

# **Year in Review: Management of Breast Cancer**

*A CME/MOC-Accredited Live Webinar*

**Tuesday, May 6, 2025  
5:00 PM – 6:00 PM ET**

## **Faculty**

**Ian E Krop, MD, PhD  
Sara M Tolaney, MD, MPH**

## **Moderator**

**Neil Love, MD**

# Faculty



**Ian E Krop, MD, PhD**

Professor of Internal Medicine  
Associate Cancer Center Director for Clinical Research  
Yale Cancer Center  
New Haven, Connecticut



**MODERATOR**

**Neil Love, MD**

Research To Practice  
Miami, Florida



**Sara M Tolaney, MD, MPH**

Chief, Division of Breast Oncology  
Dana-Farber Cancer Institute  
Associate Professor of Medicine  
Harvard Medical School  
Boston, Massachusetts

## Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Genentech, a member of the Roche Group, Lilly, Novartis, and Puma Biotechnology Inc.

## Dr Love — Disclosures

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# 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 Krop — Disclosures

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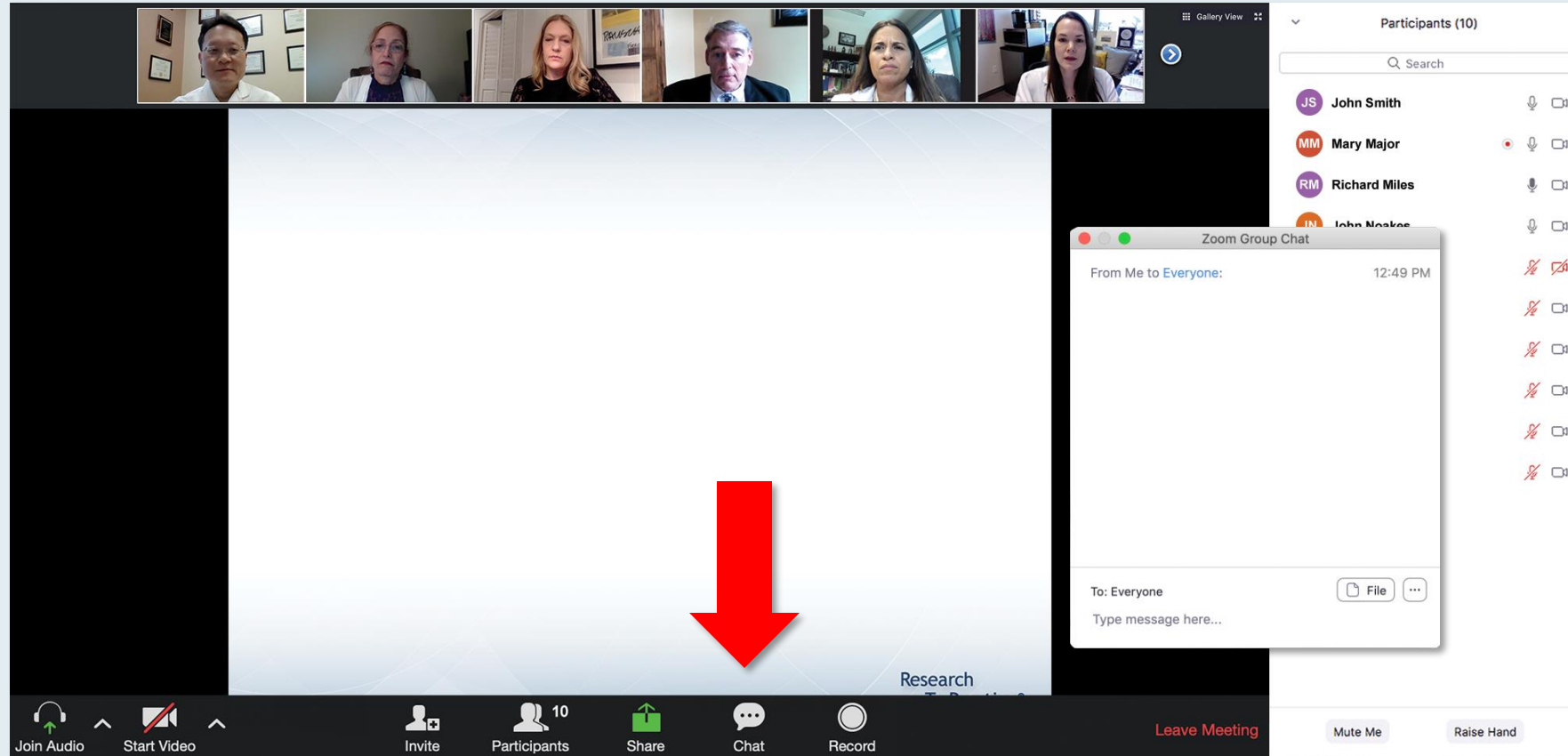
# Dr Tolaney — Disclosures

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**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.

# Familiarizing Yourself with the Zoom Interface

## Expand chat submission box

The screenshot shows a Zoom meeting interface. At the top, there's a header bar with participant names: RTP Coordinat..., Kirsten Miller, RTP Mike Rivera, and Lisa Suarez. Below this is a slide titled "Meet The Professor Program Participating Faculty" featuring six faculty members with their photos and titles. To the right is a chat window. The chat window has a header "Chat" and a dropdown menu set to "Me to Panelists". It contains two messages from "Me to Panelists" dated 4:31 PM, each with a welcome message and a link to a PDF. Below these is another message from "Me to Panelists and Attendees" dated 4:32 PM, also with a welcome message and a link. At the bottom of the chat window is a submission box with a dropdown menu set to "Panelists and Attendees" and a text input field labeled "Type message here...". A red arrow points to the white line above the submission box, indicating where to drag to expand the box.

**Meet The Professor Program Participating Faculty**

**Nancy L Bartlett, MD**  
Professor of Medicine  
Koman Chair in Medical Oncology  
Washington University School of Medicine  
St Louis, Missouri

**Jonathan W Friedberg, MD, MMSc**  
Samuel E Durand Professor of Medicine  
Director, James P Wilmot Cancer Institute  
University of Rochester  
Rochester, New York

**Carla Casulo, MD**  
Associate Professor of Medicine  
Division of Hematology/Oncology  
Director, Hematology/Oncology Fellowship Program  
University of Rochester  
Wilmot Cancer Institute  
Rochester, New York

**Brian T Hill, MD, PhD**  
Director, Lymphoid Malignancy Program  
Cleveland Clinic Taussig Cancer Institute  
Cleveland, Ohio

**Christopher R Flowers, MD, MS**  
Chair, Professor  
Department of Lymphoma/Myeloma  
The University of Texas MD Anderson Cancer Center  
Houston, Texas

**Brad S Kahl, MD**  
Professor of Medicine  
Washington University School of Medicine  
Director, Lymphoma Program  
Siteman Cancer Center  
St Louis, Missouri

**Chat**

Me to **Panelists** 4:31 PM

Welcome and thank you for attending! To access the slides from today's session please use the link below.  
[http://images.researchtopractice.com/2021/Meetings/Slides/MTP\\_ToGo\\_CLL\\_2021\\_April1.pdf](http://images.researchtopractice.com/2021/Meetings/Slides/MTP_ToGo_CLL_2021_April1.pdf)

Me to **Panelists and Attendees** 4:32 PM

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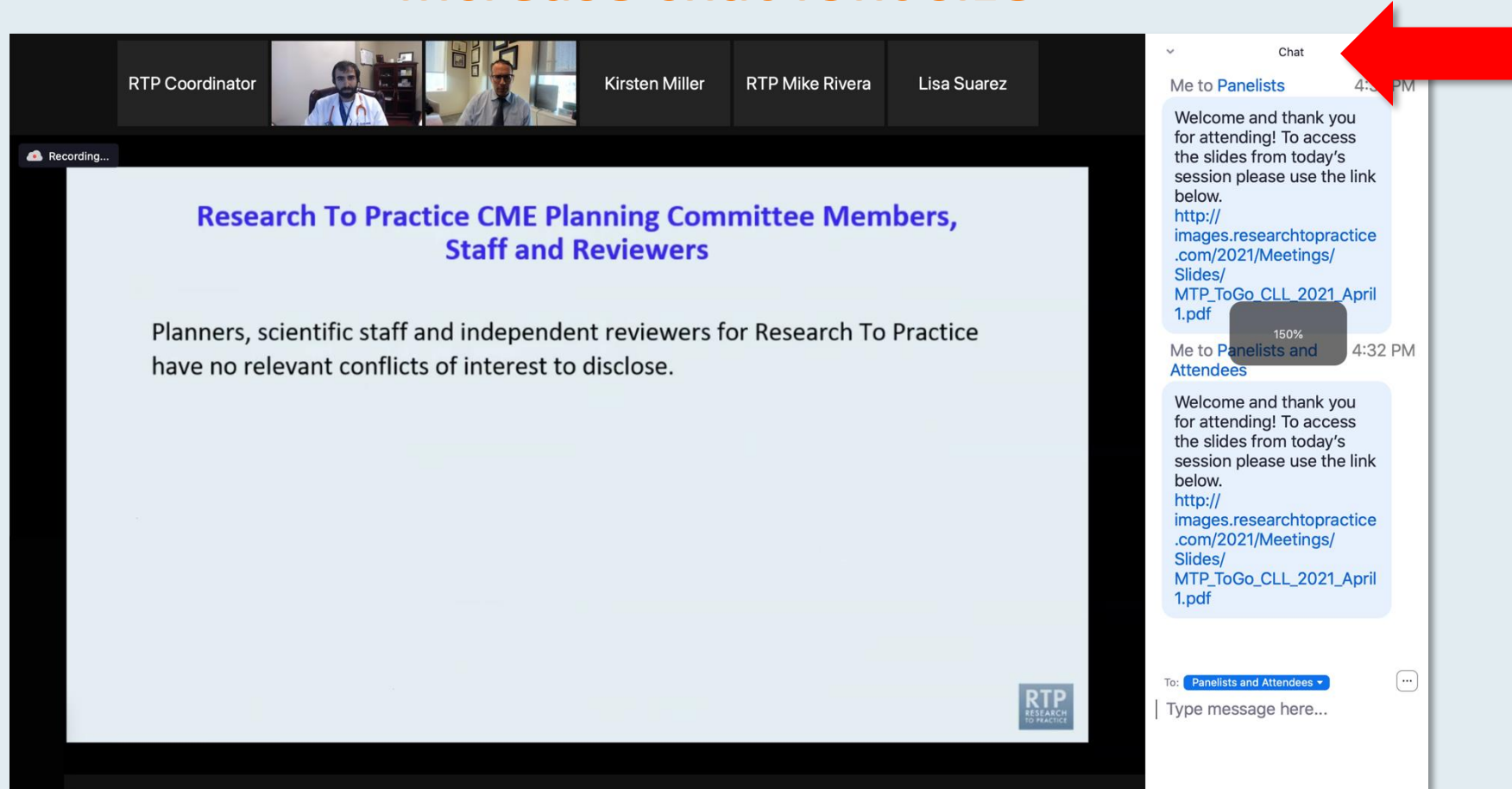
To: **Panelists and Attendees**

Type message here...

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

# Familiarizing Yourself with the Zoom Interface

Increase chat font size



The screenshot displays a Zoom meeting interface. At the top, a gallery view shows participants: RTP Coordinator, Kirsten Miller, RTP Mike Rivera, and Lisa Suarez. The main area shows a presentation slide titled "Research To Practice CME Planning Committee Members, Staff and Reviewers" with the text: "Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose." The bottom right corner of the slide features the RTP Research To Practice logo. On the right side, the chat window is open, showing a message from "Me to Panelists" with a link to a PDF. A red arrow points to the font size icon (a square with "150%") in the chat window's header area.

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

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

The screenshot shows a Zoom meeting interface. At the top, a gallery view displays seven participants. The main content area features a presentation slide with the following text:

**Meet The Professor**  
**Optimizing the Selection and Sequencing of Therapy for Patients with Metastatic Gastrointestinal Cancer**  
**Wednesday, August 25, 2022**  
**5:00 PM – 6:00 PM EST**  
**Faculty**  
**Wells A Messersmith, MD**  
**Moderator**  
**Neil Love, MD**

A "Quick Survey" pop-up is displayed over the slide, listing treatment options with radio buttons for selection:

- ☐ Ceritinib +/- dexamethasone
- ☐ Pomalidomide +/- dexamethasone
- ☐ Ceritinib + pomalidomide +/- dexamethasone
- ☐ Elotuzumab + lenalidomide +/- dexamethasone
- ☐ Elotuzumab + pomalidomide +/- dexamethasone
- ☐ Daratumumab + lenalidomide +/- dexamethasone
- ☐ Daratumumab + pomalidomide +/- dexamethasone
- ☐ Daratumumab + bortezomib +/- dexamethasone
- ☐ Isaxozim + Rd
- ☐ Other

The "Participants (10)" list on the right includes: John Smith, Mary Major, Richard Miles, John Noakes, Alice Suarez, Jane Perez, Robert Stiles, Juan Fernandez, Ashok Kumar, and Jeremy Smith. The bottom toolbar contains icons for Join Audio, Start Video, Invite, Participants, Share, Chat, Record, and a "Leave Meeting" button.

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**Regulatory and reimbursement issues aside, what would you recommend for a 65-year-old patient with clear cell renal cell carcinoma (ccRCC) if follow-up 3 years later is found to have asymptomatic (PS 0)?**

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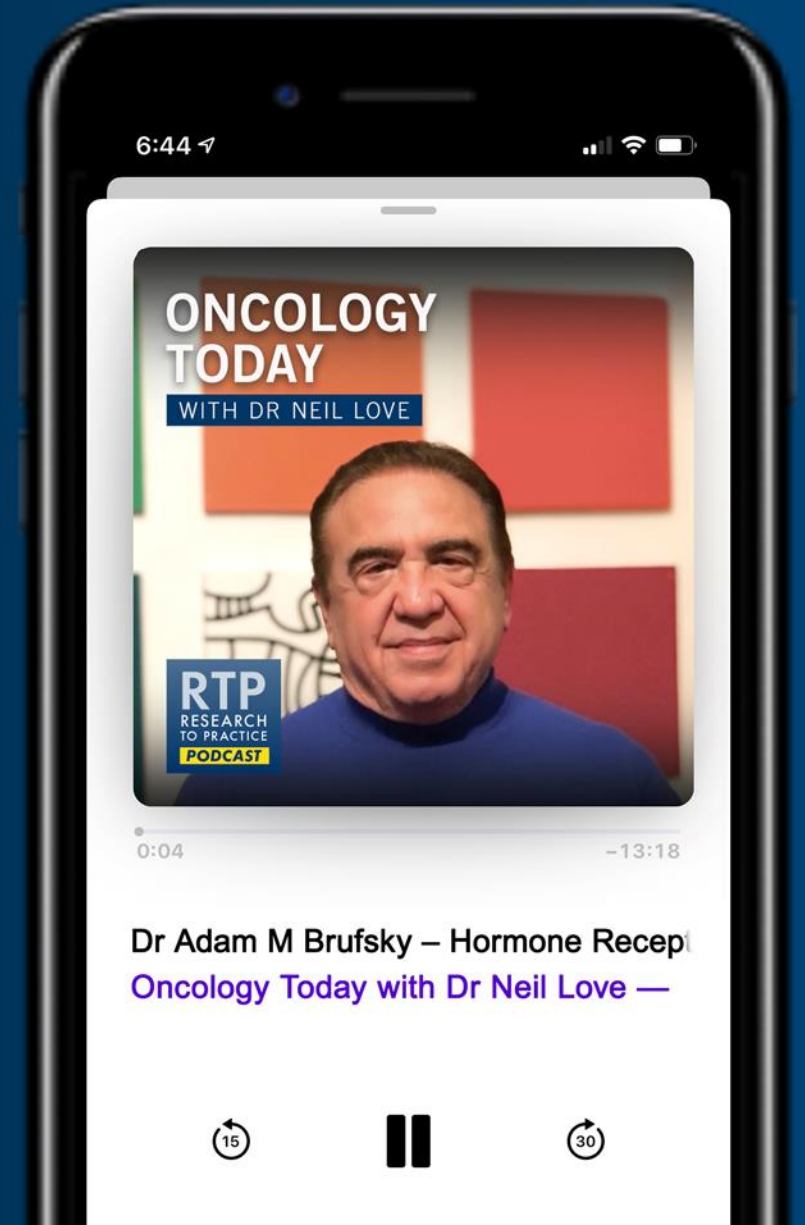
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WITH DR NEIL LOVE

**Hormone Receptor-Positive Metastatic Breast Cancer — An Interview with Dr Adam M Brufsky on the Impact of Biomarkers and Existing Comorbidities on the Selection of First-Line Therapy**



DR ADAM M BRUFSKY  
UNIVERSITY OF PITTSBURGH



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

## **Management of Multiple Myeloma**

*A CME/MOC-Accredited Live Webinar*

**Thursday, May 8, 2025**

**5:00 PM – 6:00 PM ET**

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**Meletios-Athanasios (Thanos) C Dimopoulos, MD**

**Robert Z Orlowski, MD, PhD**

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**Jessica J Lin, MD**

**Joel W Neal, MD, PhD**

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# Practical Perspectives: Experts Review Actual Cases of Patients with Advanced Gastroesophageal Cancers

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# AGENDA

## Year in Review: Management of Breast Cancer

**INTRODUCTION:** Adjuvant CDK4/6 Inhibition

**MODULE 1:** HER2-Positive Disease

**MODULE 2:** PARP Inhibition

**MODULE 3:** Antibody-Drug Conjugates

**MODULE 4:** Up-Front Treatment of HR-Positive Metastatic Disease

***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.***

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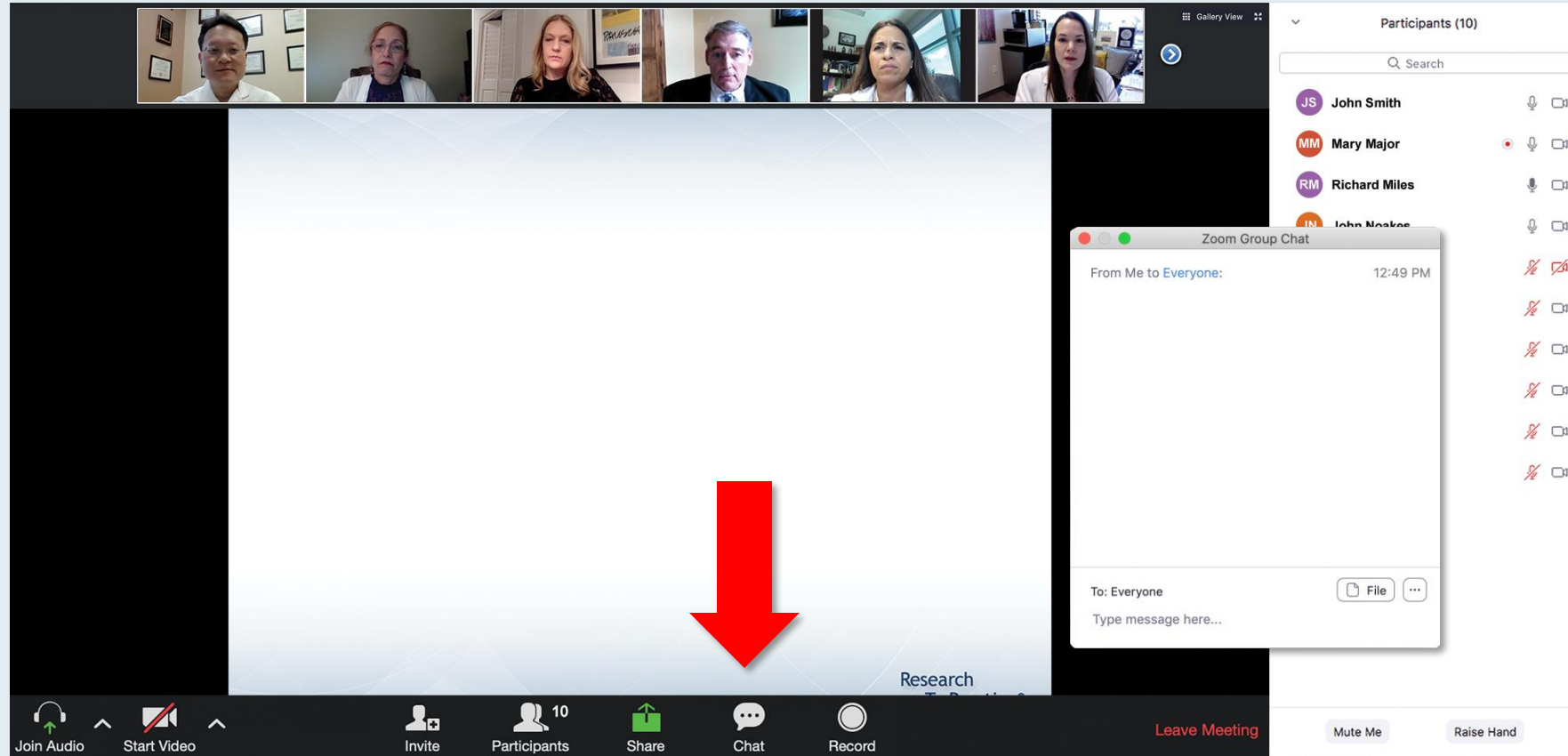
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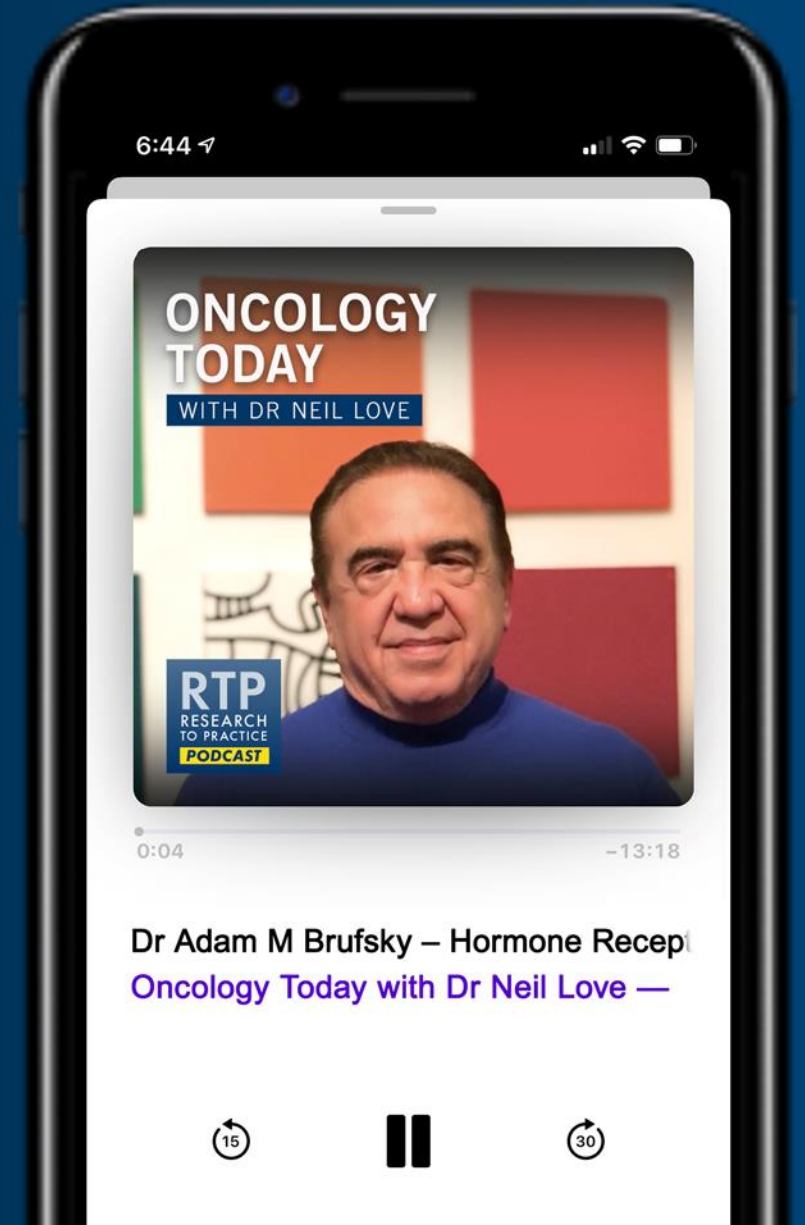
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# **Year in Review: Management of Breast Cancer**

*A CME/MOC-Accredited Live Webinar*

**Wednesday, March 26, 2025  
5:00 PM – 6:00 PM ET**

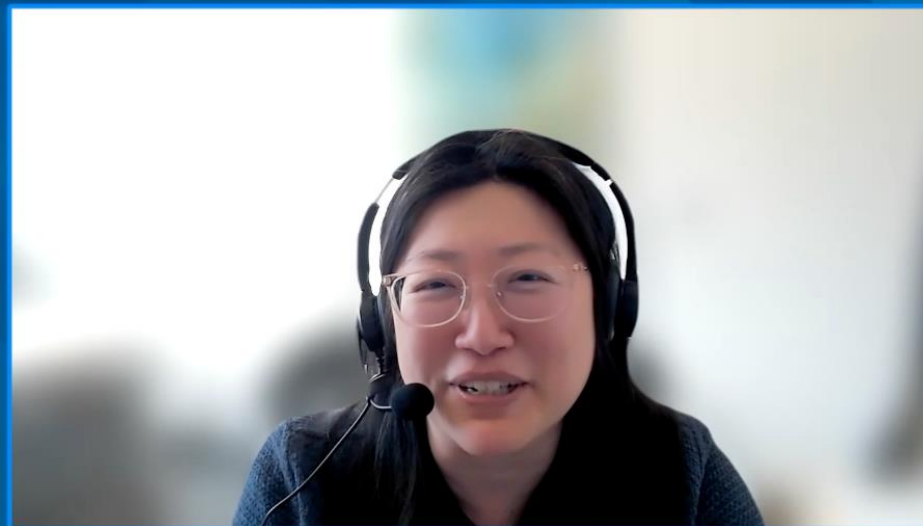
## **Faculty**

**Rebecca A Dent, MD, MSc  
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## **Moderator**

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# AGENDA

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### MODULE 1: HER2-Positive Disease


### MODULE 2: PARP Inhibition

### MODULE 3: Antibody-Drug Conjugates

### MODULE 4: Up-Front Treatment of HR-Positive Metastatic Disease

Comments and Controversies

# Why We Do Not Recommend That Women With Breast Cancer Receive Adjuvant Treatment With a CDK4/6 Inhibitor

Ian F. Tannock, MD, PhD, FRCPC, FASCO<sup>1</sup> ; Qamar J. Khan, MD<sup>2</sup>; and Tito Fojo, MD, PhD<sup>3,4</sup>

DOI <https://doi.org/10.1200/JCO-24-02683>

*J Clin Oncol* 2025 April 14;[Online ahead of print].

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# ***Meet The Professor***

## **Optimizing the Selection and Sequencing of Therapy for Patients with HER2-Positive Breast Cancer**

**Sara M Tolaney, MD, MPH**

Associate Director, Susan F Smith Center for Women's Cancers

Director of Clinical Trials, Breast Oncology

Director of Breast Immunotherapy Clinical Research

Senior Physician

Breast Oncology Program

Dana-Farber Cancer Institute

Associate Professor of Medicine

Harvard Medical School

Boston, Massachusetts

# Trastuzumab Deruxtecan Significantly Improved Progression-Free Survival in Comparison to T-DM1 for HER2-Positive Metastatic Breast Cancer

Press Release – August 9, 2021

“Trastuzumab deruxtecan demonstrated superior progression-free survival (PFS) outcomes over trastuzumab emtansine (T-DM1) in patients with HER2-positive metastatic breast cancer, based on the phase 3 DESTINY-Breast03 trial (NCT03529110). The study’s planned interim analysis identified a statistically significant and clinically meaningful improvement in the primary end point of PFS as assessed by an Independent Data Monitoring Committee (IDMC) for patients with HER2-positive, unresectable and/or metastatic breast cancer who received prior treatment with trastuzumab and a taxane.

Approximately 500 patients were enrolled in the DESTINY-Breast03 trial, who were randomized to either the experimental trastuzumab deruxtecan arm or the comparator T-DM1 arm. The primary end point was PFS assessed by IDMC, with secondary end points including overall survival (OS), objective response rate (ORR), duration of response, and PFS based on investigator assessment.

While patients treated with trastuzumab deruxtecan trended toward OS improvement, the data were immature. Furthermore, the safety profile was consistent with previously reported data regarding trastuzumab deruxtecan, with no new safety signals or grade 4/5 treatment-related interstitial lung disease events observed.”

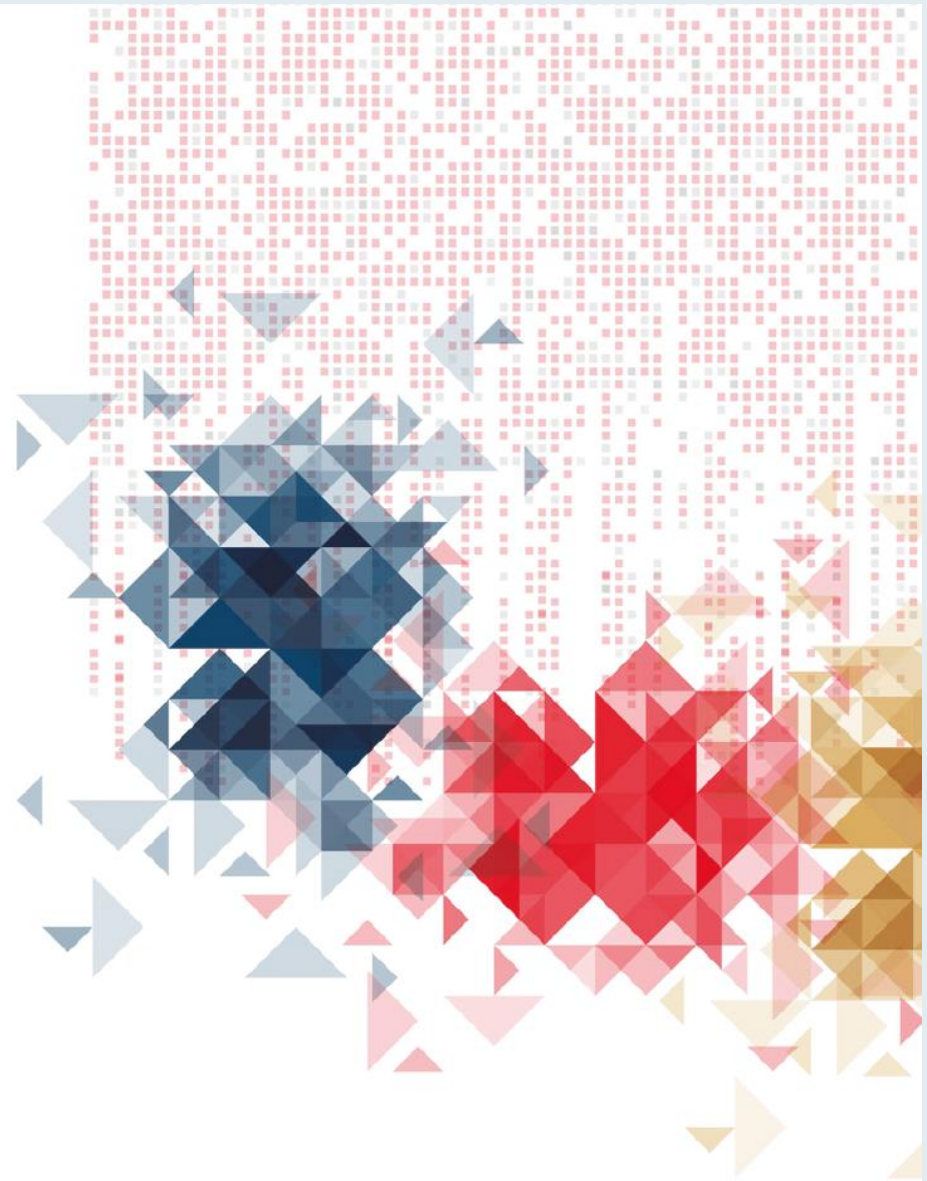




# Trastuzumab Deruxtecan (T-DXd) vs Trastuzumab Emtansine (T-DM1) in Patients With HER2+ Metastatic Breast Cancer: Results of the Randomized, Phase 3 Study DESTINY-Breast03

**Javier Cortés, MD<sup>a</sup>**, Sung-Bae Kim, Wei-Pang Chung, Seock-Ah Im, Yeon Hee Park, Roberto Hegg, Min-Hwan Kim, Ling-Ming Tseng, Vanessa Petry, Chi-Feng Chung, Hiroji Iwata, Erika Hamilton, Giuseppe Curigliano, Binghe Xu, Caleb Lee, Yali Liu, Jillian Cathcart, Emarjola Bako, Sunil Verma, Sara Hurvitz  
**On behalf of the DESTINY-Breast03 investigators**

<sup>a</sup>Medical Oncology, International Breast Cancer Center (IBCC), Quironsalud Group, and Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; Universidad Europea de Madrid, Faculty of Biomedical and Health Sciences, Department of Medicine, Madrid, Spain.



# DESTINY-Breast03 Phase III Trial Schema

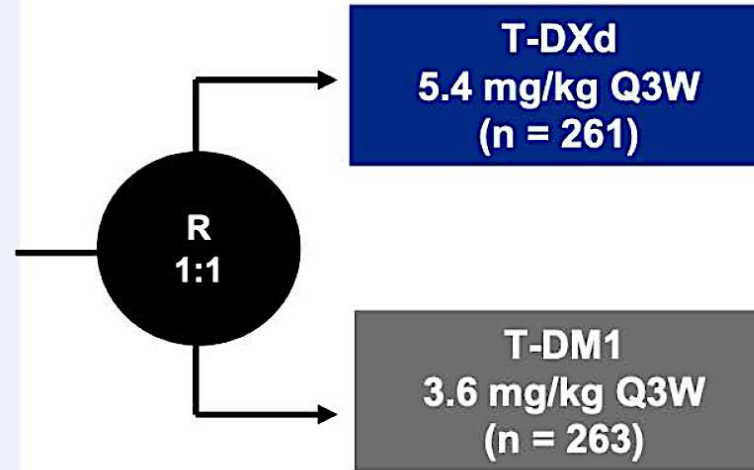
An open-label, multicenter study (NCT03529110)

## Patients

- Unresectable or metastatic HER2-positive<sup>a</sup> breast cancer
- Previously treated with trastuzumab and taxane in advanced/metastatic setting<sup>b</sup>
- Could have clinically stable, treated brain metastases

## Stratification factors

- Hormone receptor status
- Prior treatment with pertuzumab
- History of visceral disease



## Primary endpoint

- PFS (BICR)

## Key secondary endpoint

- OS

## Secondary endpoints

- ORR (BICR and investigator)
- DOR (BICR)
- PFS (investigator)
- Safety

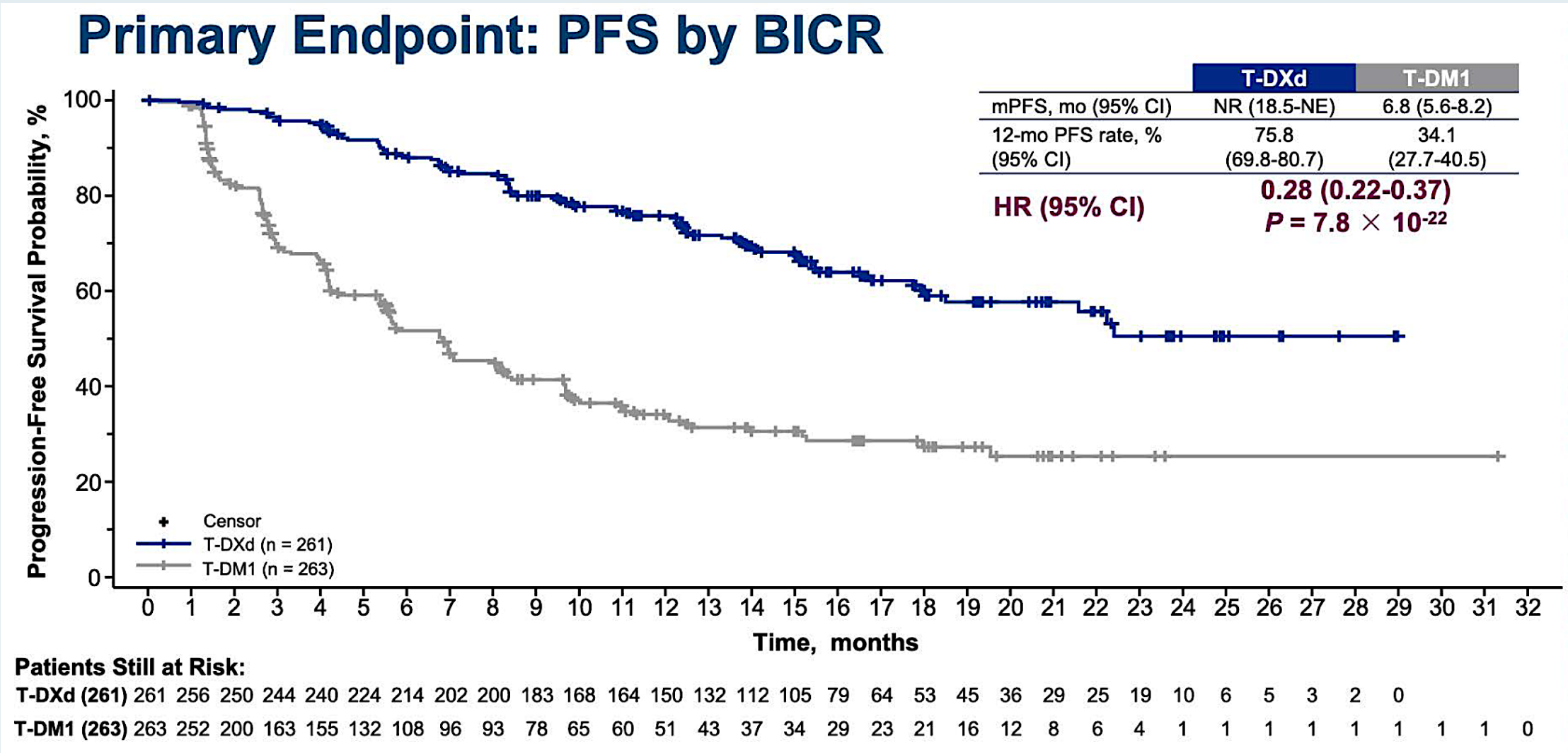
## Interim analysis for PFS (data cutoff: May 21, 2021)

- Efficacy boundary for superiority:  $P < 0.000204$  (based on 245 events)
- IDMC recommendation to unblind study (July 30, 2021)

**Key secondary endpoint, OS:** boundary for efficacy:  $P < 0.000265$  (based on 86 events)

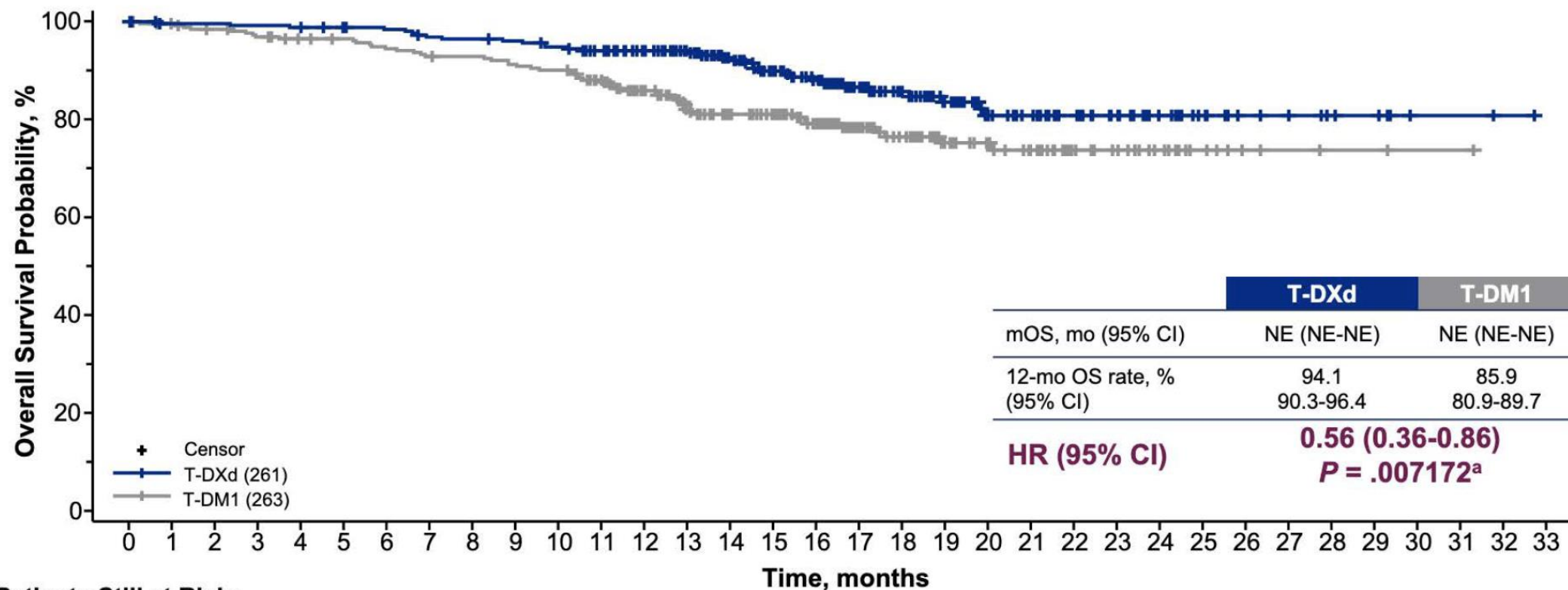


# DESTINY-Breast03: PFS by Blinded Independent Central Review (BICR)



# DESTINY-Breast03: Overall Survival (OS) by BICR

## Key Secondary Endpoint: OS



### Patients Still at Risk:

|                    |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |    |    |    |    |    |    |    |    |    |    |   |   |   |   |   |   |
|--------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|----|----|----|----|----|----|----|----|----|---|---|---|---|---|---|
| <b>T-DXd (261)</b> | 261 | 256 | 256 | 255 | 254 | 251 | 249 | 244 | 243 | 241 | 237 | 230 | 218 | 202 | 180 | 158 | 133 | 108 | 86 | 71 | 56 | 50 | 42 | 33 | 24 | 18 | 11 | 10 | 7 | 6 | 2 | 2 | 1 | 0 |
| <b>T-DM1 (263)</b> | 263 | 258 | 253 | 248 | 243 | 241 | 236 | 232 | 231 | 227 | 224 | 210 | 188 | 165 | 151 | 140 | 120 | 91  | 75 | 58 | 52 | 44 | 32 | 27 | 18 | 11 | 5  | 4  | 3 | 3 | 1 | 1 | 0 |   |



Early OS data with relatively few events (33 in the T-DXd arm, 53 in the T-DM1 arm)

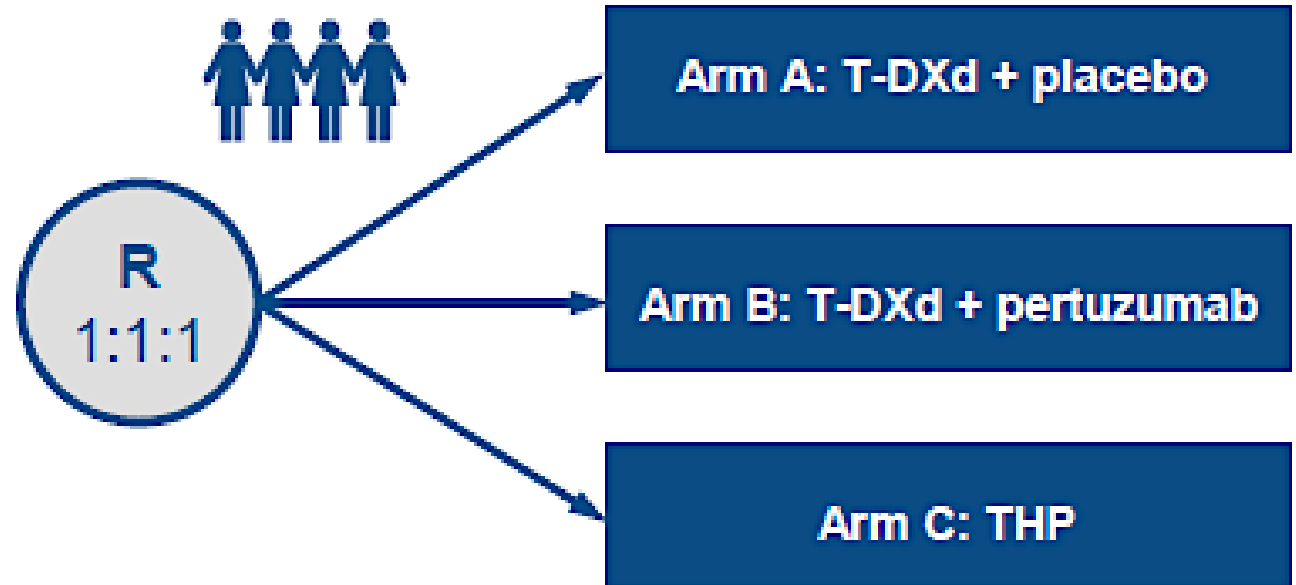
<sup>a</sup>P = .007172, but does not cross pre-specified boundary of P < .000265



# DESTINY-Breast09 Phase III Trial Design

## Patient population (N≈1134)

- Advanced and/or metastatic breast cancer
- HER2 positive (IHC 3+ or ISH+) by central confirmation
- No previous chemotherapy or HER2-targeted therapy for advanced or metastatic breast cancer
- Patients will be stratified by prior treatment status (de novo vs recurrent), HR status (positive vs negative), and *PIK3CA* mutation status (detected vs not detected)



# Trastuzumab Deruxtecan with Pertuzumab Demonstrated Highly Statistically Significant and Clinically Meaningful Improvement in PFS in Comparison to THP as First-Line Therapy for Patients with HER2-Positive Metastatic Breast Cancer

**Press Release: April 21, 2025**

“Positive high-level results from a planned interim analysis of the DESTINY-Breast09 Phase III trial showed trastuzumab deruxtecan in combination with pertuzumab demonstrated a highly statistically significant and clinically meaningful improvement in progression-free survival (PFS) compared to a taxane, trastuzumab and pertuzumab (THP) as a 1st-line treatment for patients with HER2-positive metastatic breast cancer.

The PFS improvement was seen across all pre-specified patient subgroups with trastuzumab deruxtecan in combination with pertuzumab. The key secondary endpoint of overall survival (OS) was not mature at the time of this planned interim analysis; however, interim OS data showed an early trend favoring the trastuzumab deruxtecan combination compared with THP. The second arm assessing trastuzumab deruxtecan monotherapy versus THP remains blinded to patients and investigators and will continue to the final PFS analysis.”

# Trastuzumab Deruxtecan (T-DXd) + Pertuzumab (P) vs Taxane + Trastuzumab + Pertuzumab (THP) for First-Line (1L) Treatment of Patients (pts) with Human Epidermal Growth Factor Receptor 2-Positive (HER2+) Advanced/Metastatic Breast Cancer (a/mBC): Interim Results from DESTINY-Breast09

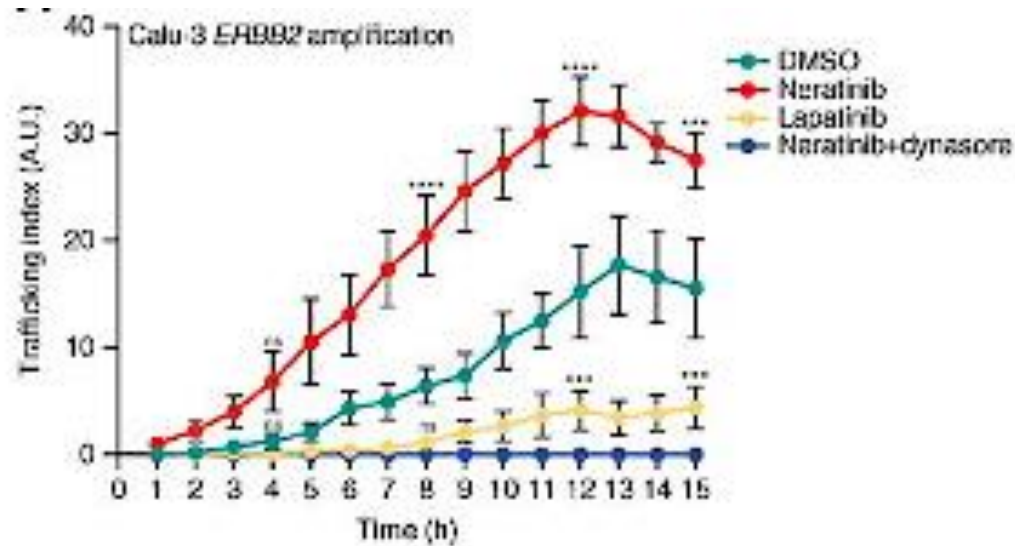
Tolaney S et al.

ASCO 2025;Abstract LBA1008.

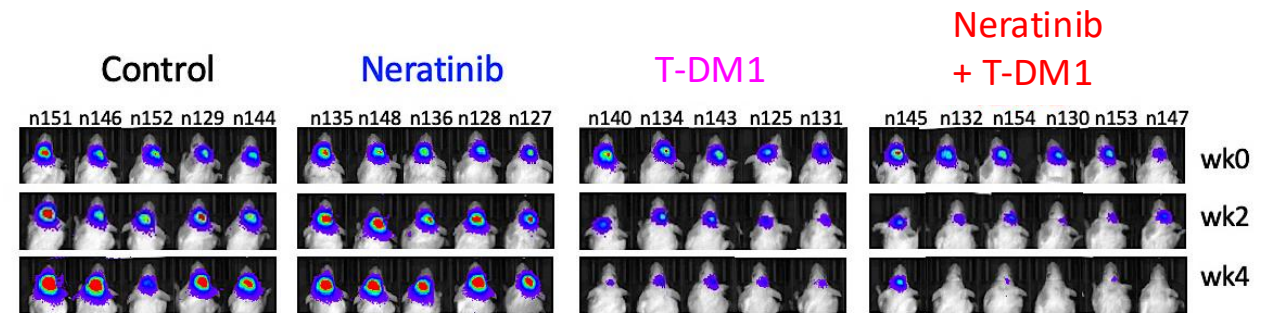
**MONDAY, JUNE 2 | 7:30 AM CDT**

# TBCRC 022: T-DM1 + Neratinib for HER+ Brain Mets

## *Rationale for the Combination*



Neratinib increases HER2 trafficking  
and may overcome T-DM1 resistance



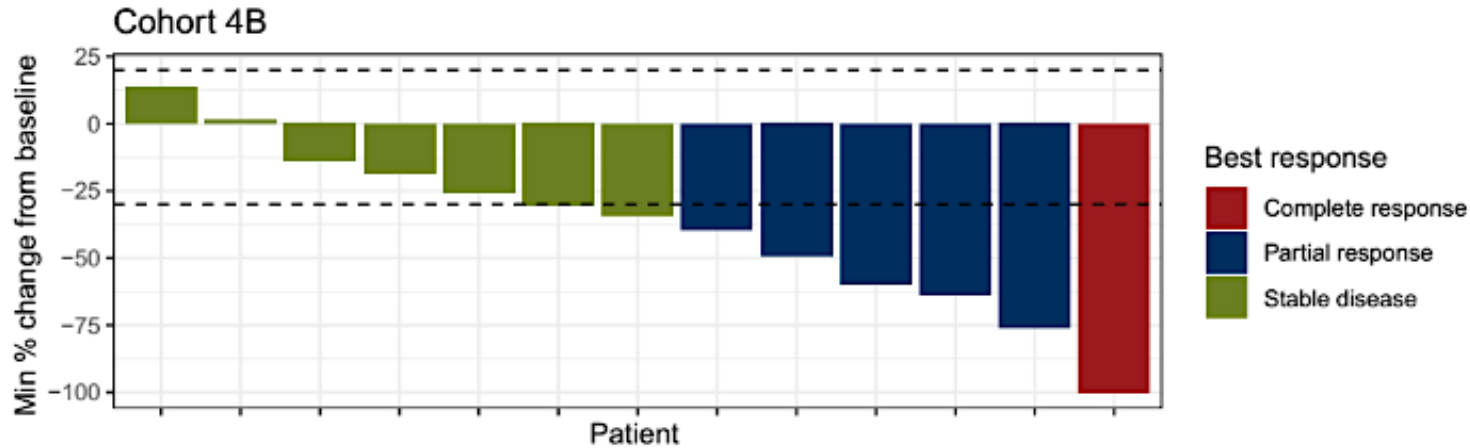
PDX model of HER2+ breast cancer brain mets  
Deeper and more durable responses with the combination

Freedman RA et al. Ann Oncol 2024;35(11):993-1002.

Li et al, Cancer Discov 2020



# TBCRC 022: T-DM1 + neratinib for HER+ Brain Mets



Progressing after prior local tx

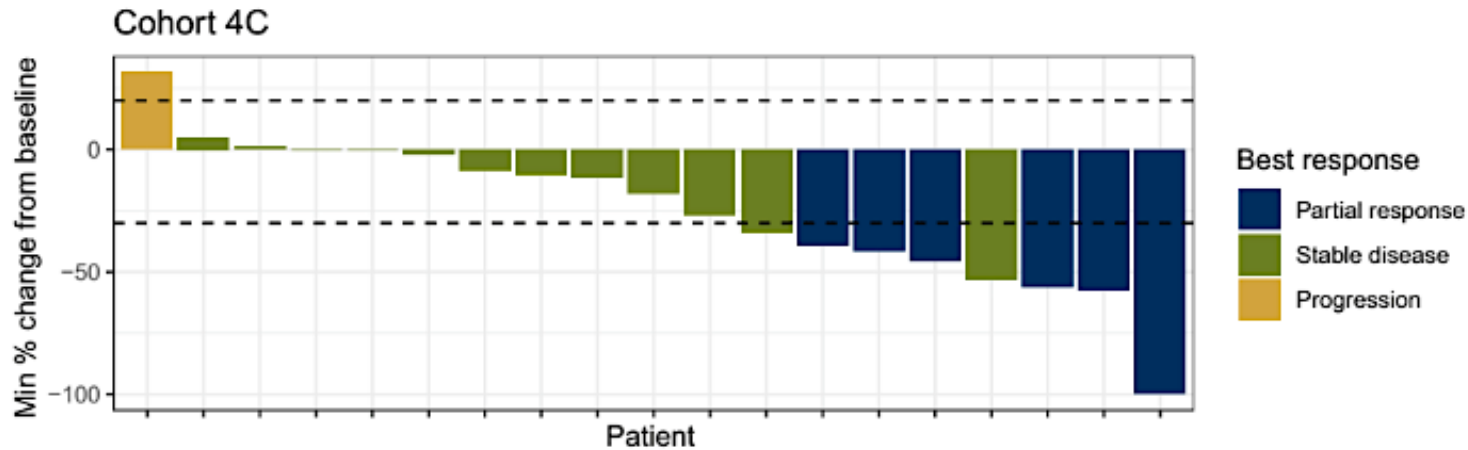
No prior T-DM1

**CNS ORR 35.3%**

**Median PFS 4.1 mo**

**Median OS 23.3 mo**

**12 mo OS 87%**



Progressing after prior local tx

Prior T-DM1 exposure

**CNS ORR 28.6%**

**Median PFS 4.1 mo**

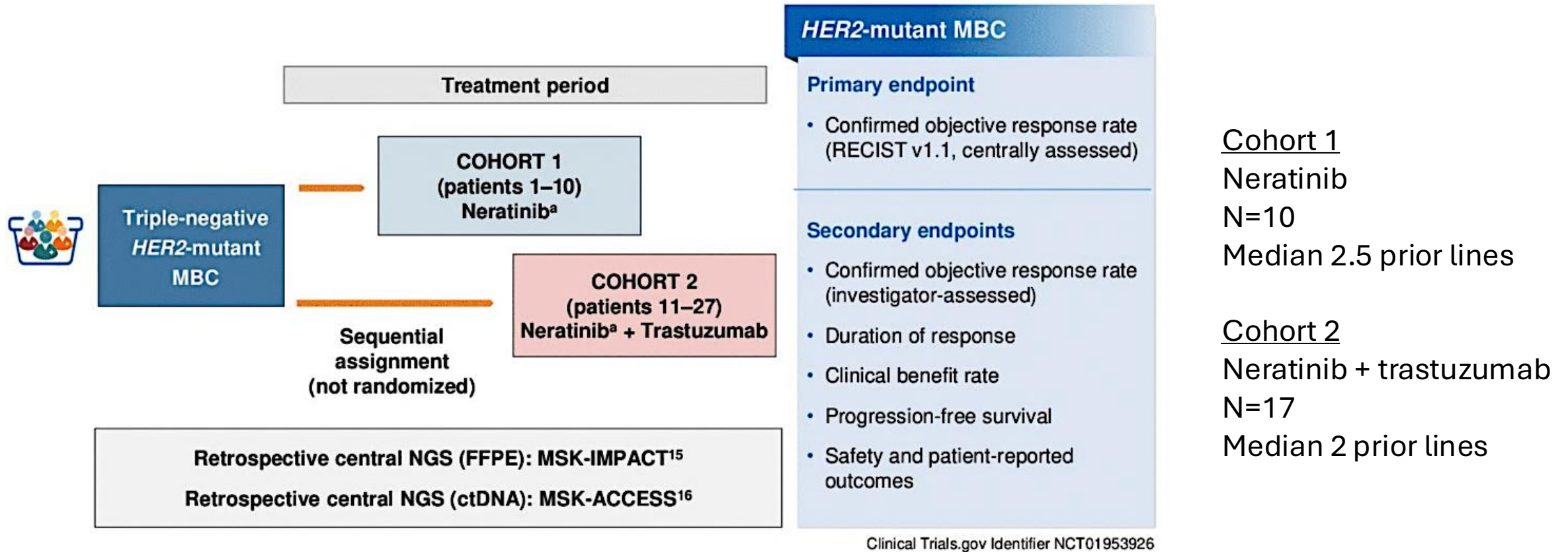
**Median OS 20.9 mo**

**12 mo OS 80%**

# TBCRC 022: Conclusions and Thoughts

- Even with the advent of T-DXd and tucatinib, there is a substantial need for multiple lines of systemic therapy for patients with active brain metastases
- CNS ORR to T-DM1 + neratinib exceeds that of neratinib monotherapy (CNS ORR 8%)
- CNS responses are seen in about 1/3 of patients with prior T-DM1 exposure
- Limitations: no patients had received prior tucatinib, and only a few had prior T-DXd
- Await more granular CNS data from HER2CLIMB-02
- Provides another systemic option for patients with HER2+ BM

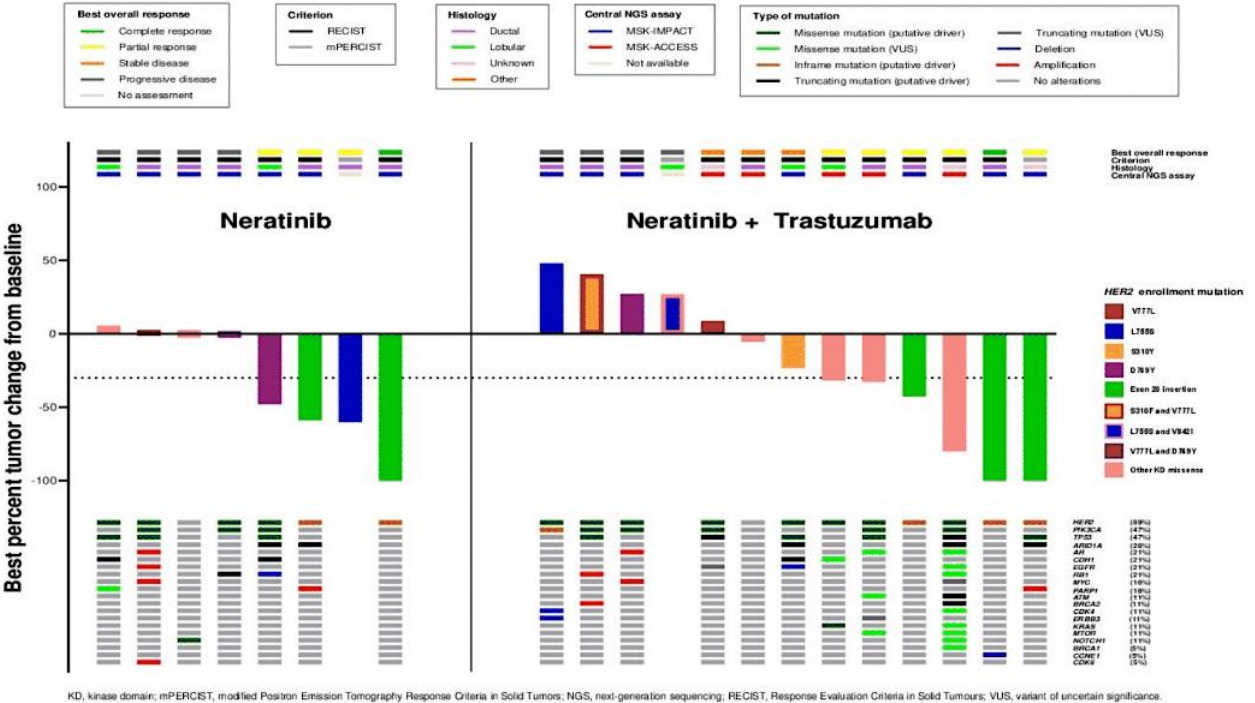
# SUMMIT Trial: HER2-mutant TNBC treated with Neratinib or Neratinib + Trastuzumab



# SUMMIT Trial: HER2-mutant TNBC treated with Neratinib or Neratinib + Trastuzumab

| Parameter   | Neratinib (n=10) | Neratinib + Trastuzumab (n=17) |
|---|------------------|--------------------------------|
| <b>Objective response (confirmed PR or CR)<sup>a</sup>, n (%)</b>       |                  |                                |
| CR  | 1 (10.0)         | 2 (11.8)                       |
| PR  | 3 (30.0)         | 4 (23.5)                       |
| Objective response rate, % (95% CI)                                     | 40.0 (12.2–73.8) | 35.3 (14.2–61.7)               |
| <b>Best overall response (confirmed or unconfirmed PR or CR), n (%)</b> |                  |                                |
| CR  | 1 (10.0)         | 2 (11.8)                       |
| PR  | 4 (40.0)         | 5 (29.4)                       |
| Best overall response rate (95% CI)                                     | 50.0 (18.7–81.3) | 41.2 (18.4–67.1)               |
| <b>Median duration of response<sup>b</sup>, months (95% CI)</b>         | 3.78 (3.75–3.88) | 6.14 (4.17–9.49)               |
| <b>Clinical benefit rate, %<sup>c</sup> (95% CI)</b>                    |                  |                                |
| CR  | 1 (10.0)         | 2 (11.8)                       |
| PR  | 3 (30.0)         | 4 (23.5)                       |
| SD ≥24 weeks  | 0                | 2 (11.8)                       |
| <b>Median PFS<sup>b</sup>, months (95% CI)</b>                          | 2.89 (0.95–5.52) | 6.24 (2.10–8.18)               |

Confirmed ORR 40% (N), 35.3% (N+T)  
Median PFS 2.89 mo (N), 6.24 mo (N+T)



Deepest responses in those with Exon 20 insertions

Jhaveri K et al. ASCO 2024;Abstract 1094.

# SUMMIT Trial TNBC basket: Conclusions and Thoughts

- Impressive response rates (40%) in pre-treated HER2-mut TNBC
- Longer DoR and PFS with the doublet of N+T
- Small numbers but compares favorably to “nth-line” chemo in TNBC
- Previously published data in HR+/HER2-mut MBC
  - ORR 38.6%, median PFS 8.3 months with neratinib + fulvestrant + trastuzumab
- New data for tucatinib + trastuzumab in HER2-mut MBC
  - Confirmed ORR 41.9%; median PFS 9.5 months
  - Pts with HR+ disease also received fulvestrant
  - Only 4 pts with TNBC included

Jhaveri K et al. ASCO 2024;Abstract 1094.

Jhaveri et al, Ann Oncol 2023

Okines et al, Nat Med 2025

# 2018 and 2024 Surveys of Clinical Investigator (CI) Use of Postoperative Systemic Therapy After Prior Neoadjuvant Treatment of HER2-Positive Breast Cancer (HER2+ BC)

Wallace T et al.

SABCS 2024;Abstract P3-11-20.

## Survey Participants

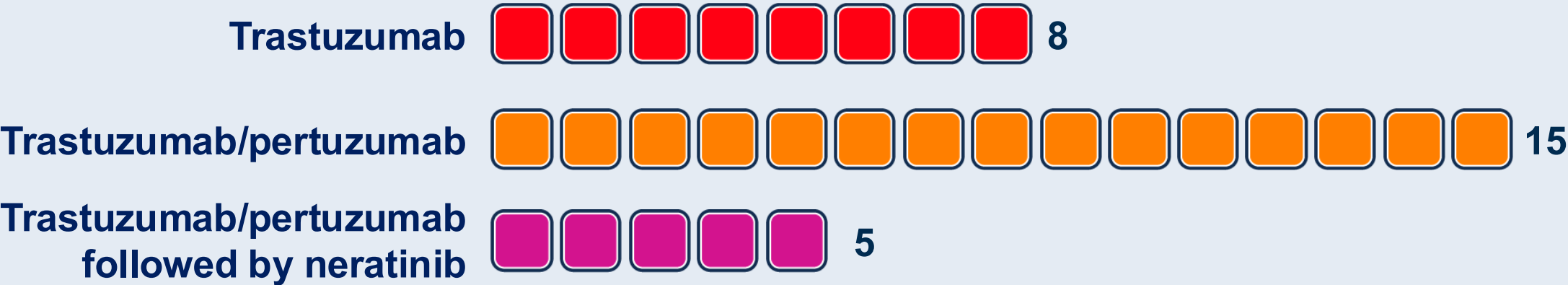
Virginia F Borges, MD, MMSc  
Adam M Brufsky, MD, PhD  
Harold J Burstein, MD, PhD  
Karen A Gelmon, MD  
Matthew P Goetz, MD  
Virginia Kaklamani, MD, DSc  
Kevin Kalinsky, MD, MS  
Ian E Krop, MD, PhD  
Erica Mayer, MD, MPH, FASCO  
Jane Lowe Meisel, MD

Kathy D Miller, MD  
Ruth O'Regan, MD  
Joyce O'Shaughnessy, MD  
Lajos Pusztai, MD, DPhil, FASCO  
Mark E Robson, MD  
Hope S Rugo, MD  
Priyanka Sharma, MD  
Laura Spring, MD  
Sara M Tolaney, MD, MPH  
Seth Wander, MD, PhD

What adjuvant anti-HER2 treatment would you most likely recommend in the following scenario?

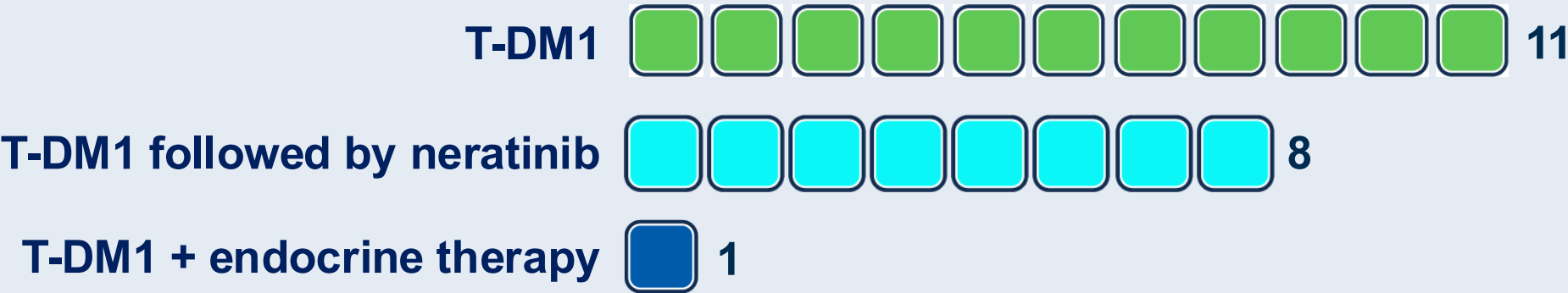
HER2-positive, ER-positive  
Neoadjuvant TCHP  
Minimal residual disease at surgery

2018



Survey of 28 US-based clinical investigators November 2018

2024



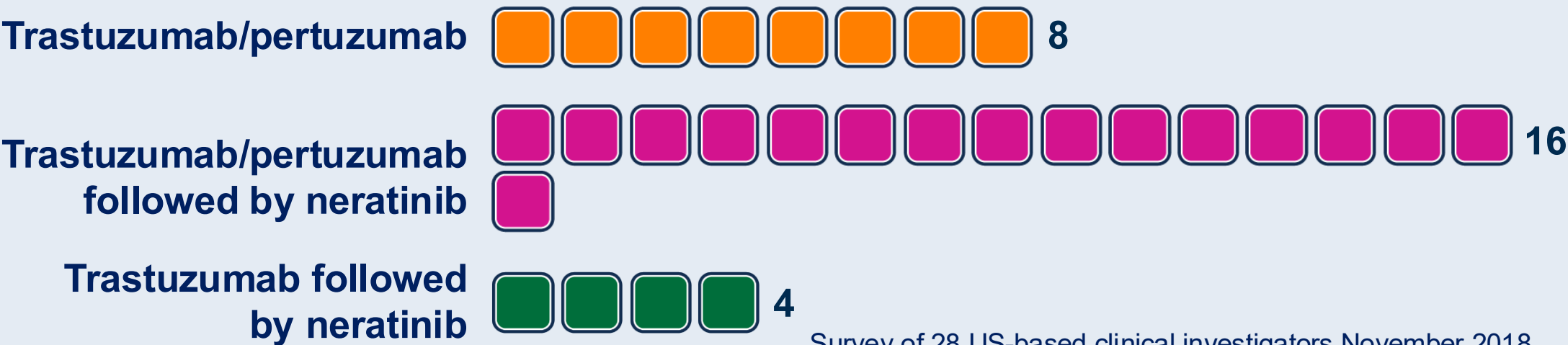
Survey of 20 US-based clinical investigators April-May 2024



What adjuvant anti-HER2 treatment would you most likely recommend in the following scenario?

HER2-positive, ER-positive  
Neoadjuvant TCHP  
Macroscopic residual disease at surgery

2018



2024



# **ASCO 2025: HER2-Positive Breast Cancer**

# **Phase IB and II Study of Ribociclib with Trastuzumab plus Endocrine Therapy in HR+/HER2+ Advanced Breast Cancer Patients: Korean Cancer Study Group BR 18-2 MINI Trial**

Sohn J et al.

ASCO 2025;Abstract 1016.

**FRIDAY, MAY 30 | 3:15 PM CDT**

# Treatment Rechallenge After Trastuzumab-Deruxtecan-Related Interstitial Lung Disease: A Multi-Institution Cohort Study

Rugo H et al.

ASCO 2025;Abstract 1015.

**FRIDAY, MAY 30 | 2:57 PM CDT**

# AGENDA

## Year in Review: Management of Breast Cancer

**INTRODUCTION:** Adjuvant CDK4/6 Inhibition

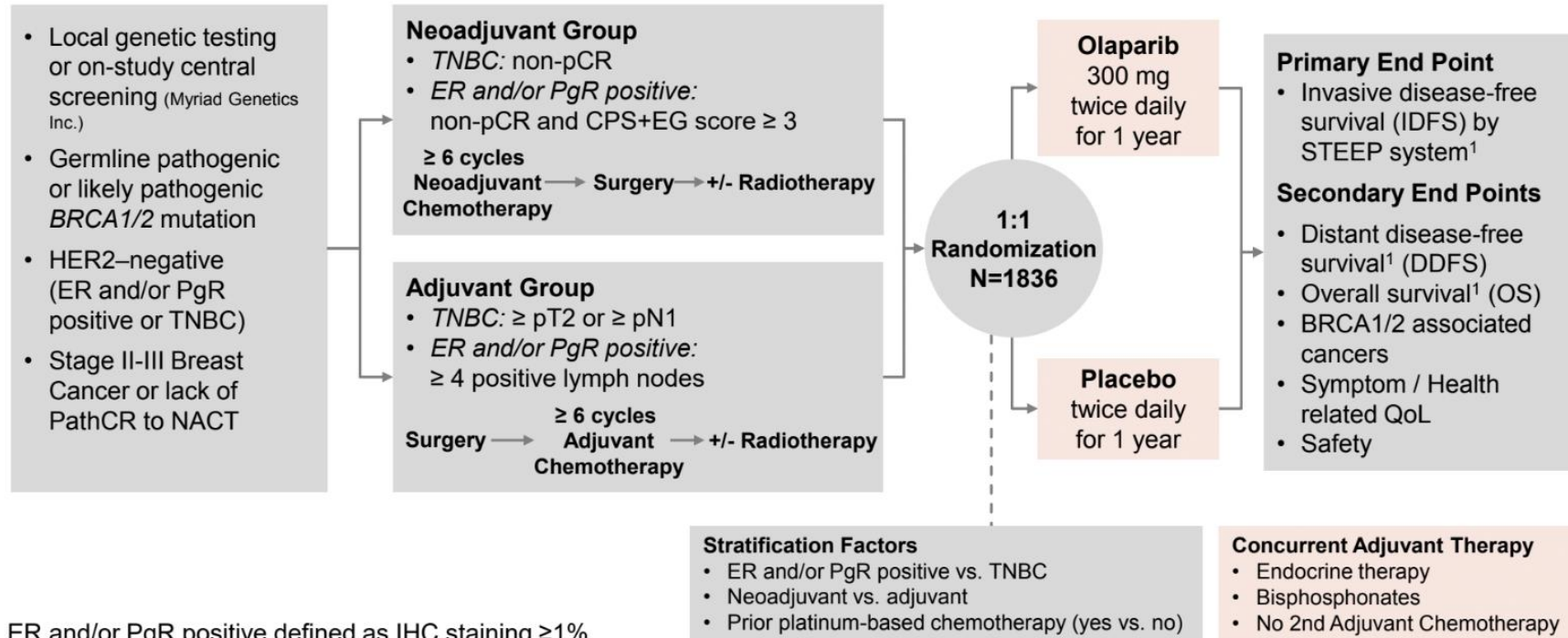
**MODULE 1:** HER2-Positive Disease

**MODULE 2:** PARP Inhibition

**MODULE 3:** Antibody-Drug Conjugates

**MODULE 4:** Up-Front Treatment of HR-Positive Metastatic Disease

# OlympiA: Adjuvant Olaparib in gBRCA1/2 carriers



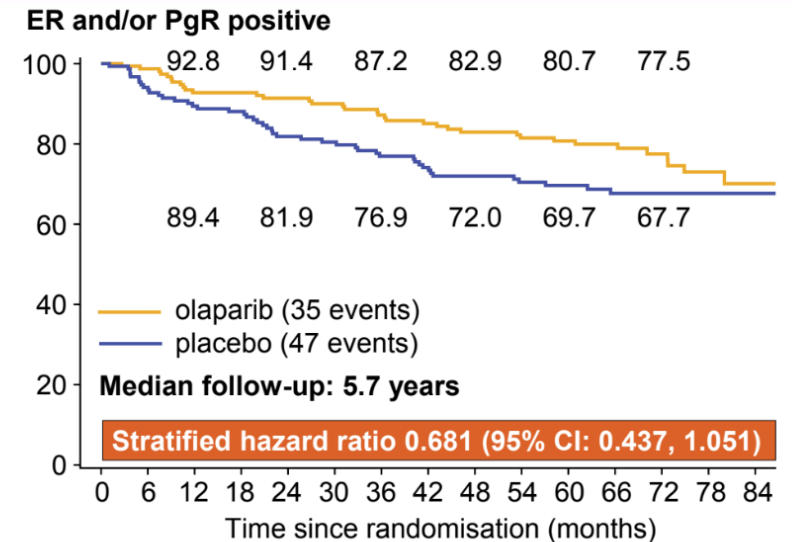
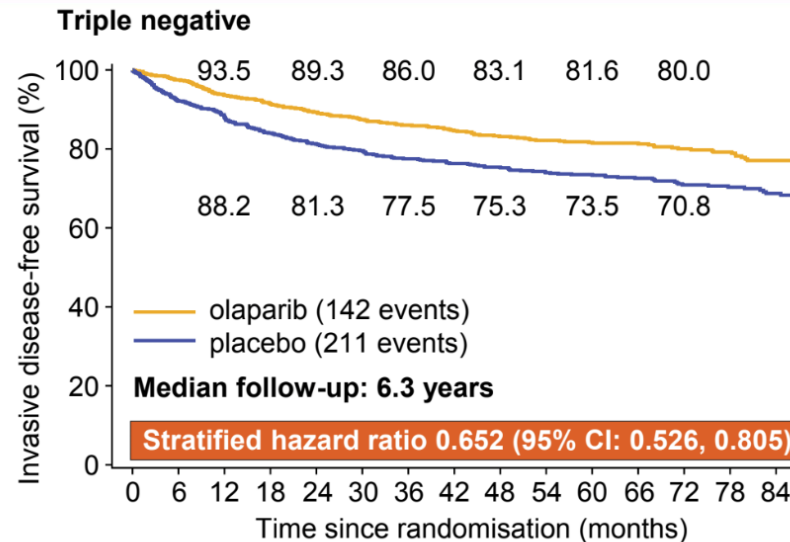
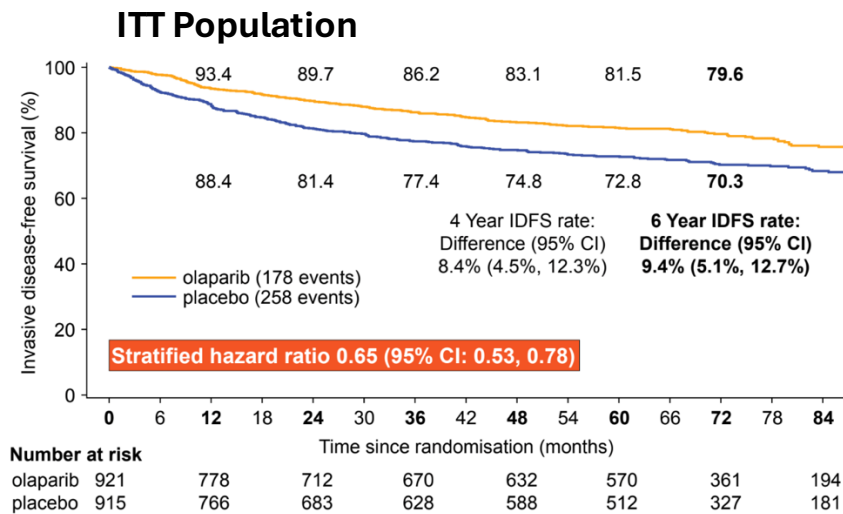
ER and/or PgR positive defined as IHC staining  $\geq 1\%$ .  
Triple Negative defined as ER and PgR negative (IHC staining  $< 1\%$ )

>70% enrolled pts were gBRCA1  
>80% had TNBC

~50% adjuvant  
~50% post neoadjuvant

- Third pre-specified analysis at 10 years from first patient in
- Median follow up of 6.1 years (additional 2.6 y f/u since previous)

# OlympiA: iDFS

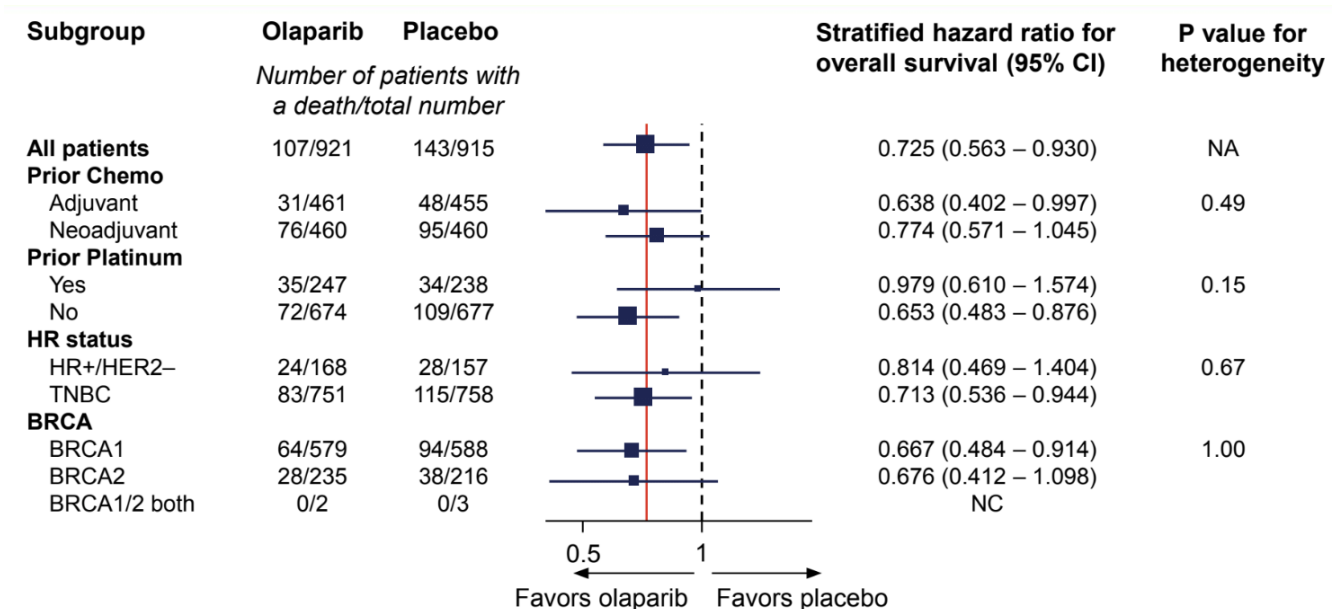
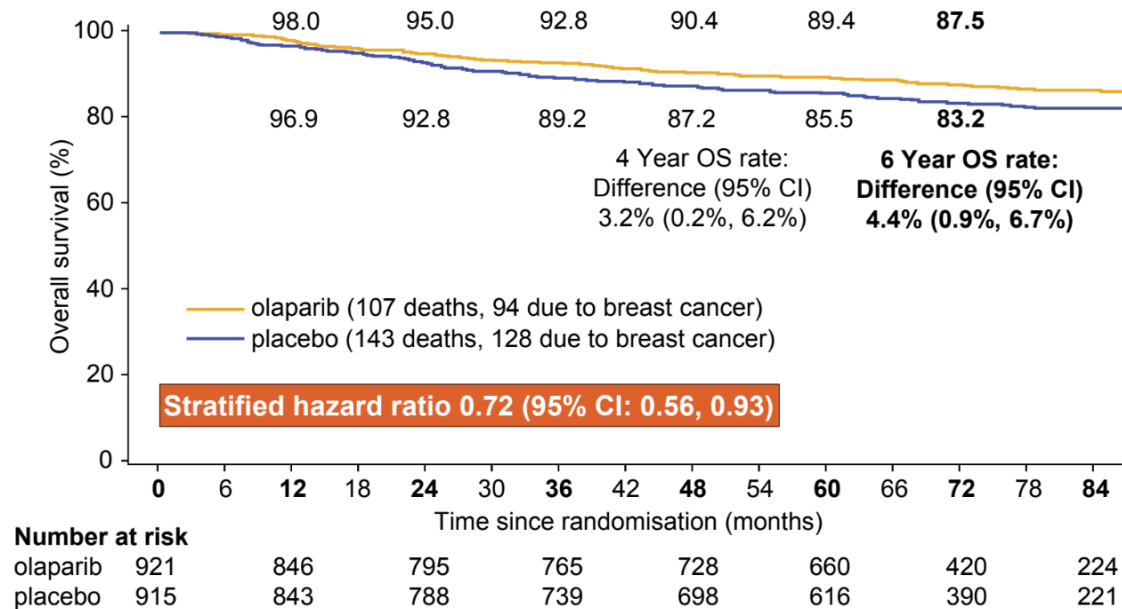


- Similar magnitude of benefit for DDFS
- Similar rates of MDS/AML (4 events (0.4%) for Olaparib; 6 events (0.7%) in placebo arm)
- Numerically fewer CNS events as 1<sup>st</sup> iDFS event (2.8% vs 4.4%)
- Fewer new primary cancers with olaparib (contralateral breast cancer, new primary ovarian/fallopian tube cancer)

Garber J et al. SABCS 2024;Abstract GS1-09.

# OlympiA: OS

## ITT Population





# OlympiA: Conclusions and Thoughts

- Significant benefit in iDFS (HR 0.65), DDFS, and OS (HR 0.72) with adjuvant Olaparib
- Effect seen in both HR+ and TN patients and in BRCA1 or BRCA2 carriers
- No signal of increase in MDS/AML at 6.1 y median f/u
- All patients who meet anatomic eligibility criteria for Olaparib (with drug access) *should be offered germline genetic testing*
- TNBC: Cape vs Olaparib post NAC?
  - No direct comparison
  - CREATE-X OS HR 0.52, 8% absolute gain
  - GEICAM (adjuvant cape) suggested more benefit of capecitabine in non-basal subtypes
  - OlympiAD – Olaparib outperformed chemo of provider choice (~1/2 capecitabine) in MBC setting
- ER+: Abema or Ribo vs Olaparib?
  - No direct comparison
  - MONARCHE @ 54 mo median f/u, HR 0.68 for iDFS (7.6% absolute gain); no statistically significant OS benefit
  - NATALEE @ 34 mo median f/u, HR 0.75 for iDFS (3% gain at 3y); no difference yet in OS
  - For 4+ positive nodes, generally prefer Olaparib (or a sequence of ola -> CDK4/6i in very high-risk patients)
  - For 1-3 positive nodes (OlympiA did not include if adjuvant only), could consider CDK4/6i but lean towards olaparib: shorter duration of therapy and OS benefit already demonstrated
  - For node negative disease, olaparib has not been studied, and would consider ribo in carefully selected patients who would have met eligibility for NATALEE

## **“Beyond the Guidelines” Questions**

**What would be your most likely adjuvant treatment approach for a patient with an ER-positive, HER2-negative 1.8-cm IDC, 3 positive nodes and a germline BRCA mutation?**

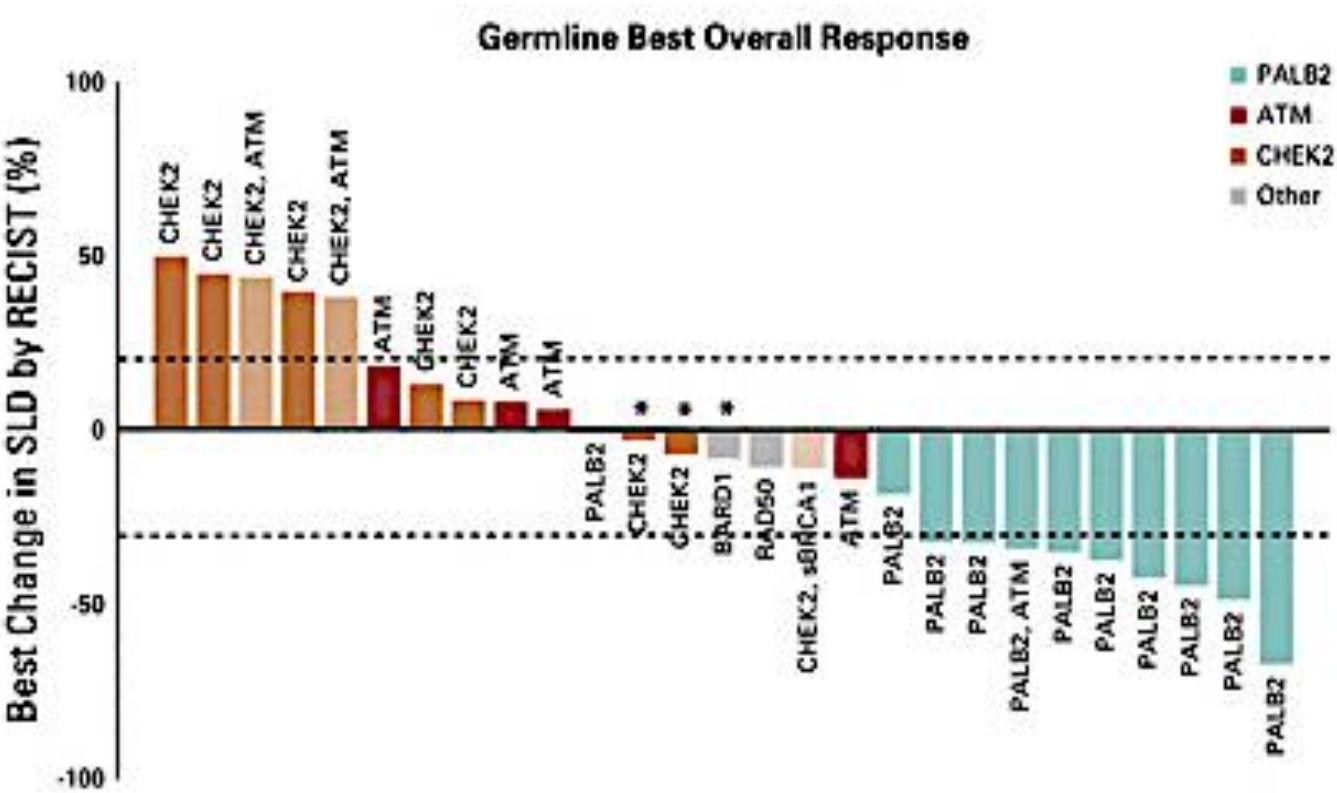
**How, if at all, would you integrate a PARP inhibitor into current or future treatment?**

## **“Beyond the Guidelines” Questions**

**What would be your most likely adjuvant treatment approach for a patient with a 1.8-cm ER/PR-negative, HER2-negative, node-negative IDC and a germline BRCA mutation?**

**How, if at all, would you integrate a PARP inhibitor into current or future treatment?**

# TBCRC 048: Olaparib Expanded Initial Cohort



| Gene              | ORR (90% CI) |
|-------------------|--------------|
| gPALB2 (n=11)     | 82% (48-98%) |
| sBRCA (n=16)      | 50% (25-75%) |
| ATM, CHEK2 (n=18) | 0%           |

# TBCRC 048: Olaparib Expanded Expansion Cohorts

| <b>gPALB2<br/>N=24</b>                      |                     |
|---|---------------------|
| Best Response                               | Responses (rate, %) |
| Complete Response (CR)                      | 1 (4%)              |
| Partial Response (PR)                       | 17 (71%)            |
| Stable Disease (SD)                         | 5 (21%)             |
| Progressive Disease (PD)                    | 1 (4%)              |
| ORR = 75% (18/24, 80%-CI: 60%-86%)          |                     |
| CBR (18 wks) = 83% (20/24, 90%-CI: 66%-94%) |                     |

Median PFS 9.6 months

Key Eligibility: 0-2 prior chemo for MBC  
Key exclusion: prior PARP, progression on platinum

| <b>sBRCA1/2<br/>N=30</b>                    |                      |
|---|----------------------|
| Best Response                               | Responses, (rate, %) |
| Complete Response (CR)                      | 1 (3%)               |
| Partial Response (PR)^                      | 10 (33%)             |
| Stable Disease (SD)                         | 13 (43%)             |
| Progressive Disease (PD)                    | 6 (20%)              |
| ORR = 37% (11/30, 80%-CI: 25%-50%)          |                      |
| CBR (18 wks) = 53% (16/30, 90%-CI: 37%-69%) |                      |

Median PFS 7.2 months

Tung NM et al. ASCO 2024;Abstract 1021.

# TBCRC 048: Olaparib Expanded Expansion Cohorts

**Exploratory objectives: predictors of olaparib response  
in sBRCAm (Cohorts 2\* and 2a\*)**

| Clinical/ Molecular factor                                   | Total # response/ total                |   |
|--|--|---|
| Tumor subtype (primary)<br>TNBC<br>ER+/HER2-<br>HER2+        | 7/10 (70%)<br>12/33 (36%)<br>0/3 (0%)  | <ul style="list-style-type: none"> <li>All subtypes respond                             <ul style="list-style-type: none"> <li>↑RR in TNBC</li> </ul> </li> </ul> |
| BRCA1<br>BRCA2   | 8/22 (36%)<br>10/24 (42%)              | <ul style="list-style-type: none"> <li>No <math>\Delta</math> BRCA1 vs BRCA2</li> </ul>   |
| 1L met RX<br>> 1L metastatic Rx                              | 12/17 (71%)<br>7/29 (24%)              | <ul style="list-style-type: none"> <li>↑ RR if olaparib given before chemo in MBC</li> </ul>  |
| Prior platinum<br>No prior platinum                          | 1/4 (25%)<br>18/42 (43%)               |   |
| Method of dx sBRCAm<br>cfDNA<br>Tumor bx                     | 1/10 (10%)<br>18/36 (50%)              | <ul style="list-style-type: none"> <li>↓ RR if sBRCAm identified by cfDNA only</li> </ul>   |
| PV/LPV*<br>Single BRCA copy loss<br>Biallelic BRCA copy loss | 16/39 (41%)<br>1/5 (20%)<br>2/2 (100%) | <ul style="list-style-type: none"> <li>If sBRCA loss, ↑RR if confirmed biallelic loss</li> </ul>  |

\* (L)PV: (Likely) pathogenic variant

\* Cohort 2: 16 pts ; Cohort 2a: 30 pts

# TBCRC 048: Conclusions and Thoughts

- Confirms very high response rates and durability of benefit in *gPALB2* carriers
- Activity in *sBRCA* numerically less than in initial cohort but still respectable (37%, median PFS 7.2 mo)
- Estimates of frequency of *sBRCA* in primary tumors ~3-4%
- Frequency in MBC esp in later lines is not well-described
- Sufficient activity to consider on a routine basis and to justify:
  - Routine germline testing in MBC patients
  - NGS testing to identify somatic alterations



## **“Beyond the Guidelines” Questions**

**A 65-year-old woman presents with de novo HR-positive, HER2-negative (IHC 0) metastatic breast cancer (mBC) with a germline BRCA1 mutation. Biomarker evaluation is negative for ESR1 mutations and PIK3CA/AKT1/PTEN alterations. Regulatory and reimbursement issues aside, what would be your most likely treatment?**

**How, if at all, would you integrate a PARP inhibitor into current or future treatment?**



## **“Beyond the Guidelines” Questions**

**A 65-year-old woman presents with de novo HR-positive, HER2-low (IHC 1+) mBC with a germline BRCA1 mutation. Biomarker evaluation is negative for ESR1 mutations and PIK3CA/AKT1/PTEN alterations. Regulatory and reimbursement issues aside, what would be your most likely treatment?**

**How, if at all, would you integrate a PARP inhibitor into current or future treatment?**

## **“Beyond the Guidelines” Questions**

**A 65-year-old woman presents with de novo HR-negative, HER2-negative (IHC 0) PD-L1-positive mBC with a germline BRCA1 mutation. Regulatory and reimbursement issues aside, what would be your most likely treatment?**

**How, if at all, would you integrate a PARP inhibitor into current or future treatment?**

## **“Beyond the Guidelines” Questions**

**A 65-year-old woman presents with de novo HR-negative, HER2-negative (IHC 0) PD-L1-negative mBC with a germline BRCA1 mutation. Regulatory and reimbursement issues aside, what would be your most likely treatment?**

**How, if at all, would you integrate a PARP inhibitor into current or future treatment?**

**ASCO 2025:  
PARP Inhibitors; BRCA-Positive Disease**

# Prospective Randomized Phase II Trial to Assess the Efficacy and Safety of Neo-Adjuvant Olaparib/Carboplatin (OC) in Comparison to Docetaxel/Epirubicin/Cyclophosphamide (TAC) in Patients with Early Triple-Negative Breast Cancer (TNBC) with Homologous Recombination Deficiency (HRD): Primary Results from the ABCSG 45 Trial

Singer C et al.

ASCO 2025;Abstract 510.

**SUNDAY, JUNE 1 | 8:06 AM CDT**

# Menopausal Hormone Therapy After a Diagnosis of Breast Cancer in Women with a BRCA Pathogenic Variant and Risk of Death

Kotsopoulos J et al.

ASCO 2025;Abstract 10506.

**SUNDAY, JUNE 1 | 1:30 PM CDT**

# Video-Based Genetic Counseling to Reduce Physician Workload and Enhance Consalter Understanding: A Prospective Randomized Clinical Trial

Pfeiler G et al.

ASCO 2025;Abstract 1502.

**MONDAY, JUNE 2 | 3:24 PM CDT**



# AGENDA

## Year in Review: Management of Breast Cancer

**INTRODUCTION:** Adjuvant CDK4/6 Inhibition

**MODULE 1:** HER2-Positive Disease

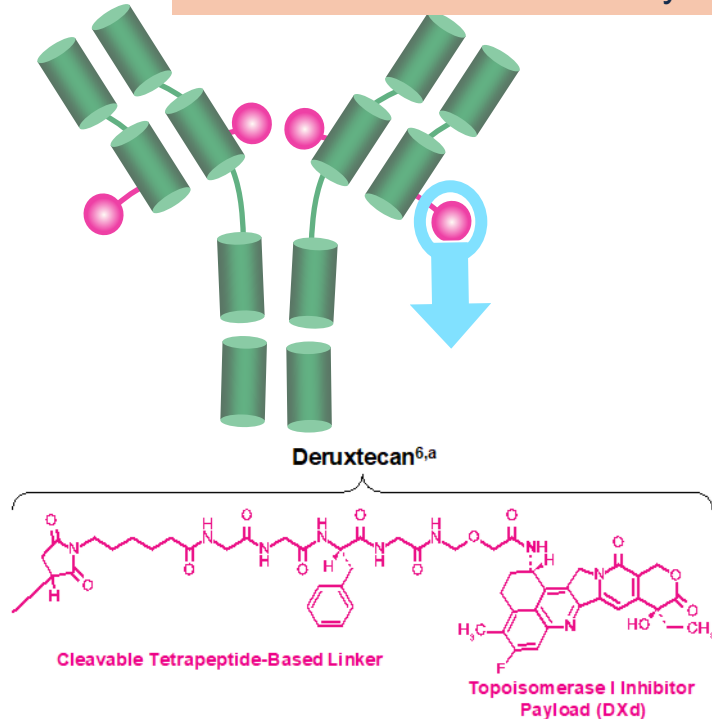
**MODULE 2:** PARP Inhibition

**MODULE 3:** Antibody-Drug Conjugates

**MODULE 4:** Up-Front Treatment of HR-Positive Metastatic Disease

# TROPION-Breast01: Ph 3 trial of Dato-DXd in HR+/HER2- MBC

**Dato-DXd:** Humanised anti-TROP2 monoclonal antibody



## Key inclusion criteria

Patients with HR+/HER2- breast cancer\*  
(HER2- 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

1:1

## Dato-DXd

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

## ICC

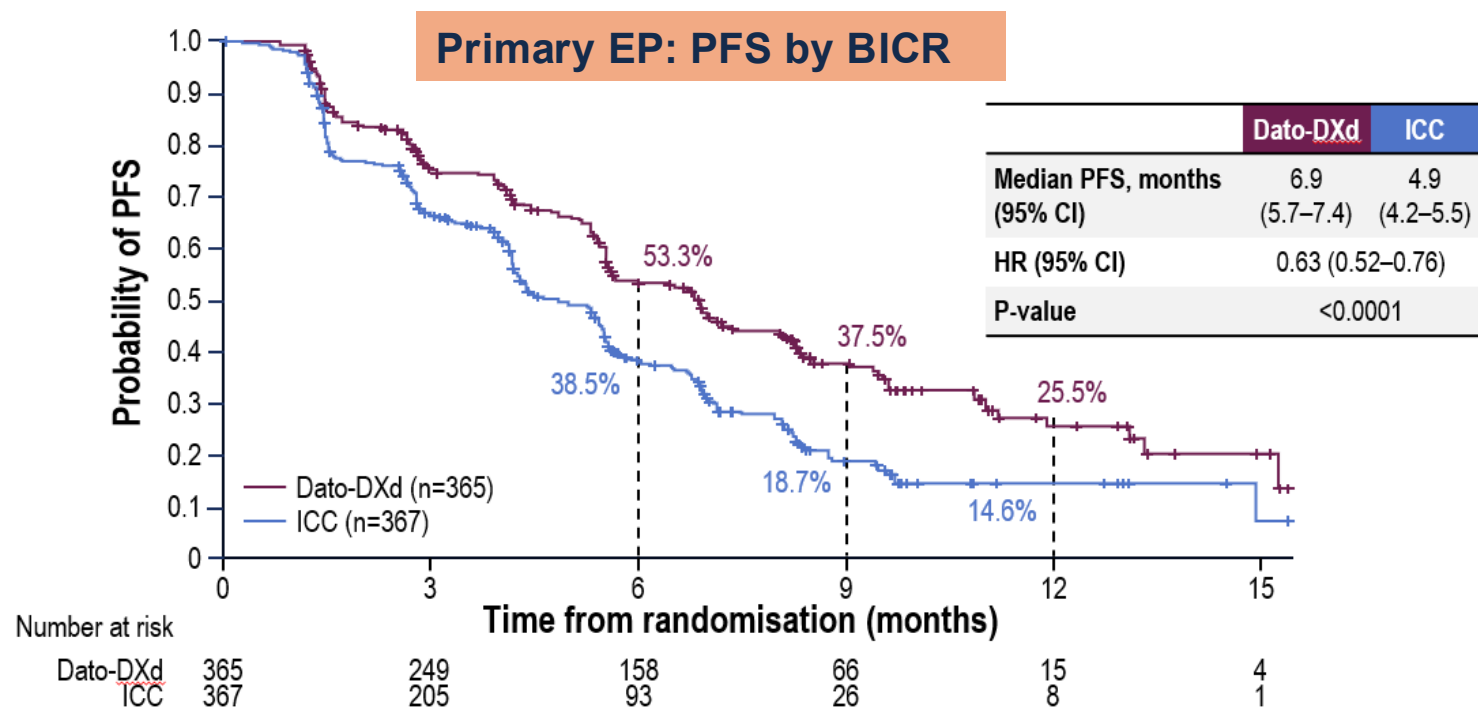
Q3W as per protocol directions†  
(eribulin mesylate, vinorelbine, capecitabine, or gemcitabine)  
(n=367)

## Endpoints:

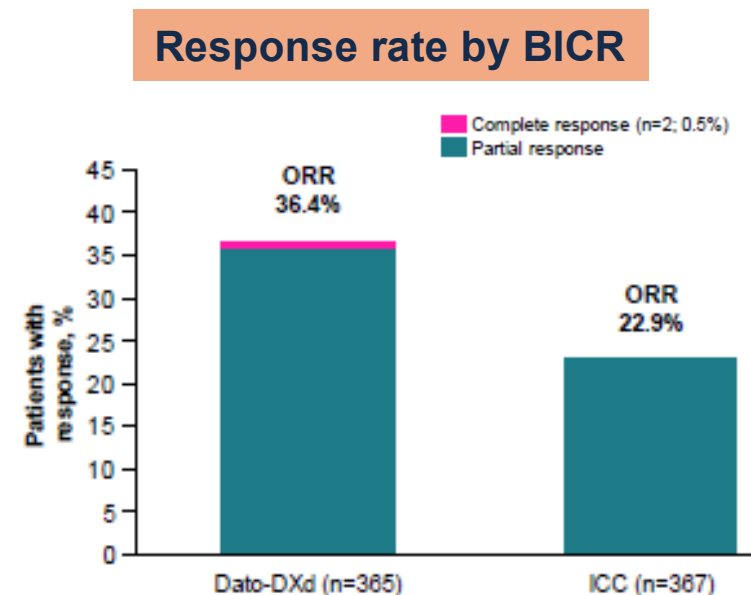
- **Dual primary:** PFS by BICR per RECIST v1.1, and OS
- **Key secondary:** ORR, PFS (investigator assessed) and safety

- High-potency TOPO1 payload
- Payload with short systemic half-life
- Optimised DAR ~4
- Tumour-selective cleavable linker
- Bystander anti-tumour effect

# TROPION-Breast01: Efficacy outcomes



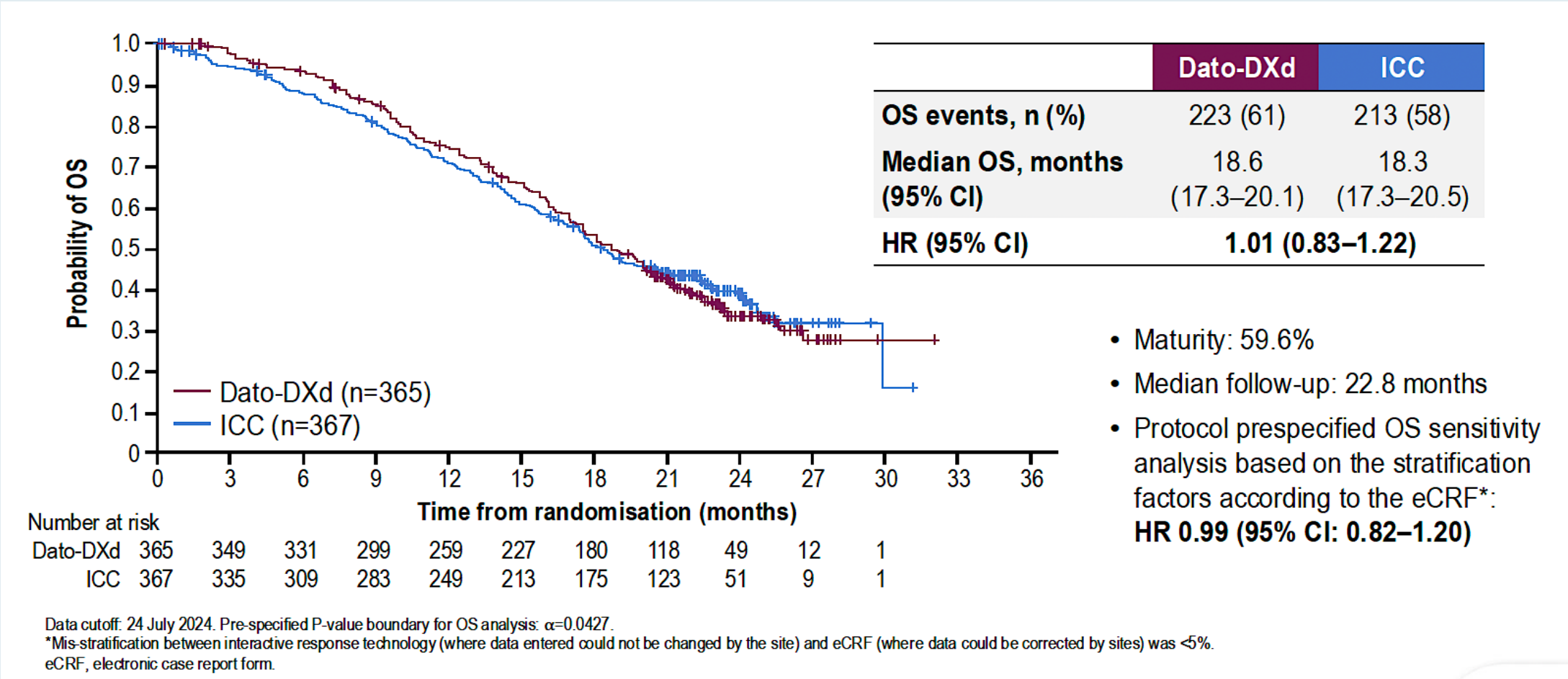
**PFS by investigator assessment:** Median 6.9 vs 4.5 months; HR 0.64 (95% CI 0.53–0.76)



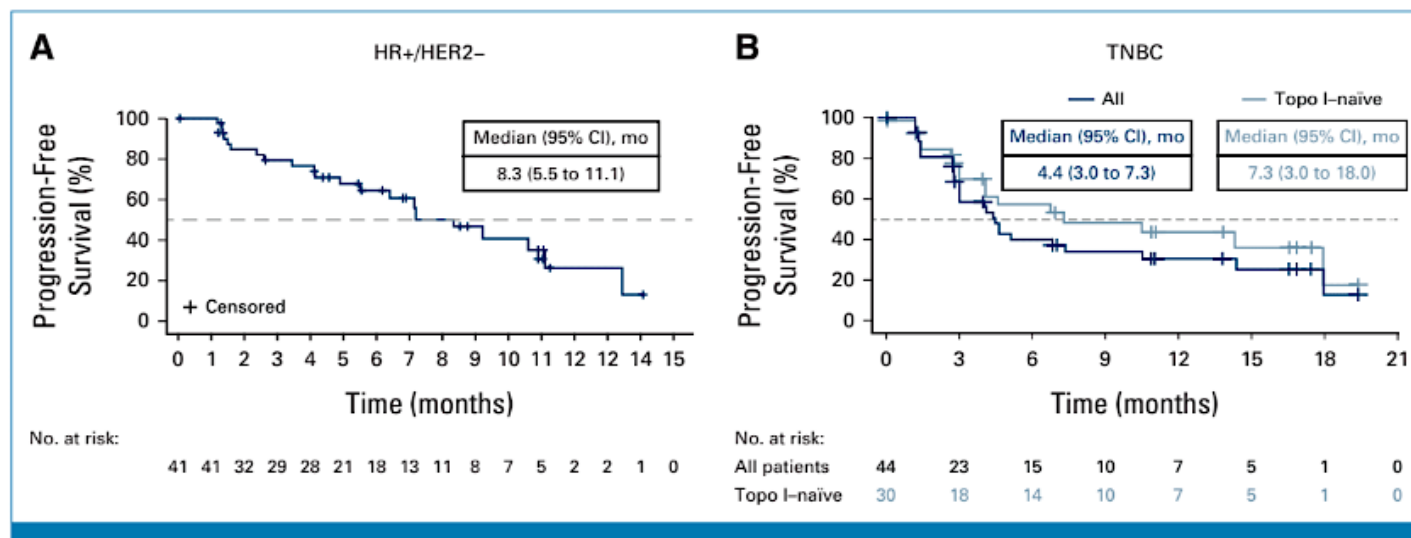
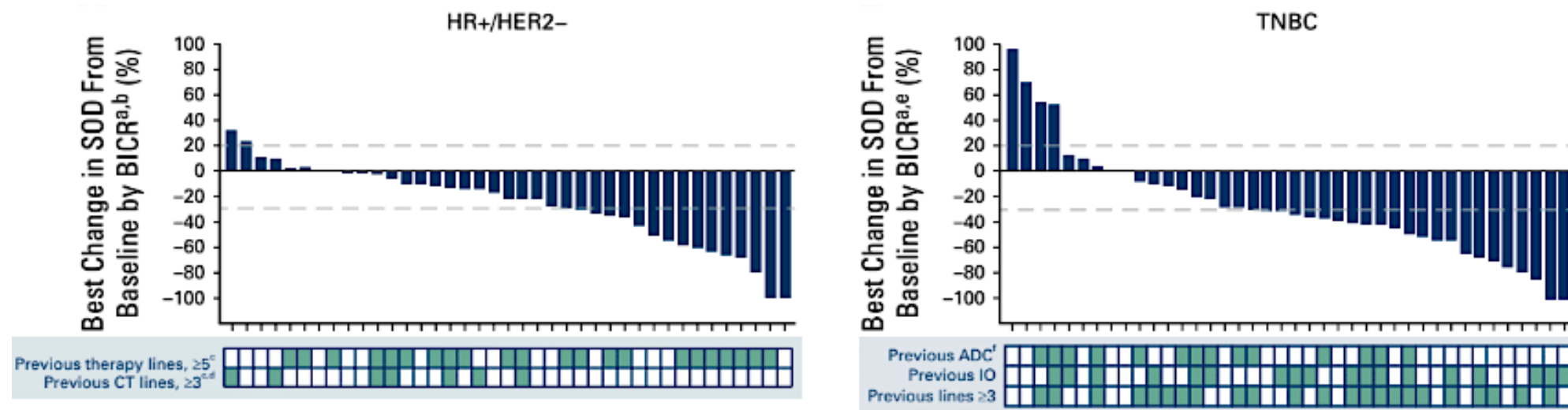
## Overall survival (dual primary endpoint)

OS data were not mature (information fraction 39%): median follow-up 9.7 months. A trend favoring Dato-DXd was observed: HR 0.84 (95% CI 0.62–1.14).

# TROPION-Breast01: Final Overall Survival Analysis with Datopotamab Deruxtecan (Dato-DXd) for Previously Treated HR-Positive mBC



# TROPION-PanTumor01: Phase 1 Dato-DXd for HR+ or TN MBC



# TROPION-PanTumor01: Phase 1 Dato-DXd for HR+ or TN MBC

| Treatment Response <sup>a</sup> | HR+/HER2- BC (N = 41)    | TNBC (N = 44)            |                          |
|---------------------------------|--------------------------|--------------------------|--------------------------|
|                                 |                          | All (N = 44)             | Topo I-Naïve (n = 30)    |
| Confirmed ORR                   | 11 (26.8) [14.2 to 42.9] | 14 (31.8) [18.6 to 47.6] | 12 (40.0) [22.7 to 59.4] |
| Confirmed CR, No. (%)           | 0                        | 1 (2.3)                  | 1 (3.3)                  |
| Confirmed PR, No. (%)           | 11 (26.8)                | 13 (29.5)                | 11 (36.7)                |
| Non-CR/non-PD, No. (%)          | 1 (2.4) <sup>b</sup>     | 3 (6.8) <sup>b</sup>     | 3 (10.0) <sup>b</sup>    |
| SD, No. (%)                     | 23 (56.1)                | 18 (40.9)                | 10 (33.3)                |
| PD, No. (%)                     | 5 (12.2)                 | 8 (18.2)                 | 4 (13.3)                 |
| NE for BOR, No. (%)             | 1 (2.4)                  | 1 (2.3)                  | 1 (3.3)                  |
| DCR                             | 35 (85.4) [70.8 to 94.4] | 35 (79.5) [64.7 to 90.2] | 25 (83.3) [65.3 to 94.4] |
| CBR <sup>c</sup>                | 18 (43.9) [28.5 to 60.3] | 17 (38.6) [24.4 to 54.5] | 15 (50.0) [31.3 to 68.7] |
| DOR, months, median [95% CI]    | NE [4.4 to NE]           | 16.8 [5.6 to NE]         | 16.8 [5.6 to NE]         |
| TTR, months, median (range)     | 2.8 (1.2-5.6)            | 1.36 (1.2-2.8)           | 1.38 (1.2-2.8)           |
| PFS, months, median [95% CI]    | 8.3 [5.5 to 11.1]        | 4.4 [3.0 to 7.3]         | 7.3 [3.0 to 18.0]        |
| OS, months, median [95% CI]     | NE [10.1 to NE]          | 13.5 [10.1 to 16.3]      | 14.3 [10.5 to NE]        |

Bardia A et al. J Clin Oncol 2024;42(19):2281-94.

# TROPION-PanTumor01: Where does Dato-DXd fit in?

|                           | HR+/HER2- MBC                         |  |                    |                                      |  |
|---------------------------|---------------------------------------|--|--------------------|--------------------------------------|--|
|                           | DESTINY-Breast06                      | DESTINY-Breast04                       | TROPION-PanTumor01 | TROPION-Breast01                     | TROPiCS-02                             |
| Treatment arms            | T-DXd vs TPC                          | T-DXd vs TPC                           | Dato-DXd           | Dato-DXd vs TPC                      | SG vs TPC                              |
| HER2 status               | Low or ultralow                       | Low (1+, 2+/ISH-)                      | Any HER2-neg       | Any HER2-neg                         | Any HER2-neg                           |
| Prior chemo for MBC       | 0                                     | 1-2                                    | No upper limit*    | 1-2                                  | 2-4                                    |
| Median PFS<br>HR (95% CI) | 13.2 vs 8.1 mo<br>HR 0.63 (0.53-0.75) | 9.6 vs 4.2 mo<br>HR 0.37 (0.30-0.56)   | 8.3 mo             | 6.9 vs 4.9 mo<br>HR 0.63 (0.52-0.76) | 5.5 vs 4.9 mo<br>HR 0.65 (0.53-0.81)   |
| Median OS<br>HR (95% CI)  | N/A<br>HR 0.81 (0.65-1.00)            | 23.9 vs 17.6 mo<br>HR 0.69 (0.55-0.87) | NE                 | N/A<br>HR 0.84 (0.62-1.14)           | 14.5 vs 11.2 mo<br>HR 0.79 (0.65-0.95) |
| ORR                       | 57.3% vs 31.2%                        | 52.6% vs 16.3%                         | 26.8%              | 36.4% vs 22.9%                       | 21% vs 14%                             |

\*median of 5 prior lines for MBC



# TROPION-PanTumor01: Where does Dato-DXd fit in?

|                           | Triple-Negative MBC                   |  |   |                                       |                                      |
|---------------------------|---------------------------------------|--|---|---------------------------------------|--------------------------------------|
|                           | DESTINY-Breast04                      | TROPION-PanTumor01                     | TROPION-Breast02  | ASCENT                                | OptiTROP-Breast01                    |
| Treatment arms            | T-DXd vs TPC                          | Dato-DXd                               | Dato-DXd vs TPC   | SG vs TPC                             | Sac-TMT vs TPC                       |
| HER2 status               | Low (1+, 2+/ISH-)                     | Any HER2-neg                           | Any HER2-neg;<br>Not a candidate for PD1/PDL1 inhibitor | Any HER2-neg                          | Any HER2-neg                         |
| Prior chemo for MBC       | 1-2                                   | No upper limit*                        | 0   | ≥1                                    | ≥2                                   |
| Median PFS<br>HR (95% CI) | 6.3 vs 2.9 mo<br>HR 0.29 (0.15-0.57)  | 4.4 mo (all)<br>7.3 mo (topo1-naïve)   | ??  | 5.6 vs 1.7 mo<br>HR 0.41 (0.32-0.52)  | 6.7 vs 2.5 mo<br>HR 0.32 (0.22-0.44) |
| Median OS<br>HR (95% CI)  | 17.1 vs 8.3 mo<br>HR 0.58 (0.31-1.08) | 13.5 mo (all)<br>14.3 mo (topo1-naïve) | ??  | 12.1 vs 6.7 mo<br>HR 0.48 (0.38-0.59) | NR vs 9.4 mo<br>HR 0.53 (0.36-0.78)  |
| ORR                       | 50.0% vs 16.7%                        | 31.8% (all)<br>40.0% (topo1-naïve)     | ??  | 35% vs 5%                             | 45.4% vs 12.0%                       |

\*median of 3 prior lines for MBC

Courtesy of Nancy U Lin, MD

## **“Beyond the Guidelines” Questions**

**A 65-year-old woman presents with de novo HR-positive, HER2-negative (IHC 0), BRCA wild-type (WT) mBC. She receives first-line ribociclib with anastrozole followed by second-line elacestrant on disease progression. Recent imaging shows evidence of asymptomatic bone and soft tissue metastases which are biopsy confirmed to be consistent with the primary. Biomarker evaluation is negative for PIK3CA/AKT1/PTEN alterations. Regulatory and reimbursement issues aside, what would be your most likely treatment?**

## “Beyond the Guidelines” Questions

**A 65-year-old woman presents with de novo HR-positive, HER2-low (IHC 1+, FISH negative), BRCA WT mBC. She receives first-line ribociclib with anastrozole followed by second-line elacestrant then trastuzumab deruxtecan on disease progression. Recent imaging shows evidence of asymptomatic bone and soft tissue metastases which are biopsy confirmed to be consistent with the primary. Biomarker evaluation is negative for PIK3CA/AKT1/PTEN alterations. Regulatory and reimbursement issues aside, what would be your most likely treatment?**

## **“Beyond the Guidelines” Questions**

**In general, what is your approach to the prevention and management of mucositis associated with datopotamab deruxtecan?**

# **ASCO 2025: Antibody-Drug Conjugates**

# Sacituzumab Govitecan with Pembrolizumab Demonstrated a Statistically Significant and Clinically Meaningful Improvement in PFS for Patients with Previously Untreated PD-L1-Positive Metastatic Triple-Negative Breast Cancer

**Press Release: April 21, 2025**

“[The manufacturer] today announced positive topline results from the Phase 3 ASCENT-04/KEYNOTE D19 study, demonstrating that sacituzumab govitecan-hziy plus pembrolizumab significantly improved progression-free survival (PFS) compared to pembrolizumab and chemotherapy in patients with inoperable (unresectable) locally advanced or metastatic triple-negative breast cancer (mTNBC) whose tumors express PD-L1 (CPS  $\geq$  10). The study met its primary endpoint, showing a statistically significant and clinically meaningful improvement in PFS.

The safety profile of sacituzumab govitecan plus pembrolizumab in the ASCENT-04 study was consistent with the known safety profile of each agent. No new safety signals were identified with the combination.”

# **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**

Tolaney S et al.

ASCO 2025;Abstract LBA109.

**SATURDAY, MAY 31 | 3:35 PM CDT**



# **A Phase 2 Study of Response-Guided Neoadjuvant Sacituzumab Govitecan and Pembrolizumab (SG/P) in Patients with Early-Stage Triple-Negative Breast Cancer: Results from the NeoSTAR Trial**

Abelman R et al.

ASCO 2025;Abstract 511.

**SUNDAY, JUNE 1 | 8:12 AM CDT**

# Exploratory Biomarker Analysis of Trastuzumab Deruxtecan (T-DXd) vs Physician's Choice of Chemotherapy (TPC) in HER2-Low/Ultralow, Hormone Receptor-Positive (HR+) Metastatic Breast Cancer (mBC) in DESTINY-Breast06 (DB-06)

Dent R et al.

ASCO 2025;Abstract 1013.

**SATURDAY, MAY 31 | 3:23 PM CDT**

# Use of Artificial Intelligence-Assistance Software for HER2-Low and HER2-Ultralow IHC Interpretation Training to Improve Diagnostic Accuracy of Pathologists and Expand Patients' Eligibility for HER2-Targeted Treatment

De Brot M et al.

ASCO 2025;Abstract 1014.

**FRIDAY, MAY 30 | 2:51 PM CDT**

# Patritumab Deruxtecan (HER3-DXd) in Active Brain Metastases (BM) from Metastatic Breast (mBC) and Non-Small Cell Lung Cancers (aNSCLC), and Leptomeningeal Disease (LMD) from Advanced Solid Tumors: Results from the TUXEDO-3 Phase II Trial

Preusser M et al.

ASCO 2025;Abstract 2005.

**FRIDAY, MAY 30 | 4:09 PM CDT**

# **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**

Yin Y et al.

ASCO 2025;Abstract 1019.

**FRIDAY, MAY 30 | 3:45 PM CDT**

# AGENDA

## Year in Review: Management of Breast Cancer

**INTRODUCTION:** Adjuvant CDK4/6 Inhibition

**MODULE 1:** HER2-Positive Disease

**MODULE 2:** PARP Inhibition

**MODULE 3:** Antibody-Drug Conjugates

**MODULE 4:** Up-Front Treatment of HR-Positive Metastatic Disease

# **Optimizing Therapy for Patients with Hormone Receptor-Positive Metastatic Breast Cancer Harboring PI3K/AKT/PTEN Pathway Abnormalities**

## **Beyond the Guidelines Survey**



## Breast Cancer Survey Respondents

Aditya Bardia, MD, MPH

Virginia F Borges, MD, MMSc

Adam M Brufsky, MD, PhD

Harold J Burstein, MD, PhD

Karen A Gelmon, MD

Stephanie L Graff, MD, FACP

Sara A Hurvitz, MD, FACP

Komal Jhaveri, MD, FACP

Virginia Kaklamani, MD, DSc

Kevin M Kalinsky, MD, MS

Ian E Krop, MD, PhD

Erica Mayer, MD, MPH, FASCO

Kathy D Miller, MD

Ruth O'Regan, MD

Joyce A O'Shaughnessy, MD

Lajos Pusztai, MD, DPhil, FASCO

Hope S Rugo, MD

Priyanka Sharma, MD

Paolo Tarantino, MD

Sara M Tolaney, MD, MPH

Seth Wander, MD, PhD

A 65-year-old woman with ER-positive, HER2-negative (HER2 IHC 0), node-negative breast cancer has developed multiple metastases 2 years after starting adjuvant anastrozole.

ESR1 mutation-negative      PIK3CA mutation-negative      AKT1 and PTEN mutation-negative

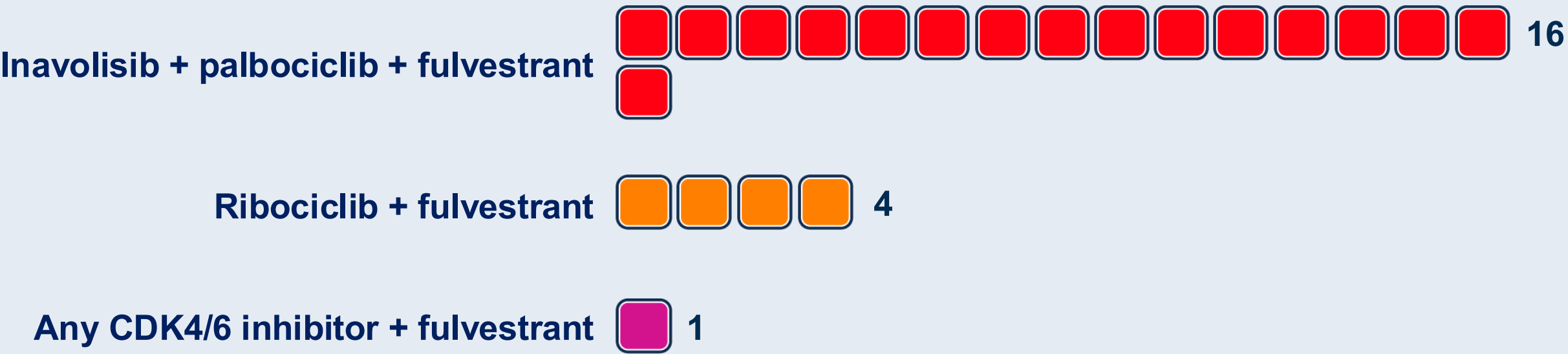


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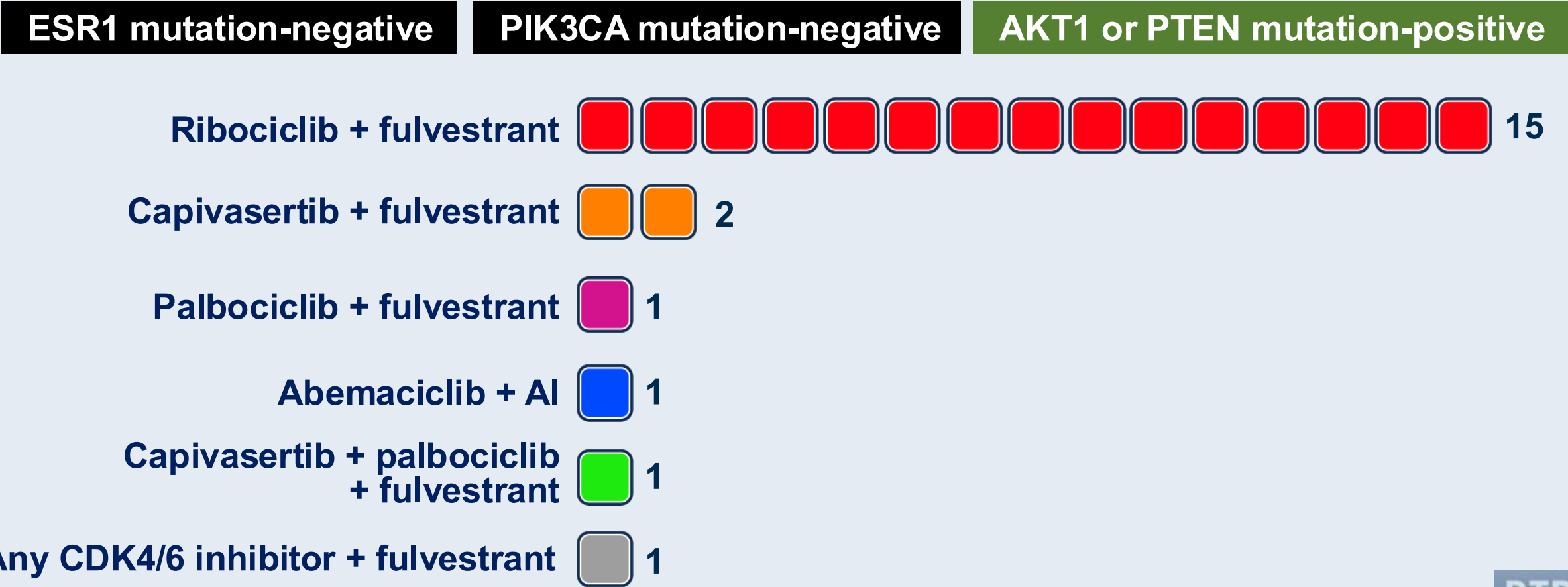
ESR1 mutation-negative

PIK3CA mutation-positive

AKT and PTEN mutation-negative



A 65-year-old woman with ER-positive, HER2-negative (HER2 IHC 0), node-negative breast cancer has developed multiple metastases 2 years after starting adjuvant anastrozole.

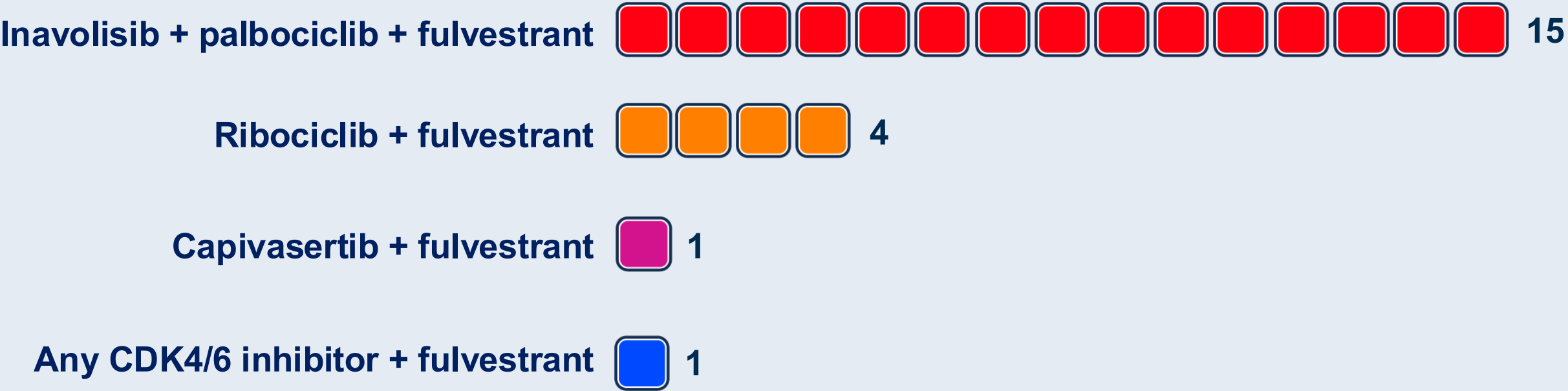


A 65-year-old woman with ER-positive, HER2-negative (HER2 IHC 0), node-negative breast cancer has developed multiple metastases 2 years after starting adjuvant anastrozole.

ESR1 mutation-positive

PIK3CA mutation-positive

AKT1 and PTEN mutation-negative

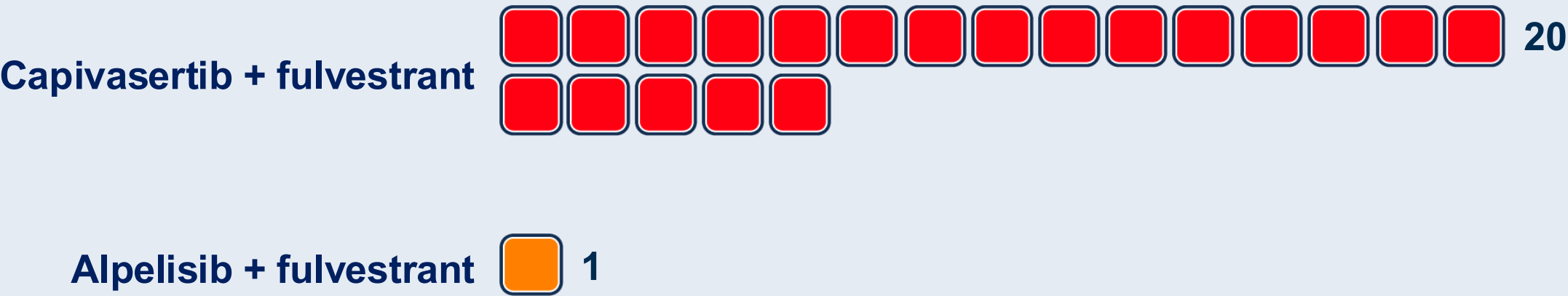


A 65-year-old woman with ER-positive, HER2-negative (HER2 IHC 0), node-negative mBC receives a CDK4/6 inhibitor with an AI and initially responds but then experiences disease progression 18 months later.

ESR1 mutation-negative

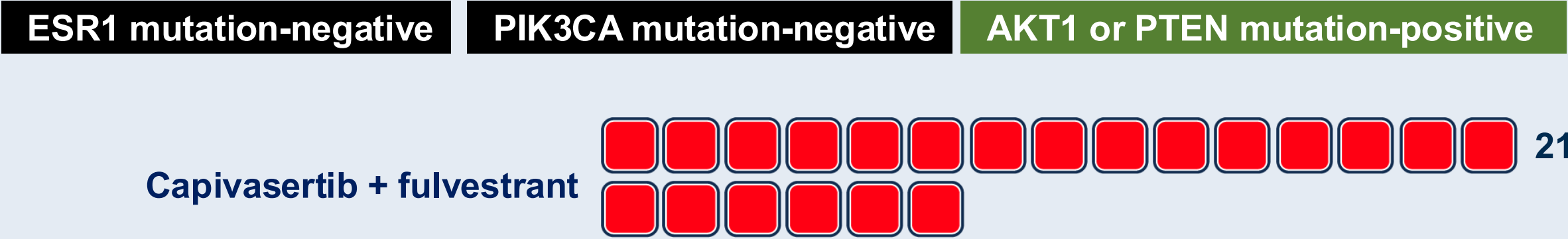
PIK3CA mutation-positive

AKT1 and PTEN mutation-negative



AI = aromatase inhibitor

A 65-year-old woman with ER-positive, HER2-negative (HER2 IHC 0), node-negative mBC receives a CDK4/6 inhibitor with an AI and initially responds but then experiences disease progression 18 months later.



A 65-year-old woman with ER-positive, HER2-negative (HER2 IHC 0), node-negative mBC receives a CDK4/6 inhibitor with an AI and initially responds but then experiences disease progression 18 months later.

ESR1 mutation-positive

PIK3CA mutation-positive

AKT1 and PTEN mutation-negative

Capivasertib + fulvestrant



Elacestrant



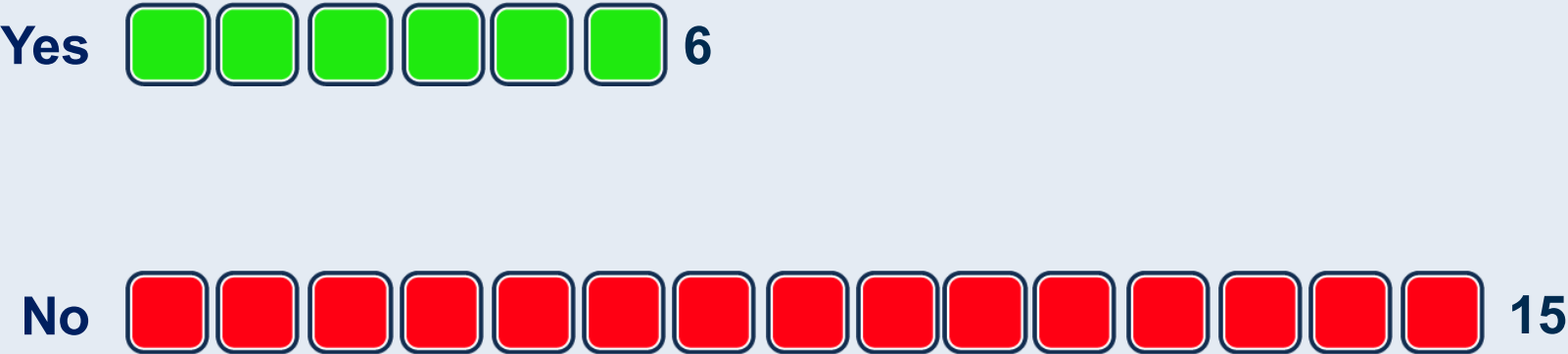
Other\*



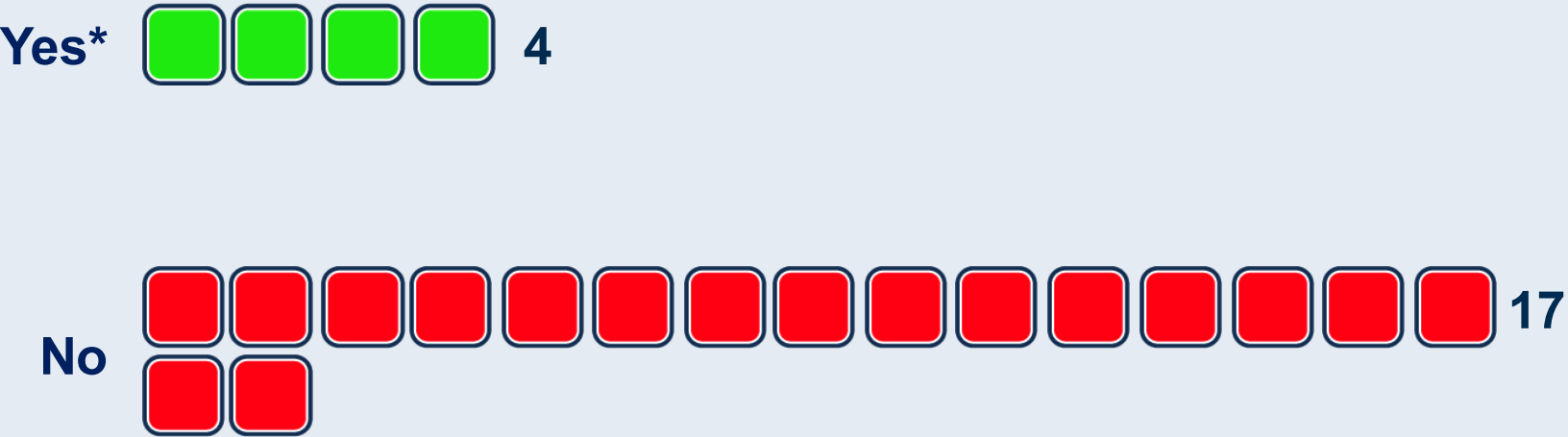
\* Depends on extent of progression: Elacestrant if progression is less aggressive/asymptomatic, capivasertib + fulvestrant or combined with ET if progression is more aggressive/asymptomatic



Would you administer alpelisib and capivasertib in sequence to the same patient?



For patients about to receive capiwasertib, do you take any prophylactic measures to prevent hyperglycemia?



\* Check HbA1C, finger stick blood glucose, dietary education, metformin

Survey of 21 US-based breast cancer clinical investigators, October 2024

For patients about to receive capivasertib, do you take any prophylactic measures to prevent cutaneous reactions?

Yes\*  11

No  10

\* Antihistamines

Survey of 21 US-based breast cancer clinical investigators, October 2024

For patients about to receive capiwasertib, do you take any prophylactic measures to prevent gastrointestinal toxicity?

Yes\*  6

No  15

\* Loperamide/antidiarrheal agents

Survey of 21 US-based breast cancer clinical investigators, October 2024

# **ASCO 2025: HR-Positive Breast Cancer**

# First-Line Camizestrant Demonstrated Highly Statistically Significant and Clinically Meaningful Improvement in PFS for Advanced HR-Positive Breast Cancer with an Emergent ESR1 Tumor Mutation in the SERENA-6 Phase III Trial

Press Release: February 26, 2025

“Positive high-level results from a planned interim analysis of the SERENA-6 Phase III trial showed that camizestrant in combination with a cyclin-dependent kinase (CDK) 4/6 inhibitor (palbociclib, ribociclib or abemaciclib) demonstrated a highly statistically significant and clinically meaningful improvement in the primary endpoint of progression-free survival (PFS). The trial evaluated switching to the camizestrant combination versus continuing standard-of-care treatment with an aromatase inhibitor (AI) (anastrozole or letrozole) in combination with a CDK4/6 inhibitor in the 1st-line treatment of patients with hormone receptor (HR)-positive, HER2-negative advanced breast cancer whose tumors have an emergent ESR1 mutation.

The key secondary endpoints of time to second disease progression (PFS2) and overall survival (OS) were immature at the time of this interim analysis. However, the camizestrant combination demonstrated a trend toward improvement in PFS2. The trial will continue as planned to further assess key secondary endpoints.”

# **Camizestrant + CDK4/6 Inhibitor (CDK4/6i) for the Treatment of Emergent ESR1 Mutations During First-Line (1L) Endocrine-Based Therapy (ET) and Ahead of Disease Progression in Patients (pts) with HR+/HER2-Advanced Breast Cancer (ABC): Phase 3, Double-Blind ctDNA-Guided SERENA-6 Trial**

Turner N et al.

ASCO 2025;Abstract LBA4.

**Plenary | SUNDAY, JUNE 1 | 2:41 PM CDT**

# Patient-Reported Outcomes (PROs) in Patients with ER+, HER2- Advanced Breast Cancer (ABC) Treated with Imlunestrant, Investigator's Choice Standard Endocrine Therapy, or Imlunestrant + Abemaciclib: Results from the Phase III EMBER-3 Trial

Curigliano G et al.

ASCO 2025;Abstract 1001.

**SATURDAY, MAY 31 | 1:27 PM CDT**



# Vepdegestrant, A PROTAC Estrogen Receptor (ER) Degradar, vs Fulvestrant in ER-Positive/Human Epidermal Growth Factor Receptor 2 (HER2)-Negative Advanced Breast Cancer: Results of the Global, Randomized, Phase 3 VERITAC-2 Study

Hamilton E et al.

ASCO 2025;Abstract LBA1000.

**SATURDAY, MAY 31 | 1:15 PM CDT**

# **INAVO120: Phase III Trial Final Overall Survival (OS) Analysis of First-Line Inavolisib (INAVO)/Placebo (PBO) + Palbociclib (PALBO) + Fulvestrant (FULV) in Patients (pts) with PIK3CA-Mutated, Hormone Receptor-Positive (HR+), HER2-Negative (HER2-), Endocrine-Resistant Advanced Breast Cancer (aBC)**

Turner N et al.

ASCO 2025;Abstract 1003.

**SATURDAY, MAY 31 | 2:07 PM CDT**

# Phase I/Ib Study of Inavolisib (INAVO) Alone and in Combination with Endocrine Therapy $\pm$ Palbociclib (PALBO) in Patients (pts) with PIK3CA-Mutated, Hormone Receptor-Positive, HER2-Negative Locally Advanced/Metastatic Breast Cancer (HR+, HER2-LA/mBC): Analysis of Hyperglycemia (HG) in Prediabetic/Obese Patients

Oliveira M et al.

ASCO 2025;Abstract 1004.

**SATURDAY, MAY 31 | 2:19 PM CDT**

# **A Double-Blind Placebo Controlled Randomized Phase III Trial of Fulvestrant and Ipatasertib as Treatment for Advanced HER-2 Negative and Estrogen Receptor Positive (ER+) Breast Cancer Following Progression on First Line CDK 4/6 Inhibitor and Aromatase Inhibitor: The CCTG/BCT MA.40/FINER Study (NCT04650581)**

Chia S et al.

ASCO 2025;Abstract LBA1005.

**SATURDAY, MAY 31 | 2:31 PM CDT**

# 15-Year Outcomes for Women with Premenopausal Hormone Receptor-Positive Early Breast Cancer (BC) in the SOFT and TEXT Trials Assessing Benefits from Adjuvant Exemestane (E) + Ovarian Function Suppression (OFS) or Tamoxifen (T)+OFS

Francis P et al.

ASCO 2025;Abstract 505.

**MONDAY, JUNE 2 | 4:48 PM CDT**

# **ASCO 2025: Other Topics**

# A Randomized Controlled Trial of Cognitive Behavioral Therapy and Bright Light Therapy for Insomnia and Fatigue During Breast Cancer Treatment: SleepCaRe Trial

Wiley J et al.

ASCO 2025;Abstract 12009.

**SUNDAY, JUNE 1 | 9:45 AM CDT**

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

## **Management of Multiple Myeloma**

*A CME/MOC-Accredited Live Webinar*

**Thursday, May 8, 2025**

**5:00 PM – 6:00 PM ET**

### **Faculty**

**Meletios-Athanasios (Thanos) C Dimopoulos, MD**

**Robert Z Orlowski, MD, PhD**

### **Moderator**

**Neil Love, MD**



*Thank you for joining us!*

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