumab, and pertuzumab for **high-risk HER2-positive early breast cancer (DESTINY-Breast11):** A randomised, open-label, multicentre, phase III trial. *Ann Oncol* 2026;37(2):166-79.
- Loibl S et al. **Trastuzumab deruxtecan in residual HER2-positive early breast cancer**. *N Engl J Med* 2025;[Online ahead of print].
- Tolaney SM et al. **Trastuzumab deruxtecan plus pertuzumab for HER2-positive metastatic breast cancer**. *N Engl J Med* 2025;[Online ahead of print].
- Wildiers H et al. Outcomes by hormone receptor (HR) status in patients (pts) with **HER2+ advanced/metastatic breast cancer (mBC)** with brain metastases (BM) treated with **trastuzumab deruxtecan (T-DXd):** A post-hoc **subgroup analysis of DESTINY-Breast12**. San Antonio Breast Cancer Symposium 2025;Abstract PS5-01-27.
- Hu X et al. **Patient-reported outcomes with trastuzumab deruxtecan** in hormone receptor-positive, HER2-low or HER2-ultralow metastatic breast cancer: Results from the randomized **DESTINY-Breast06** trial. *ESMO Open* 2025;10(5):105082.

Key Datasets

Hope S Rugo, MD (continued)

- Modi S et al. **Trastuzumab deruxtecan in HER2-low metastatic breast cancer**: Long-term survival analysis of the randomized, phase 3 **DESTINY-Breast04** trial. *Nat Med* 2025;31(12):4205-13.
- Sakai H et al. A randomized, double-blind, **placebo-controlled phase II study of olanzapine-based prophylactic antiemetic therapy** for delayed and persistent nausea and vomiting in patients with HER2-positive or HER2-low breast cancer treated with **trastuzumab deruxtecan: ERICA study** (WJOG14320B). *Ann Oncol* 2025;36(1):31-42.
- Natsuhara KH et al. **Treatment rechallenge after trastuzumab-deruxtecan–related interstitial lung disease**: A multi-institution cohort study. ASCO 2025;Abstract 1015.
- Hu X et al. **Trastuzumab botidotin vs trastuzumab emtansine (T-DM1)** in HER2-positive unresectable or metastatic breast cancer: Results from a randomized **phase III study**. ESMO 2025;Abstract LBA24.
- Song E et al. **SHR-A1811 versus pyrotinib plus capecitabine** in human epidermal growth factor receptor 2-positive (HER2+) advanced/metastatic breast cancer (BC): A multicenter, open-label, randomized, **phase III study (HORIZON-Breast01)**. ESMO 2025;Abstract LBA19.

Key Datasets

Sara M Tolaney, MD, MPH

- Tolaney SM et al. **Sacituzumab govitecan (SG) + pembrolizumab (pembro)** vs chemotherapy (chemo) + pembro in **previously untreated PD-L1–positive advanced triple-negative breast cancer (TNBC):** Primary results from the randomized **phase 3 ASCENT-04/KEYNOTE-D19 study**. ASCO 2025;Abstract LBA109.
- Cortés J et al. **Sacituzumab govitecan in untreated, advanced triple-negative breast cancer.** *N Engl J Med* 2025;393(19):1912-25.
- Dent RA et al. **First-line (1L) datopotamab deruxtecan (Dato-DXd)** vs chemotherapy in patients with locally recurrent inoperable or **metastatic triple-negative breast cancer (mTNBC)** for whom immunotherapy was not an option: Primary results from the randomised, **phase III TROPION-Breast02** trial. ESMO 2025;Abstract LBA21.
- Yin Y et al. **Sacituzumab tirumotecan (sac-TMT) as first-line treatment** for unresectable locally **advanced/metastatic triple-negative breast cancer** (a/mTNBC): Initial results from the phase II OptiTROP-Breast05 study. ASCO 2025;Abstract 1019.
- Rugo HS et al. Q-TWiST analysis of **sacituzumab govitecan vs chemotherapy** in previously treated patients with **HR+/HER2- metastatic breast cancer**. *Curr Oncol* 2025;32(3):169.

Key Datasets

Sara M Tolaney, MD, MPH (continued)

- Bardia A et al. **Datopotamab deruxtecan versus chemotherapy** in previously treated inoperable/metastatic hormone receptor-positive human epidermal growth factor receptor 2-negative breast cancer: Primary results from **TROPION-Breast01**. *J Clin Oncol* 2025;43(3):285-96.
- Pistilli B et al. **Datopotamab deruxtecan (Dato-DXd) vs chemotherapy (CT)** in previously-treated inoperable or metastatic hormone receptor-positive, HER2-negative (HR+/HER2–) breast cancer (BC): **Final overall survival (OS) from the phase III TROPION-Breast01 trial.** ESMO Virtual Plenary 2025;Abstract VP1-2025.
- Jhaveri K et al. **Sacituzumab govitecan vs chemotherapy as first therapy** after endocrine therapy in HR+/HER2– (IHC 0, 1+, 2+/ISH–) metastatic breast cancer: Primary results from **ASCENT-07**. San Antonio Breast Cancer Symposium 2025;Abstract GS1-09.
- Fan Y et al. **Sacituzumab tirumotecan (sac-TMT) vs investigator's choice of chemotherapy (ICC)** in previously treated locally advanced or metastatic hormone receptor-positive, HER2-negative (HR+/HER2-) breast cancer (BC): Results from the randomized, multi-center **phase III OptiTROP-Breast02** study. ESMO 2025;Abstract LBA23.
- Yin Y et al. **Sacituzumab tirumotecan** in previously treated **metastatic triple-negative breast cancer**: A randomized **phase 3 trial.** *Nat Med* 2025;31(6):1969-75.

Year in Review:
Antibody-Drug Conjugates (ADCs) for Breast Cancer

INTRODUCTION: Long-Term Outcomes with ADCs

MODULE 1: HER2-Positive Breast Cancer

- First-line treatment for metastatic disease (current role of endocrine therapy?)
- Brain metastases
- Neoadjuvant and adjuvant therapy
- Olanzapine prophylaxis with T-DXd; rechallenge after ILD

MODULE 2: HER2-Negative Breast Cancer

- TROP2-targeted ADCs for triple-negative metastatic breast cancer (mBC)
- TROP2-targeted ADCs for HR-positive, HER2-negative mBC

RTP Year in Review 2026

Year in Review:
Antibody-Drug Conjugates (ADCs) for Breast Cancer

INTRODUCTION: Long-Term Outcomes with ADCs

MODULE 1: HER2-Positive Breast Cancer

- First-line treatment for metastatic disease (current role of endocrine therapy?)
- Brain metastases
- Neoadjuvant and adjuvant therapy
- Olanzapine prophylaxis with T-DXd; rechallenge after ILD

MODULE 2: HER2-Negative Breast Cancer

- TROP2-targeted ADCs for triple-negative metastatic breast cancer (mBC)
- TROP2-targeted ADCs for HR-positive, HER2-negative mBC

Year in Review:
Antibody-Drug Conjugates (ADCs) for Breast Cancer

INTRODUCTION: Long-Term Outcomes with ADCs

MODULE 1: HER2-Positive Breast Cancer

- First-line treatment for metastatic disease (current role of endocrine therapy?)
- Brain metastases
- Neoadjuvant and adjuvant therapy
- Olanzapine prophylaxis with T-DXd; rechallenge after ILD

MODULE 2: HER2-Negative Breast Cancer

- TROP2-targeted ADCs for triple-negative metastatic breast cancer (mBC)
- TROP2-targeted ADCs for HR-positive, HER2-negative mBC

RTP Year in Review 2026

Optimal Therapy for HER2+ MBC in 2026?

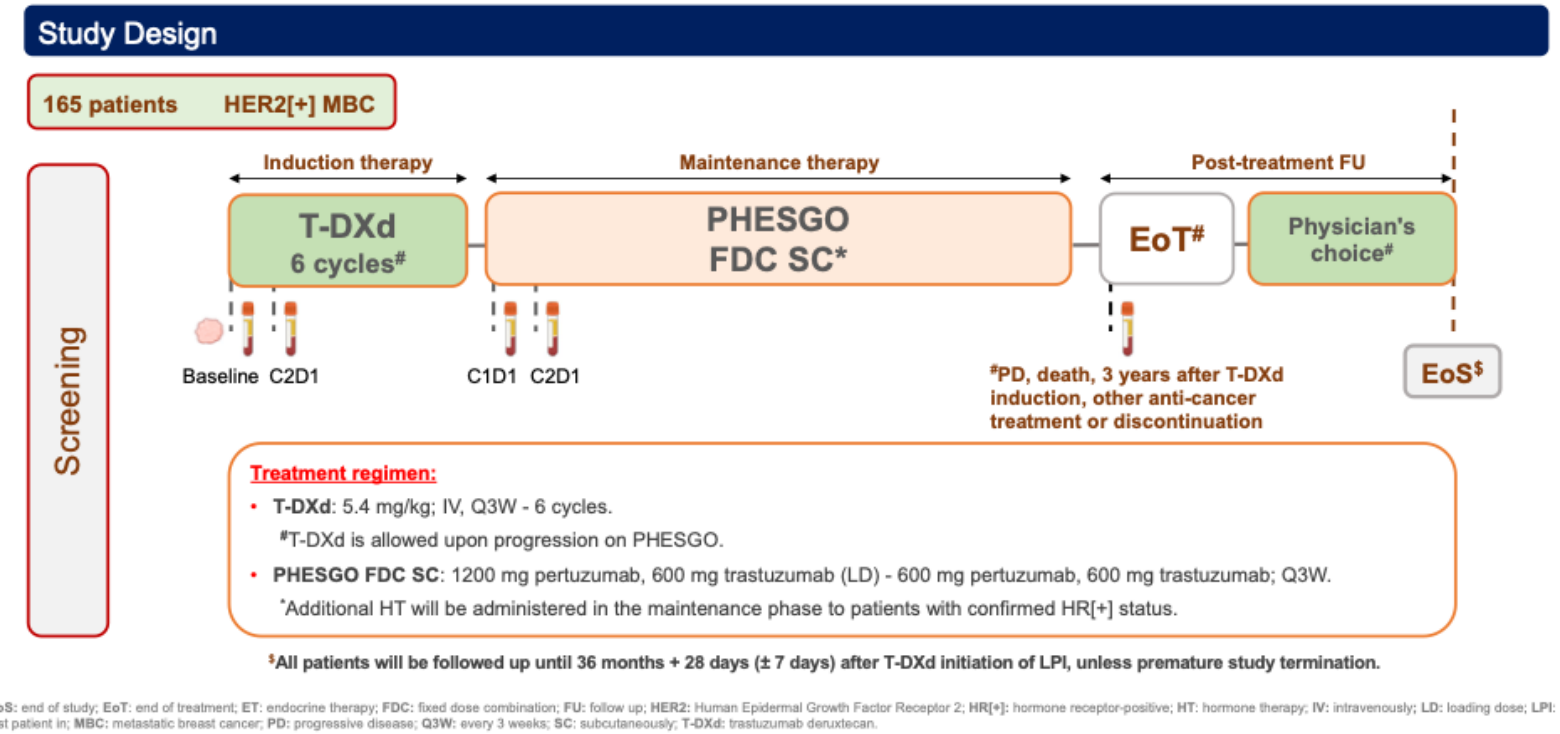
- Accessibility is clearly a key issue around the world; THP remains the standard of care
  - T-DXd has regulatory approval in the US as first-line therapy based on DB09
  - When to use T-DXd in the first-line setting - Early relapse, patients presenting with brain metastases?
  - T-DXd + P is associated with more nausea, less neuropathy than THP
    - Higher mortality by 1%; 0.5% grade 5 ILD
  - Maintenance therapy is a critical question given ongoing nausea with T-DXd/risk of ILD
- Optimal treatment?
  - T-DXd or THP induction, and in those with responding or stable disease followed by:
    - ER+: ET+ trastuzumab/pertuzumab + palbociclib
    - ER-: trastuzumab/pertuzumab + tucatinib
    - Sequencing therapy is a critical issue in interpreting trials and a key factor in improving outcome

1st Line Study	PFS, months	
TH vs THP	18.7	12.4
T-DXd/P vs THP	40.7	26.9
Palbociclib plus ET/HP vs ET/HP in responding pts	44.3	29.1
Tucatinib plus HP in responding pts	24.9	16.3

Courtesy of Hope S Rugo, MD

Ongoing Maintenance Studies

The DEMETHER Study



EoS: end of study; EoT: end of treatment; ET: endocrine therapy; FDC: fixed dose combination; FU: follow up; HER2: Human Epidermal Growth Factor Receptor 2; HR[+]: hormone receptor-positive; HT: hormone therapy; IV: intravenously; LD: loading dose; LPI: last patient in; MBC: metastatic breast cancer; PD: progressive disease; Q3W: every 3 weeks; SC: subcutaneously; T-DXd: trastuzumab deruxtecan.

Selected Group Patients

Population

HER2+

4-8 cycles of pre-study induction THP therapy

HR+ (heredERA)

PIK3CA-MUT (INAVO122)

1:1

- HP + giredestrant or inavolisib
- HP +/- ET +/- placebo

heredERA (NCT05296798)
INAVO122 (NCT05646862)

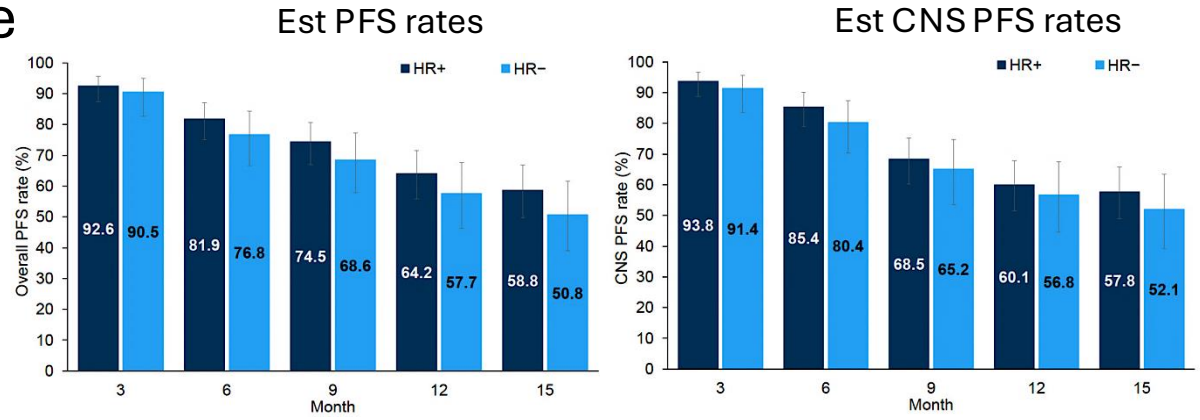
Courtesy of Hope S Rugo, MD

Questions?

RTP Year in Review 2026

Destiny Breast12: Post Hoc Analysis of Efficacy by Hormone Receptor Status

- DB12 treated 263 patients with HER2+ stable or active brain metastases with T-DXd with a primary endpoint of PFS
  - Almost all had 1-2 lines of prior therapy
  - Overall PFS 17.3 mo, 12 mo CNS PFS 58.9%
  - ORR 51.7%, 64.1% for measurable dse



Response rates in patients with BMs

Response, n (%, 95% CI)	HR+ (n-165)	HR- (n=97)
ORR	81(**49.1**) [41.5, 56.7]	54(**55.7**) [45.8, 65.6]
CNS ORR	56 (**66.7**) [56.6, 76.7])	42(**79.2**) [68.3, 90.2)
ORR in measurable dse	76(**60.8**) [52.2, 69.4]	50(**69.4**) [58.8, 80.1]

- Overall and CNS PFS similar for HR+ and HR-
- Safety similar; 3 ILD in each subgroup
- ILD rate high at 15.8 /16.5% (HR+/-) likely due to steroid use and lack of PJP prophylaxis

Conclusions

- Efficacy of T-DXd in HER2+ MBC in brain maintained regardless of HR status
- Careful management with prophylaxis to avoid opportunistic infections is critical

Harbeck N, et al. *Nat Med*. 2024;30:3717–3727; Wildiers et al, SABCS 2025

Courtesy of Hope S Rugo, MD

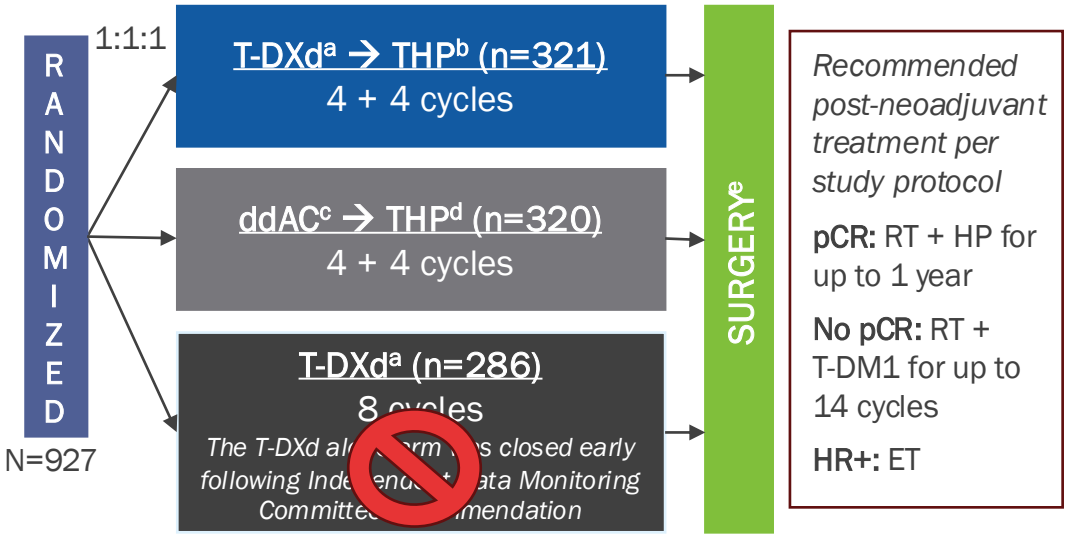
Questions?

RTP Year in Review 2026

DESTINY-Breast11 Phase 3 Trial of Neoadjuvant T-DXd Alone or Followed by THP vs SOC for High-Risk HER2+ EBC: Study Design and Patients

Key Eligibility Criteria

- Previously untreated HR+ or HR– HER2+ EBC
- High risk defined as:
  - ≥cT3 and N0-3 or cT0-4 and N1-3
  - Inflammatory breast cancer



Primary endpoint: pCR (ypT0/is ypN0) by BCR
Secondary endpoints: pCR (ypT0 ypN0) by BCR, EFS, safety, PK and immunogenicity, IDFS, OS, HRQoL

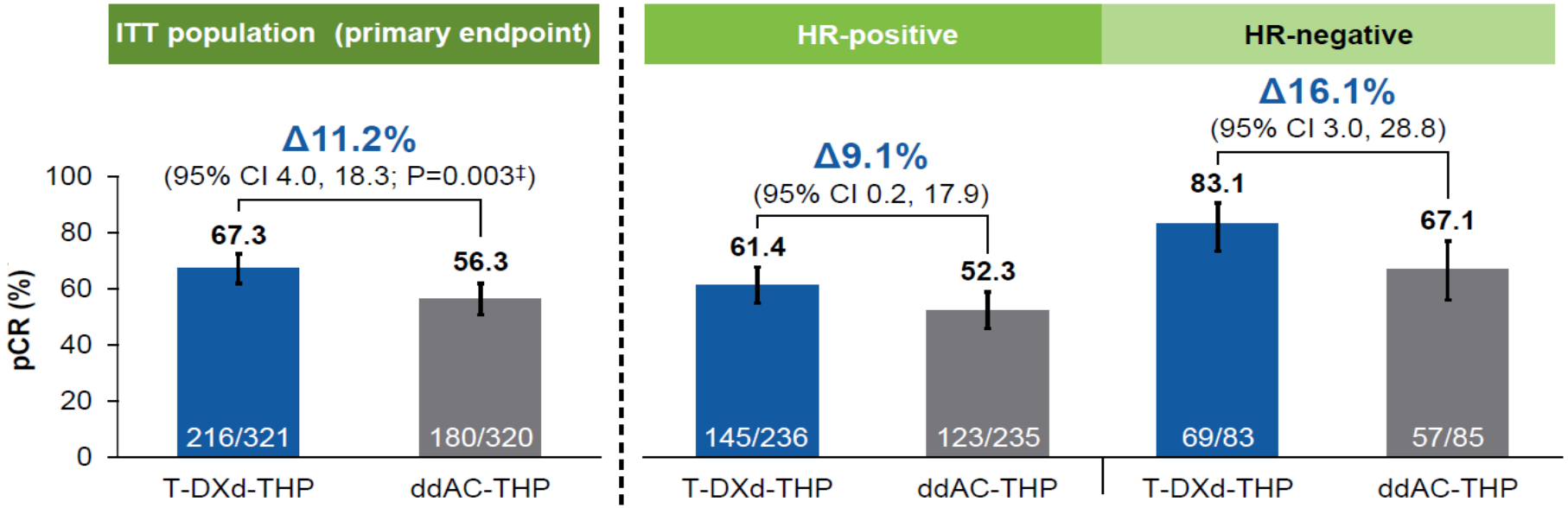
Patient Characteristics, n (%)		T-DXd-THP (n=321)	ddAC-THP (n=320)	T-DXd (n=286)
Median (range) age, years		50 (25-82)	50 (23-79)	50 (23-79)
Geographic region	**Asia**	**152 (47.4)**	**152 (47.5)**	**124 (43.4)**
	Western Europe	69 (21.5)	77 (24.1)	66 (23.1)
	North America	43 (13.4)	41 (12.8)	52 (18.2)
	Rest of world	57 (17.8)	50 (15.6)	44 (15.4)
HR+		**236 (73.5)**	**235 (73.4)**	**205 (71.7)**
Clinical tumor stage	cT0-2	176 (54.8)	188 (58.8)	157 (54.9)
	cT3-4	145 (45.2)	132 (41.3)	129 (45.1)
Nodal status	N0	26 (8.1)	35 (10.9)	20 (7.0)
	N+	**287 (89.4)**	**281 (87.8)**	**254 (88.8)**

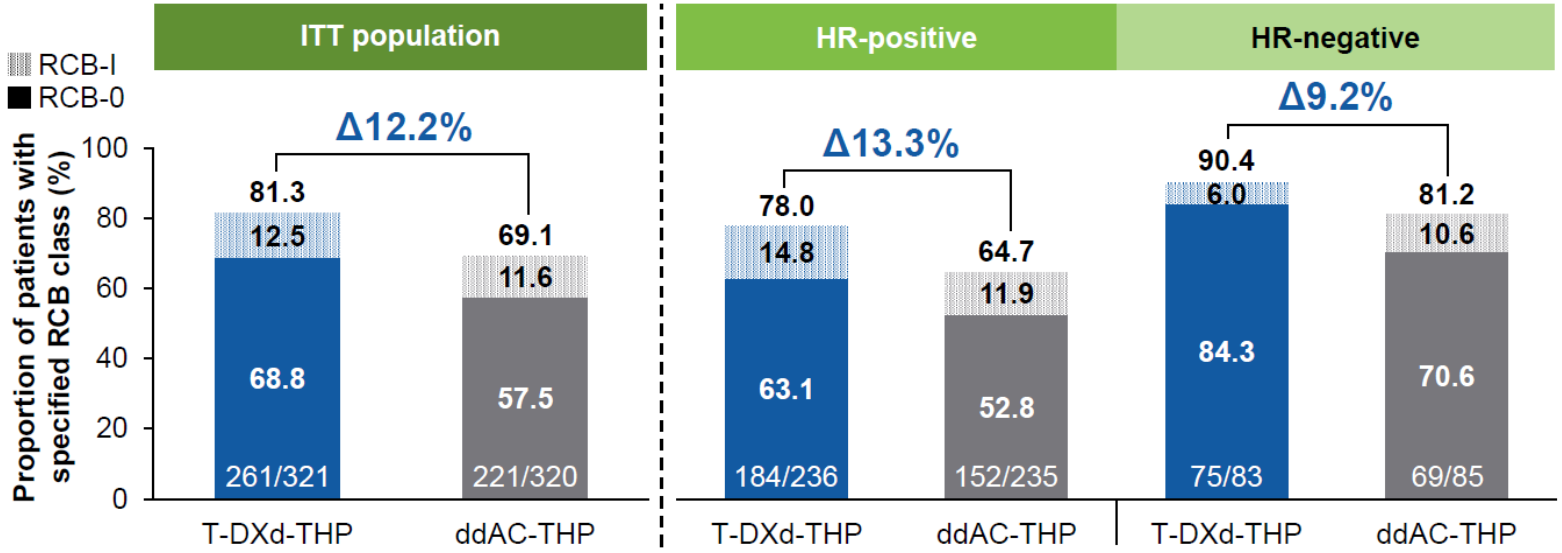
[a] 5.4 mg/kg q3w. [b] Paclitaxel (80 mg/m^2 qw) + trastuzumab (6 mg/kg q3w) + pertuzumab (840 mg loading dose followed by 420 mg q3w). [c] Doxorubicin (60 mg/m^2 q2w) + cyclophosphamide (600 mg/m^2 q2w). [d] Paclitaxel (80 mg/m^2 qw) + trastuzumab (8 mg/kg loading dose followed by 6 mg/kg q3w) + pertuzumab (840 mg loading dose followed by 420 mg q3w). [e] Recommended window for surgery was 3-6 weeks following administration of the last dose of neoadjuvant study treatment.

Harbeck N, et al. ESMO 2025. Abstract 2190; Ann Oncol 2025.

Courtesy of Hope S Rugo, MD

DESTINY-Breast11: pCR and RCB with T-DXd-THP vs ddAC-THP



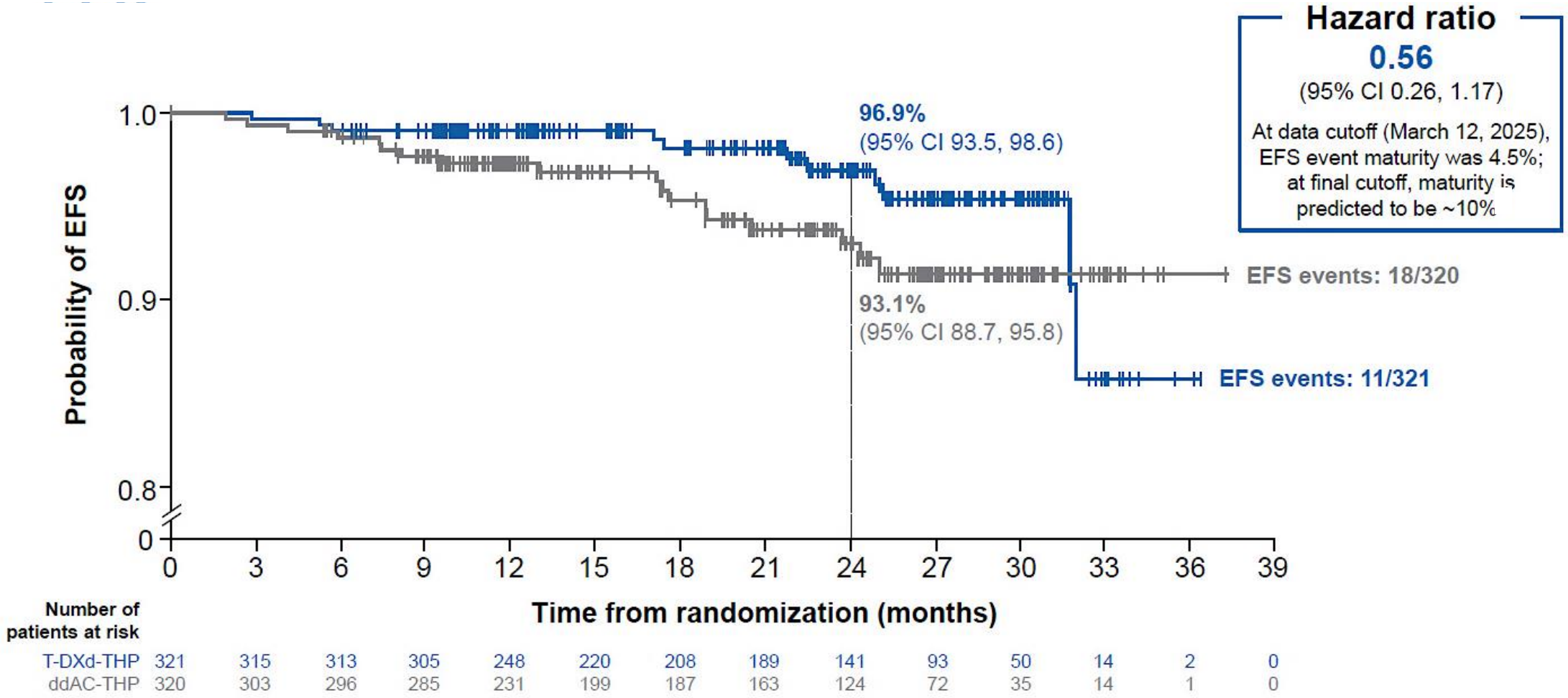


Harbeck N, et al. ESMO 2025.
Abstract 2190, Ann Oncol 2025

Courtesy of Hope S Rugo, MD

DESTINY-Breast11: EFS Immature

Trial was not powered for EFS or OS



- Post-neoadjuvant treatments were generally well balanced between T-DXd-THP and ddAC-THP arms
- In both arms, more than half of patients without pCR received post-neoadjuvant T-DM1

Harbeck N, et al. ESMO 2025. Abstract 2190, Ann Oncol 2025.

Courtesy of Hope S Rugo, MD

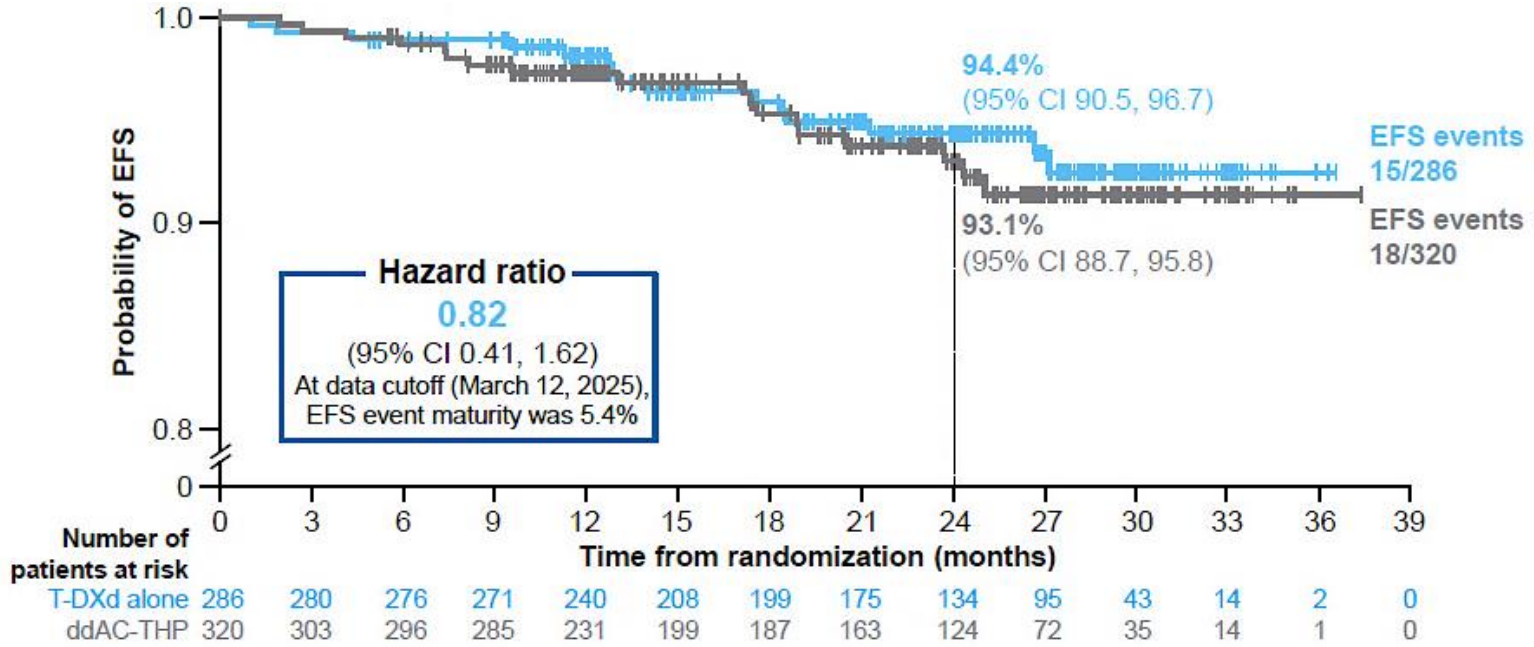
DESTINY-Breast11 Phase 3 Trial of Neoadjuvant T-DXd Alone or Followed by THP vs SOC for High-Risk HER2+ EBC: pCR and EFS in T-DXd vs ddAC-THP

On March 13, 2024, the T-DXd alone arm closed following Independent Data Monitoring Committee recommendation.[a] Patients who were still receiving T-DXd alone could remain on therapy or immediately switch to local SOC.

pCR Rate

%	T-DXd (n=286)	ddAC-THP (n=320)
Primary analysis Switch to local SOC classified as non-pCR		
pCR	43.0	56.3
Δ (95% CI)	−13.2 (−20.8, −5.4)	
Prespecified supplementary analysis Switch to local SOC not automatically classified as non-pCR		
pCR	51.4	57.2
Δ (95% CI)	−5.8 (−13.4, 1.9)	

EFS



- The overall safety profile of T-DXd alone was favorable vs ddAC-THP, with reduced rates of grade ≥3 AEs, SAEs, treatment reductions/interruptions, and left ventricular dysfunction; ILD incidence was low and similar in both arms

[a] The reasons were multifactorial, including a lower pCR rate, low likelihood that T-DXd alone would be superior to ddAC-THP, and the timing of surgery.

Harbeck N, et al. ESMO 2025. Abstract 2190; Ann Oncol 2025.

Courtesy of Hope S Rugo, MD

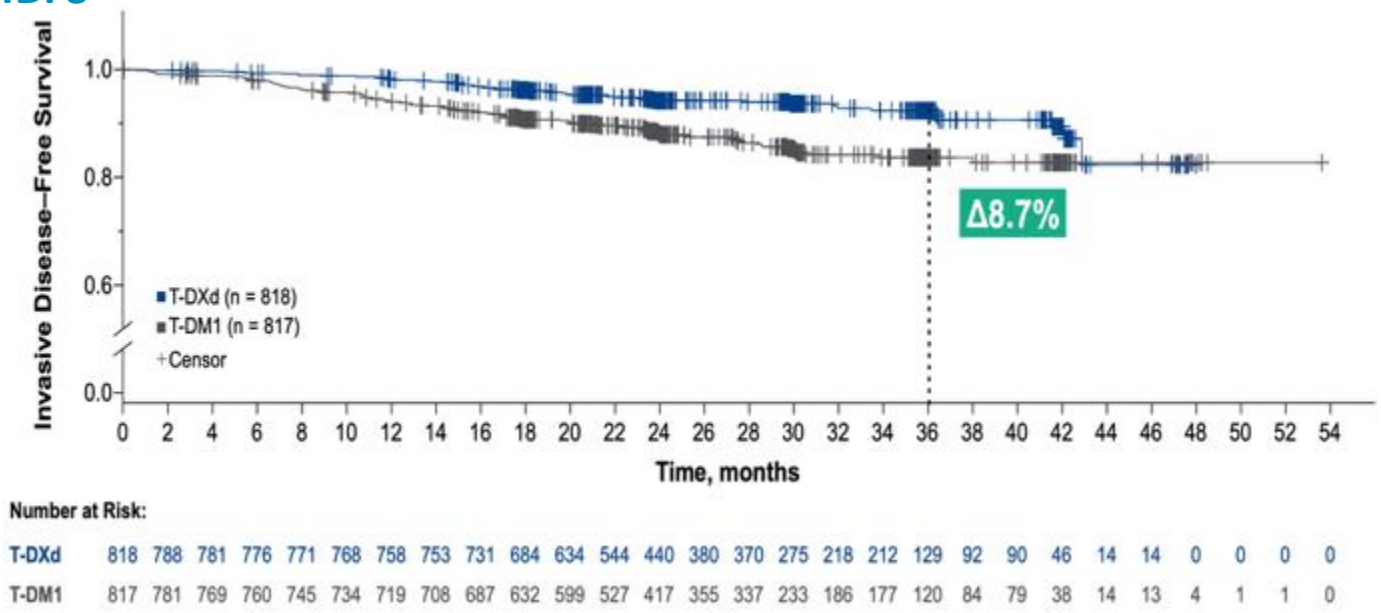
What did we Learn?

- T-DXd-THP showed the highest reported pCR rate in HER2+ EBC for a registrational study in the neoadjuvant setting, despite high prevalence of HR+ disease and a high-risk population
- Definitive data – and the 4th trial – to show that anthracyclines do not improve pCR in HER2+ breast cancer and are less safe than non-anthracycline based chemotherapy/ADCs
- Sequential non-cross resistant chemotherapy remains the best treatment approach for high-risk early stage HER2+ breast cancer
  - T-DXd alone was inferior in this high-risk patient population
- T-DXd-THP associated with lower rates of hematologic AEs, left ventricular dysfunction, and fatigue, with similar rates of ILD
  - Control arm imperfect as TCHP is the SOC in many countries although that is due to equivalency in randomized phase III trials
  - Safety comparison impacted the most

Courtesy of Hope S Rugo, MD

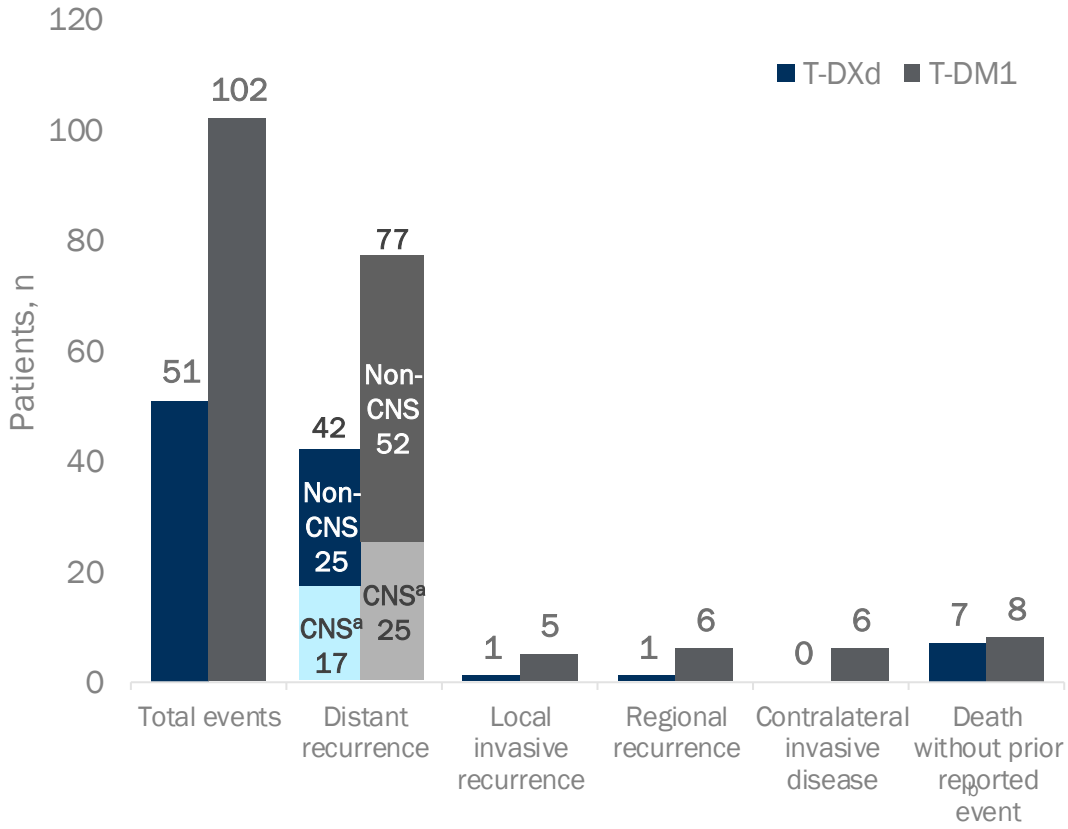
Interim Analysis of DESTINY-Breast05: IDFS with T-DXd vs T-DM1 in High-Risk HER2+ EBC

IDFS



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

Categories of First IDFS Events



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

Geyer CE, et al. ESMO 2025. Abstract LBA1.

Courtesy of Hope S Rugo, MD

What did we Learn?
How to Incorporate T-DXd into treatment for early stage HER2+ BC?

- T-DXd for patients with high risk HER2+ disease and residual disease in breast and/or node following at least 6 cycles of neoadjuvant chemotherapy containing HER2 targeted therapy significantly improved IDFS and DFS compared to T-DM1 – with short follow-up
  - Effect seen across all prespecified subgroups
  - At interim analysis there are less CNS metastases in the T-DXd group
  - T-DXd was associated with more ILD compared to DB11, presumably due to longer exposure and perhaps prior treatment, as well as more nausea than T-DM1
    - Less cytopenias and liver enzyme elevations
    - Similar deaths attributed to treatment (2 v 1)
- Neoadjuvant or adjuvant?
  - More T-DXd (8 cycles vs 4 followed by THP) was definitely not better
  - T-DXd x 4 followed by THP is associated with less toxicity and increases pCR, thereby sparing a subset of patients 14 cycles of T-DXd
  - But in patients with no pCR, next steps are unclear!
  - THP is sufficient for a subset of patients, as is T-DXd x 4: individualizing therapy to risk is critical
    - Ex: I-SPY 2.2
  - T-DXd in patients with residual disease (and high-risk) will become the SOC

Courtesy of Hope S Rugo, MD

Questions?

RTP Year in Review 2026

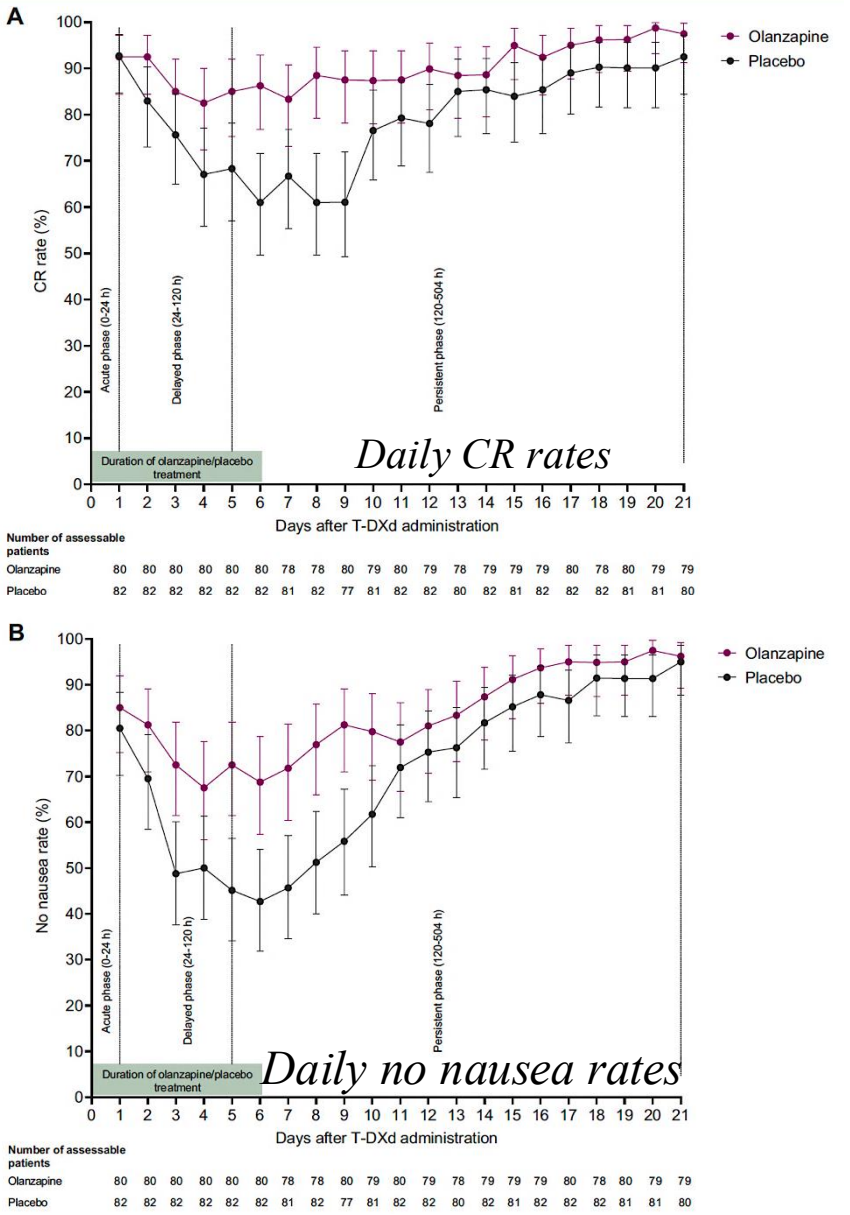
ERICA Trial: Randomized Trial of Olanzapine Prophylaxis for T-DXd Delayed/Persistent Nausea and Vomiting

- 162 evaluable patients were enrolled at 43 sites in Japan
- Study design: placebo controlled, dbl blind
  - Olanzapine/pla 5 mg/d day 1-6
  - Day 1: 5-HT3 RA, dexamethasone (6.6mg IV, 8 mg PO)
  - Primary endpoint CR in 21d observation period
    - No emetic events, no rescue meds in delayed phase (24-120hr post T-DXd)
  - Secondary endpoints
    - No nausea in delayed/persistent phases (120-504 hrs, 21d)
    - Adverse events
- Results
  - Delayed phase CR (olanzapine vs pla)
    - 70 vs 56.1%. P 0.047
  - Persistent phase
    - 63.9 vs 44.4%
  - No nausea
    - 57.5 vs 37.8%
  - Less appetite loss, low-grade somnolence and hyperglycemia with olanzapine
    - Hyperglycemia: 7.5% vs 0
    - Somnolence: 25 vs 10.8%

Sakai et al, Ann Oncol 2025

Courtesy of Hope S Rugo, MD

Results and Conclusions



- Nausea is the most common toxicity from T-DXd impacting QOL and adherence
  - Affects >70% with standard antiemetics
- Recommendations for prophylaxis include a 3-drug regimen with 5-HT3 RA, NK1 RA and dexamethasone
  - Delayed and long-delayed nausea remain an issue
- Olanzapine at bedtime d1-4+ is remarkably effective at reducing nausea, also effective when extended for delayed nausea
  - Start at 2.5 mg* and increase as needed (1.25mg for some!)
  - Indian study: Mainly AC showed 2.5 mg as effective as 10 mg d1-4 with much less somnolence

Courtesy of Hope S Rugo, MD

*Bajpai et al, Lancet Oncology 2024

Outcomes after Rechallenge with T-DXd

- **3 patients with recurrent grade 1 ILD were rechallenged with T-DXd a 2nd time**
  - 1 patient rechallenged with a dose reduction, 2 without
  - 2 remained on T-DXd until disease progression for 63 and 211 days and 1 remains on therapy as of 5/8/25
- **19 patients with grade 2 ILD were re-challenged with T-DXd**, outside of the guidelines
  - Median time to rechallenge was 49 days (IQR 42-126 days)
  - Patients remained on T-DXd after rechallenge for a median of 91 days (IQR 27-162)
  - 3 patients (16%) developed recurrent ILD (1-G2, 1-G3, 1-G4)

**** No grade 5 cases of recurrent ILD were seen after rechallenge***

Abbreviations: IQR = interquartile range, G = grade

Courtesy of Hope S Rugo, MD

Conclusion

Rechallenge with T-DXd after grade 1 ILD was safe; patients in a diverse real-world population had ongoing clinical benefit from T-DXd.

- High rates of rechallenge after grade 1 ILD were safe with long duration of clinical benefit
- Treatment with steroids resulted in faster radiographic improvement of ILD
- Among patients rechallenged after grade 1 ILD, rates of recurrent ILD were low, with mostly grade 1 events and no grade 5 events
- A small number of patients with grade 2 ILD were rechallenged with a similar rate of recurrent ILD, but this data must be interpreted with caution

Courtesy of Hope S Rugo, MD

Questions?

RTP Year in Review 2026

Year in Review:
Antibody-Drug Conjugates (ADCs) for Breast Cancer

INTRODUCTION: Long-Term Outcomes with ADCs

MODULE 1: HER2-Positive Breast Cancer

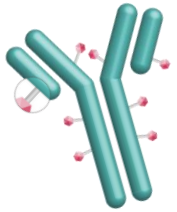
- First-line treatment for metastatic disease (current role of endocrine therapy?)
- Brain metastases
- Neoadjuvant and adjuvant therapy
- Olanzapine prophylaxis with T-DXd; rechallenge after ILD

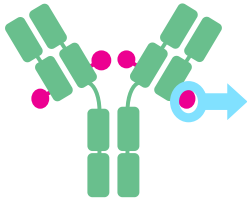
MODULE 2: HER2-Negative Breast Cancer

- TROP2-targeted ADCs for triple-negative metastatic breast cancer (mBC)
- TROP2-targeted ADCs for HR-positive, HER2-negative mBC

RTP Year in Review 2026

How To Approach Therapy for 1L mTNBC? TROP2 ADCs Moving Into The First Line Space





	Sacituzumab govitecan (SG)	Datopotamab deruxtecan (Dato-DXd)
Antibody	hRS7 Humanized IgG1 mAb	MAAP-9001a Humanized IgG1 mAb
Payload	SN38 (DNA Topoisomerase I inhibitor)	DXd (DNA Topoisomerase I inhibitor)
Linker cleavage	Enzymatic and pH-dependent	Enzymatic
Bystander effect	Yes	Yes
DAR	7.6	4
Half-life	11-14h	~5 days
Dosing	D1, D8 of Q3W schedule	Q3W

Sands J et al, ASCO 2018; Okajima D et al. Mol Cancer Ther 2021

Courtesy of Sara M Tolaney, MD, MPH

TROP2 ADC IN 1L mTNBC NOT CANDIDATE FOR PD-(L)1i

SAN ANTONIO BREAST CANCER SYMPOSIUM®

UT Health San Antonio Mays Cancer Center | AACR American Association for Cancer Research

ASCENT-03

- **Previously untreated, locally advanced inoperable or metastatic TNBC**
- Not candidate for PD-(L)1 inhibitor:
  - ✓ PD-L1- (CPS <10) OR
  - ✓ PD-L1+ AND:
    - ○ Received PD-(L)1 inhibitor in curative setting OR
    - ○ Ineligible for PD-(L)1 inhibitor due to comorbidity
- ≥6 months since treatment in curative setting
- Previously treated, stable CNS metastases allowed

1:1

Sacituzumab govitecan
(10 mg/kg IV on Days 1, 8 of 21-day cycles)

*Crossover to SG allowed after BICR-verified PD

TPC Chemotherapy*
gemcitabine/carboplatin, paclitaxel or nab-paclitaxel

Stratification Factors:

- US/Canada/Western Europe vs. other geographic regions
- De novo vs. recurrent 6-12 mo. vs. recurrent >12 mo. after treatment in curative setting

Cortés J et al. ESMO 2025.

TROPION-Breast02

- **Previously untreated, locally recurrent inoperable or metastatic TNBC**
- Not candidate for PD-(L)1 inhibitor:
  - ✓ PD-L1- (CPS <10) OR
  - ✓ PD-L1+ AND
    - ○ 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
- Any interval since treatment in curative setting (DFI ≤12 mo: ≤20%)
- Stable brain metastases[a] allowed

1:1

Datopotamab deruxtecan
(6 mg/kg IV on Day 1 of 21-day cycles)

ICC (n=321)
paclitaxel or nab-paclitaxel
(if no prior taxane or neo-/adjuvant taxane + DFI >12 mo) OR
capecitabine, carboplatin or eribulin
(if prior taxane + DFI ≤12 mo)

Stratification Factors:

- PD-L1 (positive vs. negative)
- US/Canada/Europe vs. other geographic regions
- De novo vs. DFI 0-12 mo. vs. DFI >12 mo. after treatment in curative setting

Dent R et al. ESMO 2025.

Dana-Farber Cancer Institute

Courtesy of Sara M Tolaney, MD, MPH

How to Select 1L TROP2 ADC for a Patient with PD-L1-Negative mTNBC?

SAN ANTONIO BREAST CANCER SYMPOSIUM®
UT Health San Antonio Mays Cancer Center | AACR American Association for Cancer Research

Sacituzumab govitecan

- **PFS** benefit
- **OS data immature** (impact of crossover?)
- ↑ **Neutropenia** (growth factor needed in most)
- ↑ **Nausea**
- ↑ **Diarrhea**
- **Two infusions** per 21-day cycle
- ↑ **Longer total infusion time**

Datopotamab deruxtecan

- **PFS** benefit
- **OS** benefit
- ↑ **Response** rate
- ↑ **Ocular surface toxicity** (Eye drops, avoid contact lenses, baseline eye exam)
- ↑ **Oral mucositis/stomatitis:** Mouthwash
- **ILD monitoring**
- **One infusion** per 21-day cycle
- ↓ **Shorter total infusion time**

Slide courtesy of Ana Garrido-Castro.

Dana-Farber Cancer Institute

Courtesy of Sara M Tolaney, MD, MPH

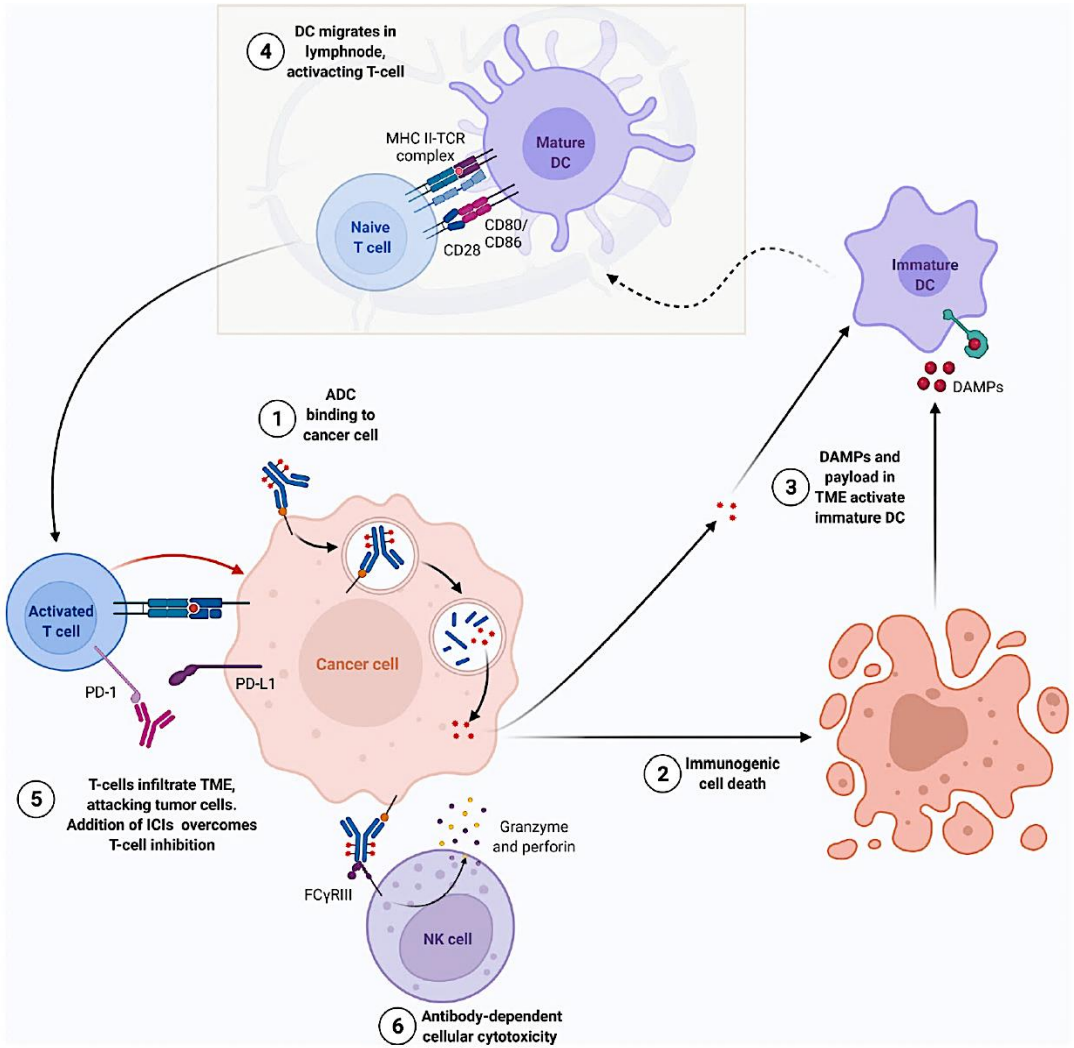
How to Select 1L TROP2 ADC for a Patient with PD-L1-Negative mTNBC?

	Sacituzumab Govitecan Preferred	Dato-DXd Preferred
Early relapse (0-6 mo)		✓
Prior or current pneumonitis	✓	
Baseline cytopenias		✓
Diarrhea at baseline/Bowel disorders		✓
Transportation challenges		✓
Corneal disorders/contact lenses/difficulty getting eye exam	✓	
Significant mucositis at baseline	✓	

Limitation: Unknown efficacy post KN522 given ~5% of pts in these trials had recv'd prior IO

Courtesy of Sara M Tolaney, MD, MPH

Rationale for Combining Immunotherapy and ADCs



- **Immunogenic cell death**
- **↑ ADCC**
- **↑ T-cell infiltration**

Nicolo E et al, Cancer Treatment Reviews 2022

Courtesy of Sara M Tolaney, MD, MPH

1L Treatment of PD-L1+ mTNBC

SAN ANTONIO BREAST CANCER SYMPOSIUM®
UT Health San Antonio Mays Cancer Center | AACR American Association for Cancer Research

	ASCENT-04	TROPION-Breast05
Patient Population	• **PD-L1+ (CPS ≥10)** untreated, inoperable/locally advanced or metastatic TNBC • **≥6 months since therapy in curative setting** (prior PD-L1 use allowed in this setting)	• **PD-L1+ (CPS ≥10)** untreated, inoperable/locally advanced or metastatic TNBC • **DFI ≥6 months since therapy in curative setting** (DFI 6–12 months capped at 20%) • Prior PD-(L)1 use allowed in this setting • History of ILD/pneumonitis and clinically significant corneal disease excluded
Study Design	R 1:1, N=440 • **SG + pembrolizumab** • **TPC chemo + pembrolizumab** (*gem + carbo; pac; nab-pac*) • **Stratification Factors** • *De novo* vs recurrent disease • Geographic region • Prior exposure to immunotherapy **Crossover to SG is allowed after BICR-verified disease progression**	R 1:1, N~625 • **Dato-DXd + durvalumab** • **Dato-DXd monotherapy** • **TPC chemo + pembrolizumab** (*gem + carbo; pac; nab-pac*) **Stratification Factors** • Geographic region • Prior PD-(L)1 • *De novo* vs prior DFI 6–12 months vs prior DFI >12 months
Key Endpoints[a]	• Primary: PFS by BICR in ITT population • Secondary: OS, ORR, PROs	• Primary: PFS by BICR • Secondary: OS, PFS (per investigator), ORR, safety, PROs

★ STILL ENROLLING

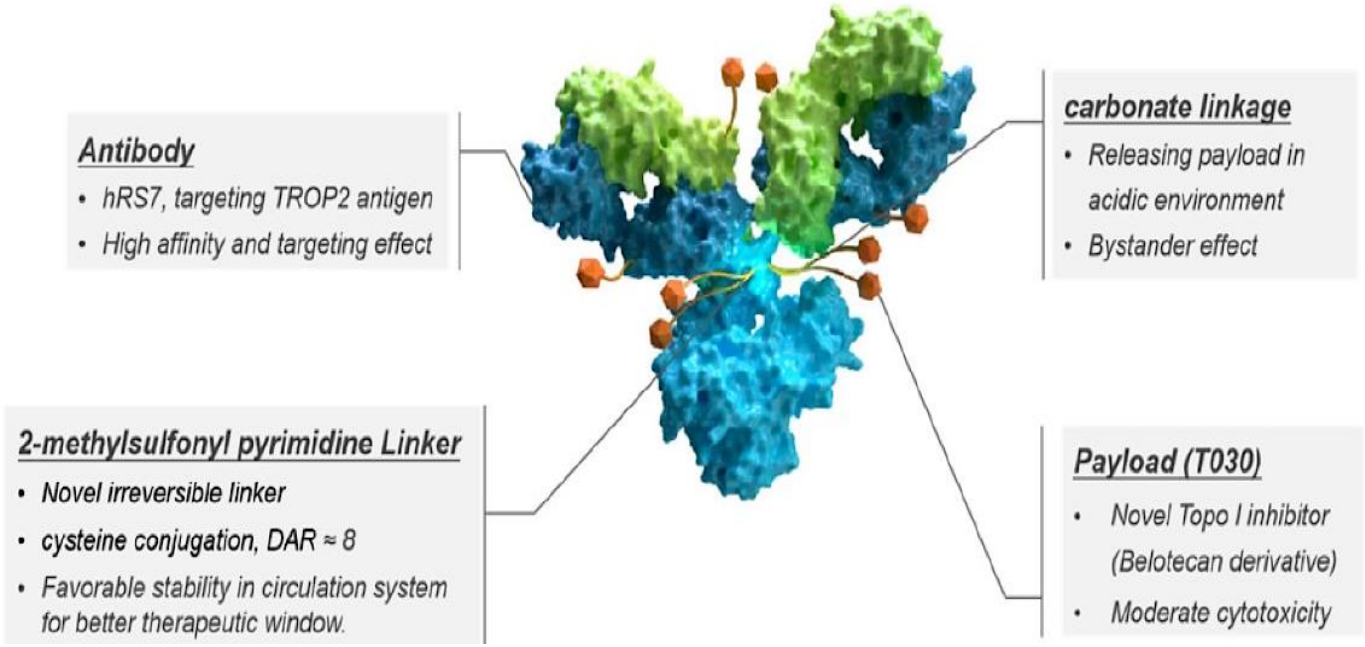
Dana-Farber Cancer Institute

Courtesy of Sara M Tolaney, MD, MPH

Novel ADCs: TROP2 ADC with Topo1 Payload: Sacituzumab Tirumotecan

Sacituzumab Tirumotecan (Sac-TMT)

anti-Trop2 ADC



	OptiTROP-Breast 01
	Sac-TMT vs TPC (2L+) in mTNBC
PFS	6.7 vs 2.5 mo (HR 0.32)
OS	NR vs 9.4 mo (HR 0.53)

Approved in China for TNBC

OptiTROP-Breast05, 1L mTNBC (n=41), mPFS=13.1 mo

Xu B, et al. J Clin Oncol. 2024;42(Suppl_16): Abstract 104.
Yin Y et al, J Clin Oncol 2025; 43 (Suppl_16): Abstract 1019

Courtesy of Sara M Tolaney, MD, MPH

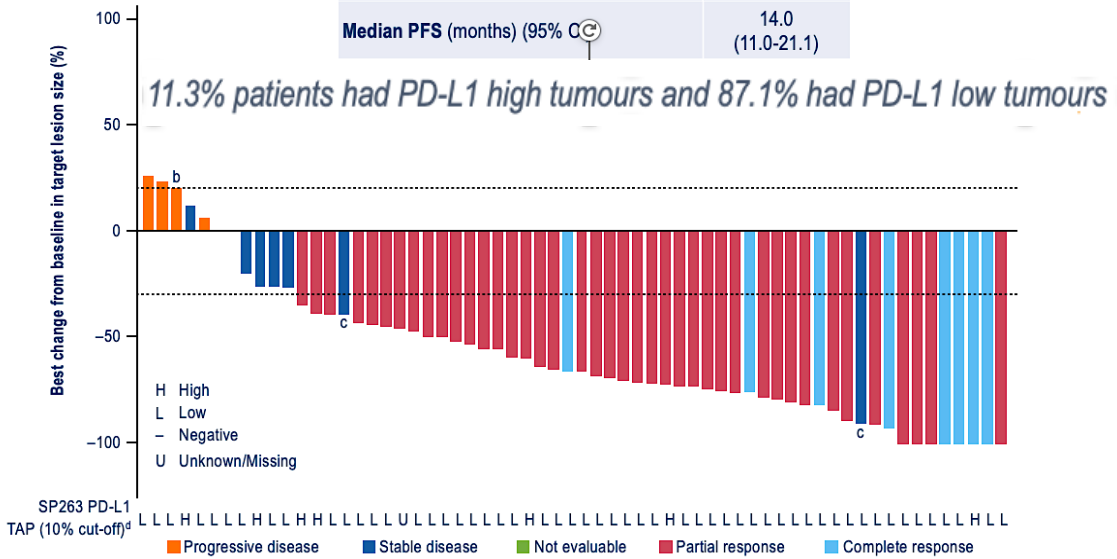
Could an ADC Allow Checkpoint Inhibition to Have Benefit in Metastatic TNBC that is PD-L1-negative?

SAN ANTONIO BREAST CANCER SYMPOSIUM®

UT Health San Antonio Mays Cancer Center | AACR American Association for Cancer Research

BEGONIA: Dato-DXd+ durvalumab

	Arm 7 (N=62)
Confirmed ORR, % (95% CI)	49 (79.0) (66.8–88.3)
Median PFS (months) (95% CI)	14.0 (11.0-21.1)



Responses were observed in patients with PD-L1 high and PD-L1 low tumours

Schmid P et al, ESMO 2025

DIAMOND (Ph 2): Dato-DXd +/- durvalumab in PD-L1- mTNBC

- Previously untreated, locally advanced inoperable or metastatic TNBC
- PD-L1- (CPS <10)
- No prior neoadj/adj IO within 6 mo

Stratification Factors:
De novo OR DFI≤12 mo OR DFI>12 mo

→ Dato-DXd

1:1

N=140

→ Dato-DXd + durvalumab

NCT06954480
PI:Peter Schmid

Dana-Farber Cancer Institute

Courtesy of Sara M Tolaney, MD, MPH

Could an ADC Allow Checkpoint Inhibition to Have Benefit in Metastatic TNBC that is PD-L1-negative?

SAN ANTONIO BREAST CANCER SYMPOSIUM®

UT Health San Antonio Mays Cancer Center | AACR American Association for Cancer Research

SACI IO TNBC (Ph 2):
SG +/- pembro in PD-L1- 1L mTNBC

mTNBC:
No Prior Chemo
No Prior PD-1/L1

PD-L1 <1% by SP-142
ER ≤ 5%
PR ≤ 5%
HER2-

Exclude prior: PD-1/L1, SG, Irinotecan

R
1:1

N=110 pts

sacituzumab govitecan
10mg/kg IV d1,8 q21 days
+
pembrolizumab
200mg/kg Q3wks

sacituzumab govitecan
10mg/kg d1,8 q21 days

NCT04468061 PI: Ana Garrido-Castro

TroFuse-011 (Ph 3):
Sac-TMT+/- pembro vs TPC in PD-L1- 1L mTNBC

Previously untreated, locally recurrent unresectable, or **metastatic TNBC**

- PD-L1− (CPS <10*)
- ≥6 months since treatment in the curative setting

N≈1000

R

Sac-TMT
4 mg/kg IV Q2W

Sac-TMT + pembrolizumab
Sac-TMT: 4 mg/kg IV Q2W
Pembrolizumab: 400 mg IV Q6W (max. 18 administrations)

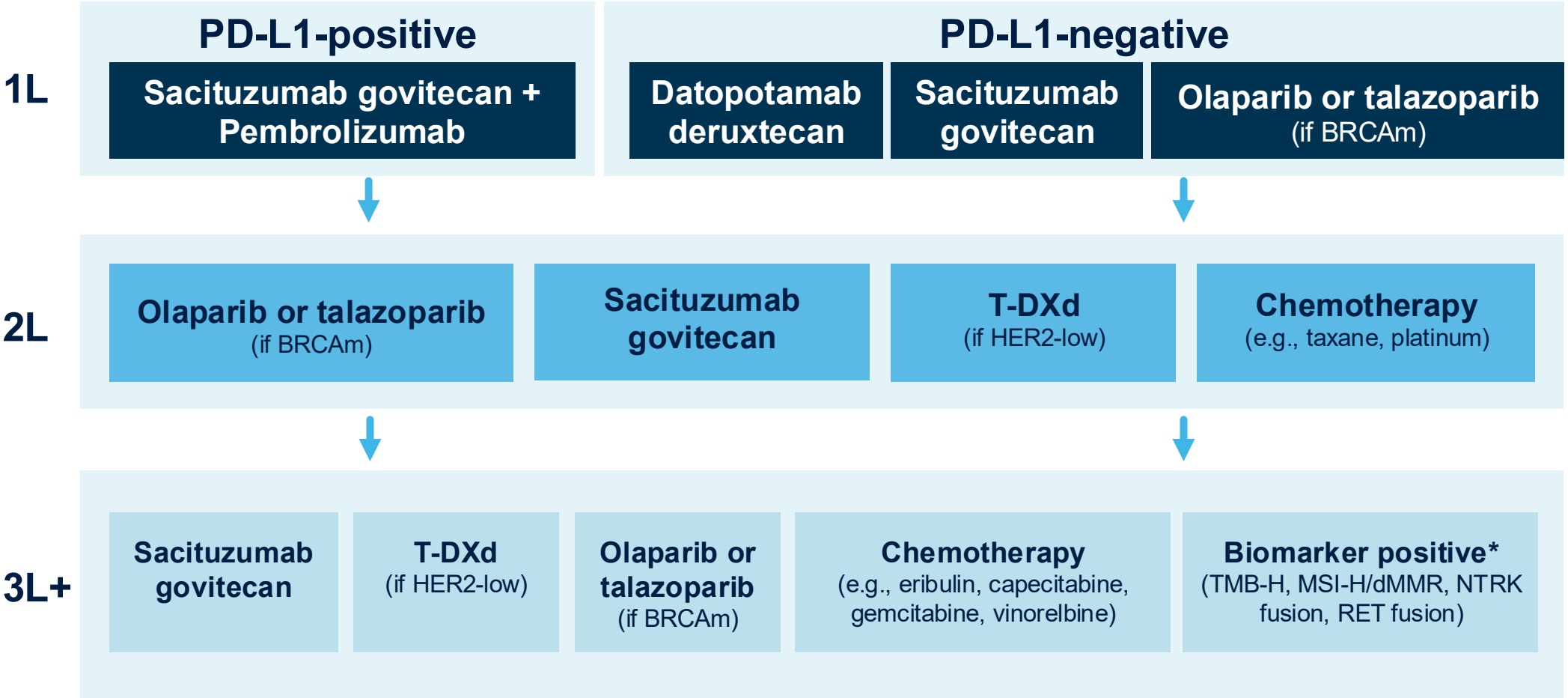
TPC
(gemcitabine and carboplatin, paclitaxel, or nab-paclitaxel)

NCT06841354

Dana-Farber Cancer Institute

Courtesy of Sara M Tolaney, MD, MPH

New Potential Treatment Algorithm for mTNBC



*TMB-H: Pembrolizumab; MSI-H: Pembrolizumab, Dostarlimab; NTRK fusion: Larotrectinib, Entrectinib, Repotrectinib; RET fusion: Selpercatinib. Slide courtesy of Ana Garrido-Castro

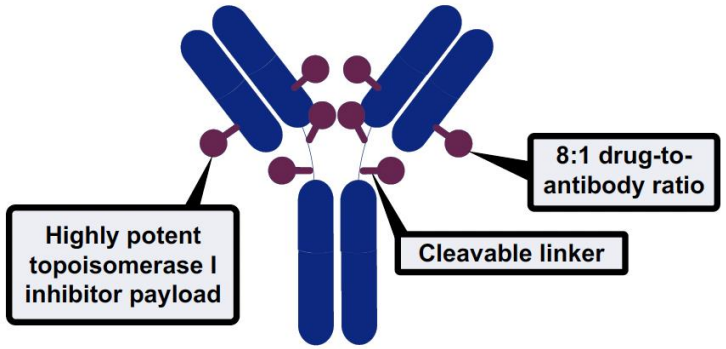
Courtesy of Sara M Tolaney, MD, MPH

Questions?

RTP Year in Review 2026

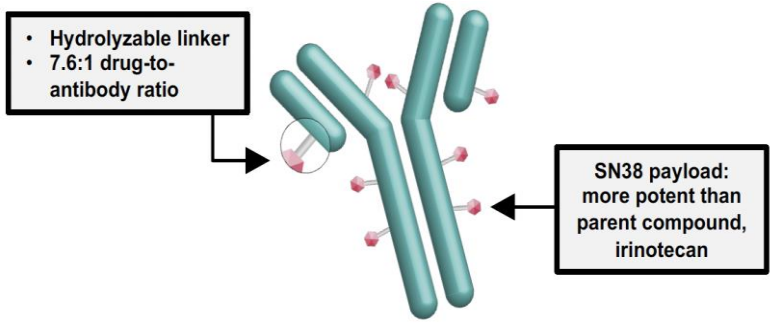
Available ADCs for HR+/HER2- MBC in 2026

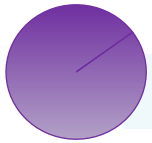
Trastuzumab deruxtecan (T-DXd)
anti-HER2 ADC



~90% (HER2-low, *-ultralow*)

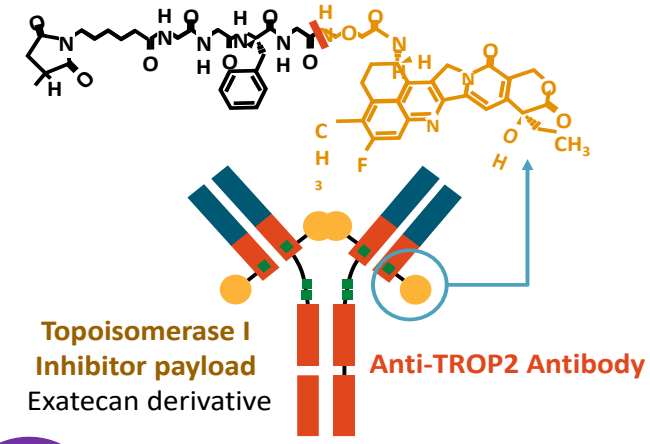
Sacituzumab Govitecan (SG)
anti-Trop2 ADC





~100% (no biomarker)

Datopotamab Deruxtecan (Dato-DXd)
anti-Trop2 ADC



~100% (no biomarker)

Courtesy of Sara M Tolaney, MD, MPH

TROPICS-02

SG demonstrated a statistically significant and clinically meaningful improvement in both PFS and OS vs chemotherapy in 3L and later HR+/HER2-negative mBC[1,2]

NCT03901339[1,3]

Metastatic or locally recurrent inoperable HR+/HER2-negative breast cancer that progressed after*

- **At least 1 endocrine therapy, taxane, and CDK4/6 inhibitor in any setting**
- **At least 2, but no more than 4, lines of chemotherapy for metastatic disease**
- Measurable disease by RECIST 1.1

Treatment was continued until progression or unacceptable toxicity

R 1:1

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

TPC†
(capecitabine, vinorelbine, gemcitabine, or eribulin)
n=271

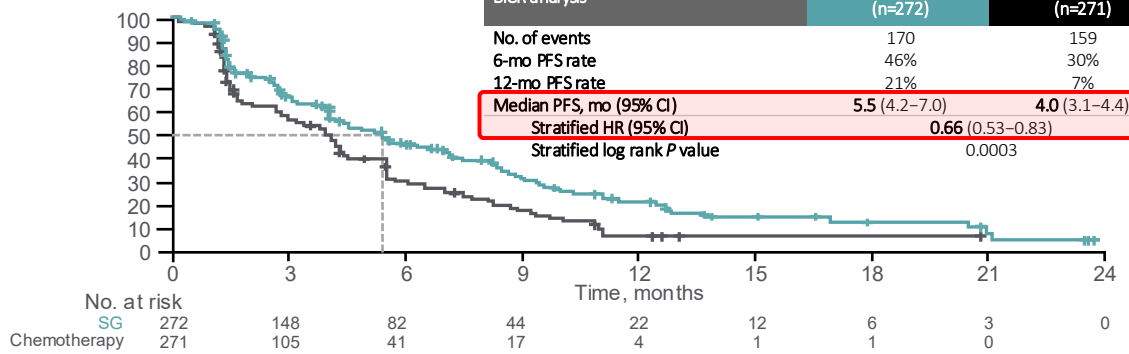
Continue treatment until progression or unacceptable toxicity

Primary endpoint:
- PFS by BICR

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

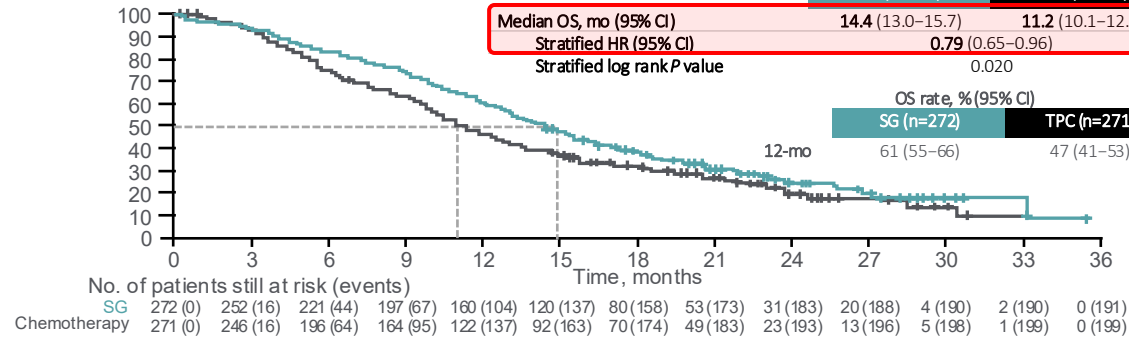
Stratification factors
- Visceral metastases (yes/no)
- Endocrine therapy in metastatic setting ≥6 months (yes/no)
- Prior lines of chemotherapies (2 vs 3/4)

PFS[1*,†]



BICR analysis	SG (n=272)	Chemotherapy (n=271)
No. of events	170	159
6-mo PFS rate	46%	30%
12-mo PFS rate	21%	7%
Median PFS, mo (95% CI)	**5.5** (4.2–7.0)	**4.0** (3.1–4.4)
Stratified HR (95% CI)	**0.66** (0.53–0.83)	
Stratified log rank *P* value	0.0003	

OS[2*,†]



	SG (n=272)	TPC (n=271)
Median OS, mo (95% CI)	**14.4** (13.0–15.7)	**11.2** (10.1–12.7)
Stratified HR (95% CI)	**0.79** (0.65–0.96)	
Stratified log rank *P* value	0.020	

OS rate, % (95% CI)

	SG (n=272)	TPC (n=271)
12-mo	61 (55–66)	47 (41–53)

Courtesy of Sara M Tolaney, MD, MPH

*Disease histology based on the ASCO/CAP criteria; †Single-agent standard-of-care treatment of physician's choice was specified prior to randomisation by the investigator.

ASCO/CAP, American Society of Clinical Oncology/College of American Pathologists; BICR, blinded independent central review; CBR, clinical benefit rate; CDK, cyclin-dependent kinase; CI, confidence interval; DOR, duration of response; HER2-negative, human epidermal growth factor receptor 2-negative; HR, hazard ratio; HR+, hormonal receptor-positive; ITT, intent-to-treat; IV, intravenously; LIR, local investigator review; mo, months; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PRO, patient-reported outcome; R, randomised; RECIST, Response Evaluation Criteria in Solid Tumours; SG, sacituzumab govitecan; TPC, treatment of physician's choice.

1. Adapted from Rugo HS, *et al*. *J Clin Oncol*. 2022;40:3365–3376 (inc. Suppl); 2. Adapted from Rugo HS, *et al*. *Lancet* 2023; 402: 1423–1433. 3. ClinicalTrials.gov, NCT03901339: https://www.clinicaltrials.gov/study/NCT03901339. Accessed: July 2025.

TROPiCS-02

SG significantly improved ORR,[1,2] and significantly extended TTD of Global Health Status and fatigue vs TPC[2]*

TTD[2–4,*]	Patients SG/TPC, n/n	SG median TTD, mo (95% CI)	TPC median TTD, mo (95% CI)	Stratified HR (95% CI)	Stratified Log Rank *P* value
Global health status QoL	234/207	4.3 (3.1–5.7)	**3.0 (2.2–3.9)**	0.75 (0.61–0.92)	0.006
Fatigue	234/205	2.2 (1.6–2.8)	**1.4 (1.1–1.9)**	0.73 (0.60–0.89)	0.002
Pain	236/210	3.8 (N/A)	**3.5 (N/A)**	0.92 (0.75–1.13)	0.42

*HRQoL was formally tested as part of the testing hierarchy in TROPiCS-02.[4]

CI, confidence interval; CR, complete response; HR, hazard ratio; mo, months; N/A, not available; OR, overall response; ORR, objective response rate; PD, progressive disease; PR, partial response; QoL, quality of life; SD, stable disease; SG, sacituzumab govitecan; TPC, treatment of physician's choice; TTD, time to deterioration.

1. Adapted from Rugo HS, et al. *J Clin Oncol*. 2022; 40(29):3365–3376; 2. Rugo HS, *et al. Lancet* 2023; 402: 1423–1433; 3. Rugo HS, *et al. Lancet* 2023; 402: 1423–1433 (Suppl); 4. Rugo HS, et al. *Oncologist*. 2024; 29: 768–779.

Courtesy of Sara M Tolaney, MD, MPH

TROPiCS-02

SG had a manageable safety profile that was consistent with previous studies[1]

Selected TRAEs*[2,3]		SG (n=268)		TPC (n=249)	
		All Grade, %	Grade ≥3, %	All Grade, %	Grade ≥3, %
Hematologic	Neutropenia†	71	52	55	39
	Anaemia‡	37	7	28	3
	Thrombocytopenia§	6	<1	16	4
Gastrointestinal	Diarrhea	62	10	23	1
	Nausea	59	1	35	3
	Vomiting	24	1	16	2
Other	Alopecia	48	0	18	0
	Fatigue	39	6	33	4

Neutropenia and diarrhoea were the most common treatment-related AEs

TEAEs associated with/leading to:[1,3]

n(%)	Sacituzumab govitecan (n=268)	TPC (n=249)
Treatment discontinuation	17 (6)	11 (4)
Dose reductions	90 (34)	82 (33)
Treatment-related leading to death**	1 (<1)	0

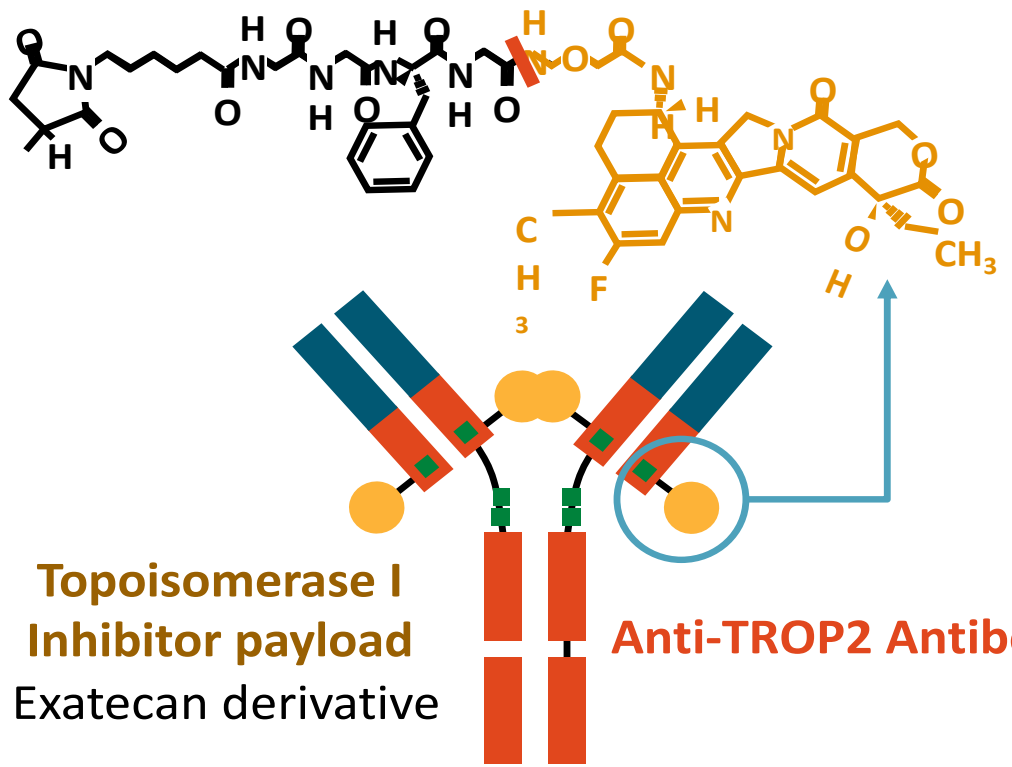
ILD events[4]	**SG: no events** **TPC: 1%**

Assessed in the safety population of patients who received ≥1 dose of study treatment.[1] *Patients may report more than one event per preferred term. AEs were coded using Medical Dictionary for Regulatory Activities v25.0, and AE severity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events v 5.0. †Combined preferred terms of neutropenia and neutrophil count decreased. ‡Combined preferred terms of anaemia, hemoglobin decreased, and red blood cell count decreased. §Combined preferred terms of "thrombocytopenia" and "platelet count decreased";[2] **Of 6 TEAEs leading to death, only 1 was considered by the investigator as treatment-related (septic shock due to neutropenic colitis). The other 5 were: COVID-19 pneumonia, pulmonary embolism, pneumonia, nervous system disorder, and arrhythmia. Upon detailed review of the TEAEs leading to death, there were no patterns identified.[3]
AE, adverse event; ILD, interstitial lung disease; LVD, left ventricular dysfunction; TPC, treatment of physician's choice; TRAE, treatment-related adverse event; TEAE, treatment-emergent adverse event.

1. Adapted from Rugo HS, *et al. Lancet* 2023; 402: 1423–1433. 2. Rugo HS, *et al. Lancet* 2023; 402: 1423–1433 (Suppl); 3. Tolaney S, et al. ASCO 2023. Abstract #1003. 4. Rugo HS, et al. *J Clin Oncol*. 2022;40:3365–3376.

Courtesy of Sara M Tolaney, MD, MPH

Dato-DXd vs T-DXd



- **Targets Trop2 like SG**
- **Same payload-linker as T-DXd**
- **Same schedule as T-DXd (Q3W)**
- **Lower DAR as other ADCs**

  DAR 4, vs 8 for SG and T-DXd
- **Same half-life as T-DXd**

  5 days, vs 1 day for SG

Courtesy of Sara M Tolaney, MD, MPH

TROPION-Breast01

Dato-DXd demonstrated significant PFS benefit, but did not show a significant difference in OS vs ICC[1,2]

NCT02574455[2]

Key inclusion criteria:

- Patients with HR+/HER2-negative breast cancer* (HER2-negative defined as IHC 0/1+/2+; ISH 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

R 1:1

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)

Dual primary endpoints:

- PFS by BICR per RECIST v1.1, and OS

Key secondary endpoints:

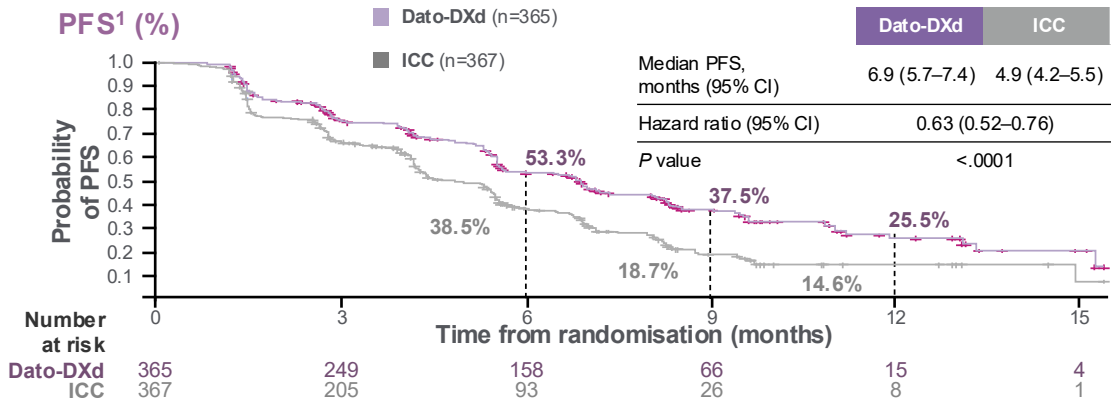
- ORR, PFS (investigator assessed), TFST,[2] Safety,[2] PROs[2]

Exploratory PRO endpoints[2]

Stratification factors

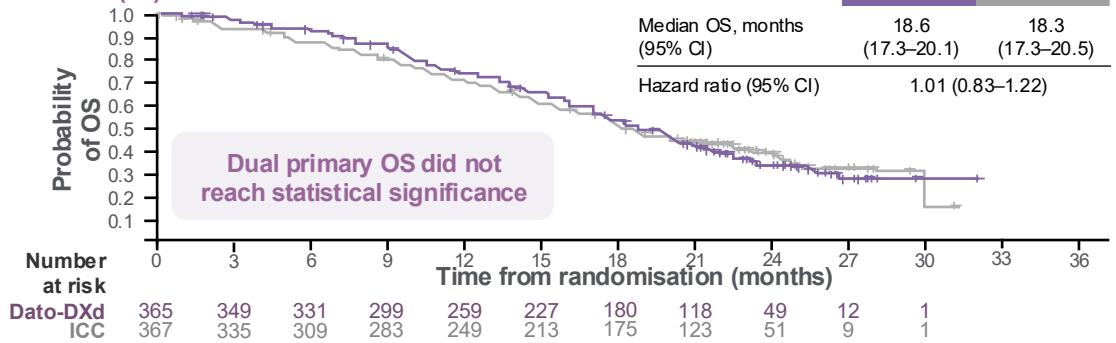
- Lines of chemotherapy (1 vs 2)
- Geographic location (USA/Canada/Europe vs other geographic regions)
- Previous CDK4/6 inhibitor (yes vs no)

PFS[1] (%)



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

OS[2] (%)



	Dato-DXd	ICC
Median OS, months (95% CI)	18.6 (17.3–20.1)	18.3 (17.3–20.5)
Hazard ratio (95% CI)	1.01 (0.83–1.22)	

*Per American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines;[2] †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.[2]

BICR, blinded independent central review; CDK4/6, cyclin-dependent kinase 4/6; CI, confidence interval; D, day; Dato-DXd, datopotamab deruxtecan; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; ICC, investigator's choice of chemotherapy; IHC, immunohistochemistry; ISH, in situ hybridisation; IV, intravenous; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PRO, patient-reported outcome; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumours; TFST, time to first subsequent therapy.

1. Bardia A, et al. *J Clin Oncol.* 2025;43:285–296; 2. Pistilli B, *et al.* Oral presentation. ESMO On Air Webinar series. 12 February 2025.

Courtesy of Sara M Tolaney, MD, MPH

ASCENT-07: Phase 3, Randomized, Open-Label Study

Locally advanced unresectable or metastatic HR+/HER2− BC:

- **No prior chemotherapy** for locally advanced or metastatic HR+/HER2− BC
- Measurable disease per RECIST v1.1
- Must have at least 1 of the following:
  - Progression on ≥ 2 previous lines of ET ± targeted therapy for mBC[a]
  - Progression < 6 mo of starting 1L ET ± CDK4/6i for mBC
  - Recurrence < 24 mo of starting adjuvant ET + CDK4/6i and no longer a candidate for additional ET for mBC

N = 690

R 2:1

Sacituzumab govitecan 10 mg/kg IV Days 1 and 8, every 21 days n = 456

Treatment of physician's choice (capecitabine, paclitaxel, nab-paclitaxel)[b] n = 234

Treatment continued until disease progression[c] or unacceptable toxicity

Stratification factors:

- Duration of prior CDK4/6i[d] for mBC (none vs ≤ 12 mo vs > 12 mo)
- HER2 IHC (HER2 IHC 0 vs HER2 IHC-low [IHC 1+ or IHC 2+/ISH–])
- Geographic region (US/Canada/UK/EU vs ROW)

End points

Primary

- PFS by BICR

Key Secondary

- OS
- ORR by BICR
- QOL

Other Secondary

- PFS by INV
- ORR by INV
- DOR by BICR and INV
- Safety

Courtesy of Sara M Tolaney, MD, MPH

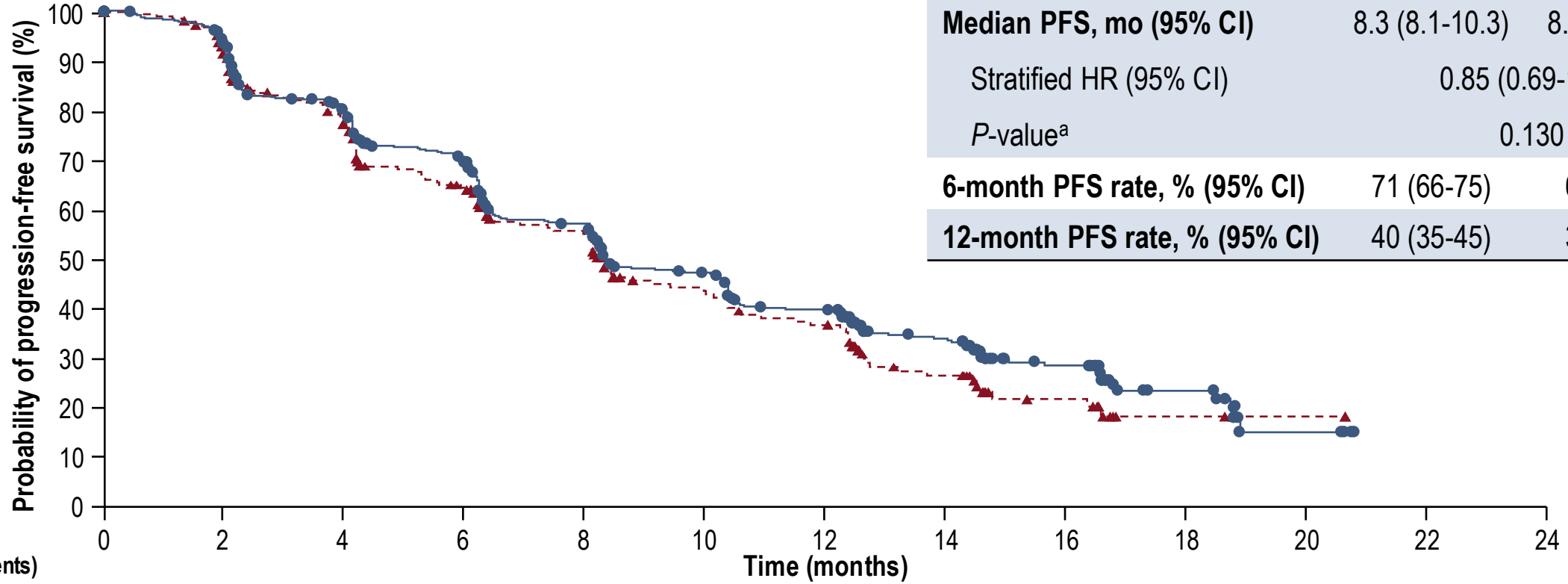
ClinicalTrials.gov identifier: NCT05840211.

[a]Disease recurrence while on the first 24 months of starting adjuvant ET will be considered a line of therapy; these participants will only require 1 line of ET in the metastatic setting. [b]Paclitaxel 80 mg/m^2 or nab-paclitaxel 100 mg/m^2 IV on days 1, 8, and 15 of 28-day cycles, or capecitabine oral 1000 or 1250 mg/m^2 twice daily for first 2 weeks of 21-day cycles. [c]Per RECIST v1.1. [d]Enrollment of CDK4/6i-naïve participants was capped at 10%.

1L, first-line; **BICR**, blinded independent central review; **CDK4/6i**, cyclin-dependent kinase 4/6 inhibitor; **DOR**, duration of response; **ET**, endocrine therapy; **EU**, European Union; **HER2−**, human epidermal growth factor receptor 2 negative; **HR+**, hormone receptor positive; **IHC**, immunohistochemistry; **INV**, investigator assessment; **ISH**, in situ hybridization; **IV**, intravenously; **mBC**, metastatic breast cancer; **mo**, months; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **QOL**, quality of life; **R**, randomized; **RECIST v1.1**, Response Evaluation Criteria in Solid Tumors, version 1.1; **ROW**, rest of the world.

Primary End Point: Progression-Free Survival by BICR

	SG (n = 456)	TPC (n = 234)
Median PFS, mo (95% CI)	8.3 (8.1-10.3)	8.3 (6.9-10.0)
Stratified HR (95% CI)	0.85 (0.69-1.05)	
P-value[a]	0.130	
6-month PFS rate, % (95% CI)	71 (66-75)	64 (57-71)
12-month PFS rate, % (95% CI)	40 (35-45)	37 (29-44)



No. at risk (events)												
SG	456 (0)	415 (25)	335 (86)	285 (126)	219 (179)	168 (216)	136 (242)	92 (260)	49 (272)	17 (278)	4 (282)	0 (282)
TPC	234 (0)	204 (16)	159 (49)	119 (74)	90 (90)	63 (108)	52 (118)	30 (131)	14 (135)	5 (137)	2 (137)	0 (137)

With a hazard ratio of 0.85, PFS by BICR did not meet statistical significance

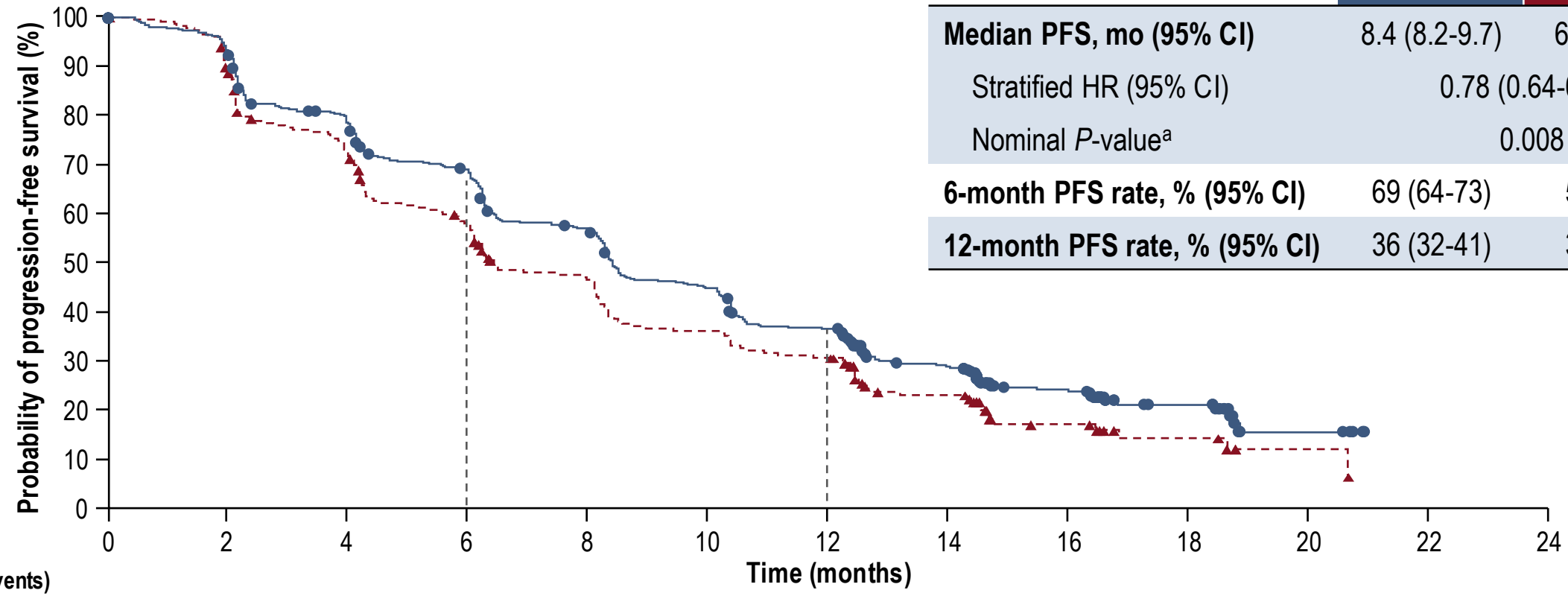
[a]Two-sided *P*-value from stratified log-rank test.
BICR, blinded independent central review; **HR**, hazard ratio; **mo**, months; **PFS**, progression-free survival; **SG**, sacituzumab govitecan; **TPC**, treatment of physician's choice.

Courtesy of Sara M Tolaney, MD, MPH

Secondary End Point: Progression-Free Survival Investigator Assessment

by SAN ANTONIO BREAST CANCER SYMPOSIUM® UT Health San Antonio Mays Cancer Center AACR American Association for Cancer Research

	SG (n = 456)	TPC (n = 234)
Median PFS, mo (95% CI)	8.4 (8.2-9.7)	6.4 (6.0-8.1)
Stratified HR (95% CI)	0.78 (0.64-0.93)	
Nominal *P*-value[a]	0.008	
6-month PFS rate, % (95% CI)	69 (64-73)	58 (51-64)
12-month PFS rate, % (95% CI)	36 (32-41)	30 (24-36)



No. at risk (events)

SG	456 (0)	417 (30)	345 (96)	298 (138)	242 (190)	188 (242)	150 (277)	98 (306)	58 (321)	24 (326)	5 (330)	0 (330)
TPC	234 (0)	203 (23)	160 (62)	124 (94)	92 (118)	71 (139)	60 (150)	34 (163)	15 (170)	8 (172)	2 (173)	0 (174)

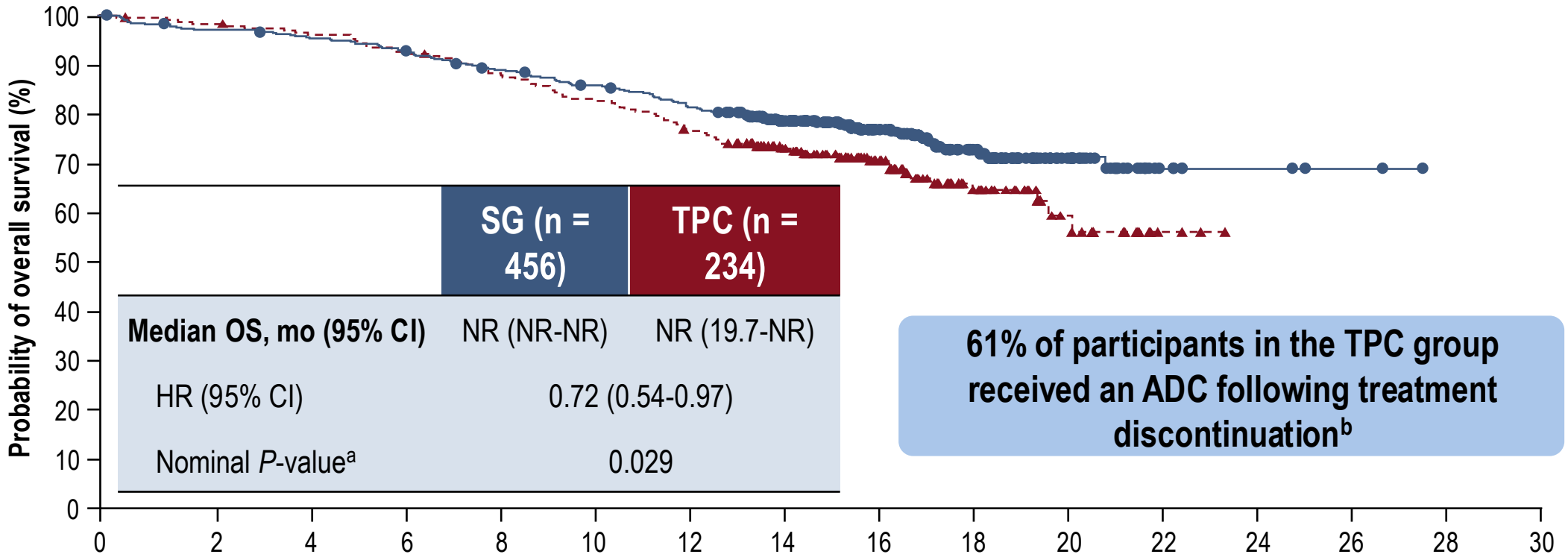
There was a numerical improvement in investigator-assessed PFS with SG versus TPC

[a]Two-sided *P*-value from stratified log-rank test

HR, hazard ratio; **mo**, months; **PFS**, progression-free survival; **SG**, sacituzumab govitecan; **TPC**, treatment of physician's choice.

Courtesy of Sara M Tolaney, MD, MPH

Overall Survival at Primary Analysis (27% maturity)



	SG (n = 456)	TPC (n = 234)
Median OS, mo (95% CI)	NR (NR-NR)	NR (19.7-NR)
HR (95% CI)	0.72 (0.54-0.97)	
Nominal *P*-value[a]	0.029	

61% of participants in the TPC group received an ADC following treatment discontinuation[b]

No. at risk (events)

SG	456 (0)	442 (12)	436 (17)	423 (30)	402 (48)	385 (64)	368 (79)	315 (95)	206 (101)	112 (109)	43 (111)	10 (112)	4 (112)	2 (112)	0 (112)
TPC	234 (0)	229 (4)	225 (7)	217 (15)	205 (26)	192 (39)	181 (50)	145 (61)	95 (65)	51 (71)	19 (74)	4 (75)	0 (75)		

While the OS data were not mature, an early trend was observed favoring SG over TPC

Median follow-up was 15.4 months. [a]The nominal P-value was reported as a descriptive measure of the observed treatment effect and does not support statistical significance. [b]97/160 participants in the TPC group received at least one ADC as subsequent therapy after treatment discontinuation.

ADC, antibody drug conjugate; **HR**, hazard ratio; **mo**, months; **NR**, not reached; **OS**, overall survival; **SG**, sacituzumab govitecan; **TPC**, treatment of physician's choice.

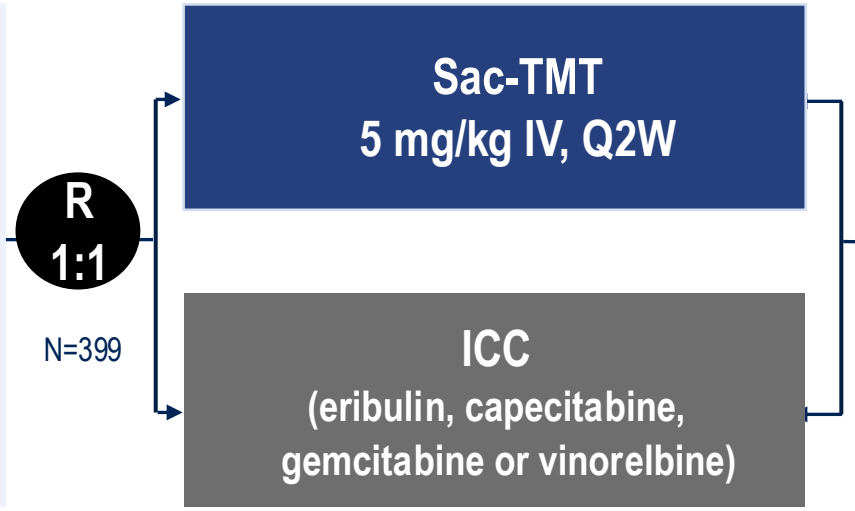
Courtesy of Sara M Tolaney, MD, MPH

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.

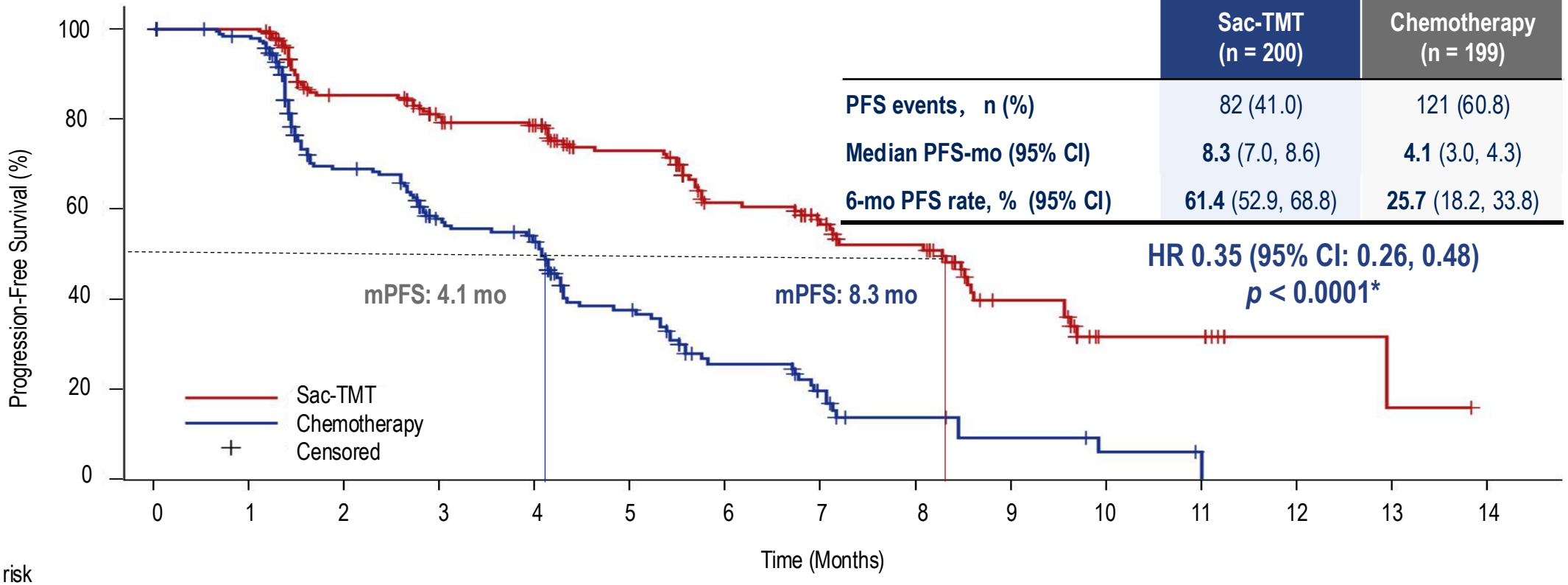
PRESENTED BY : Ying Fan, MD

Courtesy of Sara M Tolaney, MD, MPH

Progression-Free Survival by BICR

Sac-TMT significantly improved PFS over chemotherapy with 65% lower risk of disease progression or death.

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



NO.at risk

Sac-TMT	200	199	146	128	120	97	68	54	44	21	8	8	2	1	0
Chemotherapy	199	198	109	80	70	41	23	14	7	4	2	1	0		

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

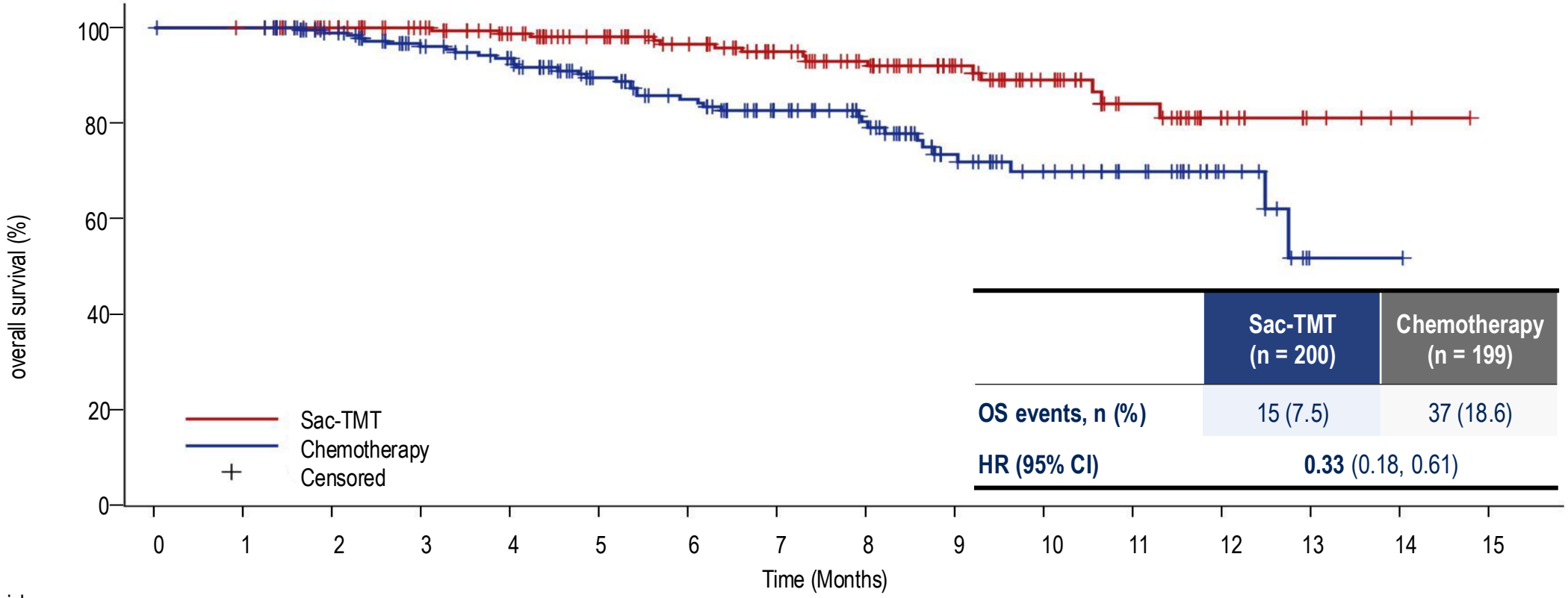
* Pre-specified efficacy boundary (one side alpha level of 0.010 determined by the O'Brien-Fleming alpha spending function).

PRESENTED BY : Ying Fan, MD

Courtesy of Sara M Tolaney, MD, MPH

Overall Survival

Survival benefit trend with sac-TMT has been observed at time of PFS interim analysis. The study is continuing to the pre-specified interim analysis for OS.



	Sac-TMT (n = 200)	Chemotherapy (n = 199)
OS events, n (%)	15 (7.5)	37 (18.6)
HR (95% CI)	**0.33** (0.18, 0.61)	

No.at risk

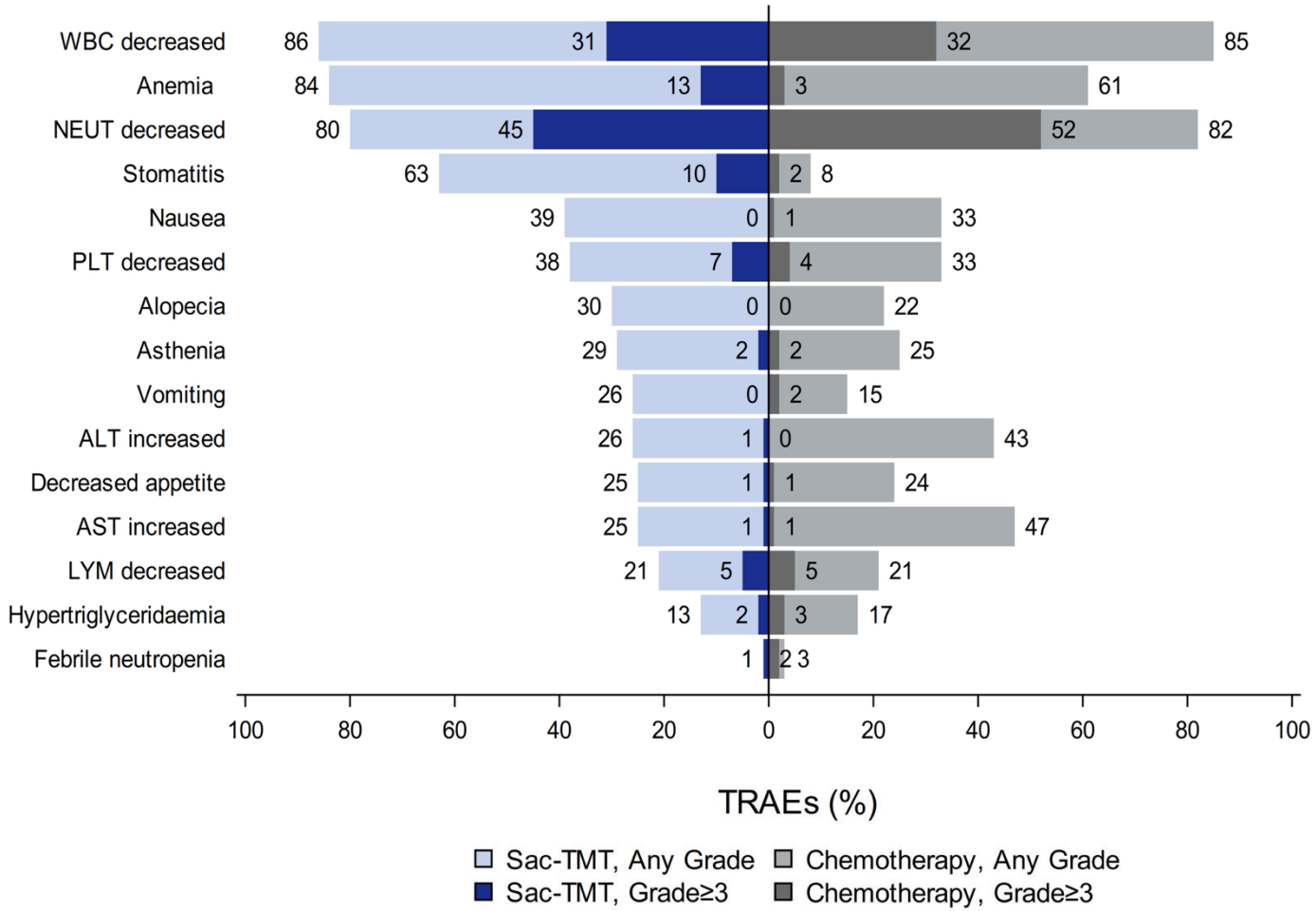
Sac-TMT	200	199	184	170	156	140	123	103	89	65	45	28	12	5	2	0
Chemotherapy	199	198	179	159	148	122	108	86	69	45	33	25	12	1	1	0

CI, confidence interval; HR, hazard ratio; OS, overall survival.

PRESENTED BY : Ying Fan, MD

Courtesy of Sara M Tolaney, MD, MPH

Common TRAEs*



- The most common TRAEs for both sac-TMT and chemotherapy were hematologic toxicities.
- Stomatitis was the common TRAE seen with sac-TMT and predominantly grade 1 or 2 with no case leading to discontinuation.
- Grade ≥ 3 diarrhea occurred in **1.0%** of patients in sac-TMT.
- Pneumonitis occurred in **1.5% and 1.0%** of patients (all grade 1-2) in sac-TMT and chemotherapy, respectively.

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

PRESENTED BY : Ying Fan, MD

Courtesy of Sara M Tolaney, MD, MPH

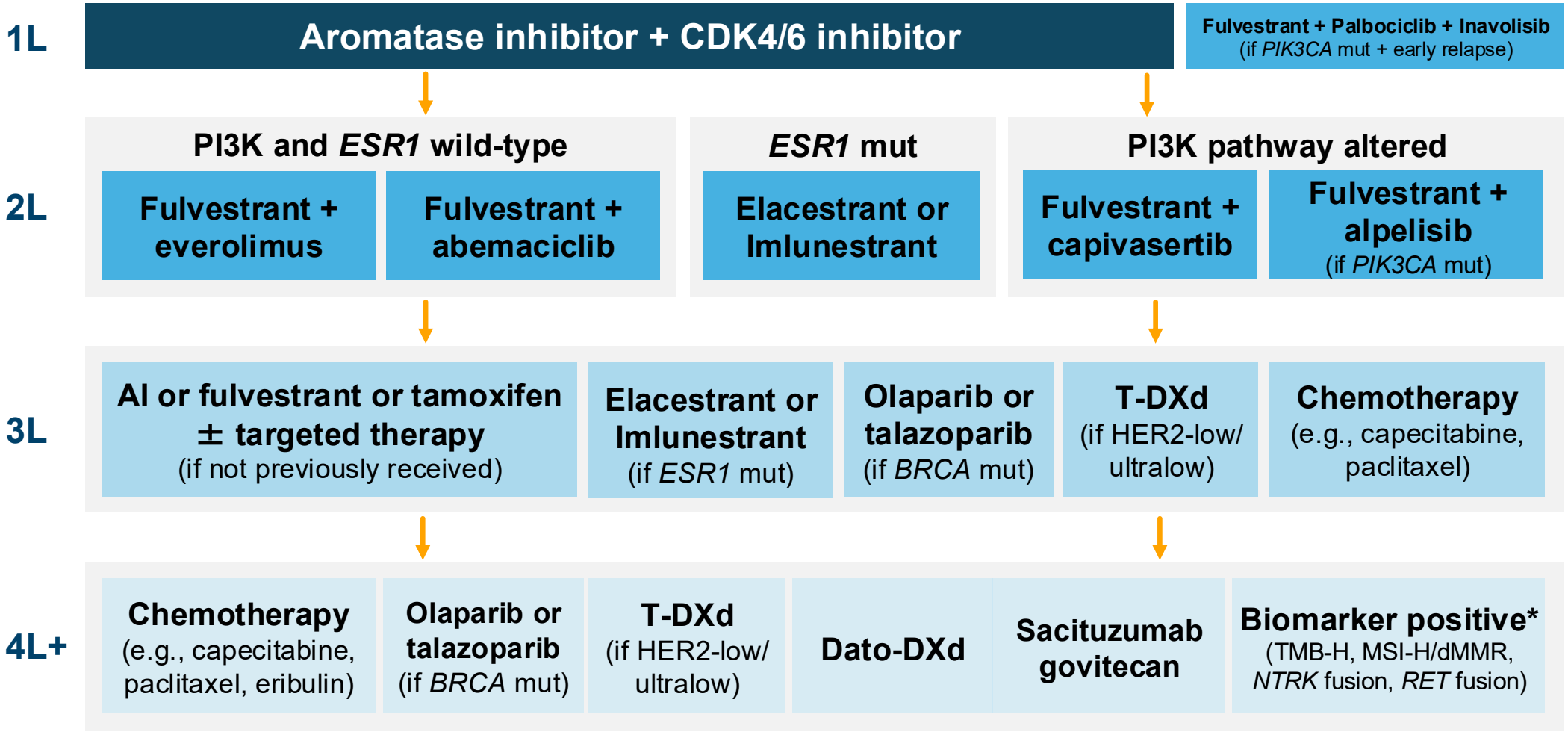
TROP2 ADCs in chemo-pretreated HR+/HER2- MBC: Phase 3 studies

	OptiTROP-Breast 02	ASCENT-07	TROPION-Breast01	TROPiCS-02
ADC Payload (MoA)	Sacituzumab tirumotecan Topo I Inhibitor	Sacituzumab govitecan Topo I inhibitor	Datopotamab deruxtecan Topo I Inhibitor	Sacituzumab govitecan Topo I Inhibitor
ADC-Target	TROP-2	TROP2	TROP-2	TROP-2
N (ADC arm)	200	690	365	272
Prior Chemo	1-4 lines	0	1-2	2-4
Prior CT lines in MBC	2 (1-≥3)	0	1 (1-2)	3 (0-8)
Prior CDK 4/6inh	100%	91%	82%	98%
Primary Objective	PFS by BICR*	PFS by BICR	PFS by BICR & OS	PFS by BICR
ORR	41.5%	37%	36.4%	21%
PFS (HR & 95% CI) Median PFS (mo)	0.35 (0.26-0.48) 8.3 mo	0.85 (0.69-1.05) 8.3 mo	0.63 (0.52-0.76) 6.9 mo	0.66 (0.63-0.83) 5.5 mo
OS (HR & 95% CI) Median OS (mo)	0.33 (0.18-0.61) NR	0.72 (0.54-0.97) NR	1.01 (0.83-1.22) 18.6 mo	0.79 (0.65-0.96) 14.4 mo

Courtesy of Sara M Tolaney, MD, MPH

1. Fan Y, 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 5. Jhaveri K et al, SABCS 2025

Current treatment algorithm for HR+/HER2- metastatic breast cancer



*TMB-H: Pembrolizumab; MSI-H: Pembrolizumab, Dostarlimab; *NTRK* fusion: Larotrectinib, Entrectinib, Repotrectinib; *RET* fusion: Selpercatinib.
Abbreviations: HR, hormone receptor; HER2, human epidermal growth factor receptor 2; AI, aromatase inhibitor; T-DXd, trastuzumab deruxtecan; Dato-DXd, datopotamab deruxtecan; PI3K, phosphatidylinositol 3-kinase; mut, mutant; CT, chemotherapy; TMB-H, tumor mutational burden-high; MSI-H, microsatellite instability-high; dMMR, mismatch repair-deficient

Courtesy of Sara M Tolaney, MD, MPH

Questions?

RTP Year in Review 2026

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Ovarian Cancer

A CME/MOC-Accredited Live Webinar

Thursday, February 19, 2026
5:00 PM – 6:00 PM ET

Faculty

Nicoletta Colombo, MD
Angeles Alvarez Secord, MD, MHSc

Moderator

Neil Love, MD

RTP Year in Review 2026

Thank you for joining us!

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

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

RTP Year in Review 2026