The Implications of Recent Datasets for the Current and Future Management of Breast Cancer — An ASCO 2025 Review

A CME/MOC-Accredited Live Webinar

Wednesday, August 13, 2025
5:00 PM – 6:00 PM ET

Faculty

Sara A Hurvitz, MD, FACP
Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

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Faculty

Sara A Hurvitz, MD, FACP
Professor of Medicine
Smith Family Endowed Chair in Women's Health
Senior Vice President, Clinical Research Division
Fred Hutchinson Cancer Center
Head, Division of Hematology/Oncology
Department of Medicine
UW Medicine
Seattle, Washington

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

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Dr Love — Disclosures

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Data and Safety Monitoring Boards/Committees	Atossa Therapeutics
Nonrelevant Financial Relationships	InClin, Quantum Leap Healthcare Collaborative

Dr Tolaney — Disclosures

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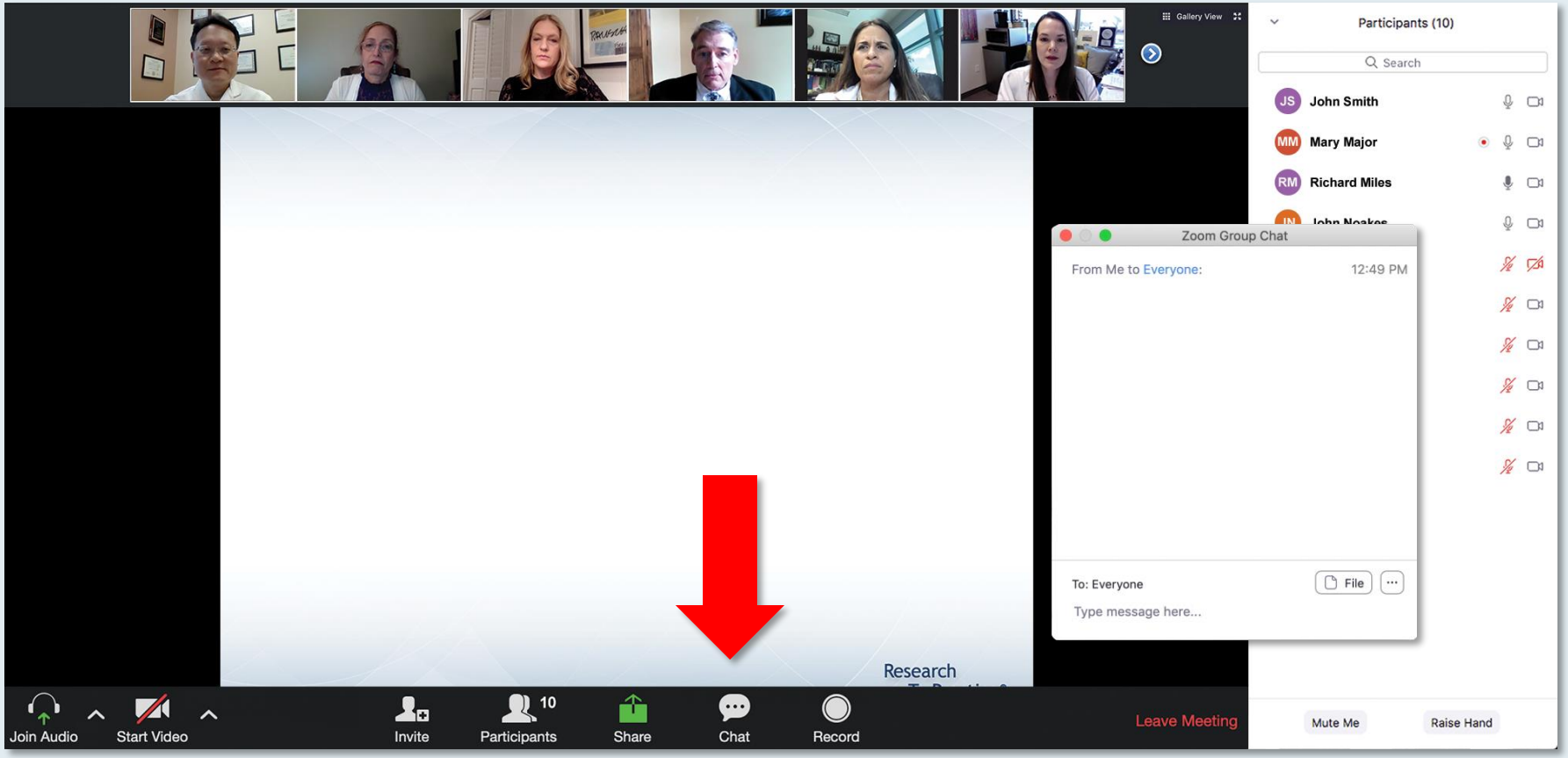

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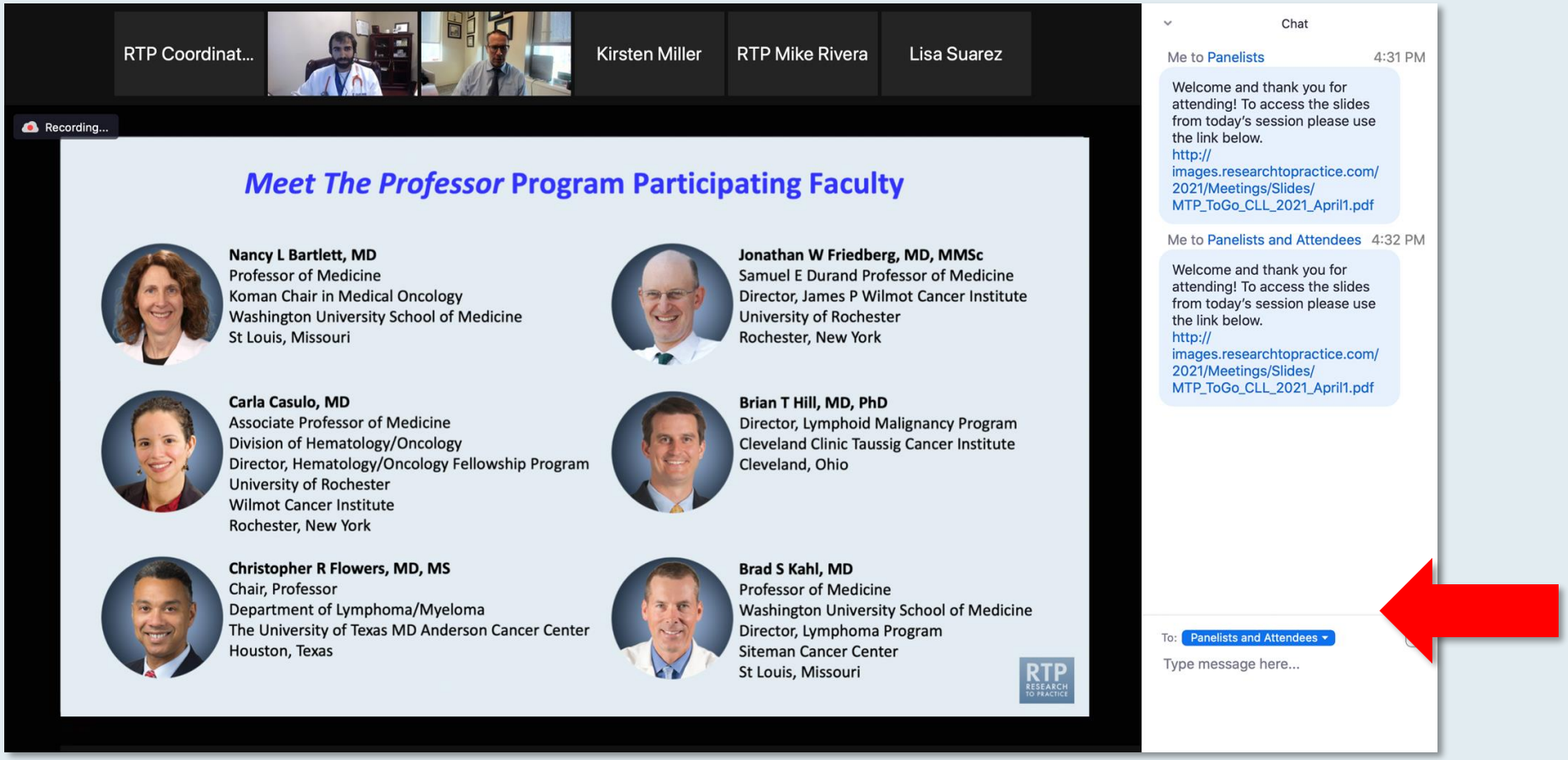

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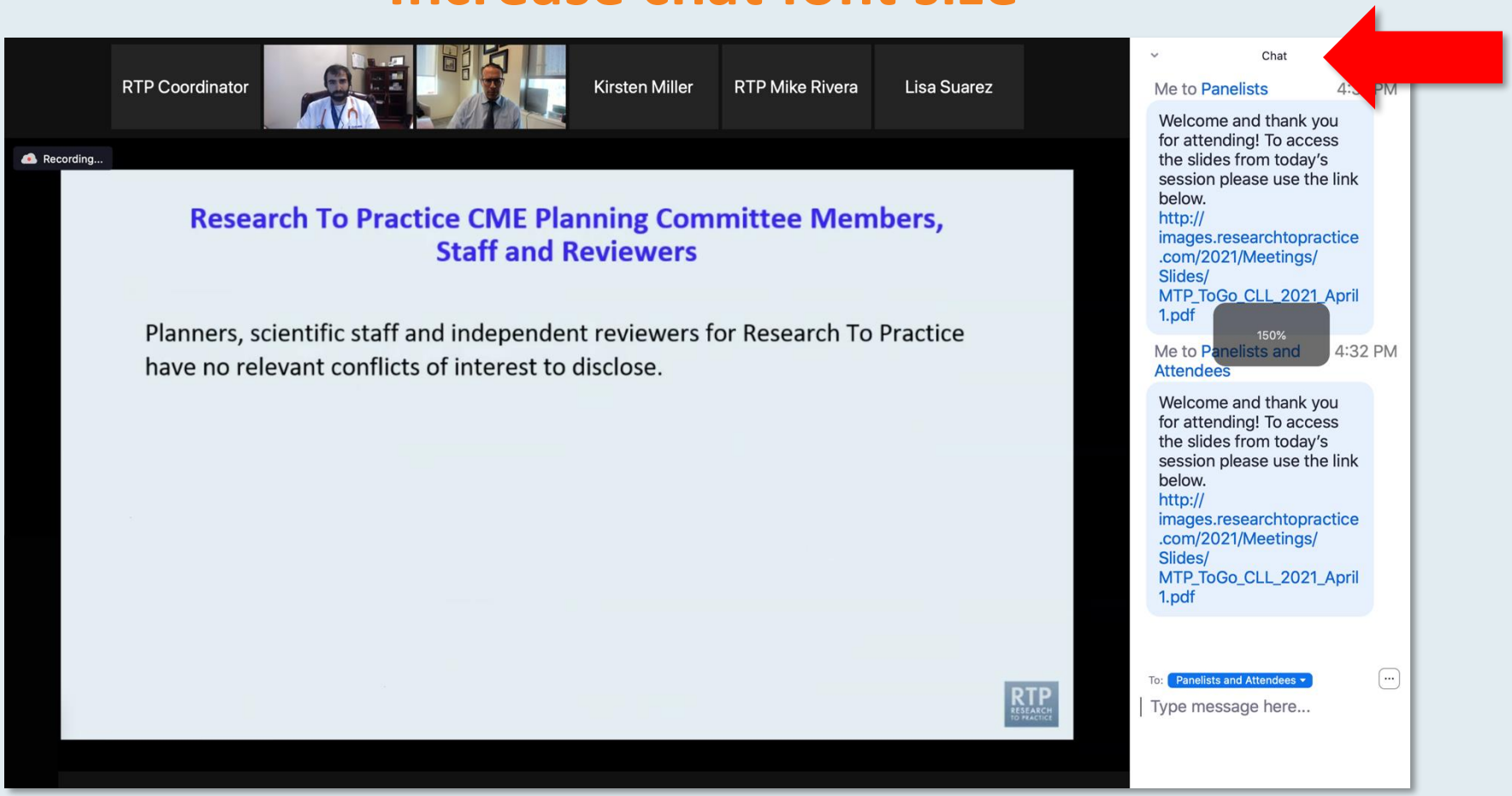

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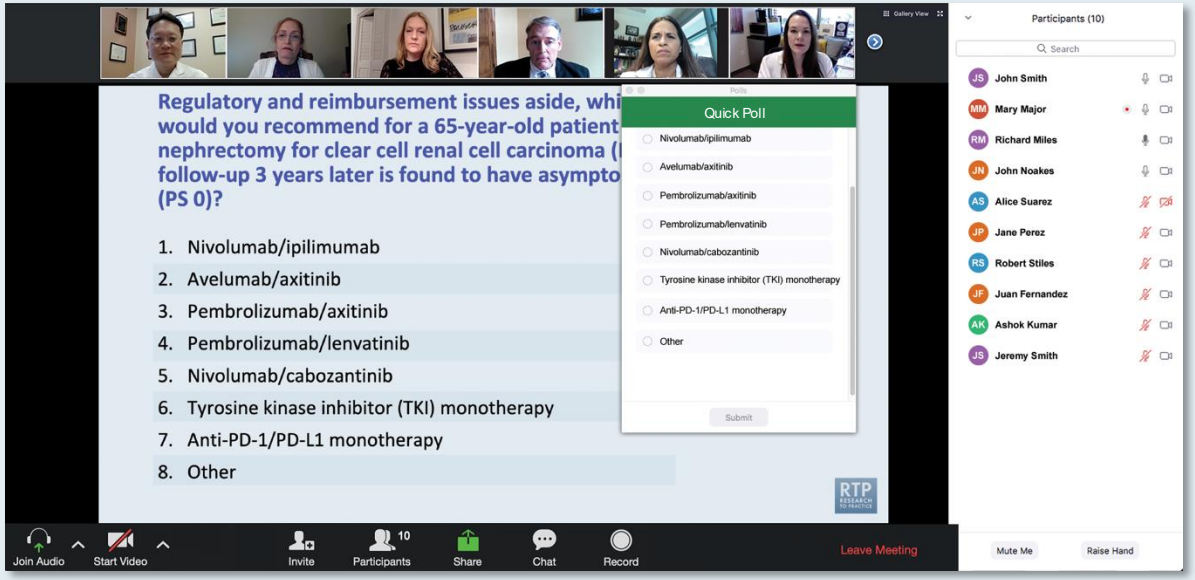

Breast Cancer — 5-Minute Journal Club Issue 1 with Dr Erika Hamilton: Defining the Role of TROP2-Directed Antibody-Drug Conjugates

DR ERIKA HAMILTON
SARAH CANNON RESEARCH INSTITUTE

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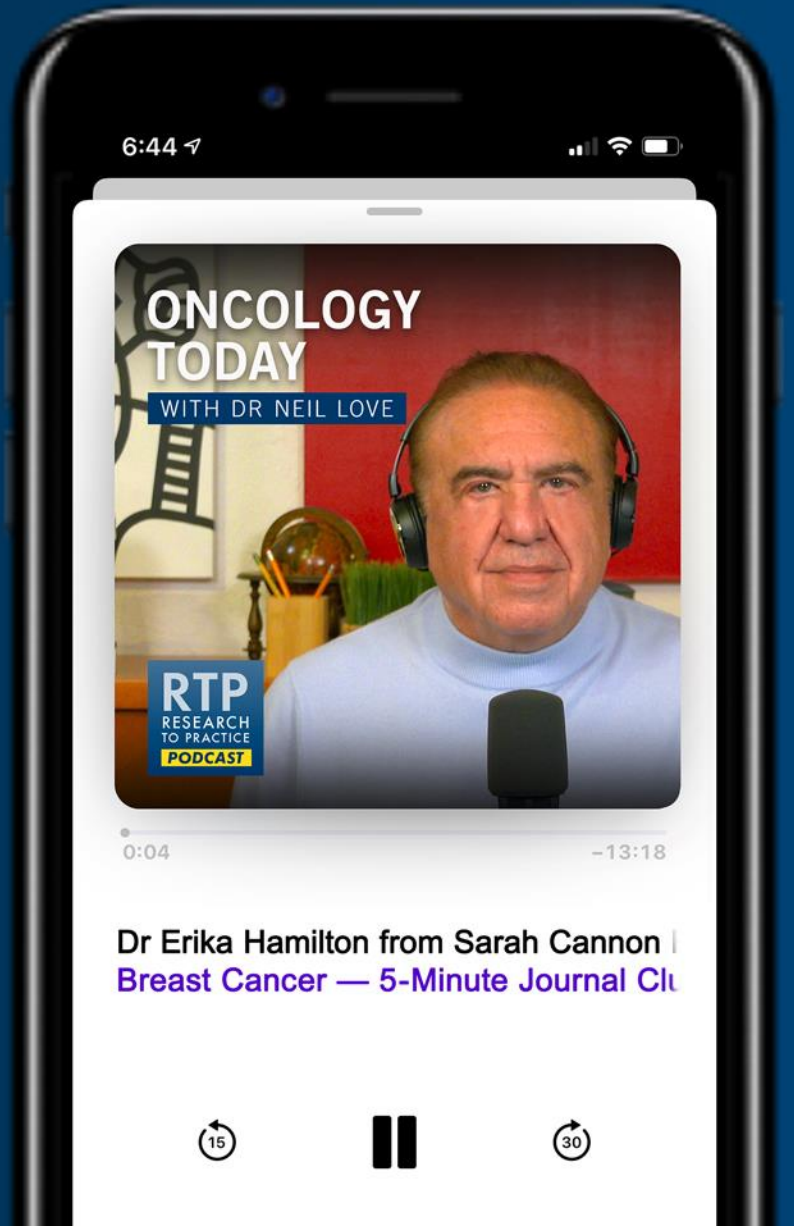

Selection and Sequencing of Therapy for Metastatic Triple-Negative Breast Cancer

A CME/MOC-Accredited Live Webinar

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

Faculty

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

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

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

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

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

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

Moderator

Joseph Mikhael, MD, MEd

RTP RESEARCH TO PRACTICE

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Friday, September 5, 2025

11:47 AM – 12:47 PM CT

Faculty

Jennifer Crombie, MD

Laurie H Sehn, MD, MPH

Moderator

Jeremy S Abramson, MD, MMSc

RTP RESEARCH TO PRACTICE

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

A CME/MOC-Accredited Live Webinar

Wednesday, October 29, 2025

5:00 PM – 6:00 PM ET

Faculty

Rinath M Jeselsohn, MD

Joyce O'Shaughnessy, MD

Moderator

Neil Love, MD

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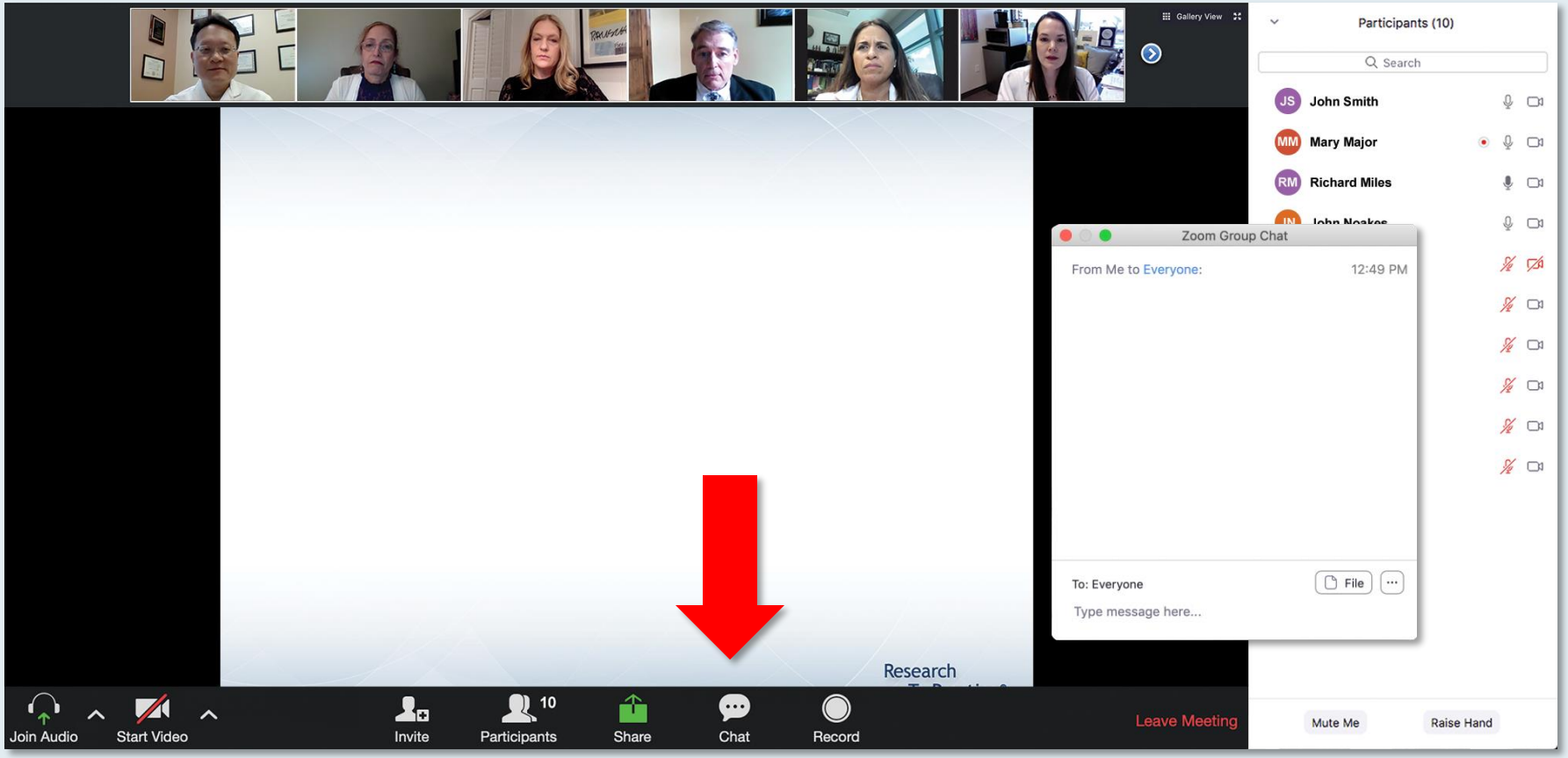

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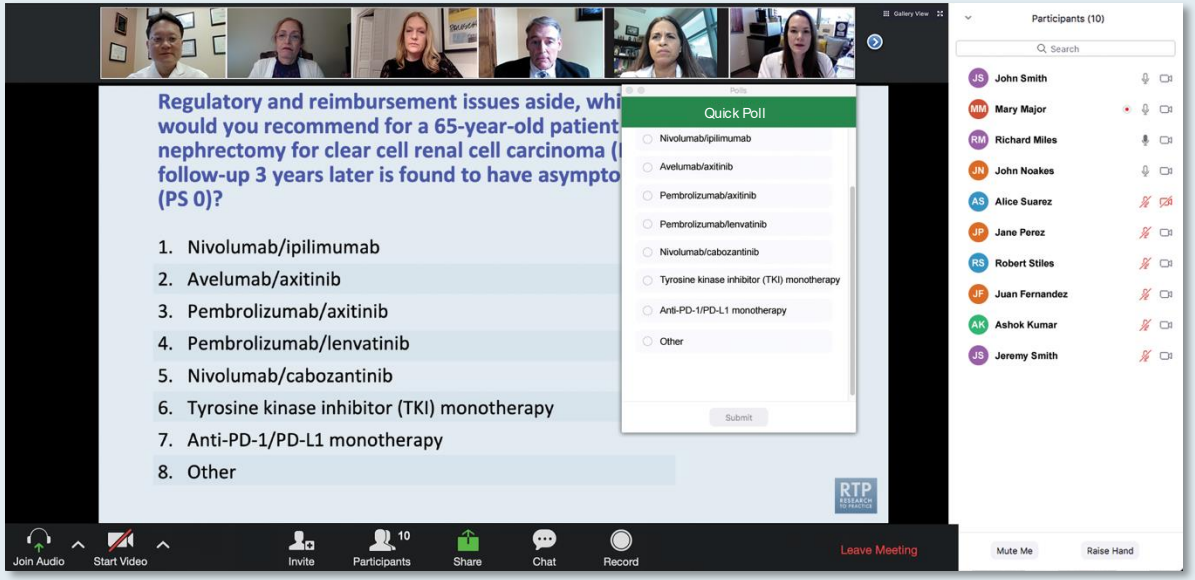

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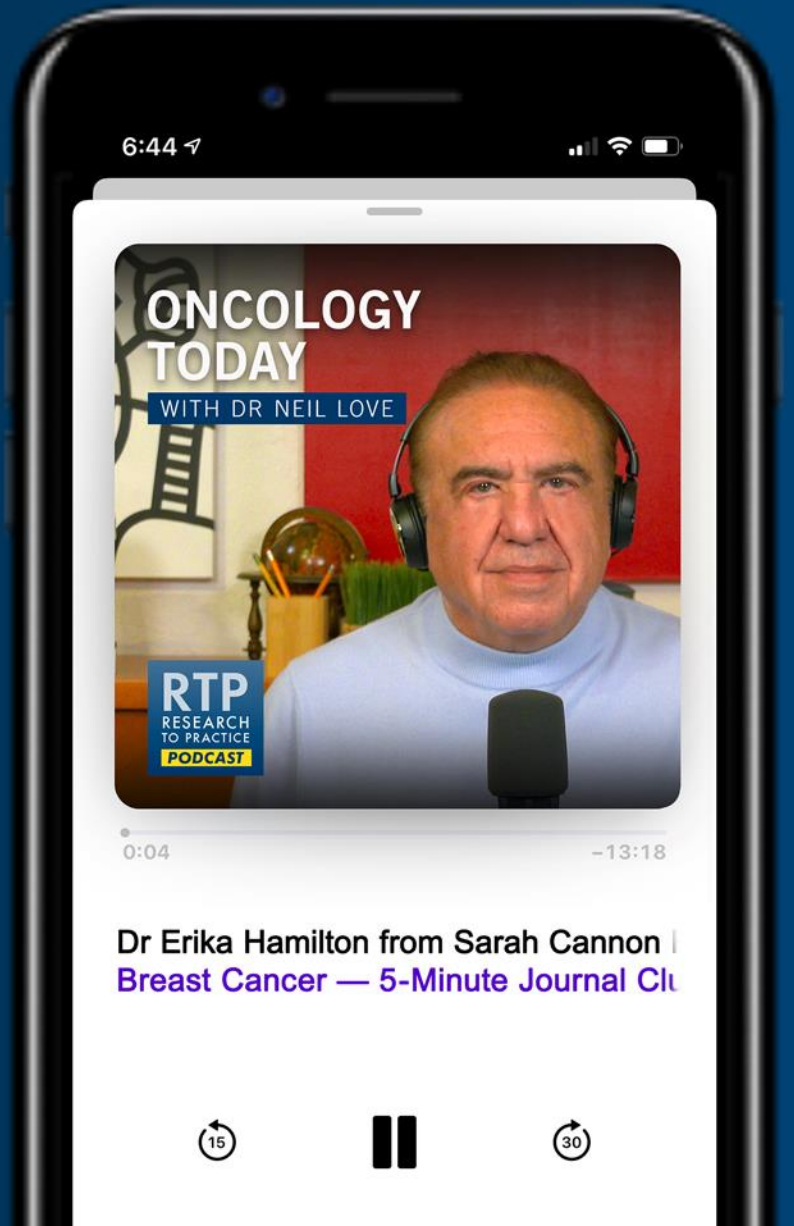

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Key Datasets

Sara A Hurvitz, MD, FACP

- Kalinsky K et al. Efficacy and safety of **ribociclib** (RIB) + **nonsteroidal aromatase inhibitor** (NSAI) in **NATALEE**: Analysis across **menopausal status and age**. ASCO 2025;Abstract 516.
- Mayer EL et al. The **TRADE** study: A phase 2 trial to assess the tolerability of **abemaciclib dose escalation** in **early-stage HR+/HER2-** breast cancer. ASCO 2025;Abstract 517.
- El Saghir NS et al. **First-line** (1L**) ribociclib** (RIB) + **endocrine therapy** (ET) vs combination chemotherapy (combo CT) in clinically aggressive **hormone receptor (HR)+/HER2–** advanced breast cancer (ABC): A subgroup analysis of patients (pts) **with or without liver metastases** (mets) from **RIGHT Choice**. ASCO 2025;Abstract 1069.
- Turner NC et al. 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). ASCO 2025;Abstract 1003.
- Turner NC et al. **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. ASCO 2025;Abstract LBA4.
- Curigliano G et al. **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. ASCO 2025;Abstract 1001.

Key Datasets

Sara A Hurvitz, MD, FACP

- O'Shaughnessy J et al. **Imlunestrant** with or without **abemaciclib** in advanced breast cancer (ABC): **Safety** analyses from the phase III **EMBER-3** trial. ASCO 2025;Abstract 1060.
- Turner NC et al. **Capivasertib** in **hormone receptor-positive** advanced breast cancer. *N Engl J Med* 2023;388(22):2058-70.
- Hamilton EP et al. **Vepdegestrant**, a PROTAC estrogen receptor (ER) degrader, 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. ASCO 2025;Abstract LBA1000.
- Dent RA et al. 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). ASCO 2025;Abstract 1013.
- De Brot M et al. 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. ASCO 2025;Abstract 1014.
- 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.

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- Tolaney SM et al. **Trastuzumab deruxtecan** (T-DXd) + **pertuzumab** (P) vs taxane + trastuzumab + pertuzumab (THP) for **first-line** (1L) treatment of patients (pts) with human epidermal growth factor receptor 2–positive **(HER2+)** advanced/metastatic breast cancer (a/mBC): Interim results from **DESTINY-Breast09**. ASCO 2025;Abstract LBA1008.
- Rugo HS et al. Treatment **rechallenge** after **trastuzumab-deruxtecan**–related **interstitial lung disease**: A multi-institution cohort study. ASCO 2025;Abstract 1015.
- Sammons SL et al. **Brain metastases** in metastatic breast cancer: **Prevalence per line of treatment** and cumulative incidence in a cohort of 18075 real-world patients. SABCS 2023;Abstract PS11-01.
- Lin NU et al. **Tucatinib** versus placebo added to **trastuzumab and capecitabine** for patients with **previously treated HER2+** metastatic breast cancer **with brain metastases (HER2CLIMB**). ASCO 2020;Abstract 1005.
- Lin NU et al. **Trastuzumab deruxtecan** (T-DXd) in patients (pts) with **HER2+** advanced/metastatic breast cancer (mBC) **with or without brain metastases** (BM): **DESTINYBreast-12** primary results. ESMO 2024; Abstract LBA18.
- Gao H-F et al**. De-escalated neoadjuvant** taxane plus trastuzumab and pertuzumab with or without carboplatin **in HER2-positive early breast cancer** (neoCARHP): A multicentre, open-label, randomised, phase 3 trial. ASCO 2025;Abstract LBA500.
- Garber J et al. **OlympiA:** A phase 3, multicenter, randomized, placebo-controlled trial of **adjuvant olaparib** after (neo)adjuvant chemotherapy in patients with **germline BRCA1 and/or BRCA2** pathogenic variants and **high risk HER2-negative** primary breast cancer: Longer term follow-up. SABCS 2024;Abstract GS1-09.

Key Datasets

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- Singer CF et al. 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. ASCO 2025;Abstract 510.
- Tolaney SM et al. **Sacituzumab govitecan** (SG) + **pembrolizumab** (pembro) vs chemotherapy (chemo) + pembro in **previously untreated PD-L1–positiv**e advanced **triple-negative breast cancer** (TNBC): Primary results from the randomized phase 3 **ASCENT-04/KEYNOTE-D19** study. ASCO 2025;Abstract LBA109.
- 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.
- O'Shaughnessy J et al. **HERTHENA-Breast03**: A phase 2, randomized, open-label study evaluating **neoadjuvant patritumab deruxtecan** + **pembrolizumab** before or after pembrolizumab + chemotherapy for **early-stage TNBC** or **HR-low+/HER2–** breast cancer. ASCO 2025;Abstract 629.

Agenda

Introduction: View from Outer Space

Module 1: Hormone Receptor (HR)-Positive Breast Cancer

Module 2: HER2-Positive Breast Cancer

Module 3: Triple-Negative Breast Cancer

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Agenda

Introduction: View from Outer Space

Module 1: HR-Positive Breast Cancer

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Post-ASCO Review

Sara A. Hurvitz, MD, FACP

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Head, Division of Hematology/Oncology,
University of Washington School of Medicine
Senior Vice President, Clinical Research Division,
Fred Hutchinson Cancer Center

Fred Hutch Cancer Center

UNIVERSITY of WASHINGTON

NATALEE Outcome by Menopausal Status/Age

- Adult pts with HR+/HER2− EBC
- Prior ET allowed ≤12 mo prior to randomization
- **Anatomical stage IIA**[a]
  - **N0** with:
    - Grade 2 and evidence of high risk:
      - Ki-67 ≥20%
      - Oncotype DX Breast Recurrence Score ≥26 ***or***
      - High risk via genomic risk profiling
    - Grade 3
  - **N1**
- **Anatomical stage IIB**[a]
  - N0 or N1
- **Anatomical stage III**
  - N0, N1, N2, or N3

N = 5101[b]

R 1:1[c]

RIB
400 mg/day
3 weeks on/1 week off
for 3 years

+

NSAI
Letrozole or anastrozole[d]
for ≥5 years
+ goserelin in men and premenopausal women

NSAI
Letrozole or anastrozole[d]
for ≥5 years
+ goserelin in men and premenopausal women

Primary end point
- iDFS using STEEP criteria

Secondary end points
- Recurrence-free survival
- Distant disease–free survival
- OS
- Safety and tolerability
- PROs
- PK

End points included in this presentation

Statistical comparisons were performed using a Cox proportional hazards model and the Kaplan-Meier method

Randomization stratification
Anatomical stage: II vs III
Menopausal status: men and premenopausal women vs postmenopausal women
Receipt of prior (neo)adjuvant chemotherapy: yes vs no
Geographic location: North America/Western Europe/Oceania vs rest of world

Data cutoff: April 29, 2024

ctDNA/RNA, circulating tumor DNA/RNA; EBC, early breast cancer; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; iDFS, invasive disease–free survival; NSAI, nonsteroidal aromatase inhibitor; OS, overall survival; PK, pharmacokinetics; PRO, patient-reported outcome; pt, patient; R, randomized; RIB, ribociclib; STEEP, Standardized Definitions for Efficacy End Points in Adjuvant Breast Cancer Trials.
[a] Enrollment of pts with stage II disease was capped at 40%. [b] 5101 pts were randomized from January 10, 2019, to April 20, 2021. [c] Open-label design. [d] Per investigator choice.
Fasching PA et al. Oral presented at: ESMO 2024; Sept 13-17, 2024; Barcelona, Spain. Oral LBA13.

Consistent Efficacy Outcomes in Premenopausal Patients[a]

n = 2238	All		<40 years		≥40 years	
	RIB + NSAI n = 1115	NSAI alone n = 1123	RIB + NSAI n = 237	NSAI alone n = 276	RIB + NSAI n = 878	NSAI alone n = 847
IDFS						
Events, n	99	136	27	37	72	99
4-y rate, %	90.6%	85.3%	88.6%	82.3%	91.2%	86.2%
4-y ΔIDFS, %	Δ5.3%		Δ6.3%		Δ5.0%	
HR[b] (95% CI)	0.671 (0.518-0.870)		0.690 (0.419-1.137)		0.662 (0.488-0.897)	
DDFS						
Events, n	88	124	24	35	64	89
4-y rate, %	91.6%	86.6%	90.0%	83.0%	92.0%	87.6%
4-y ΔDDFS, %	Δ5.0%		Δ7.0%		Δ4.4%	
HR[b] (95% CI)	0.655 (0.498-0.861)		0.647 (0.383-1.091)		0.659 (0.478-0.908)	
RFS						
Events, n	85	122	25	33	60	89
4-y rate, %	92.0%	86.6%	89.5%	84.0%	92.7%	87.4%
4-y ΔRFS, %	Δ5.4%		Δ5.5%		Δ5.3%	
HR[b] (95% CI)	0.641 (0.486-0.845)		0.723 (0.429-1.220)		0.610 (0.439-0.846)	
DRFS						
Events, n	77	113	23	33	54	80
4-y rate, %	92.7%	87.6%	90.4%	83.9%	93.3%	88.6%
4-y ΔDRFS, %	Δ5.1%		Δ6.5%		Δ4.7%	
HR[b] (95% CI)	0.627 (0.469-0.837)		0.659 (0.386-1.126)		0.615 (0.435-0.869)	

- As the trial was not powered to detect differences in these exploratory analyses, the results should be interpreted with caution

DDFS, distant disease–free survival; DRFS, distant relapse–free survival; FSH, follicle-stimulating hormone; HR, hazard ratio; IDFS, invasive disease–free survival; NSAI, nonsteroidal aromatase inhibitor; pt, patient; RFS, relapse-free survival; RIB, ribociclib.
[a] Postmenopausal status was defined as 1 of the following: bilateral oophorectomy; age ≥60 years; age <60 years with ≥12 months of amenorrhea (not due to chemotherapy, tamoxifen, toremifene, or ovarian suppression) and FSH and plasma estradiol in the postmenopausal range per local laboratoreis; or, if on tamoxifen or toremifene and age <60 years, FSH and plasma estradiol in the postmenopausal range. All women who do not meet the criteria for postmenopausal status are considered premenopausal. [b] HRs between treatment arms (RIB + NSAI; NSAI alone), stratified by stage, prior chemotherapy, and geographic region.
Data on file. NATALEE CLEE011O12301C (TRIO033). Clinical study protocol. V4.0. Novartis Pharmaceuticals Corp; August 27, 2020.

NATALEE

- Fewer dose discontinuations due to AE in premenopausal (16% vs 23%) and younger (<40 yo, 10.5% vs ≥40 yo, 17.5%)

Consistent Efficacy Outcomes in Postmenopausal Patients[a]

n = 2844	All		<60 years		≥60 years	
	RIB + NSAI n = 1424	NSAI alone n = 1420	RIB + NSAI n = 703	NSAI alone n = 735	RIB + NSAI n = 721	NSAI alone n = 685
IDFS						
Events, n	164	203	82	91	82	112
4-y rate, %	86.8%	82.2%	86.7%	84.0%	86.8%	80.4%
4-y ΔIDFS, %	Δ4.6%		Δ2.7%		Δ6.4%	
HR[b] (95% CI)	0.746 (0.607-0.917)		0.835 (0.619-1.128)		0.673 (0.506-0.896)	
DDFS						
Events, n	152	186	76	83	76	103
4-y rate, %	87.7%	83.6%	87.6%	85.4%	87.8%	81.9%
4-y ΔDDFS, %	Δ4.1%		Δ2.2%		Δ5.9%	
HR[b] (95% CI)	0.759 (0.612-0.941)		0.854 (0.625-1.168)		0.681 (0.506-0.916)	
RFS						
Events, n	139	175	72	82	67	93
4-y rate, %	88.8%	84.5%	88.3%	85.5%	89.3%	83.5%
4-y ΔRFS, %	Δ4.3%		Δ2.8%		Δ5.8%	
HR[b] (95% CI)	0.735 (0.588-0.919)		0.811 (0.590-1.114)		0.668 (0.487-0.915)	
DRFS						
Events, n	133	162	68	75	65	87
4-y rate, %	89.2%	85.6%	88.8%	86.7%	89.6%	84.6%
4-y ΔDRFS, %	Δ3.6%		Δ2.1%		Δ5.0%	
HR[b] (95% CI)	0.763 (0.606-0.960)		0.842 (0.606-1.172)		0.693 (0.502-0.956)	

TRADE Study: Dose escalation of abemaciclib

TRADE: Design

- HR-positive, HER2-negative, early breast cancer
- Adjuvant abemaciclib is indicated based on patient risk/stage

Screening

N=90

Adjuvant Endocrine Therapy

Abemaciclib 50mg BID	Abemaciclib 100mg BID	Abemaciclib 150mg BID
Days 1 – 14	Days 15 – 28	> 28 Days

→ **Endocrine Therapy + up to 2 years Abemaciclib**

Intra-patient dose escalation requirements: Absence of ongoing grade 3/4 or persistent grade 2 toxicity

Supportive care, including anti-diarrhea medication, provided as needed

PRIMARY ENDPOINT:

- **Composite Adverse Event Rate**: Discontinuation of adjuvant abemaciclib for any reason and/or inability to reach or maintain target dose of 150 mg BID by 12 weeks of therapy

SECONDARY ENDPOINTS:

- Treatment-emergent adverse effects, discontinuation / hold rates, incidence of grade ≥2 diarrhea, quality of life, adherence, dose intensity, correlative science

STATISTICAL DESIGN:

- **Experimental hypothesis**: **a dose-escalation schedule will significantly reduce the composite adverse event rate at 12 weeks from a baseline of 40%, based on monarchE**
- **Sample size**: 90 patients provides 92% power, against an alternative of 25%, with a 1-sided test at a significance level of 0.07, assuming drop-out rate of 10%

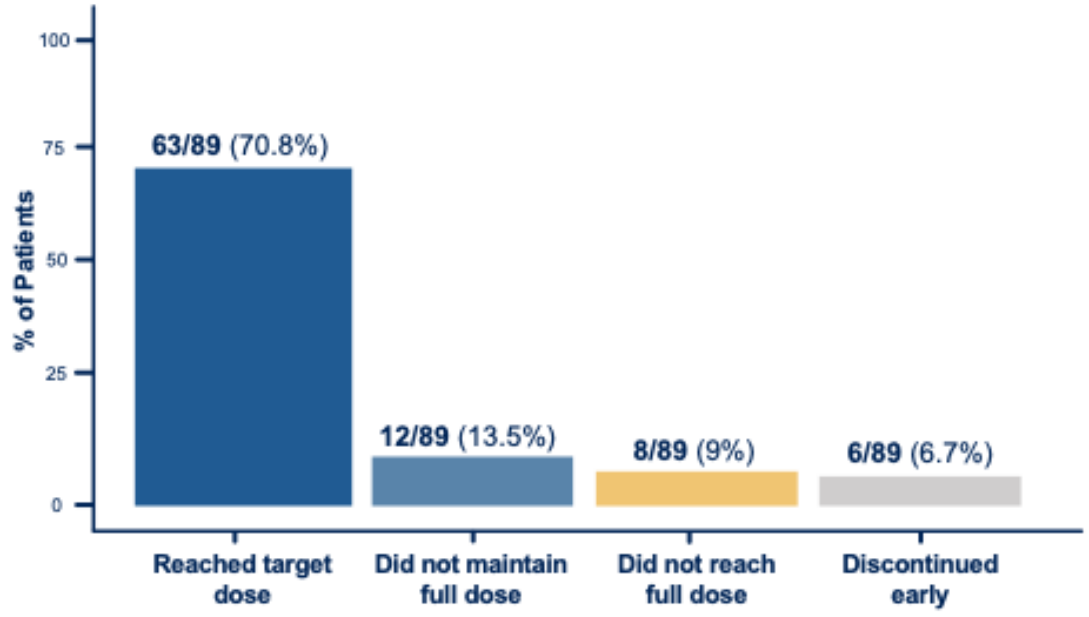
Mayer EL et al. ASCO 2025;Abstract 517

TRADE Results

Clinically Relevant TEAE	≥ Grade 2 N (%)	Grade 2 N (%)	Grade 3 N (%)	Grade 4 N (%)
Any event	67 (74.4)	49 (54.4)	17 (18.9)	1 (1.1)
Diarrhea	24 (26.7)	21 (23.3)	3 (3.3)	-
Neutropenia	22 (24.4)	19 (21.1)	2 (2.2)	1 (1.1)
Fatigue	19 (21.1)	19 (21.1)	-	-
WBC decreased	13 (14.4)	12 (13.3)	1 (1.1)	-
Pneumonitis	3 (3.3)	3 (3.3)	-	-
ALT elevation	3 (3.3)	1 (1.1)	2 (2.2)	-
AST elevation	2 (2.2)	2 2.2)	-	-
Thromboembolic event	1 (1.1)	-	1 (1.1)	-

Of 89 evaluable patients, 26 (29.2%; 90% CI [21.3-38.2]; p=0.046) **met the primary endpoint at 12 weeks:**

- 12 (13.5%) for inability to maintain target dose of 150 mg BID
- 8 (9.0%) for inability to reach 150 mg BID
- 6 (6.7%) for early discontinuation (3 [3.4%] for toxicity)



2025 ASCO ANNUAL MEETING #ASCO25

PRESENTED BY: Erica L. Mayer, MD, MPH

RIGHT Choice: Outcome based on Presence of Liver Metastases

- Pre-/perimenopausal women
- HR+/ HER2–ABC (>10% ER+)
- No prior systemic therapy for ABC
- Measurable disease per RECIST 1.1
- Aggressive disease[a]
  - Symptomatic visceral metastases
  - Rapid disease progression or impending visceral compromise
  - Markedly symptomatic non-visceral disease
- ECOG PS ≤ 2[b]
- Total bilirubin ≤ 1.5 ULN
- N = 222[c]

Stratified by (1) the presence or absence of liver metastases and by (2) DFI[d] < or ≥2 years

R 1:1

Ribociclib
(600mg, 3 weeks on/1 week off)
+
Letrozole or anastrozole + goserelin

Investigators' choice of combination CT[e]

Docetaxel + capecitabine
Paclitaxel + gemcitabine
Capecitabine + vinorelbine

Tumor imaging evaluation
Q6W for 1st 12 weeks, Q8W for next 32 weeks, then Q12W[f]

Primary endpoint
- PFS (locally assessed per RECIST 1.1)

Secondary endpoints
- TTF
- 3-month TFR
- ORR
- CBR
- TTR
- OS
- Safety
- QOL

Exploratory endpoints
- Biomarker analyses
- Healthcare resource utilization

ABC, advanced breast cancer; CBR, clinical benefit rate; CT, chemotherapy; DFI, disease-free interval; ECOG PS, Eastern Cooperative Oncology Group performance status; ER+, estrogen receptor positive; HER2–, human epidermal growth factor receptor 2 negative; HR+, hormone receptor positive; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; Q6W, every 6 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; QOL, quality of life; RECIST, Response Evaluation Criteria In Solid Tumors; TFR, treatment failure rate; TTF, time to treatment failure; TTR, time to response; ULN, upper limit of normal.

[a] Where combination CT is clinically indicated by physician's judgment; [b] For patients with ECOG 2, the poor performance status should be due to breast cancer; [c] Patients were enrolled from Feb 2019 to Nov 2021; [d] Disease-free interval is defined as the duration from date of complete tumor resection for primary breast cancer lesion to the date of documented disease recurrence; [e] If one of the combination CT drugs had to be stopped because of toxicity, the patient was allowed to continue on the other, better-tolerated CT drug (monotherapy); [f] Until disease progression, death, withdrawal of consent, loss to follow-up, or patient/guardian decision, and at end of treatment.

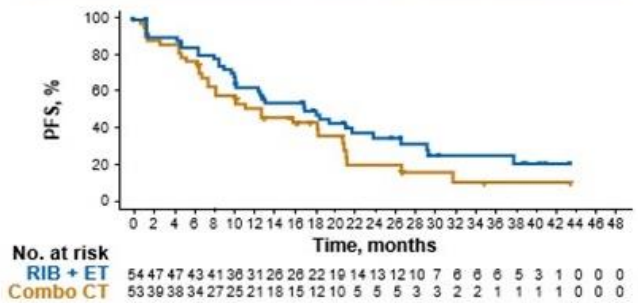
Lu Y-S, et al. J Clin Oncol 2024 Aug 10;42(23):2812-2821, https://ascopubs.org/doi/10.1200/JCO.24.00144

PFS in Patients With and Without Liver Metastases

- Patients with liver metastases receiving RIB + ET showed a 32% relative reduction in risk of disease progression or death vs those receiving combo CT, with a 5.6 mo longer median PFS (mPFS) **(Figure 2A)**
- In patients without liver metastases, RIB + ET was associated with a 43% relative reduction in risk of disease progression or death vs combo CT, with a 9.8 mo longer mPFS **(Figure 2B)**

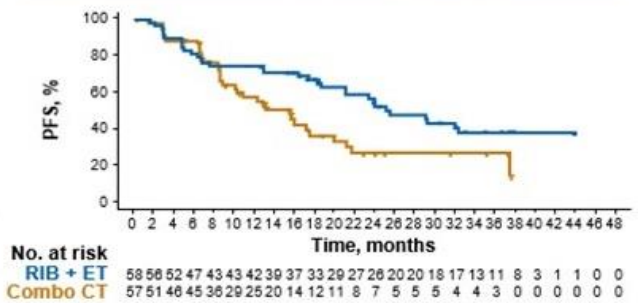
A. Liver metastases

	RIB + ET	Combo CT
Events/n	35/54	32/53
PFS, median (95% CI), mo	18.3 (10.3-24.0)	12.7 (7.5-21.0)
HR (95% CI)	**0.68 (0.42-1.11)**	



B. No liver metastases

	RIB + ET	Combo CT
Events/n	32/58	33/57
PFS, median (95% CI), mo	25.2 (18.6-NE)	15.4 (8.8-20.0)
HR (95% CI)	**0.57 (0.34-0.93)**	



RIGHT Choice (222 pts)	Patients with Liver Mets 107 pts (48%); VC in 69 pts (64%)			Pts without Liver Mets 115 pts (52%); VC in 37 pts (32%)		
Arm	Ribo + ET	Combo CT		Ribo + ET	Combo CT	
mPFS	18.3 mo	12.7 mo	(HR: 0.68)	25.3 mo	15.4 mo	(HR: 0.57)
mTTF	13.2 mo	8.3 mo	(HR: 0.60)	24.0 mo	10.0 mo	(HR: 0.44)
CBR (CR, PR, Stable 6+ mo)	77.8%	67.9%		84.5%	80.7%	
ORR (CR, PR)	64.8%	60.4%		67.2%	63.2%	
mTTR	6.4 m	3.0		4.6 mo	4.5 mo	
mTTD (FACT-B)	37.7 mo	18.4 mo		29.9-NE	15.1-NE	

El Saghir NS et al. ASCO 2025;Abstract 1069

INAVO120 Overall Survival Data

INAVO120: A Phase III, randomized, double-blind, placebo-controlled study[1,2]

Key eligibility criteria

Enrichment of patients with poor prognosis:

- ***PIK3CA*-mutated, HR+, HER2– aBC** by central ctDNA* or local tissue/ctDNA test
- **Measurable disease**
- **Progression during/within 12 months of adjuvant ET completion**
- **No prior therapy for aBC**
- **Fasting glucose <126 mg/dL and HbA_{1c} <6.0%**

Enrollment period: January 2020 to September 2023

N = 325

R 1:1

Inavolisib (9 mg PO QD) + palbociclib (125 mg PO QD D1–D21) + fulvestrant (500 mg C1D1/15 and Q4W)†

Placebo (PO QD) + palbociclib (125 mg PO QD D1–D21) + fulvestrant (500 mg C1D1/15 and Q4W)†

Until PD or toxicity

SURVIVAL FOLLOW-UP

Stratification factors:

- Visceral disease (yes vs. no)
- Endocrine resistance (primary vs. secondary)‡
- Region (North America/Western Europe vs. Asia vs. Other)

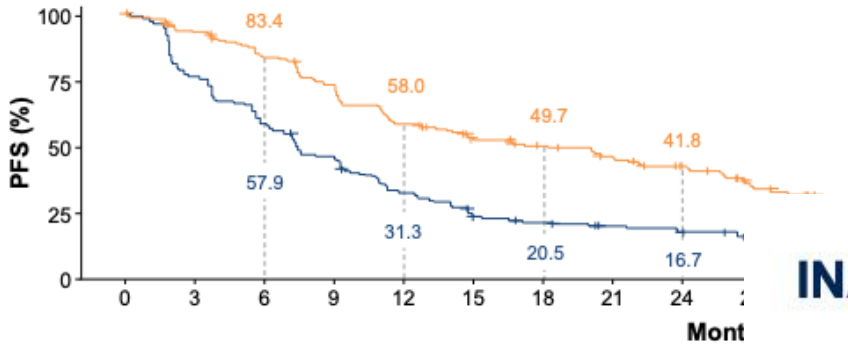
- Primary endpoint: Investigator-assessed PFS
- Secondary endpoints included: OS; investigator-assessed ORR, BOR, CBR, and DoR; PROs

ClinicalTrials.gov number, NCT04191499.
Adapted from Jhaveri KJ, *et al.* SABCS 2023 (Abstract GS03-13). * Central testing for *PIK3CA* mutations was done on ctDNA using FoundationOne®Liquid (Foundation Medicine, Inc.). In China, the central ctDNA test was the PredicineCARE NGS assay (Huidu); † Pre-menopausal women received ovarian suppression; ‡ Defined per 4th European School of Oncology (ESO)–European Society for Medical Oncology (ESMO) International Consensus Guidelines for Advanced Breast Cancer.[3]
Primary: Relapse while on the first 2 years of adjuvant ET; secondary: Relapse while on adjuvant ET after at least 2 years or relapse within 12 months of completing adjuvant ET.
aBC, advanced breast cancer; BOR, best overall response; C, cycle; CBR, clinical benefit rate; ctDNA, circulating tumor DNA; D, day; DoR, duration of response; ET, endocrine therapy; HbA_{1c}, glycated hemoglobin; HER2–, HER2-negative; HR+, hormone receptor-positive; NGS, next-generation sequencing; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PO, by mouth; PRO, patient-reported outcome; Q4W, every 4 weeks; QD, daily; R, randomization.
1. Turner NC, *et al. N Engl J Med* 2024; **391**:1584–1596; 2. Jhaveri KJ, *et al.* SABCS 2023 (Abstract GS03-13); 3. Cardoso F, *et al. Ann Oncol* 2018; **29**:1634–1657.

INAVO120 updated PFS

	Events, n (%)	Median, months (95% CI)
Inavolisib (n = 161)	103 (64.0)	17.2 (11.6–22.2)
Placebo (n = 164)	141 (86.0)	7.3 (5.9–9.2)

Stratified hazard ratio, 0.42
(95% CI = 0.32–0.55)



No. at risk									
Inavolisib	161	146	129	112	89	73	65	57	46
Placebo	164	125	95	74	50	34	30	24	21

The improvement in PFS was

Data cutoff: November 15, 2024.
CI, confidence interval; PFS, progression-free survival. © Copyright 2025.

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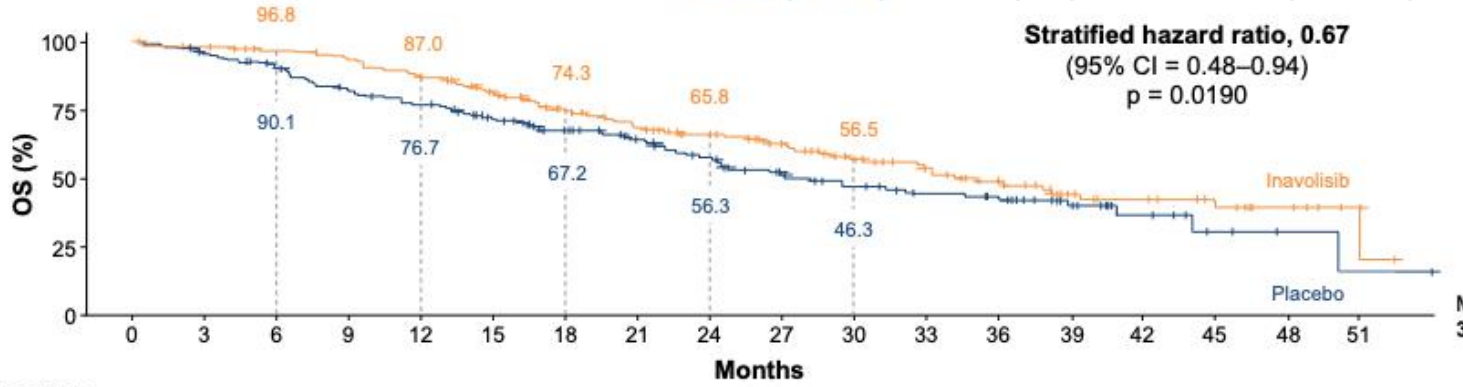
- ORR 63% vs 28%
- DOR 19.2 m vs 11.1 m

INAVO120 key secondary endpoint: OS

	Deaths, n (%)	Median, months (95% CI)
Inavolisib (n = 161)	72 (44.7)	34.0 (28.4–44.8)
Placebo (n = 164)	82 (50.0)	27.0 (22.8–38.7)

Stratified hazard ratio, 0.67
(95% CI = 0.48–0.94)
p = 0.0190



Median follow-up: **34.2 months**

No. at risk																		
Inavolisib	161	155	149	142	131	114	99	88	78	67	54	43	34	22	19	13	7	1
Placebo	164	155	142	127	119	104	90	77	63	48	42	36	32	18	10	4	2	1

Improvement in median OS: 7 months. The prespecified boundary for statistical significance (p < 0.0469) was crossed

Data cutoff: November 15, 2024.
CI, confidence interval; OS, overall survival. © Copyright 2025.

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INAVO120 Updated Safety

INAVO120 overview of AEs

Patients, n (%) with at least one:	Inavolisib (n = 161)	Placebo (n = 163)
Any-grade AE	161 (100)	163 (100)
Grade 3–4 AE	146 (90.7)	138 (84.7)
Grade 5 AE*	6 (3.7)	
Serious AE	44 (27	
AE leading to discontinuation of treatment		
Inavolisib/placebo	11 (6.	
Palbociclib	10 (6.	
Fulvestrant	6 (3.7	
AE leading to dose reduction of treatment		
Inavolisib/placebo	24 (14	
Palbociclib	65 (40	

There was a low discontinuation rate du

Data cutoff: November 15, 2024. AE severity was graded per National Cancer Institute Common Terminology Criteria for AEs v5.0. * None of the grade 5 AEs w
The grade 5 AEs reported were cerebral hemorrhage, cerebrovascular accident, gastrointestinal hemorrhage, acute coronary syndrome, death, and COVID-19 i
AE, adverse event. 1. Turner NC, *et al. N Engl J Med* 2024; **391**:1584–1596. © Copyright 2025.

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INAVO120 selected AEs*

	Inavolisib (n = 161)		Placebo (n = 163)	
Patients, n (%)	**Any grade**	**Grade 3 or 4**	**Any grade**	**Grade 3 or 4**
Neutropenia	147 (91.3)	133 (82.6)	148 (90.8)	131 (80.4)
Thrombocytopenia	80 (49.7)	22 (13.7)	75 (46.0)	8 (4.9)
Stomatitis or mucosal inflammation	89 (55.3)	9 (5.6)	47 (28.8)	0
Anemia	64 (39.8)	11 (6.8)	62 (38.0)	3 (1.8)
Hyperglycemia	102 (63.4)	11 (6.8)	22 (13.5)	0
Diarrhea†	84 (52.2)	6 (3.7)	26 (16.0)	0
Nausea	47 (29.2)	0	32 (19.6)	0
Rash	43 (26.7)	0	32 (19.6)	1 (0.6)
Ocular toxicities‡	47 (29.2)	1 (0.6)	26 (16.0)	0
Aspartate transaminase/ alanine transaminase increase	34 (21.1)	7 (4.3)	37 (22.7)	4 (2.5)
Vomiting	26 (16.1)	2 (1.2)	10 (6.1)	2 (1.2)
Lymphopenia	6 (3.7)	1 (0.6)	15 (9.2)	3 (1.8)
Pneumonitis§	5 (3.1)	1 (0.6)	2 (1.2)	0

Longer exposure to inavolisib did not lead to a new safety signal, nor changes in the safety profile

Data cutoff: November 15, 2024. AEs in bold are key risks. * Grouped by medical concept; † Grade 2 (which is impactful on quality of life) in 29 patients (18.0%) in the inavolisib group and in seven patients (4.3%) in the placebo group; All were grades 1 or 2. with the exception of one Grade 3 cataract unrelated to inavolisib treatment
‡ The most common ocular toxicities observed were dry eye in 14 patients in the inavolisib group (8.7%) and seven patients in the placebo group (4.3%), and blurred vision in eight (5.0%) and two patients (1.2%), respectively.
§ Two patients each (1.2%) at grades 1 and 2. AE, adverse event. © Copyright 2025.

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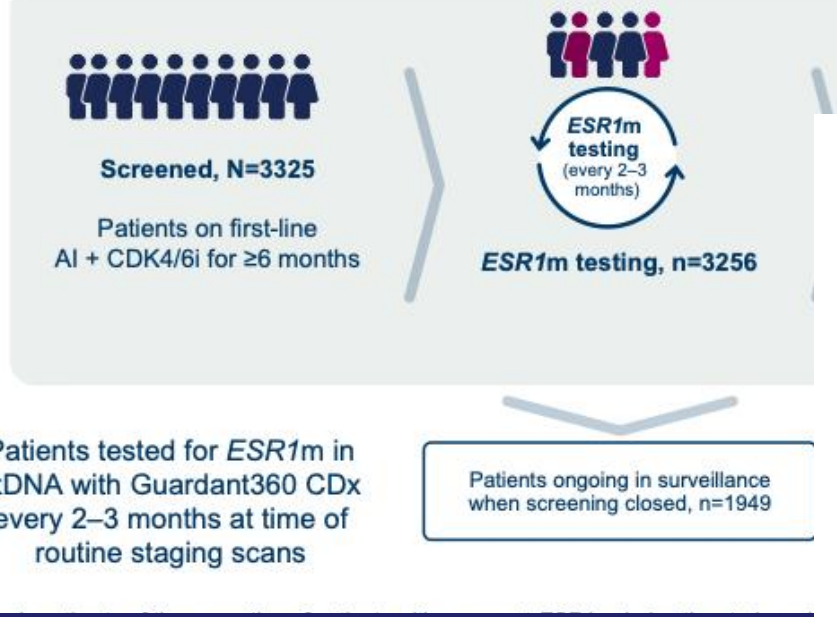
SERENA-6: Using ctDNA to guide switch

*ESR1*m surveillance during first-line AI+CDK4/6i



SERENA-6 study design

Phase III, randomized, double-blind, placebo-controlled study (NCT04964934)

- Female/male patients with ER+/HER2– ABC*
- All patients that have received AI + CDK4/6i (palbociclib, ribociclib, or abemaciclib) as initial endocrine-based therapy for ABC for at least 6 months
- *ESR1*m detected in ctDNA with no evidence of disease progression

R 1:1
N=315

Camizestrant (75 mg qd) + continuing CDK4/6i + placebo for AI

Continuing AI (anastrozole/letrozole) + CDK4/6i + placebo for camizestrant

Stratification factors

- Visceral vs non-visceral
- *ESR1*m detection at first test vs at a subsequent test
- Time from initiation of AI + CDK4/6i to randomization: <18 vs ≥18 months
- Palbociclib vs ribociclib vs abemaciclib

Treatment continued until disease progression, unacceptable toxicity, patient withdrawal or death

Primary endpoint

PFS by investigator assessment (RECIST v1.1)

Secondary endpoints

- PFS2**
- OS**
- Safety
- Patient-reported outcomes

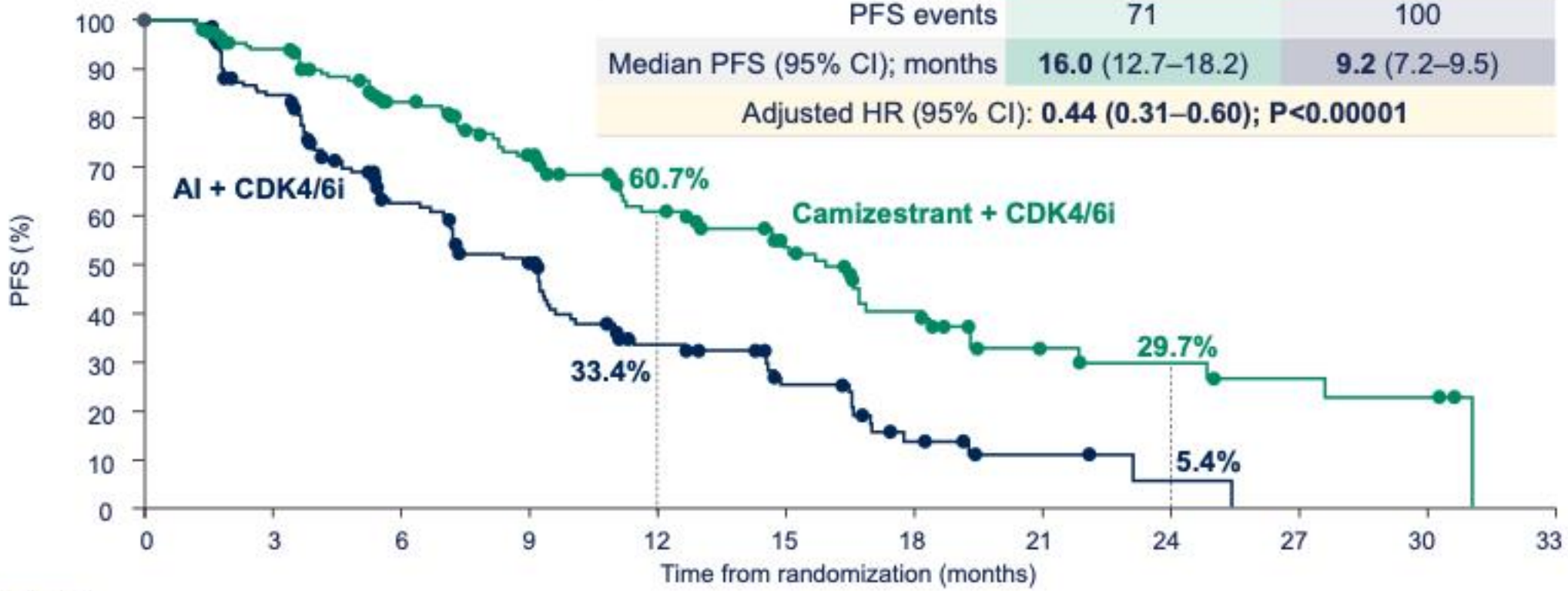
*Pre- or perimenopausal women, and men received a luteinizing hormone–releasing hormone agonist per clinical guidelines. **Key secondary endpoint.
OS, overall survival; PFS2, second progression-free survival; qd, once daily dose; R, randomized; RECIST, response evaluation criteria in solid tumors.

Turner N et al. ASCO 2025;Abstract LBA4

Primary endpoint: Investigator-assessed PFS

SERENA-6

	Camizestrant + CDK4/6i (N=157)	AI + CDK4/6i (N=158)
PFS events	71	100
Median PFS (95% CI); months	**16.0** (12.7–18.2)	**9.2** (7.2–9.5)
Adjusted HR (95% CI): **0.44 (0.31–0.60); P<0.00001**		



Number of patients at risk

Camizestrant + CDK4/6i	157	138	105	82	55	41	26	11	9	7	6	0
AI + CDK4/6i	158	124	73	55	29	17	7	3	1	0	0	0

Second progression-free survival (PFS2)

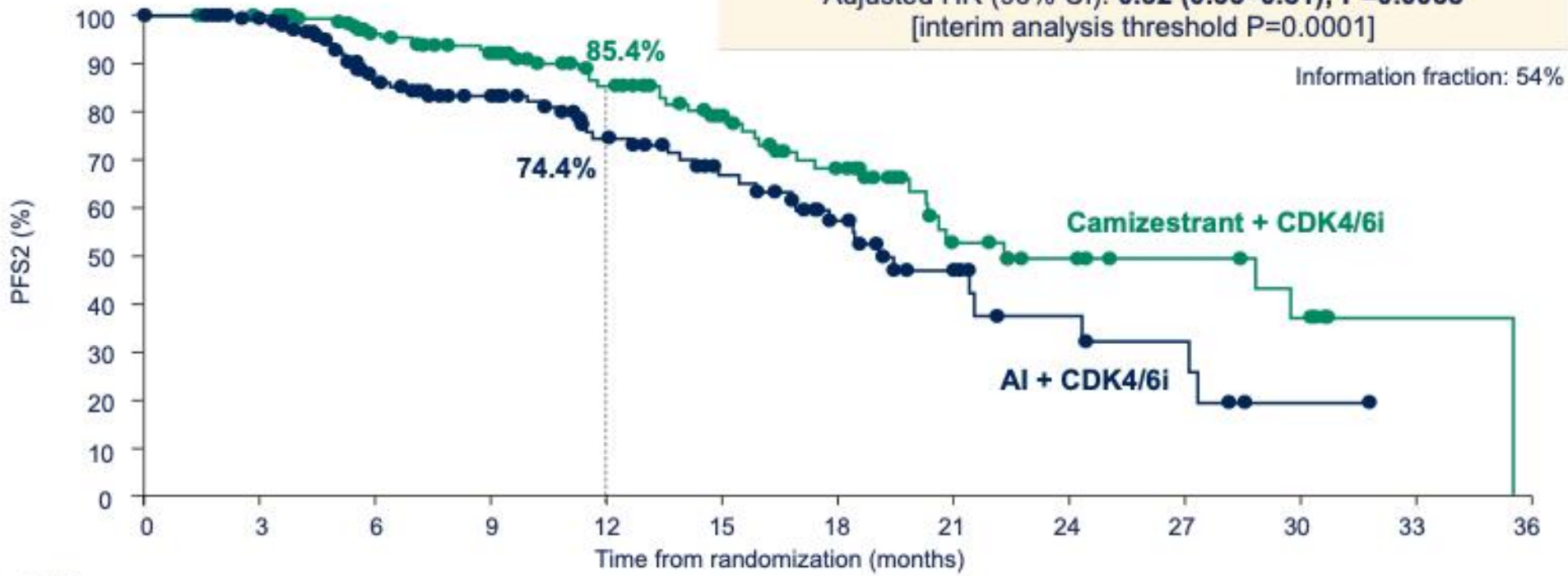
Key secondary endpoint

SERENA-6

	Camizestrant + CDK4/6i (N=157)	AI + CDK4/6i (N=158)
PFS2 events	38	47

Adjusted HR (95% CI): **0.52 (0.33–0.81); P=0.0038**
[interim analysis threshold P=0.0001]

Information fraction: 54%



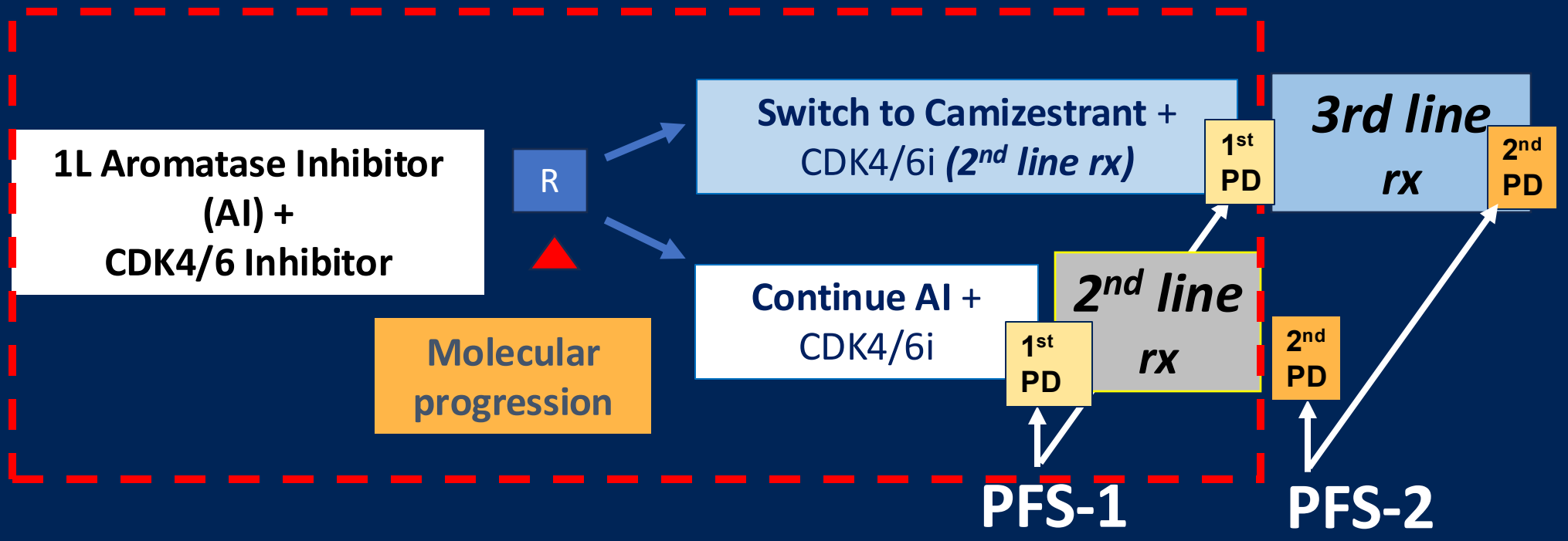
Number of patients at risk

Camizestrant + CDK4/6i	157	146	120	103	74	55	39	17	12	9	6	1	0
AI + CDK4/6i	158	144	98	78	55	38	25	12	7	5	1	0	0

HR was estimated using the Cox proportional hazard model adjusted for stratification factors. Final PFS2 analysis will occur at 158 PFS2 events.

PFS-2 in SERENA-6

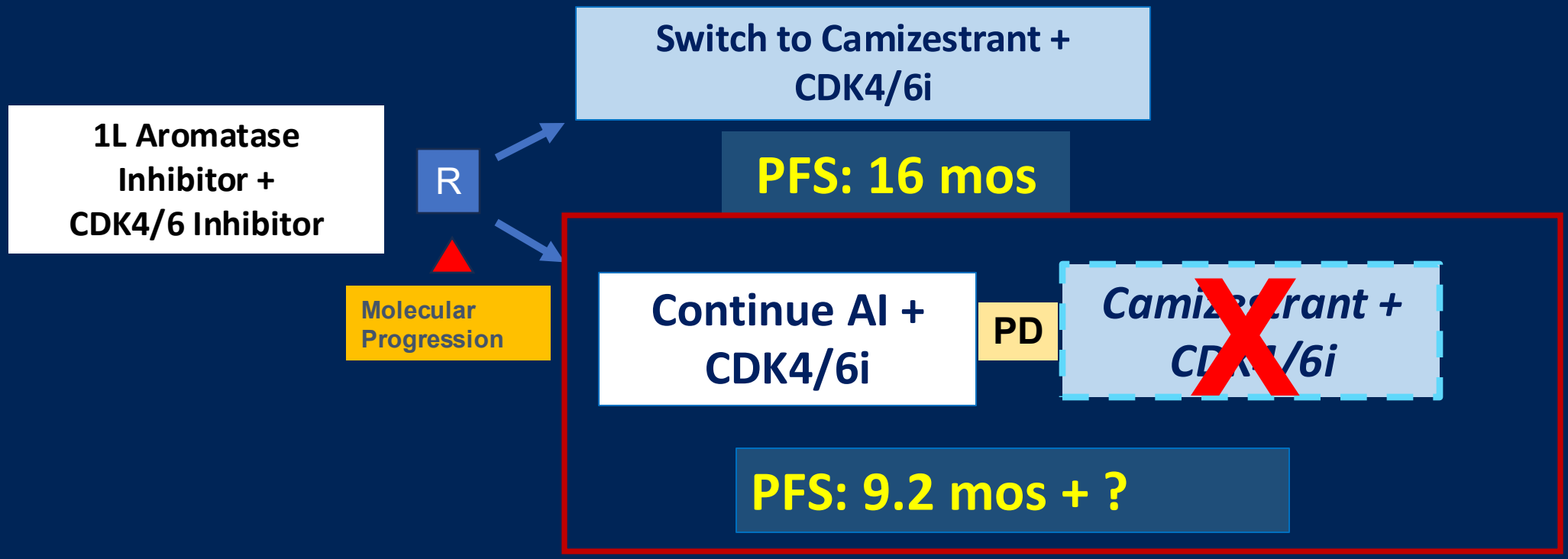
Standard PFS-2



Should PFS-2 include 3rd line therapy?

Is SERENA-6 PFS-2 a valid surrogate for overall survival?

Lack of crossover limits clinical utility assessment



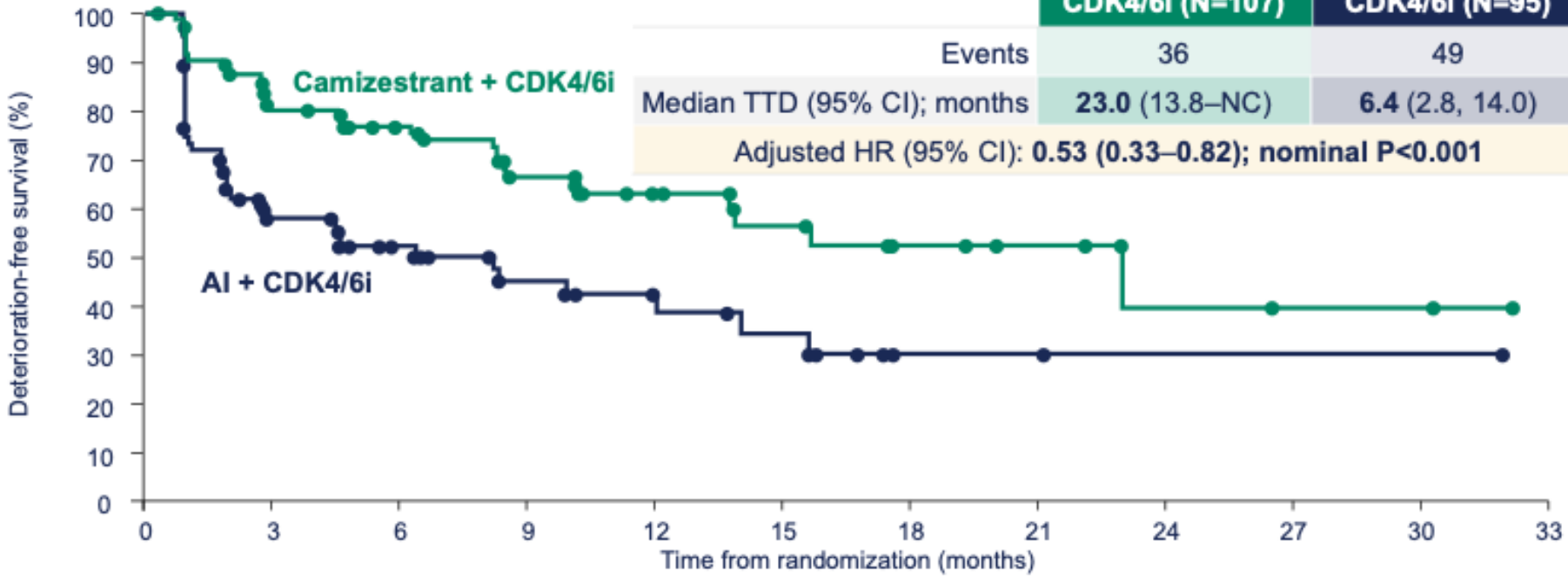
- No direct comparison of response time or overall strategy with switch at molecular vs. anatomic progression

Time to deterioration in global health status/quality of life

EORTC QLQ-C30

SERENA-6

	Camizestrant + CDK4/6i (N=107)	AI + CDK4/6i (N=95)
Events	36	49
Median TTD (95% CI); months	**23.0** (13.8–NC)	**6.4** (2.8, 14.0)
Adjusted HR (95% CI): **0.53 (0.33–0.82); nominal P<0.001**		



Number of patients at risk

Camizestrant + CDK4/6i	107	72	59	40	24	16	9	6	3	2	2	0
AI + CDK4/6i	95	42	26	16	11	8	2	2	1	1	1	0

- Camizestrant + CDK4/6i also delayed the time to deterioration in pain compared with AI + CDK4/6i

Assessments were conducted at baseline, weeks 4, 8 and 12 and then every 8 weeks until PFS2. Analysis conducted in patients with a baseline score and at least one post-baseline assessment. TTD in global health status/quality of life, an exploratory endpoint, was defined as the time from randomization to first deterioration that was confirmed at a subsequent timepoint measured using the European Organization for Research and Treatment of Cancer 30-item quality-of-life questionnaire (**EORTC QLQ-30**). Deterioration was defined as a decrease from baseline ≥16.6. HR was estimated using the Cox proportional hazard model stratified by time of *ESR1*m detection (one test vs more than one test), and time from initiation of AI + CDK4/6i to randomization (<18 months vs. ≥18 months). NC, not calculable; TTD, time-to-deterioration.

Turner N et al. ASCO 2025;Abstract LBA4

EMBER-3 Safety Update

EMBER-3 Study Design

ER+, HER2- ABC

Men & Pre[a]/post menopausal women

Prior therapy:
- **Adjuvant**: Recurrence on or within 12 months of completion of AI ± CDK4/6i
- **ABC**: Progression on first-line AI ± CDK4/6i
- No other therapy for ABC

R 1:1:1[b]

- **A**: Imlunestrant 400 mg QD
- **B**: SOC ET[d,e] Fulvestrant or Exemestane
- **C**: Imlunestrant 400 mg QD + abemaciclib[e]

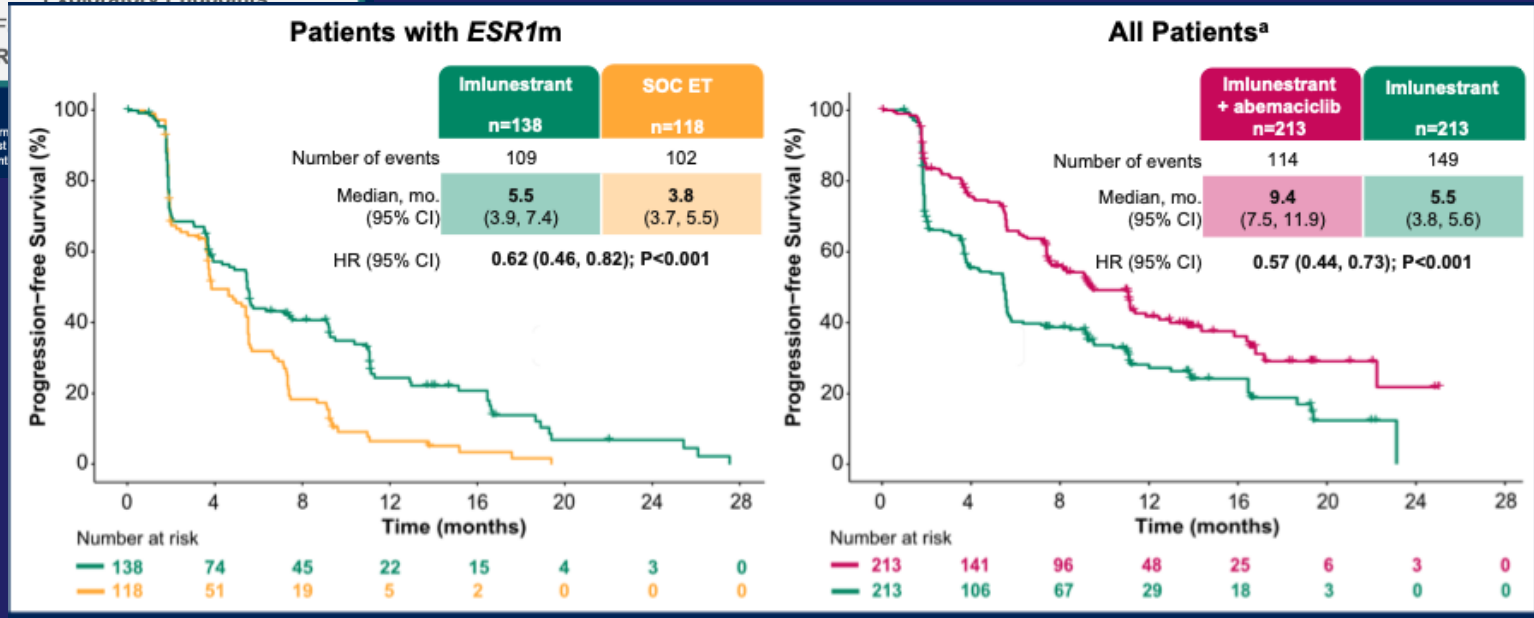
Stratification Factors:
- Prior CDK4/6i therapy (Yes/No)
- Visceral metastases (Yes/No)
- Region[c]

Primary Endpoints
Investigator-assessed PFS[f] for:
- A vs B in patients with *ESR1*m[g]
- A vs B in all patients
- C vs A in all[h] patients

Key Secondary Endpoints
- OS, PFS by BICR, and ORR
- Safety

Exploratory Endpoints
- PF
- PR

Patients were enrolled from October 2021 to November 2023 across 195 sites in 22 countries. [a] A GnRH agonist was required in men and premenopausal women; [b] Enrollment into Arm patients had been randomized across Arms A and B); [c] East Asia vs United States/European Union vs others; [d] Investigator's choice; [e] Labeled dose; [f] Scans every 8 weeks for the first determined in baseline plasma by the Guardant 360 ctDNA assay and OncoCompass Plus assay (Burning Rock Biotech) for patients from China; [h] Analysis conducted in all concurrent



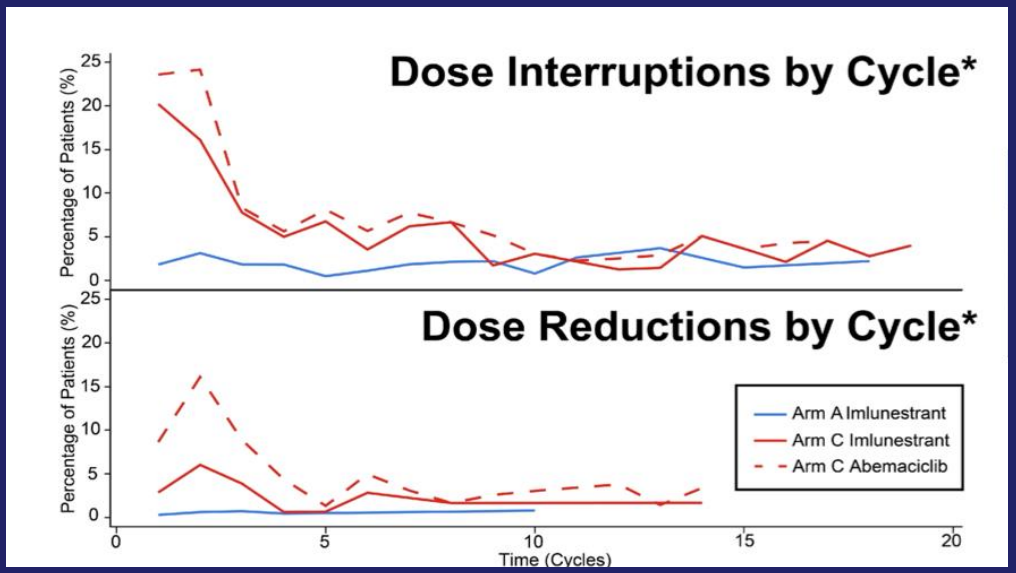
PFS improved with imlunestrant vs SOC ET in patients with *ESR1*m, and with imlunestrant + abemaciclib vs imlunestrant in all patients regardless of *ESR1*m status

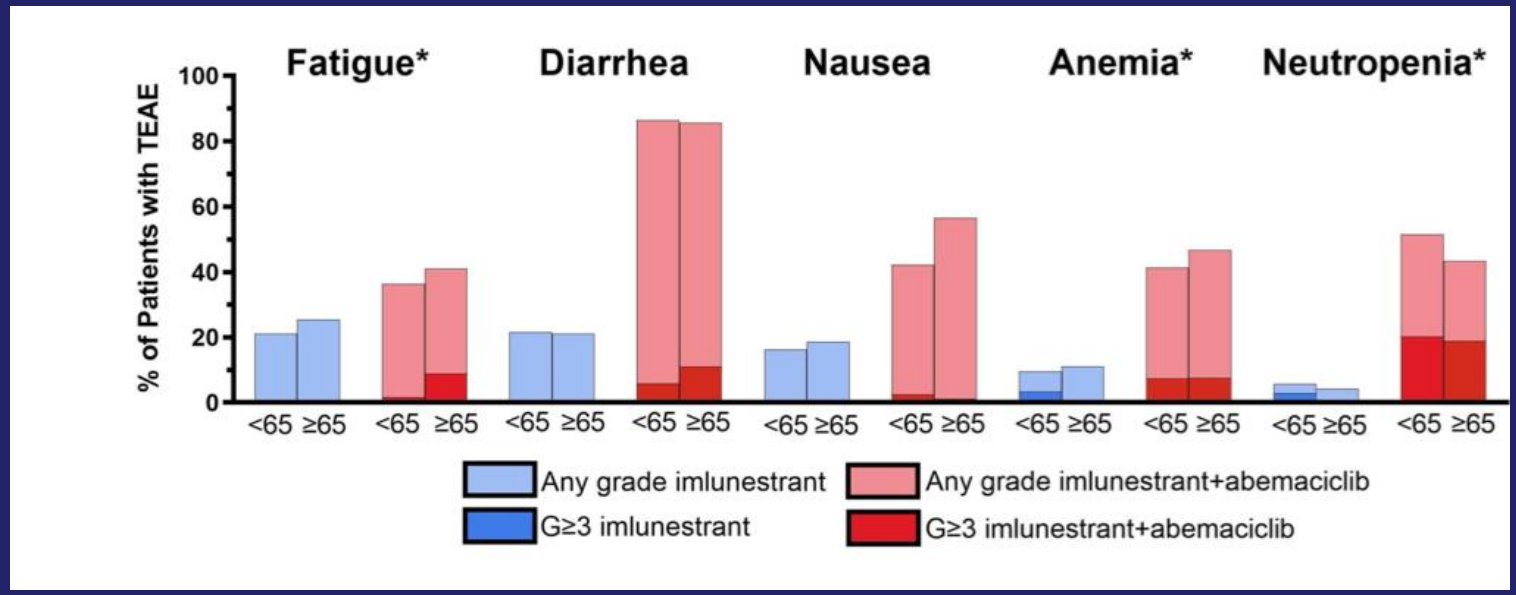
Curigliano G et al. ASCO 2025;Abstract 1001

EMBER-3 SAFETY

Diarrhea		Imlu N=327	SOC ET N=324	Imlu+Abema N=208
% pts	Any grade			
	G1 AE			
	G2 AE			
	G≥3 AE			
	Pts with >1 occurrences of AE			
	Pts with >1 occurrences of G≥3			
	Dose interruption/reduction/disc			
	Antidiarrheal medication[e]			
Median days	Time to onset (Q1-Q3)			
	Duration of G2 AE (range)			
	Duration of G≥3 AE (range)			

Nausea		Imlu N=327	SOC ET N=324	Imlu+Abema N=208
% pts	Any grade	17	13	49
	G1 AE	14	8	31
	G2 AE	3	5	15
	G≥3 AE	<1	0	2
	Pts with >1 occurrences of AE	2	1	14
	Pts with >1 occurrences of G≥3 AE	0	0	<1
	Dose interruption/reduction/discontinuation	0/<1/0	0/0/0	6[a]/5[b]/0[c,d]
	Antiemetic medication[e]	10	10	21
Median days	Time to onset (Q1-Q3)	20 (4–56)	57 (10–147)	15 (3–48)
	Duration of G2 AE (range)	16 (4–89)	10 (1–90)	19 (2–266)
	Duration of G≥3 AE (range)	24 (24–24)	–	7 (6–13)





O'Shaughnessy J et al. ASCO 2025;Abstract 1060

EMBER-3 Patient Reported Outcomes

PRO Measures and Assessment Schedule

Measure	Domains/items	Schedule of Assessments
	Global health status/quality of life (GHS/QOL)	
EORTC QLQ-C30 (30 items)	**Functional** (physical, role, social, emotional, cognitive) **Symptoms** (fatigue, pain, nausea/vomiting, dyspnea, insomnia, loss of appetite, constipation, diarrhea)	Day 1, Every 8 weeks, Short-term Follow-up
EORTC IL-19 (5 items)	**Physical functioning** (physical functioning items from QLQ-C30)	Every 8 weeks opposite the QLQ-C30
PRO-CTCAE diarrhea (1 item)	**Frequency of diarrhea** (never, rarely, occasionally, fr almost constantly)	
PRO-CTCAE ISR (1 item)	**Occurrence of Injection Site Reaction (ISR): Injection site pain, swelling or redness**	

Conclusions

- **Global health status (GHS)/QOL and Functional Domains were maintained across treatment arms in the EMBER-3 trial**
  - **Notably, GHS/QOL and functioning were maintained with imlunestrant + abemaciclib despite increased patient-reported diarrhea and nausea/vomiting**
- **Both longitudinal and Time To Deterioration analyses of GHS/QOL numerically favored imlunestrant vs SOC ET in patients with *ESR1*m (5.6 vs 3.8 months; HR 0.76, 95% CI, 0.51, 1.13), suggesting that imlunestrant delays deterioration of QOL without meaningful increases in toxicity**
- **Importance of injection site reaction (ISR) as a clinically relevant AE for patients is demonstrated by high incidence (72%) of patient-reported ISR with fulvestrant**

Consistent with the primary results from EMBER-3, these PRO results reinforce the benefit of imlunestrant, as monotherapy or combined with abemaciclib, as an all-oral targeted therapy option after progression on ET for patients with ER+, HER2- ABC

Curigliano G et al. ASCO 2025;Abstract 1001

Adjuvant CDK4/6 Inhibitor Indications

Abemaciclib

- In combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of HR-positive, HER2-negative, node-positive localized breast cancer with high risk of recurrence

Ribociclib

- In combination with an aromatase inhibitor for the adjuvant treatment of HR-positive, HER2-negative Stage II and III localized breast cancer with high risk of recurrence

Faculty Discussion Questions

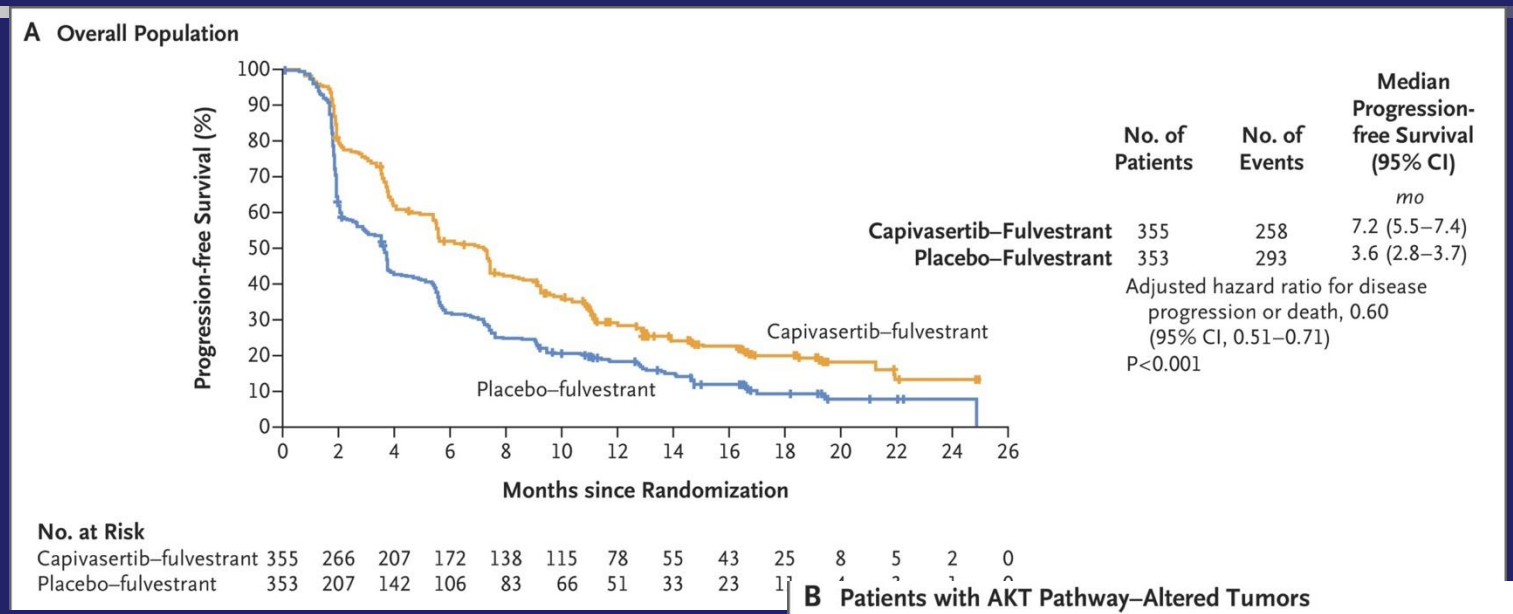
For which patients are you recommending an adjuvant CDK inhibitor (CDKi), and does this correlate with the current FDA indications? How do you choose which CDKi to use in the adjuvant setting?

Do you think the current data from SERENA-6 justify the use of serial ctDNA monitoring for patients receiving CDKi with endocrine therapy and early switching for patients with confirmed ESR1 mutations but no clinical signs of progression? If not, what outcomes would you require?

In which situations do you offer a CDKi to a patient who has already received a CDKi? Does it matter if they received the agent in the adjuvant or metastatic setting? If you could use abemaciclib/imlunestrant, in which patients, if any, would you employ it?

RTP
RESEARCH TO PRACTICE

CAPItello-291: Fulvestrant + Capivasertib or Placebo

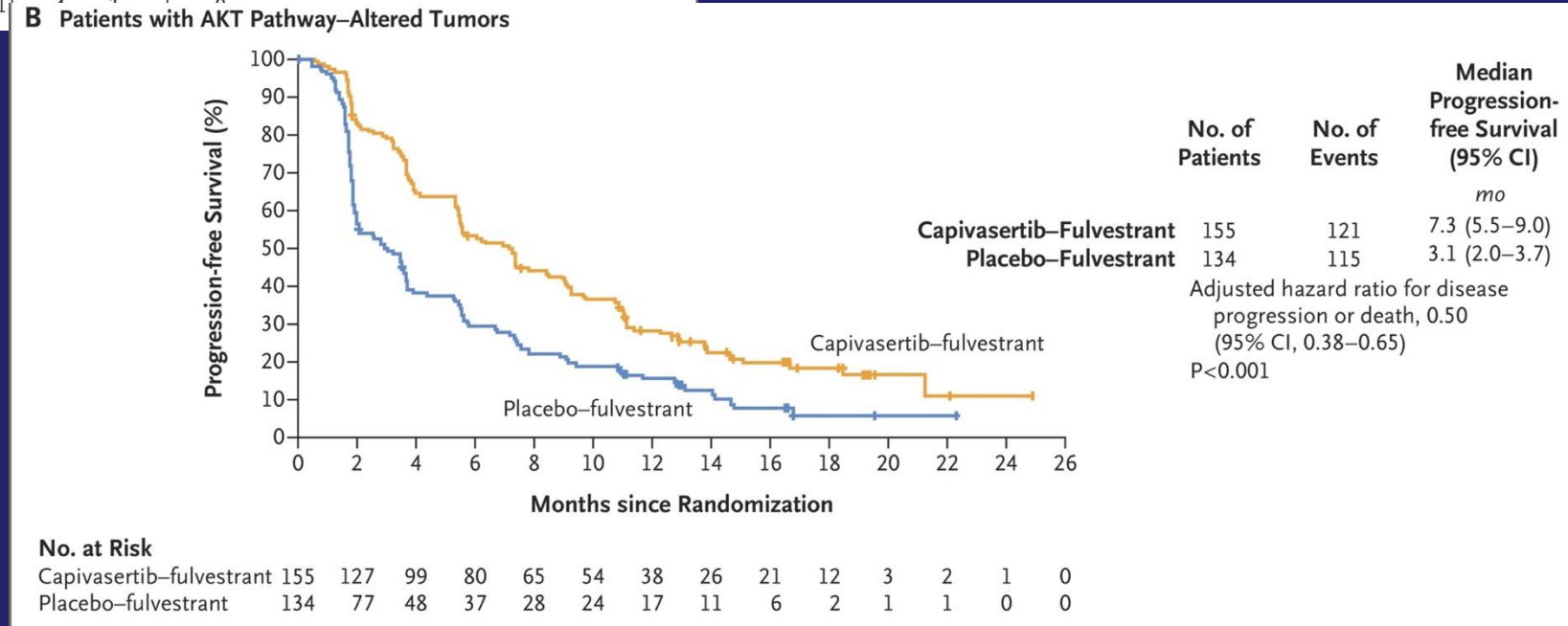


	No. of Patients	No. of Events	Median Progression-free Survival (95% CI)
			mo
Capivasertib–Fulvestrant	355	258	7.2 (5.5–7.4)
Placebo–Fulvestrant	353	293	3.6 (2.8–3.7)

Adjusted hazard ratio for disease progression or death, 0.60 (95% CI, 0.51–0.71)
P<0.001

FDA approved 11/2023:
-HR+/HER2- with PIK3CA, AKT1 and/or PTEN-alteration after PD on ≥1 endocrine therapy in MBC (or ≤12 mos from adjuvant ET)

- ~70% prior CDK4/6i
- ~18% prior chemo for MBC
- Overall survival not statistically significantly different



	No. of Patients	No. of Events	Median Progression-free Survival (95% CI)
			mo
Capivasertib–Fulvestrant	155	121	7.3 (5.5–9.0)
Placebo–Fulvestrant	134	115	3.1 (2.0–3.7)

Adjusted hazard ratio for disease progression or death, 0.50 (95% CI, 0.38–0.65)
P<0.001

Turner NC et al. N Engl J Med2023;388:2058-2070

CAPItello-291: Safety

Table 2. Most Frequent Adverse Events in the Overall Population (Safety Population).*

Event	Capivasertib–Fulvestrant (N=355)					Placebo–Fulvestrant (N=350)				
	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4
	number of patients (percent)									
Any adverse event	343 (96.6)	52 (14.6)	139 (39.2)	139 (39.2)	9 (2.5)	288 (82.3)	115 (32.9)	118 (33.7)	44 (12.6)	10 (2.9)
Diarrhea	257 (72.4)	164 (46.2)	60 (16.9)	33 (9.3)	0	70 (20.0)	60 (17.1)	9 (2.6)	1 (0.3)	0
Rash†	135 (38.0)	57 (16.1)	35 (9.9)	43 (12.1)	0	25 (7.1)	19 (5.4)	5 (1.4)	1 (0.3)	0
Nausea	123 (34.6)	85 (23.9)	35 (9.9)	3 (0.8)	0	54 (15.4)	42 (12.0)	10 (2.9)	2 (0.6)	0
Fatigue	74 (20.8)	49 (13.8)	23 (6.5)	2 (0.6)	0	45 (12.9)	35 (10.0)	8 (2.3)	2 (0.6)	0
Vomiting	73 (20.6)	54 (15.2)	13 (3.7)	6 (1.7)	0	17 (4.9)	10 (2.9)	5 (1.4)	2 (0.6)	0
Headache	60 (16.9)	47 (13.2)	12 (3.4)	1 (0.3)	0	43 (12.3)	33 (9.4)	8 (2.3)	2 (0.6)	0
Decreased appetite	59 (16.6)	37 (10.4)	21 (5.9)	1 (0.3)	0	22 (6.3)	11 (3.1)	9 (2.6)	2 (0.6)	0
Hyperglycemia	58 (16.3)	24 (6.8)	26 (7.3)	7 (2.0)	1 (0.3)	13 (3.7)	8 (2.3)	4 (1.1)	1 (0.3)	0
Stomatitis	52 (14.6)	24 (6.8)	21 (5.9)	7 (2.0)	0	17 (4.9)	15 (4.3)	2 (0.6)	0	0
Asthenia	47 (13.2)	29 (8.2)	14 (3.9)	4 (1.1)	0	36 (10.3)	31 (8.9)	3 (0.9)	2 (0.6)	0
Pruritus	44 (12.4)	32 (9.0)	10 (2.8)	2 (0.6)	0	23 (6.6)	19 (5.4)	4 (1.1)	0	0
Anemia	37 (10.4)	15 (4.2)	15 (4.2)	7 (2.0)	0	17 (4.9)	4 (1.1)	9 (2.6)	4 (1.1)	0
Urinary tract infection	36 (10.1)	8 (2.3)	23 (6.5)	5 (1.4)	0	23 (6.6)	2 (0.6)	21 (6.0)	0	0

* The safety population included all the patients who received at least one dose of capivasertib, fulvestrant, or placebo. The listed events were reported as a single term (or for rash, as a group term) in at least 10% of the patients for any grade in the capivasertib–fulvestrant group. Adverse events are reported regardless of the relationship to capivasertib, fulvestrant, or placebo.
† The group term of rash includes the preferred terms of rash, rash macular, maculopapular rash, rash papular, and rash pruritic.

- Most frequent grade ≥3 events in capi arm: rash (12.1% vs.0.3%) and diarrhea (9.3% vs. 0.3%)
- AEs leading to discontinuation: 13.0% in capivasertib and in 2.3% in placebo

Turner NC et al. N Engl J Med2023;388:2058-2070

VERITAC-2 Phase 3 Trial of Vepdegestrant

Key Eligibility Criteria

- Age ≥18 years old
- ER+/HER2- advanced or metastatic breast cancer
- Prior therapy:
  - 1 line of CDK4/6i + ET
  - ≤1 additional ET
  - Most recent ET for ≥6 months
  - No prior SERD (eg, fulvestrant, elacestrant)
  - No prior chemotherapy for advanced or metastatic disease
- Radiological progression during or after the last line of therapy

Randomization (1:1)

28-day Treatment Cycles

Vepdegestrant (n=313)
200 mg orally (once daily)

Fulvestrant (n=311)
500 mg IM
(days 1 and 15 of cycle 1; day 1 of subsequent cycles)

Stratification Factors:
- *ESR1* mutation[a] (yes vs no)
- Visceral disease (yes vs no)

Primary Endpoint:
- PFS by BICR in
  - *ESR1*m population
  - All patients

Secondary Endpoints:
- OS (key secondary)
- CBR and ORR by BICR
- AEs

VERITAC-2: Baseline Characteristics

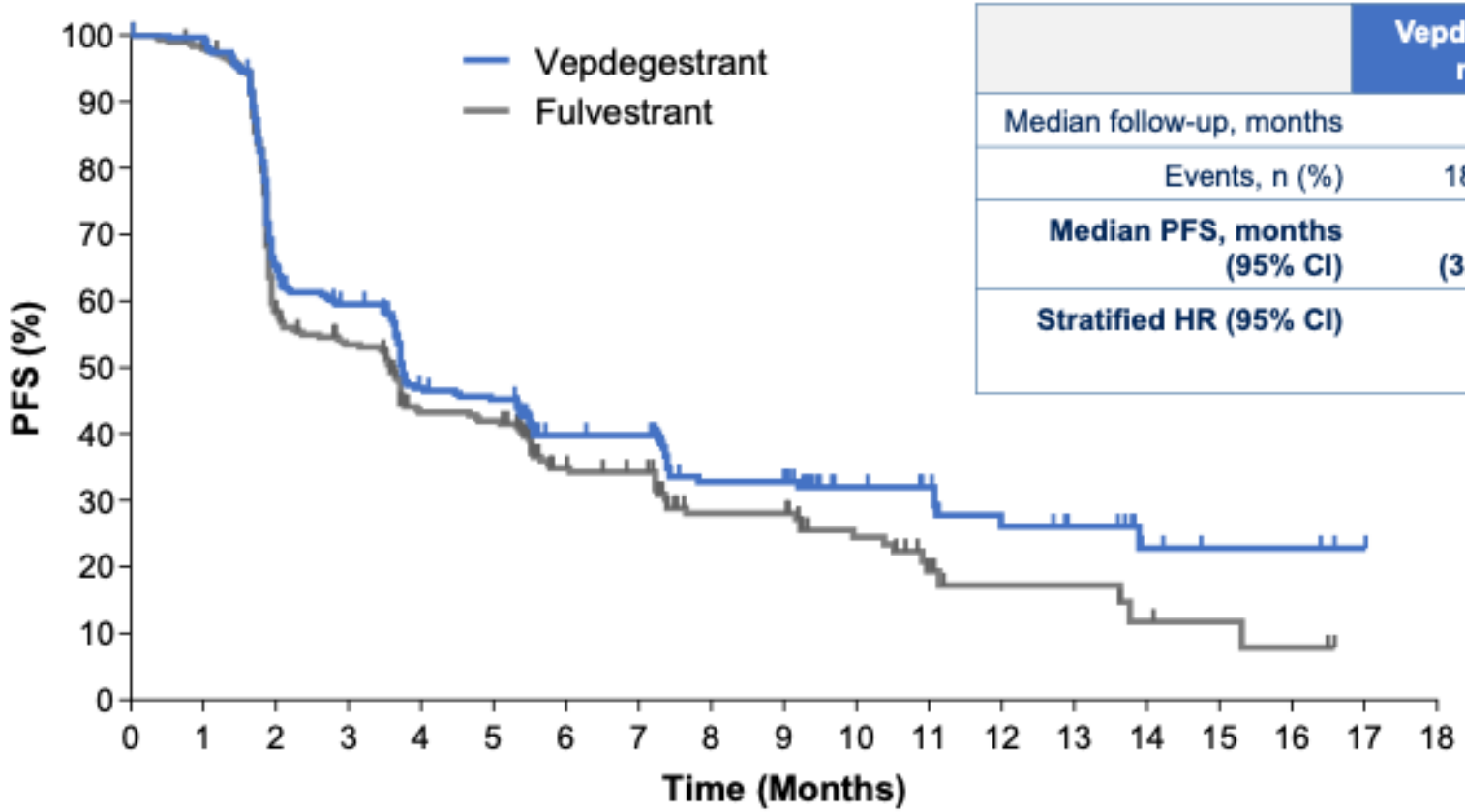
Characteristic	Patients With *ESR1*m		All Patients	
	Vepdegestrant (n=136)	Fulvestrant (n=134)	Vepdegestrant (n=313)	Fulvestrant (n=311)
Median age (range), y	60 (26–87)	60 (34–85)	60 (26–89)	60 (28–85)
Female, %	99	100	99	100
Postmenopausal, %	79	79	78	78
Race, %				
White	43	51	47	46
Black or African American	3	4	2	2
Asian	45	37	39	41
Unknown/NR	9	7	12	9
ECOG PS, %				
0	57	57	61	64
1	43	43	39	36
*ESR1*m, %[a]	100	100	43	43
Sites of disease, %				
Visceral disease	68	68	63	63
Liver metastasis	46	44	40	36
Bone-only disease	18	18	18	20

Characteristic, %	Patients With *ESR1*m		All Patients	
	Vepdegestrant (n=136)	Fulvestrant (n=134)	Vepdegestrant (n=313)	Fulvestrant (n=311)
Measurable disease[b]	71	75	71	71
Prior lines of therapy in advanced/metastatic setting[c]				
1	82	80	82	76
2	18	20	18[d]	23[d]
Prior endocrine therapy	100	100	100	100[e]
Aromatase inhibitor	99	100	99	99
SERM	15	16	16	20
Prior CDK4/6 inhibitor	100	100	100	100
Palbociclib	50	54	46	52
Ribociclib	38	28	36	31
Abemaciclib	16	25	20	21
Other[f]	1	5	4	4

CDK4/6=cyclin-dependent kinase 4/6; ECOG PS=Eastern Cooperative Oncology Group performance status; *ESR1*m=estrogen receptor 1 gene mutation; NR=not reported; SERD= selective estrogen receptor degrader; SERM=selective estrogen receptor modulator.
[a]*ESR1*m status was assessed in pretreatment circulating tumor DNA. [b]Measurable disease assessed by blinded independent central review using Response Evaluation Criteria for Solid Tumors v1.1. [c]Disease progression during or within 12 months from the end of adjuvant therapy was counted as a line of therapy in the advanced/metastatic setting. [d]1 additional patient in the vepdegestrant group and 3 additional patients in the fulvestrant group received 3 prior lines of therapy. [e]1 patient received a prior SERD. [f]Other CDK4/6 inhibitors included birociclib, dalpiciclib, lerociclib.

Hamilton EP et al. ASCO 2025;Abstract LBA1000

VERITAC-2 Primary Endpoint: PFS by BICR in All Patients



	Vepdegestrant n=313	Fulvestrant n=311
Median follow-up, months	7.4	7.2
Events, n (%)	186 (59)	198 (64)
Median PFS, months (95% CI)	**3.7 (3.6–5.3)**	**3.6 (2.2–3.8)**
Stratified HR (95% CI)	**0.83 (0.68–1.02)**	
	2-sided *P*=0.07	

No. at risk

Vepdegestrant	313	306	189	168	113	108	74	72	46	46	28	24	15	12	6	4	4	2	0
Fulvestrant	311	292	162	143	101	98	58	54	36	36	23	12	7	7	4	3	2	0	0

BICR=blinded independent central review; HR=hazard ratio; PFS=progression-free survival.

VERITAC-2: Safety and Tolerability (All Treated Patients)

Overview

TEAEs, %	Vepdegestrant (n=312)	Fulvestrant (n=307)
Any grade	87	81
Grade ≥3	23	18
Serious	10	9
Leading to treatment discontinuation	3	1
Leading to dose reduction	2	NA
TRAEs, %		
Any grade	57	40
Grade ≥3	8	3

QT prolongation

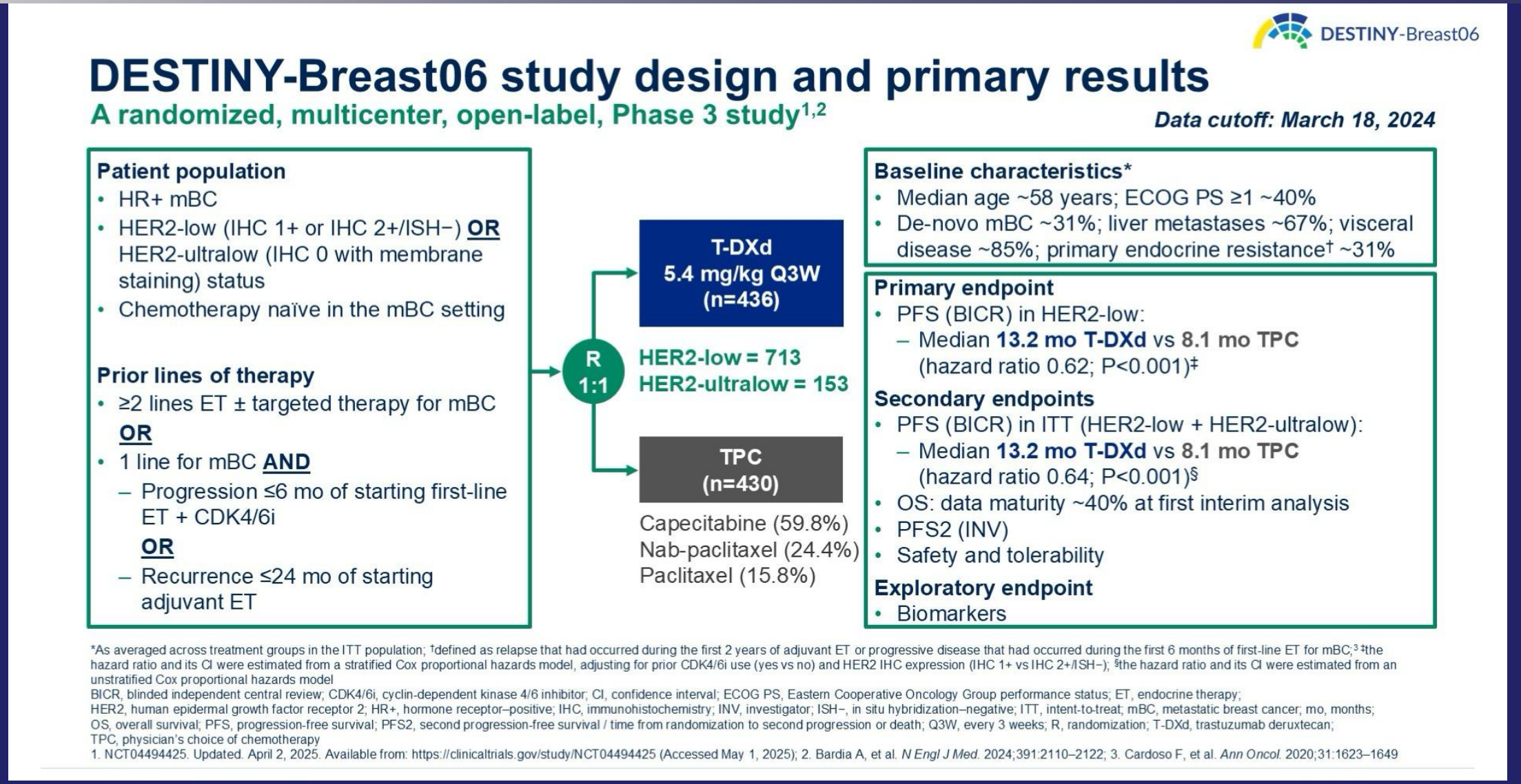
- TEAEs: vepdegestrant,10%; fulvestrant, 1%
- A QT interval sub-study (n=88) confirmed a mild increase (11.1 ms) from baseline in mean QTcF, with upper 90% CI (13.7 ms) <20 ms,[f] **indicating no large QT-prolonging effect**

TEAEs in >10% of Patients in Either Group

TEAE, %	Vepdegestrant (n = 312)		Fulvestrant (n = 307)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Fatigue[a]	27	1	16	1
ALT increased[b]	14	1	10	1
AST increased[b]	14	1	10	3
Nausea	13	0	9	1
Anemia[b, c]	12	2	8	3
Neutropenia[d]	12	2[e]	5	1[e]
Back pain	11	1	7	<1
Arthralgia	11	1	11	0
Decreased appetite	11	<1	5	0

ALT=alanine aminotransferase; AST=aspartate aminotransferase; GI=gastrointestinal; QTcF=corrected QT interval using Fridericia's method; TEAE=treatment-emergent adverse event; TRAE=treatment-related adverse event.
[a]Includes fatigue and asthenia. [b]No between-group differences were observed for ALT/AST increases or anemia based on laboratory values. [c]Includes anemia, hemoglobin decreased, and iron deficiency anemia. [d]Includes neutropenia and neutrophil count decreased. No events led to dose reductions or treatment discontinuation in either treatment group. There were no events of febrile neutropenia in the vepdegestrant group and 1 event of grade 2 febrile neutropenia in the fulvestrant group. [e]1 patient with grade 4 event. [f]Based on a concentration-QTc population modeling analysis.

DESTINY-Breast06: Biomarker Results



*As averaged across treatment groups in the ITT population; †defined as relapse that had occurred during the first 2 years of adjuvant ET or progressive disease that had occurred during the first 6 months of first-line ET for mBC;[3] ‡the hazard ratio and its CI were estimated from a stratified Cox proportional hazards model, adjusting for prior CDK4/6i use (yes vs no) and HER2 IHC expression (IHC 1+ vs IHC 2+/ISH−); §the hazard ratio and its CI were estimated from an unstratified Cox proportional hazards model

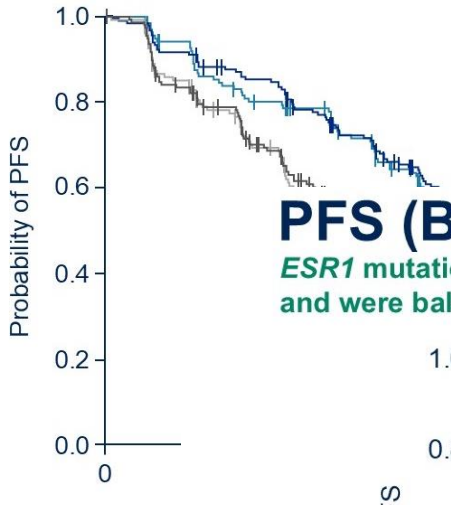
BICR, blinded independent central review; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR+, hormone receptor–positive; IHC, immunohistochemistry; INV, investigator; ISH−, in situ hybridization–negative; ITT, intent-to-treat; mBC, metastatic breast cancer; mo, months; OS, overall survival; PFS, progression-free survival; PFS2, second progression-free survival / time from randomization to second progression or death; Q3W, every 3 weeks; R, randomization; T-DXd, trastuzumab deruxtecan; TPC, physician's choice of chemotherapy

1. NCT04494425. Updated. April 2, 2025. Available from: https://clinicaltrials.gov/study/NCT04494425 (Accessed May 1, 2025); 2. Bardia A, et al. *N Engl J Med.* 2024;391:2110–2122; 3. Cardoso F, et al. *Ann Oncol.* 2020;31:1623–1649

Dent RA et al. ASCO 2025;Abstract 1013

PFS (BICR) by baseline PI3K/AKT pathway* mutation status

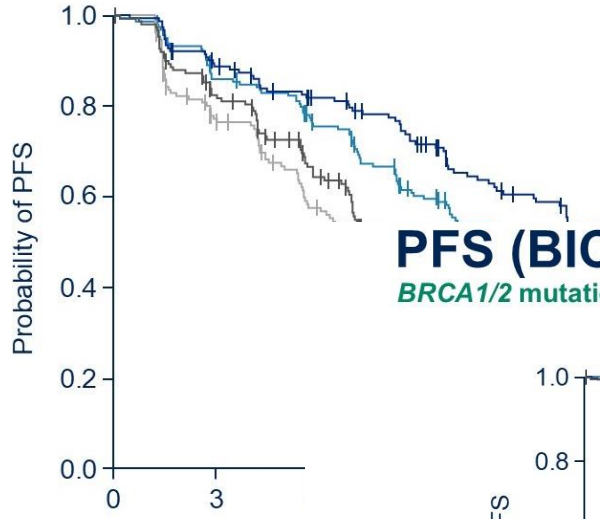
PI3K/AKT pathway mutations were observed in 45.0% (n=281) of patients in the biomarker-evaluable population and were balanced across treatment groups



	WT		Mut	
	T-DXd	TPC	T-DXd	TPC
No. of events/patients†	113/179	111/165	89/139	92/142
Median PFS, months (95% CI)	13.1 (11.1, 15.4)	8.1 (6.8, 9.6)	13.2 (9.9, 15.5)	7.1 (6.0, 9.5)
PFS hazard ratio (95% CI)‡	0.61 (0.47, 0.79)		0.65 (0.48, 0.87)	

PFS (BICR) by baseline *ESR1* mutation status

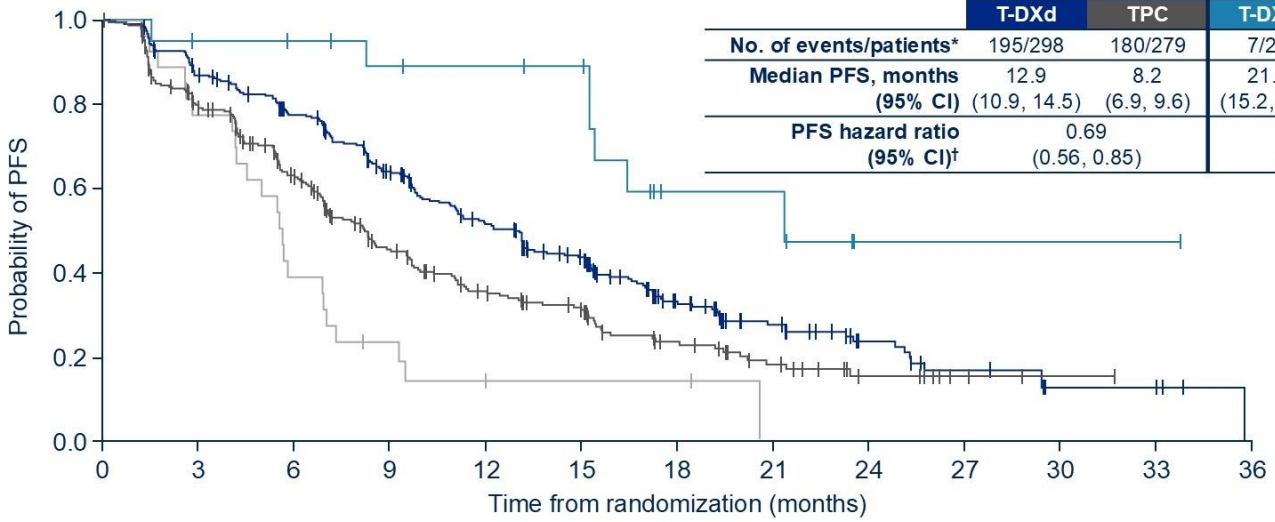
***ESR1* mutations were observed in 51.5% (n=322) of patients in the biomarker-evaluable population and were balanced across treatment groups**



	WT		Mut	
	T-DXd	TPC	T-DXd	TPC
No. of events/patients*	87/152	96/151	115/166	107/156
Median PFS, months (95% CI)	15.2 (12.3, 17.3)	8.1 (6.9, 9.6)	11.3 (9.8, 13.5)	7.0 (5.6, 9.3)
PFS hazard ratio (95% CI)†	0.59 (0.44, 0.79)		0.64 (0.49, 0.83)	

PFS (BICR) by baseline *BRCA1/2* mutation status

***BRCA1/2* mutations were observed in 7.7% (n=48) of patients in the biomarker-evaluable population**



	WT		Mut	
	T-DXd	TPC	T-DXd	TPC
No. of events/patients*	195/298	180/279	7/20	23/28
Median PFS, months (95% CI)	12.9 (10.9, 14.5)	8.2 (6.9, 9.6)	21.4 (15.2, NE)	5.6 (4.1, 6.9)
PFS hazard ratio (95% CI)†	0.69 (0.56, 0.85)		0.14 (0.05, 0.33)	

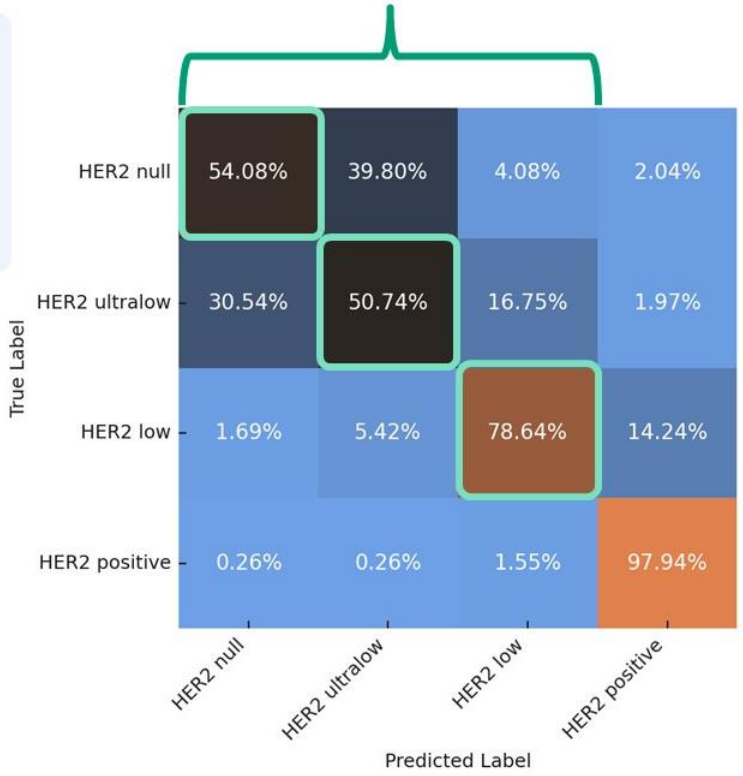
Use of AI for HER2 low and ultralow determination

Aims

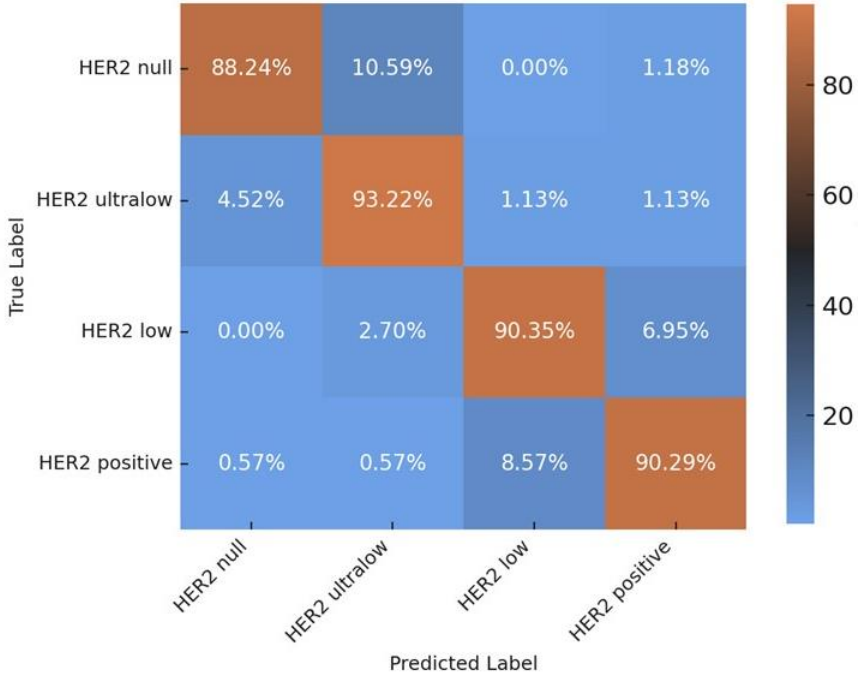
- **Goals of this study:**
  - To c
    exa
  - To e
    ass
    utiliz

Results

Manual scoring sensitivity was the lowest for cases with absence or low levels of HER2 expression



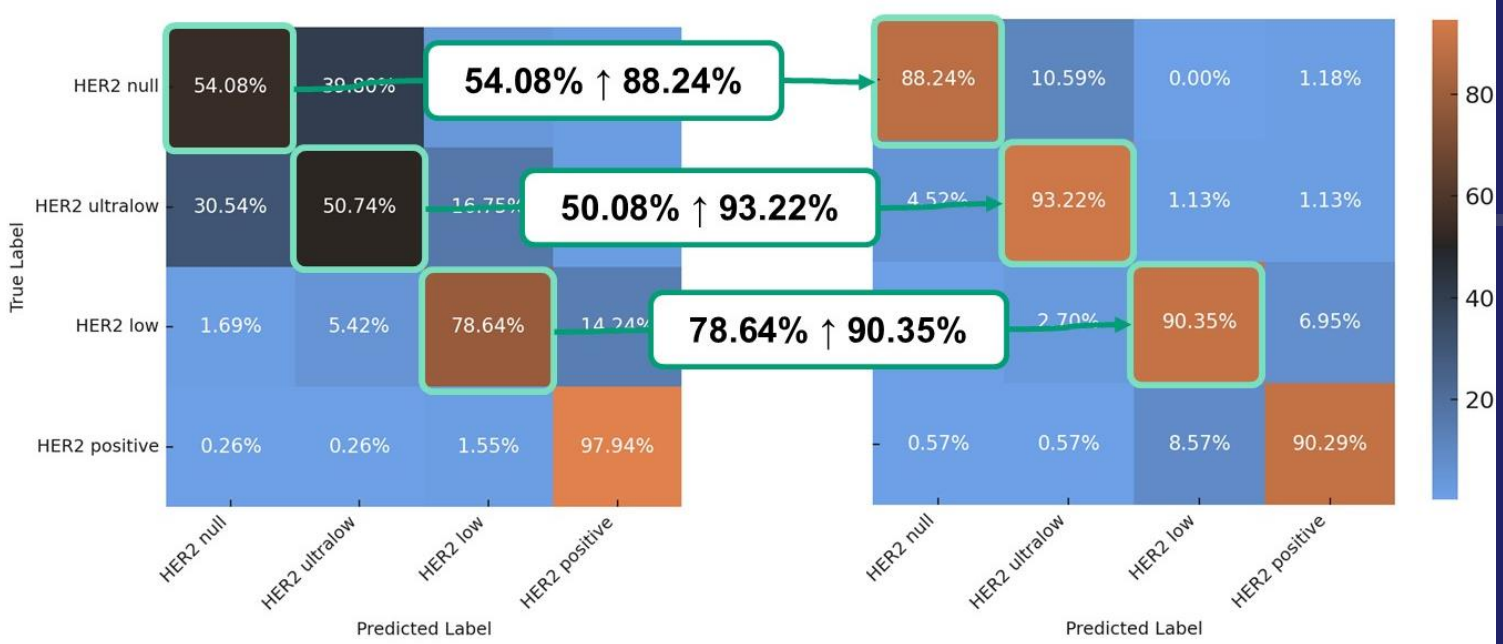
Exam A+B (manual scoring)



Exam C (with AI support)

DeBrot M et al. ASCO 2025;Abstract 1014

AI support raises sensitivity across HER2 Null/Ultralow/Low expression classifications



Exam A+B (manual scoring)

Exam C (with AI support)

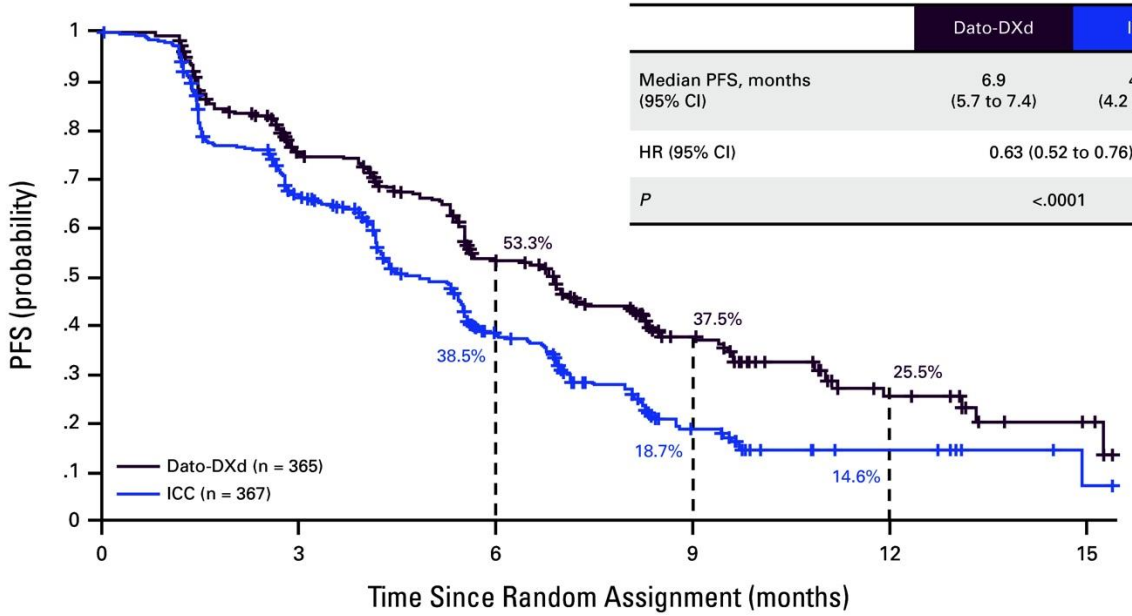
HER2-Ultralow underscoring manually in 30.5% of instances, compared to 4.5% with AI

Exam A+B (manual scoring)

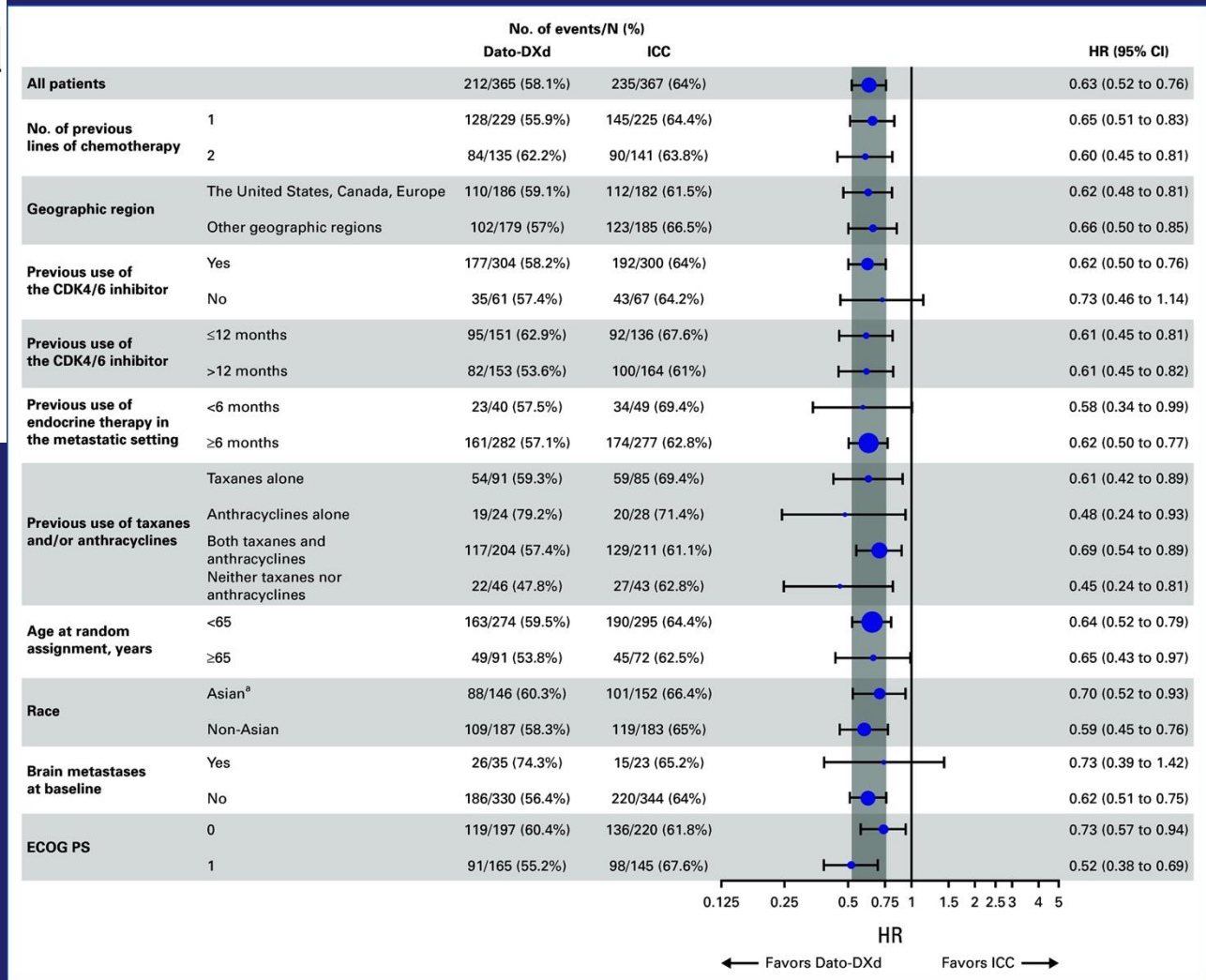
Exam C (with AI support)

DeBrot M et al.
ASCO 2025;Abstract 1014

TROPION-Breast01: Datopotamab Deruxtecan in HR+ HER2 negative MBC



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



		No. of events/N (%) Dato-DXd	ICC	HR (95% CI)
All patients		212/365 (58.1%)	235/367 (64%)	0.63 (0.52 to 0.76)
No. of previous lines of chemotherapy	1	128/229 (55.9%)	145/225 (64.4%)	0.65 (0.51 to 0.83)
	2	84/135 (62.2%)	90/141 (63.8%)	0.60 (0.45 to 0.81)
Geographic region	The United States, Canada, Europe	110/186 (59.1%)	112/182 (61.5%)	0.62 (0.48 to 0.81)
	Other geographic regions	102/179 (57%)	123/185 (66.5%)	0.66 (0.50 to 0.85)
Previous use of the CDK4/6 inhibitor	Yes	177/304 (58.2%)	192/300 (64%)	0.62 (0.50 to 0.76)
	No	35/61 (57.4%)	43/67 (64.2%)	0.73 (0.46 to 1.14)
Previous use of the CDK4/6 inhibitor	≤12 months	95/151 (62.9%)	92/136 (67.6%)	0.61 (0.45 to 0.81)
	>12 months	82/153 (53.6%)	100/164 (61%)	0.61 (0.45 to 0.82)
Previous use of endocrine therapy in the metastatic setting	<6 months	23/40 (57.5%)	34/49 (69.4%)	0.58 (0.34 to 0.99)
	≥6 months	161/282 (57.1%)	174/277 (62.8%)	0.62 (0.50 to 0.77)
Previous use of taxanes and/or anthracyclines	Taxanes alone	54/91 (59.3%)	59/85 (69.4%)	0.61 (0.42 to 0.89)
	Anthracyclines alone	19/24 (79.2%)	20/28 (71.4%)	0.48 (0.24 to 0.93)
	Both taxanes and anthracyclines	117/204 (57.4%)	129/211 (61.1%)	0.69 (0.54 to 0.89)
	Neither taxanes nor anthracyclines	22/46 (47.8%)	27/43 (62.8%)	0.45 (0.24 to 0.81)
Age at random assignment, years	<65	163/274 (59.5%)	190/295 (64.4%)	0.64 (0.52 to 0.79)
	≥65	49/91 (53.8%)	45/72 (62.5%)	0.65 (0.43 to 0.97)
Race	Asian[a]	88/146 (60.3%)	101/152 (66.4%)	0.70 (0.52 to 0.93)
	Non-Asian	109/187 (58.3%)	119/183 (65%)	0.59 (0.45 to 0.76)
Brain metastases at baseline	Yes	26/35 (74.3%)	15/23 (65.2%)	0.73 (0.39 to 1.42)
	No	186/330 (56.4%)	220/344 (64%)	0.62 (0.51 to 0.75)
ECOG PS	0	119/197 (60.4%)	136/220 (61.8%)	0.73 (0.57 to 0.94)
	1	91/165 (55.2%)	98/145 (67.6%)	0.52 (0.38 to 0.69)

Bardia A et al. J Clin Oncol. 2025 Jan 20;43(3):285-296.

TROPION-Breast01: Datopotamab Deruxtecan

TABLE 3. TRAEs (all grades) Occurring in ≥10% of Patients and Grade ≥3 TRAEs in ≥1% of Patients in Either Arm (safety population)

	Dato-DXd (n = 360), No. (%)		ICC (n = 351), No. (%)	
TRAE	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any TRAE	337 (93.6)	75 (20.8)	303 (86.3)	157 (44.7)
Nausea	184 (51.1)	5 (1.4)	83 (23.6)	2 (0.6)
Stomatitis	180 (50)	23 (6.4)	46 (13.1)	9 (2.6)
Alopecia	131 (36.4)	0	72 (20.5)	0
Fatigue	85 (23.6)	6 (1.7)	64 (18.2)	7 (2)
Dry eye	78 (21.7)	2 (0.6)	27 (7.7)	0
Vomiting	71 (19.7)	4 (1.1)	27 (7.7)	2 (0.6)
Constipation	65 (18.1)	0	32 (9.1)	0
Keratitis[a]	52 (14.4)	2 (0.6)	17 (4.8)	0
Decreased appetite	50 (13.9)	3 (0.8)	41 (11.7)	2 (0.6)
Asthenia	45 (12.5)	3 (0.8)	46 (13.1)	4 (1.1)
Anemia	40 (11.1)	4 (1.1)	69 (19.7)	7 (2)
Neutropenia[b]	39 (10.8)	4 (1.1)	149 (42.5)	108 (30.8)
AST increased	31 (8.6)	2 (0.6)	39 (11.1)	2 (0.6)
Diarrhea	27 (7.5)	0	43 (12.3)	4 (1.1)
Leukopenia[c]	26 (7.2)	2 (0.6)	60 (17.1)	24 (6.8)
Palmar-plantar erythrodysesthesia syndrome	7 (1.9)	0	42 (12)	7 (2)
Platelet count decreased	7 (1.9)	0	18 (5.1)	4 (1.1)
Febrile neutropenia	0	0	8 (2.3)	8 (2.3)

Bardia A et al. J Clin Oncol. 2025 Jan 20;43(3):285-296.

Faculty Discussion Questions

What second-line therapy do you typically prefer for a patient with ER-positive, ESR1-negative, PIK3CA-positive disease? What toxicities are most common with this approach? What second-line treatment do you favor for a patient with both ESR1 and PIK3CA mutations?

If elacestrant, imlunestrant or vepdegestrant were all available, which one would you likely use as second-line treatment for a patient with ESR1-positive, PIK3CA wild-type disease?

How do you typically sequence available agents/regimens for patients with ER-positive, HER2-low (IHC 1+) and ER-positive, HER2-negative (IHC 0) disease who are no longer candidates for endocrine therapy?

Agenda

Introduction: View from Outer Space

Module 1: HR-Positive Breast Cancer

Module 2: HER2-Positive Breast Cancer

Module 3: Triple-Negative Breast Cancer

RTP RESEARCH TO PRACTICE

SUSAN F. SMITH CENTER FOR WOMEN'S CANCERS

Dana-Farber Cancer Institute

HARVARD MEDICAL SCHOOL

HER2+ and TNBC Highlights from ASCO 2025

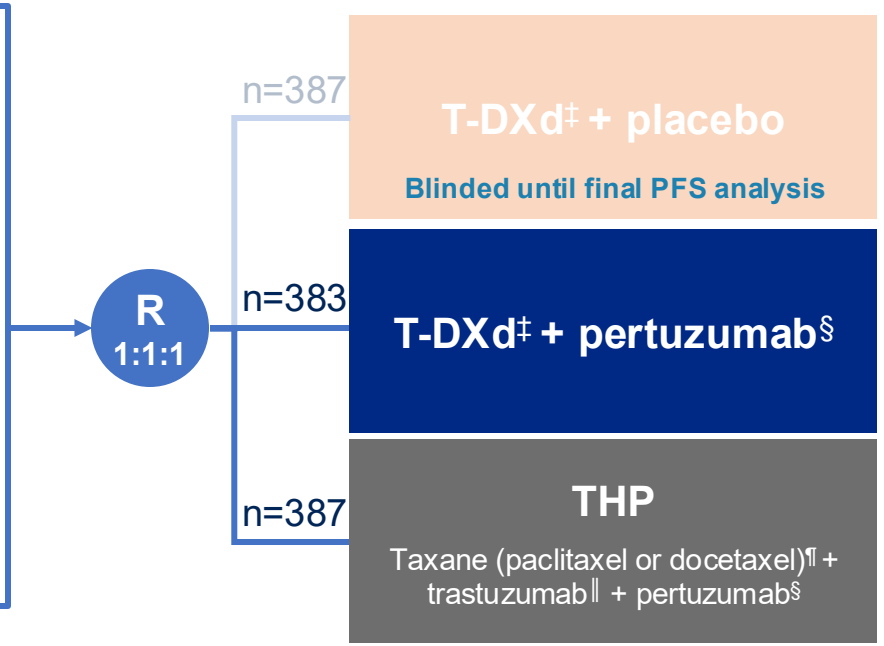
Sara M. Tolaney

DESTINY-Breast09 study design

A randomized, multicenter, open-label,* Phase 3 study (NCT04784715)

Eligibility criteria

- HER2+ a/mBC
- Asymptomatic/inactive brain mets allowed
- DFI >6 mo from last chemotherapy or HER2-targeted therapy in neoadjuvant/ adjuvant setting
- One prior line of ET for mBC permitted
- **No other prior systemic treatment for mBC†**



Endpoints

Primary

- PFS (BICR)

Key secondary

- OS

Secondary

- PFS (INV)
- ORR (BICR/INV)
- DOR (BICR/INV)
- PFS2 (INV)
- Safety and tolerability

Stratification factors

- De-novo vs recurrent mBC
- HR+ or HR−
- *PIK3CA*m (detected vs non-detected)

At this planned interim analysis (DCO Feb 26, 2025), results are reported for the T-DXd + P and THP arms

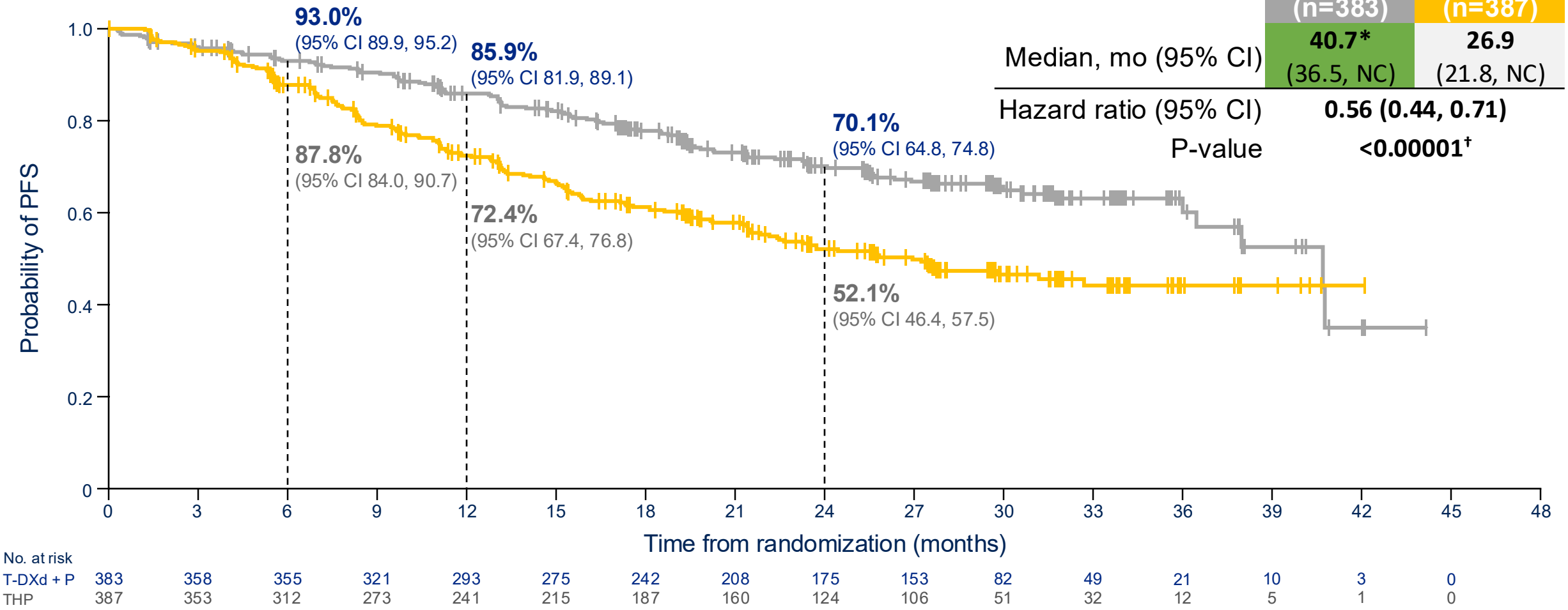
*Open label for THP arm. Double blinded for pertuzumab in experimental arms; †HER2-targeted therapy or chemotherapy; ‡5.4 mg/kg Q3W; §840 mg loading dose, then 420 mg Q3W; ¶paclitaxel 80 mg/m² QW or 175 mg/m² Q3W, or docetaxel 75 mg/m² Q3W for a minimum of six cycles or until intolerable toxicity; ‖8 mg/kg loading dose, then 6 mg/kg Q3W

a/mBC, advanced/metastatic breast cancer; BICR, blinded independent central review; DCO, data cutoff; DFI, disease-free interval; DOR, duration of response; HER2, human epidermal growth factor receptor 2; HER2+, HER2-positive; HR+/−, hormone receptor–positive/–negative; INV, investigator; mBC, metastatic breast cancer; mets, metastases; mo, months; ORR, objective response rate; OS, overall survival; P, pertuzumab; PFS, progression-free survival; PFS2, second progression-free survival; *PIK3CA*m, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha mutation; Q3W, every 3 weeks; QW, once every week; R, randomization; T-DXd, trastuzumab deruxtecan

NCT04784715. Updated. May 6, 2025. Available from: https://clinicaltrials.gov/study/NCT04784715 (Accessed May 29, 2025)

PRESENTED BY: Sara M Tolaney, MD, MPH

PFS (BICR): primary endpoint



	T-DXd + P (n=383)	THP (n=387)
Median, mo (95% CI)	40.7* (36.5, NC)	26.9 (21.8, NC)
Hazard ratio (95% CI)	0.56 (0.44, 0.71)	
P-value	<0.00001†	

No. at risk

T-DXd + P	383	358	355	321	293	275	242	208	175	153	82	49	21	10	3	0
THP	387	353	312	273	241	215	187	160	124	106	51	32	12	5	1	0

Statistically significant and clinically meaningful PFS benefit with T-DXd + P (median Δ 13.8 mo)

*Median PFS estimate for T-DXd + P is likely to change at updated analysis; †stratified log-rank test. A P-value of <0.00043 was required for interim analysis superiority
BICR, blinded independent central review; CI, confidence interval; mo, months; (m)PFS, (median) progression-free survival; NC, not calculable; P, pertuzumab; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

Conclusions

- T-DXd + P demonstrated a **statistically significant and clinically meaningful PFS benefit** by BICR vs THP, which was consistently observed across subgroups
  - Hazard ratio of **0.56** vs THP (**P<0.00001**)
  - Median PFS was **40.7 months (T-DXd + P)** vs **26.9 months (THP)**
- Median DOR of **>3 years with T-DXd + P**, with CRs in **15.1% (T-DXd + P)** vs **8.5% (THP)**
- Early OS data suggest a positive trend favoring T-DXd + P, with a supportive hazard ratio of **0.60** for PFS2
- T-DXd + P safety data were **consistent with known profiles of individual treatments**

PFS by BICR

44%

Reduction in risk of disease progression or death with T-DXd + P vs THP

T-DXd + P demonstrated a statistically significant and clinically meaningful PFS benefit vs THP and may represent a new first-line standard of care for patients with HER2+ a/mBC

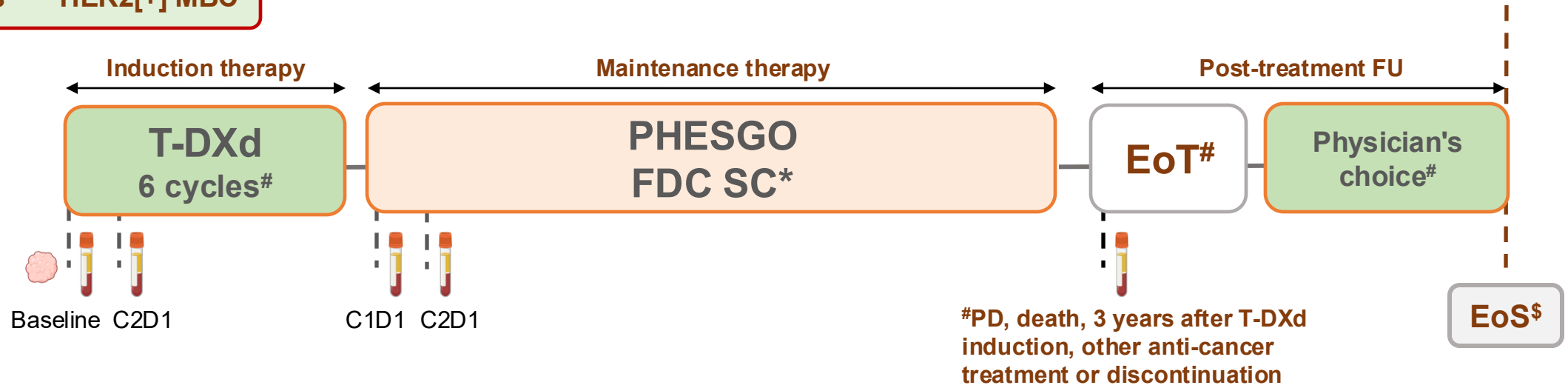
a/mBC, advanced/metastatic breast cancer; BICR, blinded independent central review; CR, complete response; DOR, duration of response; HER2+, human epidermal growth factor receptor 2–positive; OS, overall survival; P, pertuzumab; PFS, progression-free survival; PFS2, second progression-free survival; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

The DEMETHER Study

Study Design

165 patients **HER2[+] MBC**

Screening



Treatment regimen:

- **T-DXd**: 5.4 mg/kg; IV, Q3W - 6 cycles.

  #T-DXd is allowed upon progression on PHESGO.
- **PHESGO FDC SC**: 1200 mg pertuzumab, 600 mg trastuzumab (LD) - 600 mg pertuzumab, 600 mg trastuzumab; Q3W.

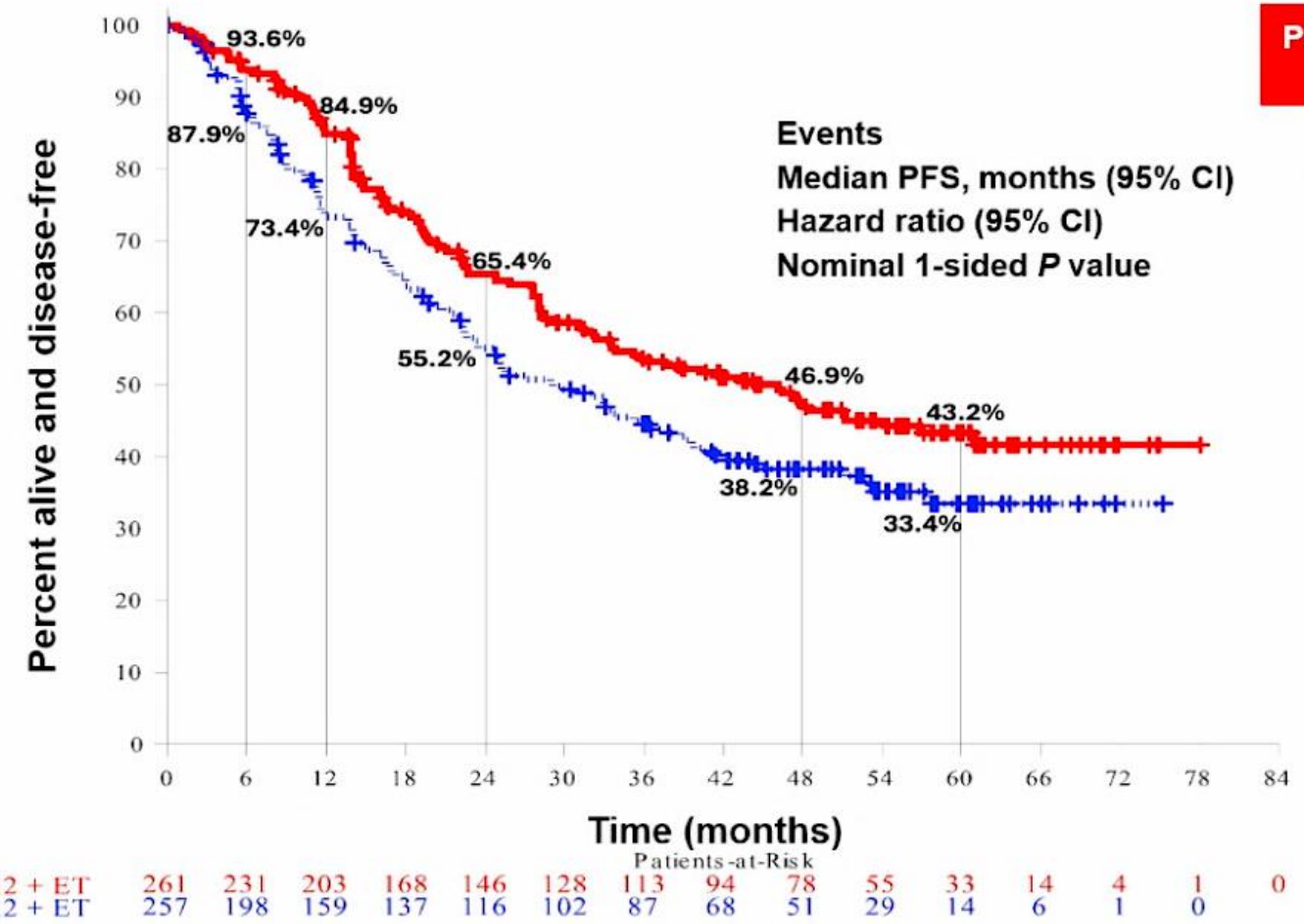
  *Additional HT will be administered in the maintenance phase to patients with confirmed HR[+] status.

$All patients will be followed up until 36 months + 28 days (± 7 days) after T-DXd initiation of LPI, unless premature study termination.

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.

1L HR+/HER2+ mBC: PATINA Trial

PFS

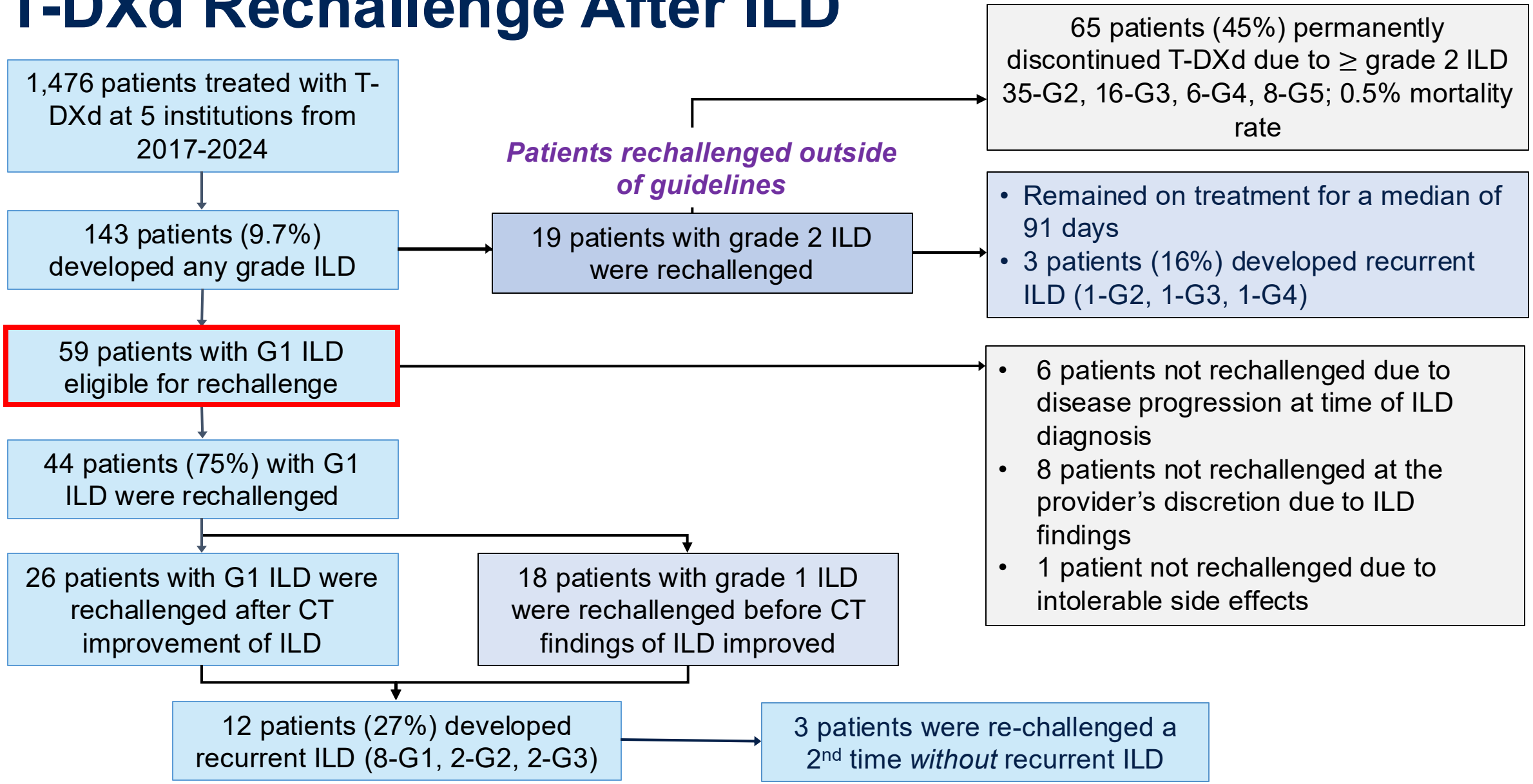


	Palbo + anti-HER2 and ET	Anti-HER2 and ET
Events	126/261	136/257
Median PFS, months (95% CI)	**44.3** (32.4-60.9)	**29.1** (23.3-38.6)
Hazard ratio (95% CI)	0.74 (0.58-0.94)	
Nominal 1-sided *P* value	0.0074	

Median follow-up on patients who are alive and disease-free, 52.6 months

CI=confidence interval; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; palbo=palbociclib.

T-DXd Rechallenge After ILD



PRESENTED BY: Hope S. Rugo, M.D.

Abstract 1015

*G = grade

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

Incidence of BM in HER2+ MBC: Real-World Data From US Flatiron Database

Line of therapy	HR+, HER2- positive	HR–, HER2- positive	HR+, HER2– [HR+, HER2-low]	TNBC [HR–, HER2-low]
Number of pts, n				
1	3062	902	12331 [7062]	1780 [725]
2	1936	478	8120 [4721]	972 [422]
3	1232	281	5303 [3101]	526 [240]
4	761	159	3454 [2002]	283 [129]
5+	453	103	2191 [1276]	141 [70]
Prevalence of BM, %				
1	193 (6.3)	101 (11.2)	134 (2.5) [199 (2.8)]	109 (10.3) [88 (12.1)]
2	341 (17.6)	149 (31.2)	150 (4.4) [275 (5.8)]	97 (17.6) [73 (17.3)]
3	265 (21.5)	102 (36.3)	125 (6.7) [231 (7.4)]	63 (22.0) [50 (20.8)]
4	199 (26.1)	59 (37.1)	104 (7.2) [189 (9.4)]	38 (24.7) [36 (27.9)]
5+	120 (26.5)	38 (36.9)	78 (8.5) [134 (10.5)]	23 (32.4) [18 (25.7)]

Data from 18,075 patients with MBC in the Flatiron database who had initiated a 1L of therapy up to March 1, 2021 to allow at least 2y follow-up

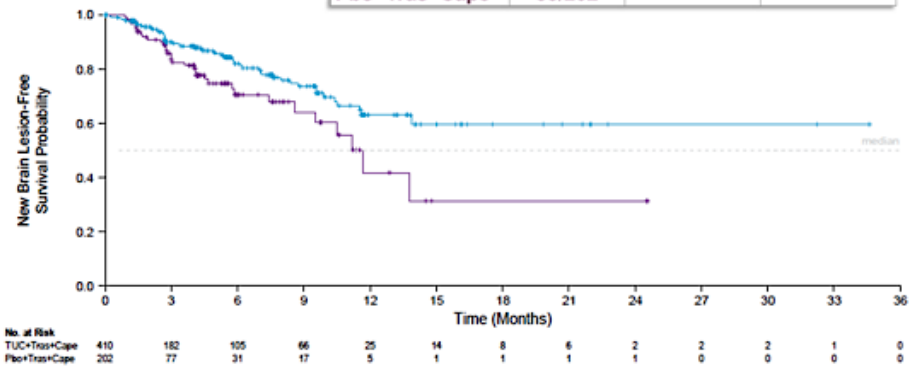
By 3L of therapy, **21.5%** of HR+/HER2+ and **36.3%** of HR-/HER2+ pts have developed brain metastases

Older data from the HERA trial (Pestalozzi et al, Lancet Oncol 2013) where HER2+ pts were followed until death reported that **47%** of trastuzumab-treated pts eventually developed brain mets

Sammons SL et al. 2023 SABCS Annual Meeting. Abstract PS11-01.

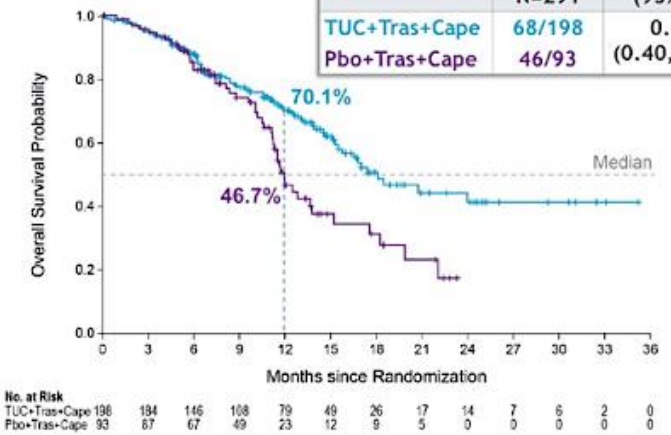
HER2CLIMB: New Brain Lesion-Free Survival

	Events N=612	HR (95% CI)	P Value
TUC+Tras+Cape	52/410	0.52 (0.33, 0.82)	0.005
Pbo+Tras+Cape	33/202		



OS Benefit in Patients with Brain Metastases

	Events N=291	HR (95% CI)	P Value
TUC+Tras+Cape	68/198	0.58 (0.40, 0.85)	0.005
Pbo+Tras+Cape	46/93		



Risk of death was reduced by 42% in patients with brain metastases

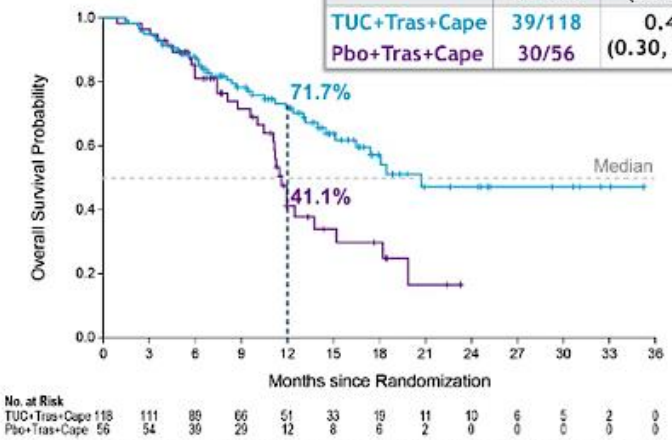
One-year OS (95% CI):	
TUC+Tras+Cape	Pbo+Tras+Cape
70.1% (62.1, 76.7)	46.7% (33.9, 58.4)
Median OS (95% CI):	
18.1 months (15.5, NE)	12.0 months (11.2, 15.2)

NE: not estimable

HR: hazard ratio computed from Cox proportional hazards model using stratification factors (ECOG performance status: 0/1, and Region of world: North America/Rest of World) at randomization. All P values are nominal.

OS Benefit in Patients with Active Brain Metastases

	Events N=174	HR (95% CI)	P Value
TUC+Tras+Cape	39/118	0.49 (0.30, 0.80)	0.004
Pbo+Tras+Cape	30/56		



Risk of death was reduced by 51% in patients with active brain metastases

One-year OS (95% CI):	
TUC+Tras+Cape	Pbo+Tras+Cape
71.7% (61.4, 79.7)	41.1% (25.5, 56.1)
Median OS (95% CI):	
20.7 months (15.1, NE)	11.6 months (10.5, 13.8)

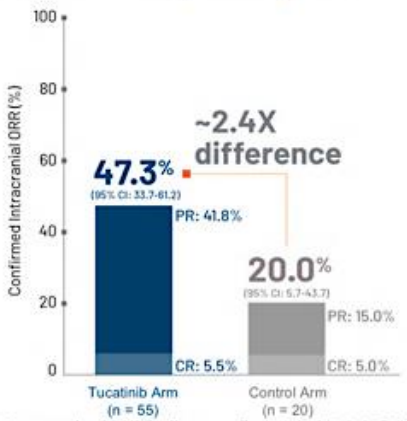
NE: not estimable

HR: hazard ratio computed from Cox proportional hazards model using stratification factors (ECOG performance status: 0/1, and Region of world: North America/Rest of World) at randomization. All P values are nominal.

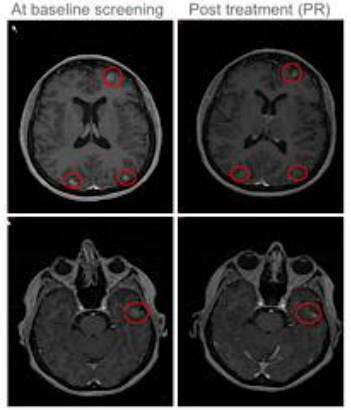
ASCO 2020 UPDATE: POST HOC EXPLORATORY ANALYSES

CONFIRMED INTRACRANIAL OBJECTIVE RESPONSE RATE[1*]

Confirmed intracranial ORR by RECIST 1.1 (n = 75) in patients with active brain metastases and measurable intracranial lesions at baseline per investigator assessment[1]



Brain CT scans of a patient in the tucatinib arm[†]



CT = computed tomography; RECIST = Response Evaluation Criteria in Solid Tumors.

* Results of this exploratory analysis are descriptive, not in the approved labeling, and not controlled for type 1 error, as HER2CLIMB was not powered to test this analysis. The results are estimates (not exact numbers). Due to a high rate of censoring of patients owing to extra-CNS progression (new or enlarging extracranial lesions) or death, results should be interpreted with caution. †Individual results may vary.

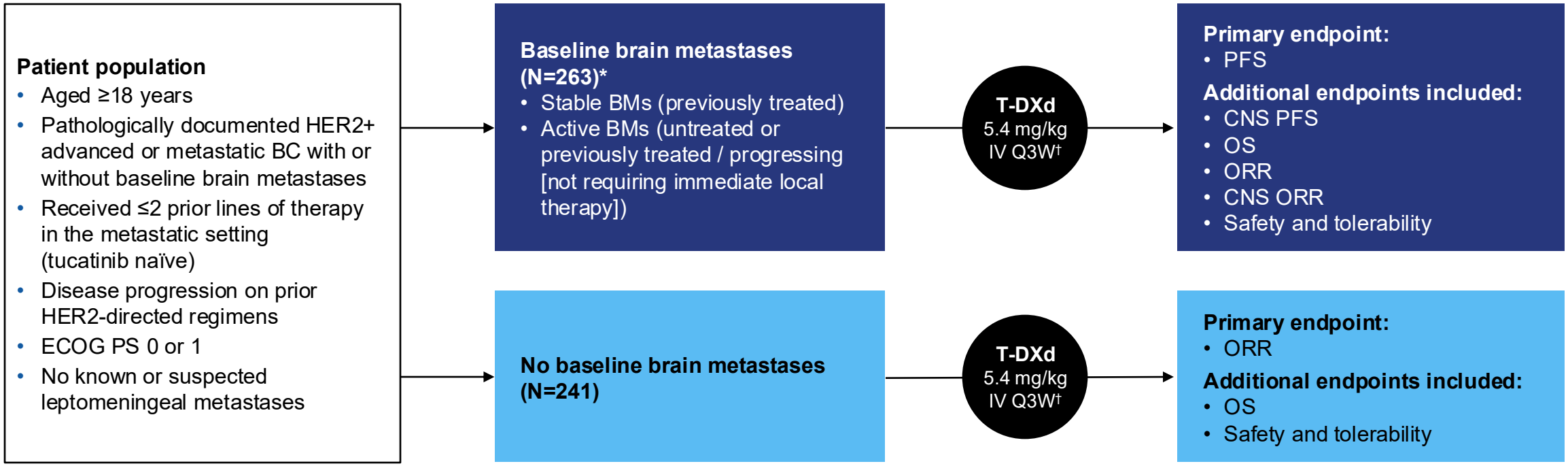
1. Lin NU et al. *J Clin Oncol*. 2020;38:2610-2619.

Lin NU et al. ASCO 2020;Abstract 1005

DESTINY-Breast12

DESTINY-Breast12 study design

Phase 3b/4, multicenter, single-arm, two-cohort, open-label study of T-DXd in previously treated HER2+ mBC with and without brain metastases (BMs); the largest prospective study of T-DXd in patients with stable or active BMs



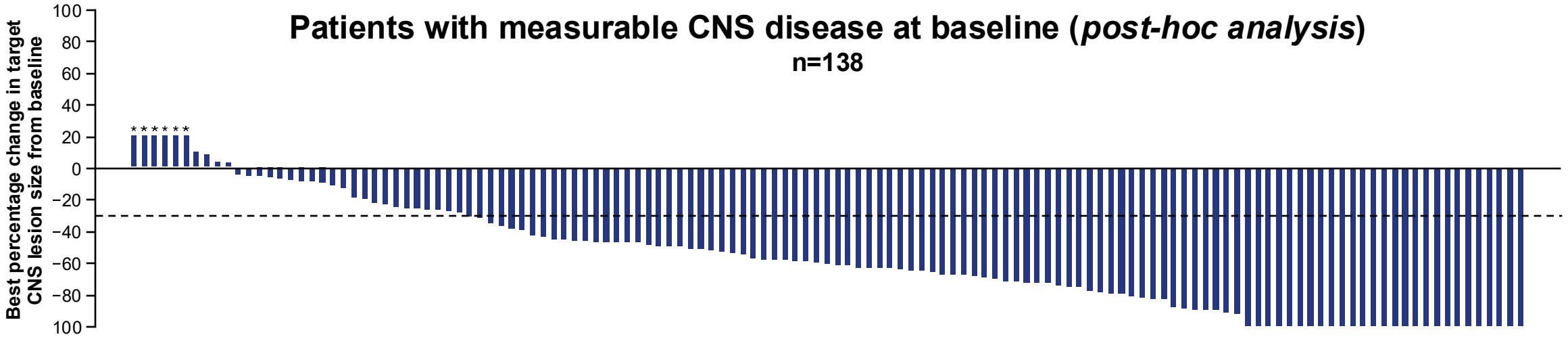
Data reported for the full analysis set (all patients enrolled in the study who received at least one treatment dose) and safety analysis set (identical to full analysis set). No hypothesis testing or comparison of cohorts. Response and progression assessed by ICR per RECIST 1.1 in both cohorts. Patients were enrolled from Australia, Canada, Europe, Japan, and United States

***Concomitant use of ≤3 mg of dexamethasone daily or equivalent allowed for symptom control of BMs (baseline BMs cohort only)**; †until RECIST 1.1-defined disease progression outside the CNS

BC, breast cancer; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; HER2+, HER2-positive; ICR, independent central review; IV, intravenous; mBC, metastatic breast cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; RECIST 1.1, Response Evaluation Criteria in Solid Tumours version 1.1; T-DXd, trastuzumab deruxtecan

NCT04739761. Updated. July 19, 2024. Available from: https://www.clinicaltrials.gov/study/NCT04739761 (Accessed September 9, 2024)

Baseline BMs: CNS ORR



Measurable CNS disease at baseline	All patients (n=138)	Stable BMs (n=77)	Active BMs (n=61)	Active BM subgroups: Untreated (n=23) *Post-hoc analysis*	Active BM subgroups: Previously treated / progressing (n=38) *Post-hoc analysis*
Confirmed CNS ORR, % (95% CI)	**71.7 (64.2, 79.3)**	79.2 (70.2, 88.3)	62.3 (50.1, 74.5)	82.6 (67.1, 98.1)	50.0 (34.1, 65.9)

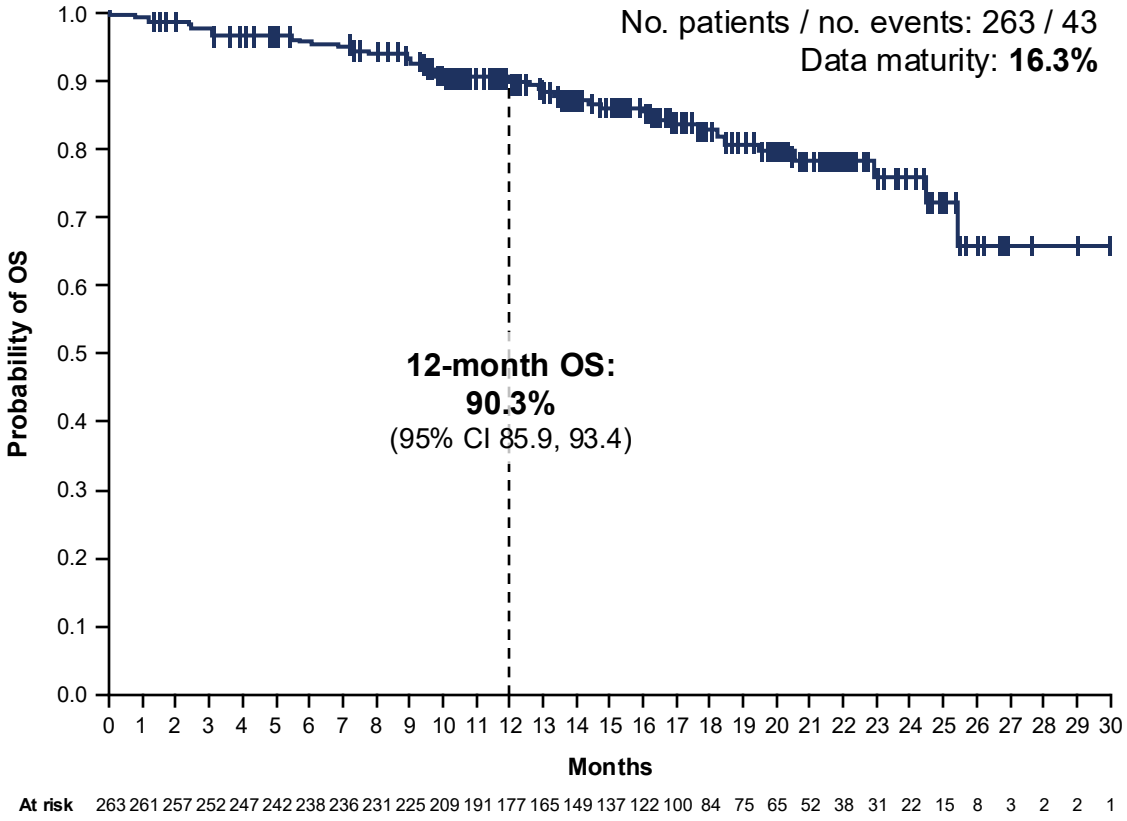
T-DXd showed substantial CNS responses in the overall BMs population, including patients with stable and active BMs

Dashed line indicates a 30% decrease in target tumor size (PR)
*Imputed values: a value of +20% was imputed if best percentage change could not be calculated because of missing data if: a patient had a new lesion or progression of non-target lesions or target lesions, or had withdrawn because of PD and had no evaluable target lesion data before or at PD
BM, brain metastasis; CI, confidence interval; CNS, central nervous system; ORR, objective response rate; PD, progressive disease; PR, partial response; T-DXd, trastuzumab deruxtecan

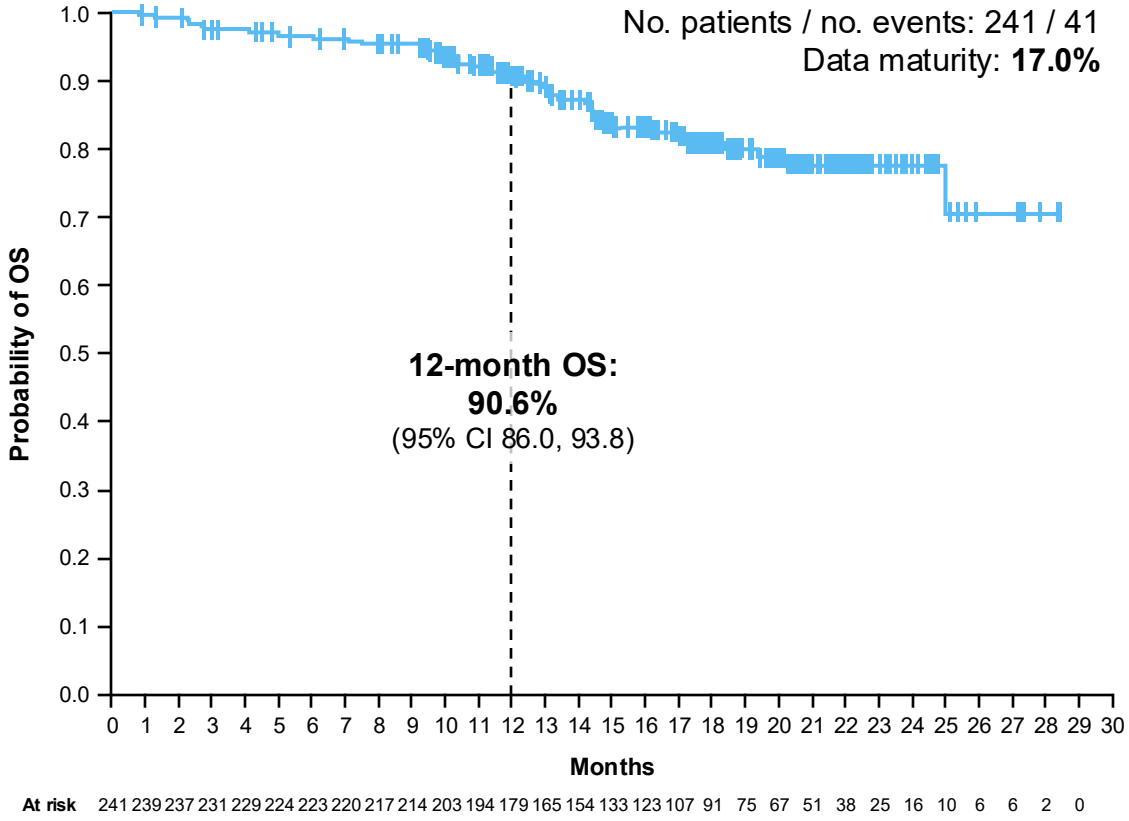
DESTINY-Breast12

OS in patients with and without baseline BMs

Baseline BMs (KM analysis)



No baseline BMs (KM analysis)



T-DXd showed consistent 12-month OS in patients with and without BMs

Median follow-up duration was 15.4 months in patients with BMs and 16.1 months in patients without BMs
BM, brain metastasis; CI, confidence interval; KM, Kaplan-Meier; no., number of; OS, overall survival; T-DXd, trastuzumab deruxtecan

T-DXd Followed by THP Before Surgery Showed Statistically Significant and Clinically Meaningful Improvement in Pathologic Complete Response in Patients with High-Risk HER2-Positive Early-Stage Breast Cancer in DESTINY-Breast11 Phase III Trial

Press Release: May 7, 2025

"Positive high-level results from the DESTINY-Breast11 Phase III trial showed trastuzumab deruxtecan (T-DXd) followed by paclitaxel, trastuzumab and pertuzumab (THP) demonstrated a statistically significant and clinically meaningful improvement in pathologic complete response (pCR) rate versus standard of care (dose-dense doxorubicin and cyclophosphamide followed by THP [ddAC-THP]) when used in the neoadjuvant setting (before surgery) in patients with high-risk, locally advanced HER2-positive early-stage breast cancer.

The secondary endpoint of event-free survival (EFS) was not mature at the time of analysis; however, EFS data showed an early positive trend favouring T-DXd followed by THP compared to standard of care. The trial will continue to follow EFS.

Data from DESTINY-Breast11 will be presented at an upcoming medical meeting and shared with regulatory authorities."

https://www.astrazeneca.com/media-centre/press-releases/2025/enhertu-improved-pcr-in-early-stage-breast-cancer.html

RTP RESEARCH TO PRACTICE

Faculty Discussion Questions

What is the optimal first-line therapy, including maintenance, for patients with HER2-positive, ER-negative mBC? What about for HER2-positive, ER-positive disease?

In which situations will you rechallenge with T-DXd for patients who have developed ILD on the drug?

What is your preferred second-line therapy for patients with HER2-positive disease who experience progression on THP with brain metastases?

Agenda

Introduction: View from Outer Space

Module 1: HR-Positive Breast Cancer

Module 2: HER2-Positive Breast Cancer

Module 3: Triple-Negative Breast Cancer

RTP RESEARCH TO PRACTICE

OlympiA: Trial schema

- Local genetic testing or on-study central screening (Myriad Genetics Inc.)
- Germline pathogenic or likely pathogenic *BRCA1/2* mutation
- HER2–negative (ER and/or PgR positive or TNBC)
- Stage II-III Breast Cancer or lack of PathCR to NACT

Neoadjuvant Group
- *TNBC:* non-pCR
- *ER and/or PgR positive:* non-pCR and CPS+EG score ≥ 3

≥ 6 cycles Neoadjuvant Chemotherapy → **Surgery** → **+/- Radiotherapy**

Adjuvant Group
- *TNBC:* ≥ pT2 or ≥ pN1
- *ER and/or PgR positive:* ≥ 4 positive lymph nodes

Surgery → **≥ 6 cycles Adjuvant Chemotherapy** → **+/- Radiotherapy**

1:1 Randomization N=1836

Olaparib 300 mg twice daily for 1 year

Placebo twice daily for 1 year

Primary End Point
- Invasive disease-free survival (IDFS) by STEEP system[1]

Secondary End Points
- Distant disease-free survival[1] (DDFS)
- Overall survival[1] (OS)
- BRCA1/2 associated cancers
- Symptom / Health related QoL
- Safety

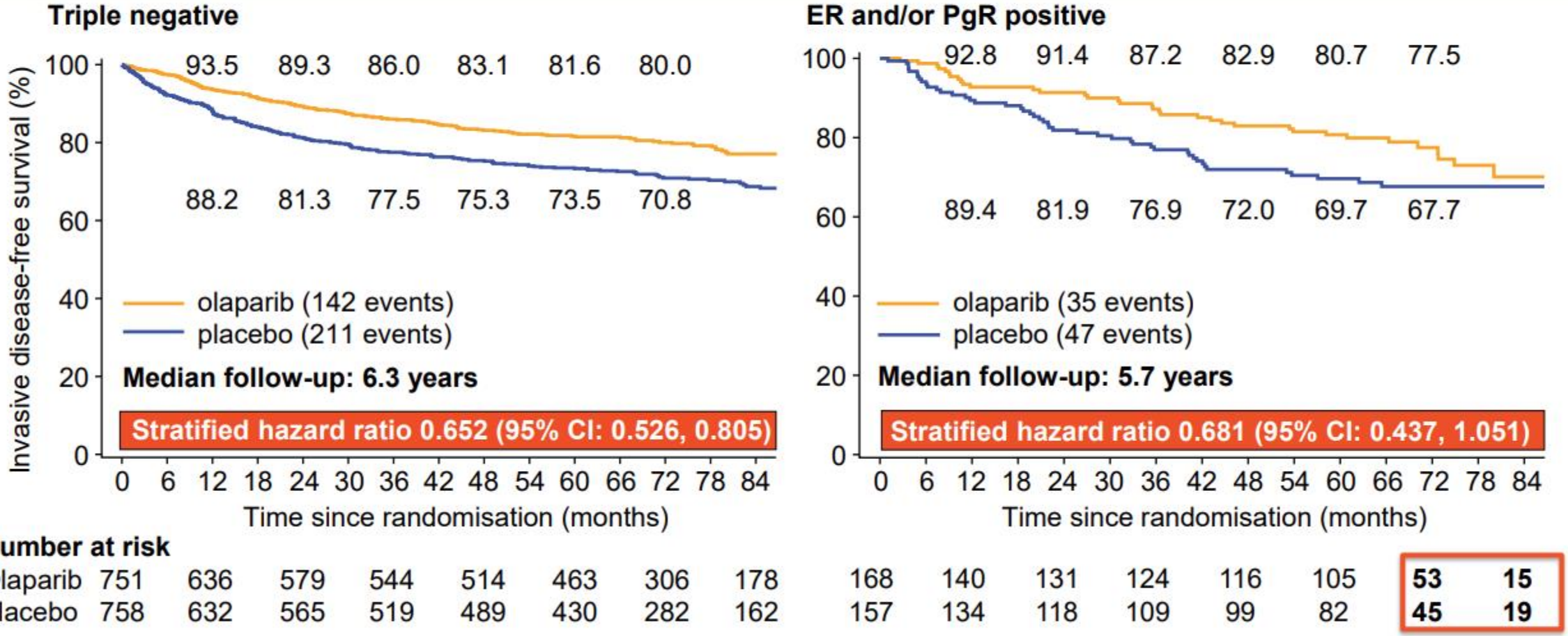
Stratification Factors
- ER and/or PgR positive vs. TNBC
- Neoadjuvant vs. adjuvant
- Prior platinum-based chemotherapy (yes vs. no)

Concurrent Adjuvant Therapy
- Endocrine therapy
- Bisphosphonates
- No 2nd Adjuvant Chemotherapy

ER and/or PgR positive defined as IHC staining ≥1%.
Triple Negative defined as ER and PgR negative (IHC staining < 1%)
[1]Hudis CA, *J Clin Oncol* 2007

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

Analysis of IDFS by HR status

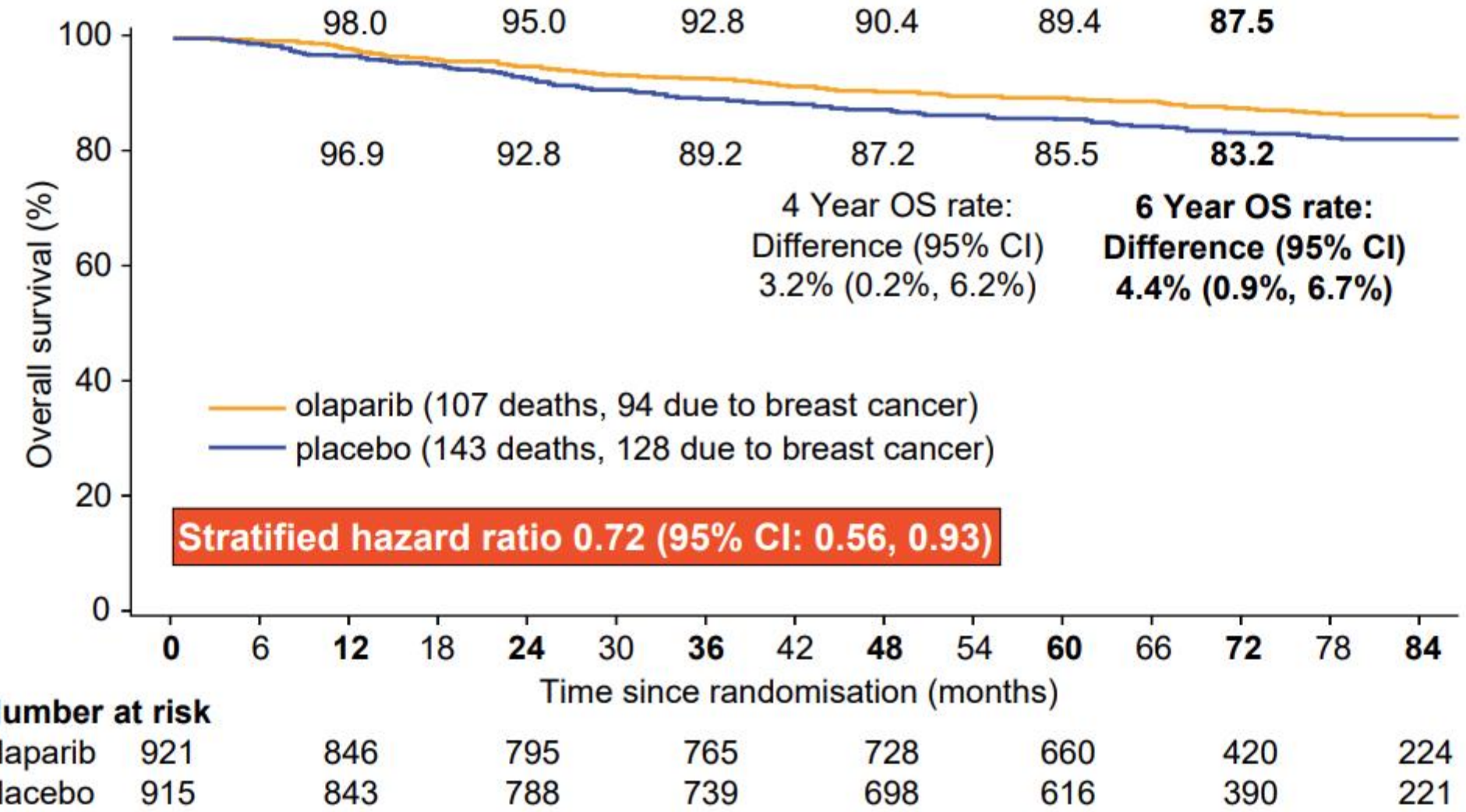


Number at risk

Olaparib	751	636	579	544	514	463	306	178	168	140	131	124	116	105	**53**	**15**
Placebo	758	632	565	519	489	430	282	162	157	134	118	109	99	82	**45**	**19**

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

Analysis of OS (ITT)



Number at risk

olaparib	921	846	795	765	728	660	420	224
placebo	915	843	788	739	698	616	390	221

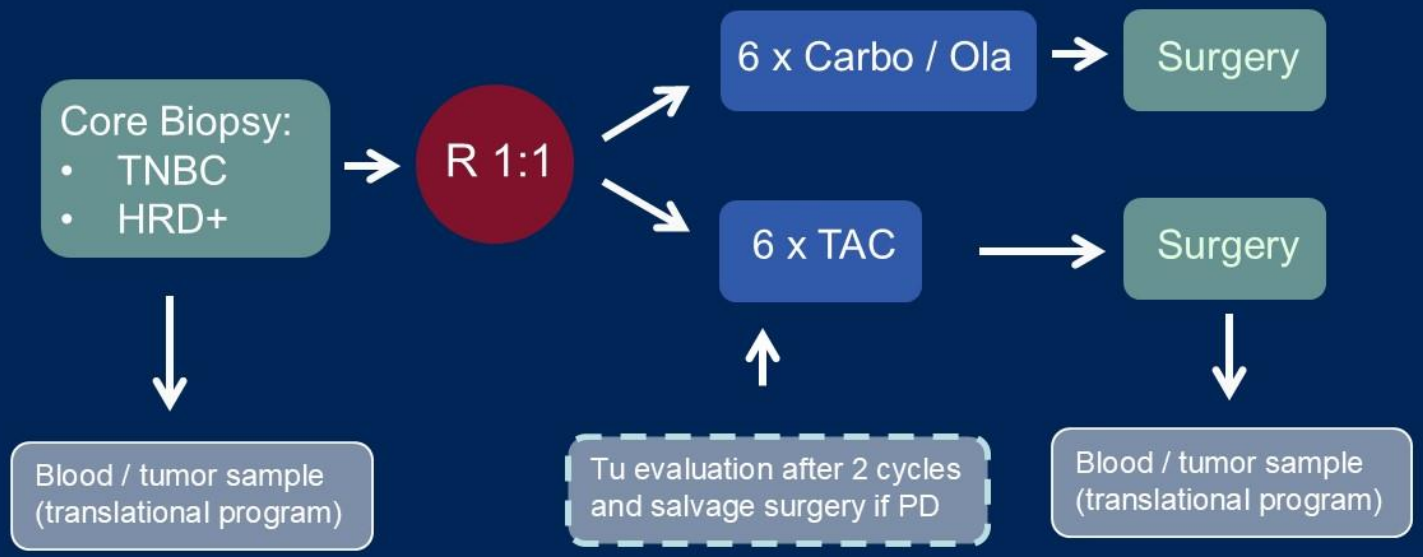
Garber JE et al. SABCS 2024; Abstract GS1-09

OlympiA: Conclusions

- At 6.1 years median follow-up (maximum, 9.6 years),12 months of olaparib after (neo)adjuvant chemotherapy continues to demonstrate clinically meaningful improvements in IDFS, DDFS and OS in patients with g*BRCA*pv and high-risk HER2-negative primary BC.
- Olaparib benefit was consistent across all key subgroups, including for patients with high-risk ER and/or PgR positive disease.
- Fewer new primary malignancies were observed in the olaparib arm.
- No new safety signals were observed with longer term follow-up, and there is no evidence of increased risk of MDS or AML.
- These data continue to support adjuvant olaparib as standard of care for patients with g*BRCA*pv high-risk HER2-negative primary BC and therefore highlight the importance of g*BRCA* testing for treatment planning.
- Blinded follow-up for the final planned analysis continues until June 2029.

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

ABCSG 45 Study Design (I)



Phase II Study

- 90 patients randomized

Strata

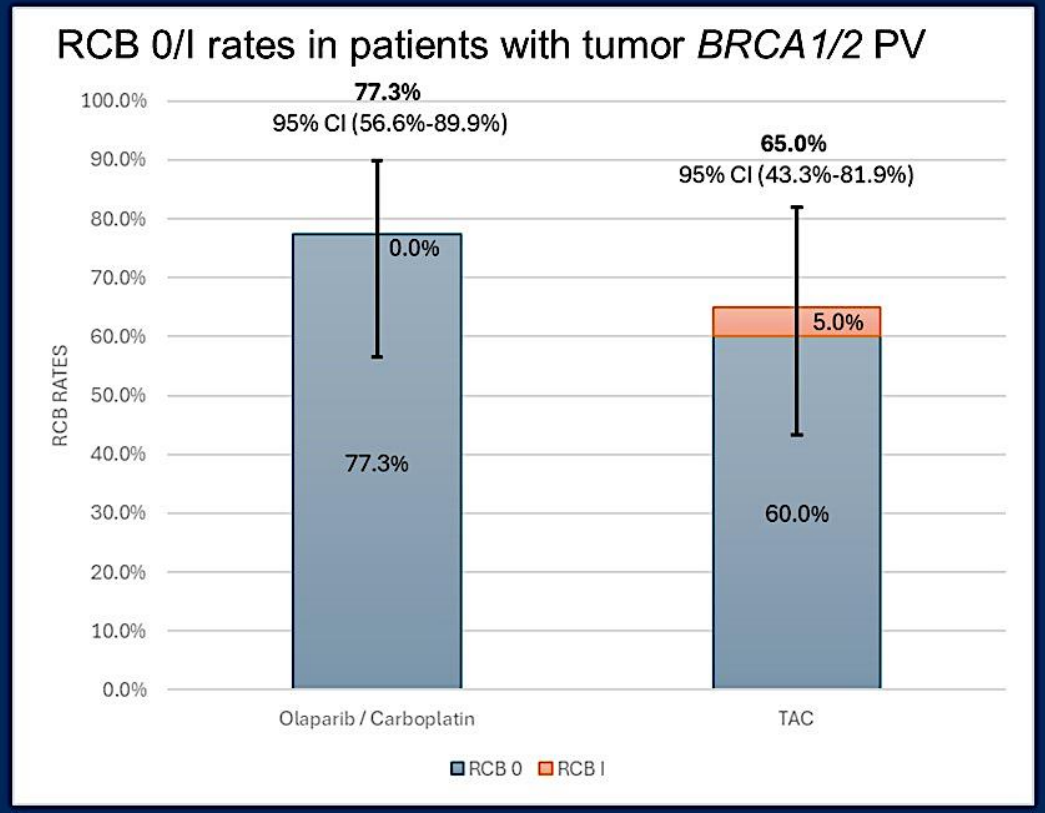
- Tumor *BRCA1/2* status
- Menopausal status

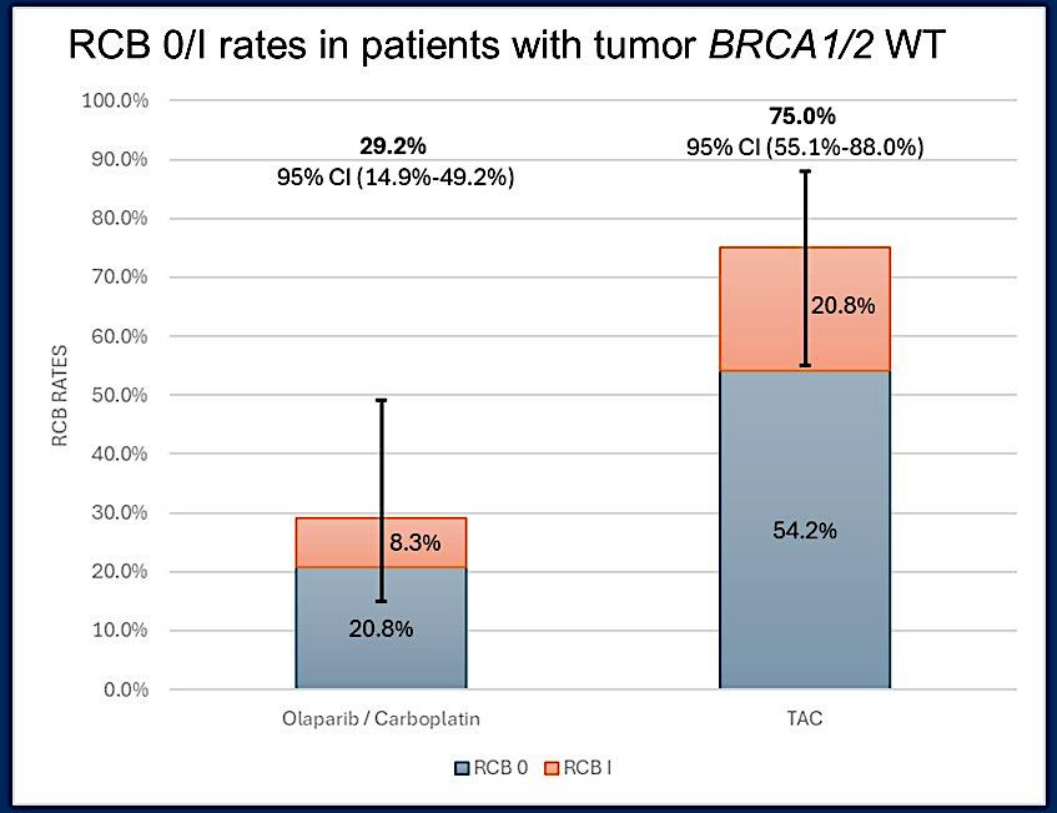
Carbo/Ola: 6 x carboplatin AUC 5 q3w + olaparib ≥ 100 bid (days 4-19)

TAC: 6 x docetaxel 75 mg q3w + epirubicin 50 mg/m^2 q3w + cyclophosphamide 500 mg/m^2 q3w

RCB 0/I and Tumor *BRCA1/2* Status

Multi-agent chemo needed in the WT group





PRESENTED BY: Christian F Singer, Medical University of Vienna, Vienna, Austria

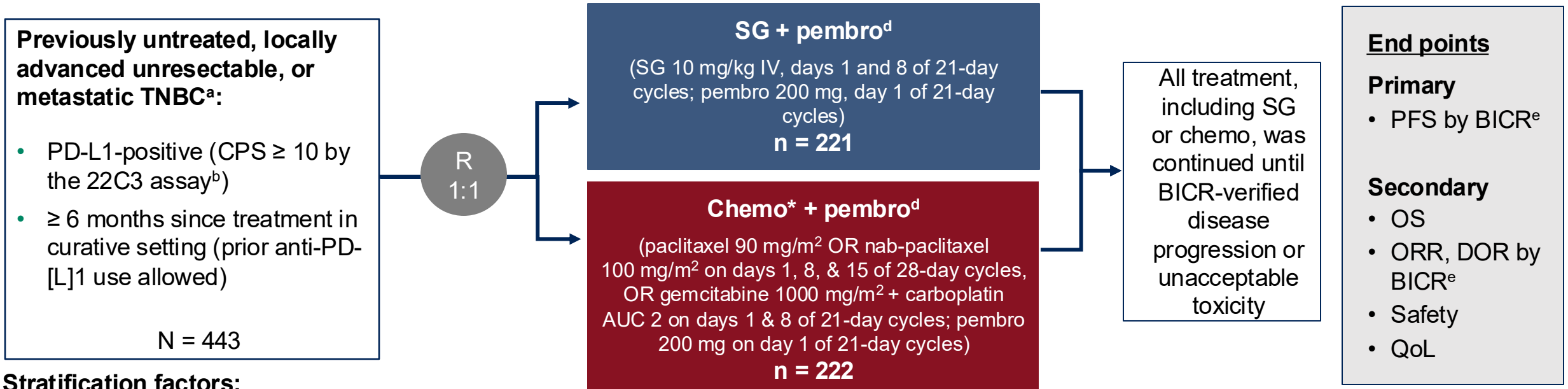
Abstract 510

TROP2-directed ADCs

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

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

ASCENT-04/KEYNOTE-D19 Study Design



Stratification factors:

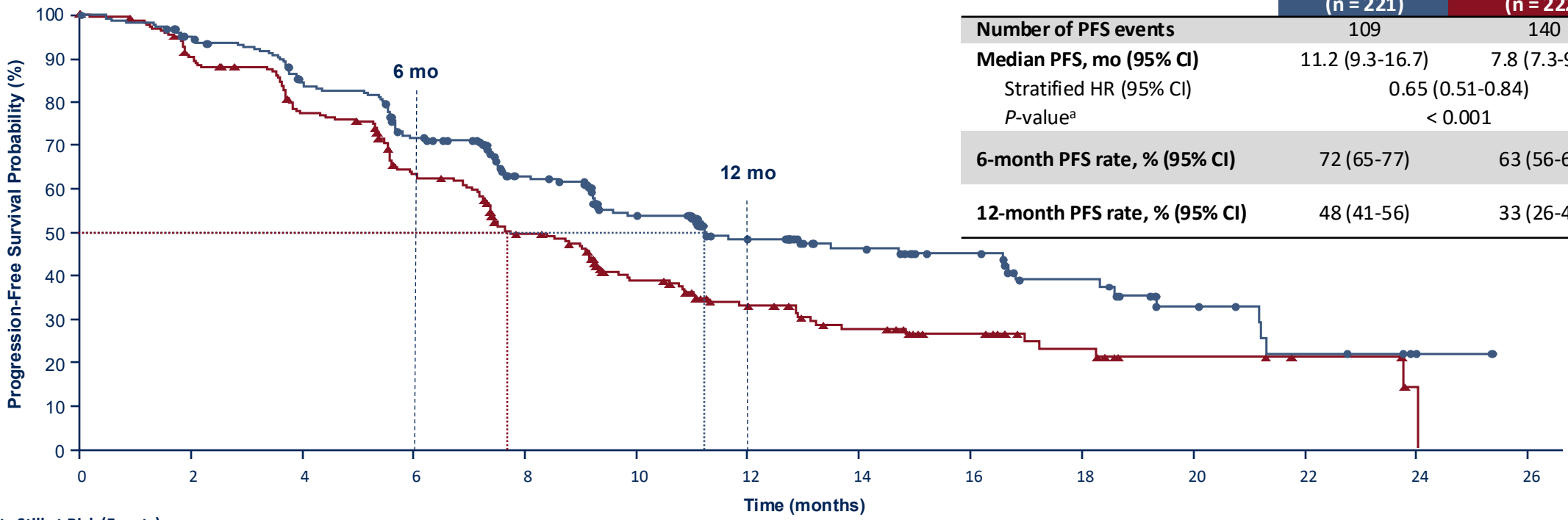
- De novo mTNBC[c] vs recurrent within 6 to 12 months from completion of treatment in curative setting vs recurrent > 12 months from completion of treatment in curative setting
- US/Canada/Western Europe vs the rest of the world
- Prior exposure to anti-PD-(L)1 (yes vs no)

- Median follow-up was 14.0 months (range, 0.1-28.6)
- 95 patients (43%) in the SG + pembro group and 52 patients (23%) in the chemo + pembro group continued to receive study treatment

ClinicalTrials.gov identifier: NCT05382286.
[a]TNBC status determined according to standard American Society of Clinical Oncology-College of American Pathologists criteria. [b]Dako, Agilent Technologies. [c]Up to 35% de novo mTNBC. [d]Pembro was administered for a maximum of 35 cycles. [e]Per RECIST v1.1.
AUC, area under the curve; BICR, blinded independent central review; chemo, chemotherapy; CPS, combined positive score; DOR, duration of response; IV, intravenously; ORR, objective response rate; OS, overall survival; PD-L1, programmed cell death ligand 1; pembro, pembrolizumab; PFS, progression-free survival; QoL, quality of life; R, randomized; RECIST v1.1; Response Evaluation Criteria inSolid Tumors, version 1.1; SG, sacituzumab govitecan; TNBC, triple-negative breast cancer; TTR, time-to-response.

Tolaney SM et al. ASCO 2025;Abstract LBA109

Progression-Free Survival by BICR



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

No. of Patients Still at Risk (Events)

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

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

Data cutoff date: March 3, 2025.
[a]Two-sided *P*-value from stratified log-rank test.
BICR, blinded independent central review; chemo, chemotherapy; HR, hazard ratio; PFS, progression-free survival; pembro, pembrolizumab; SG, sacituzumab govitecan.

Tolaney SM et al. ASCO 2025;Abstract LBA109

Conclusions

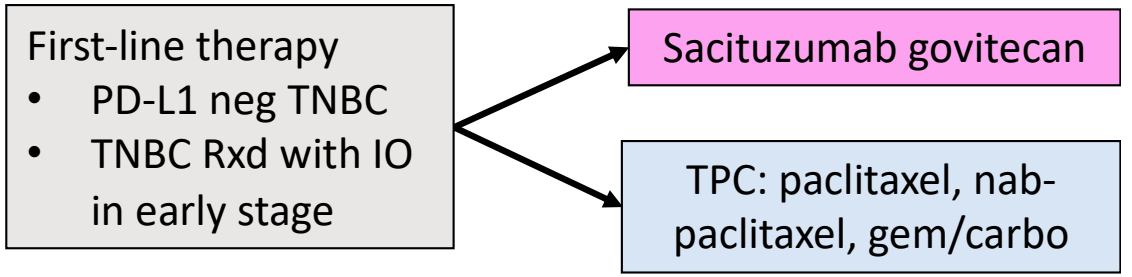
- ASCENT-04/KEYNOTE-D19 is the first randomized, phase 3 study to evaluate the efficacy and safety of an ADC/checkpoint inhibitor combination for first-line treatment of patients with PD-L1+[a] mTNBC
- SG + pembro led to a statistically significant and clinically meaningful improvement in PFS vs chemo + pembro (median 11.2 vs 7.8 months; HR, 0.65; 95% CI, 0.51-0.84; *P* < 0.001)
  - PFS benefit was observed across prespecified subgroups
- OS data are immature, but an early trend in improvement was observed
- ORR was higher (including an increased complete response rate), and responses were more durable with SG + pembro vs chemo + pembro
- The safety profile of SG + pembro was consistent with the established profiles of either agent; no additive toxicity was observed

Results from ASCENT-04/KEYNOTE-D19 support the use of SG + pembro as a potential new standard of care for patients with previously untreated, PD-L1+, locally advanced unresectable or metastatic TNBC

Data cutoff date: March 3, 2025
[a]CPS ≥ 10 per IHC 22C3 assay (Dako, Agilent Technologies).
ADC, antibody drug conjugate; chemo, chemotherapy; CPS, combined positive score; DOR, duration of response; HR, hazard ratio; IHC, immunohistochemistry; mTNBC; metastatic triple-negative breast cancer; ORR, objective response rate; OS, overall survival; PD-L1, programmed cell death ligand 1; pembro, pembrolizumab; PFS, progression-free survival; SG, sacituzumab govitecan; TNBC, triple-negative breast cancer.

Tolaney SM et al. ASCO 2025;Abstract LBA109

ASCENT-03 (NCT05382299): PD-L1 negative
N=540



May 23, 2025

ASCENT-03: Sacituzumab Govitecan Demonstrates Highly Statistically Significant & Clinically Meaningful Improvement in Progression Free Survival in Patients With First-line Metastatic Triple-Negative Breast Cancer Who Are Not Candidates for Checkpoint Inhibitors

The study met its primary endpoint, demonstrating a highly statistically significant and clinically meaningful improvement in progression-free survival (PFS) compared to chemotherapy in patients with first-line mTNBC who are not candidates for PD-1/PD-L1 inhibitors, meaning they are PD-L1 negative or are ineligible to receive immunotherapy.

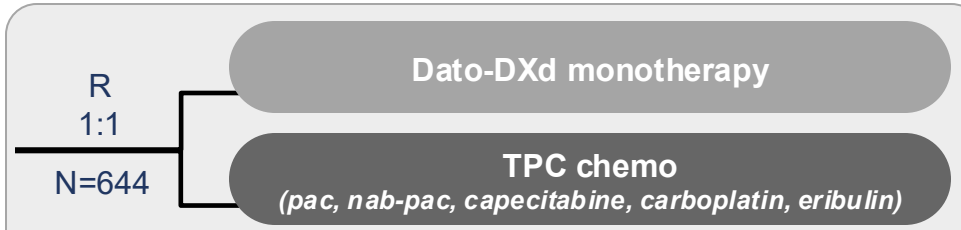
TROPION-Breast02 + TROPION-Breast05 Study Design

TROPION-Breast02[1,2]

Patient Population

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

Study Design



Stratification Factors

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

Key Endpoints[a]

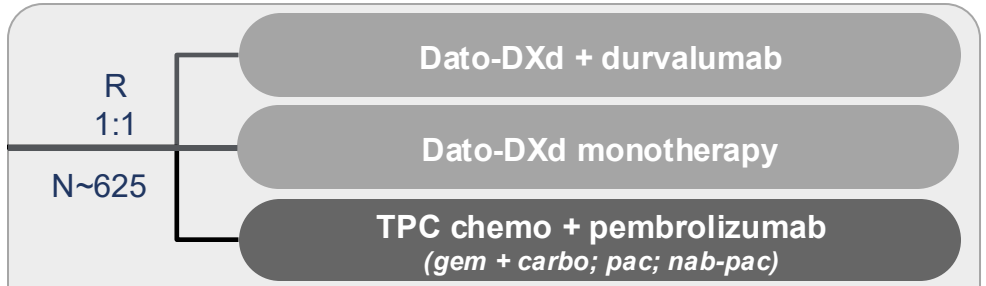
- Primary: PFS by BICR, OS
- Secondary: ORR, DOR, PFS (investigator), safety, PROs

TROPION-Breast05[3]

Patient Population

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

Study Design



Stratification Factors

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

Key Endpoints[a]

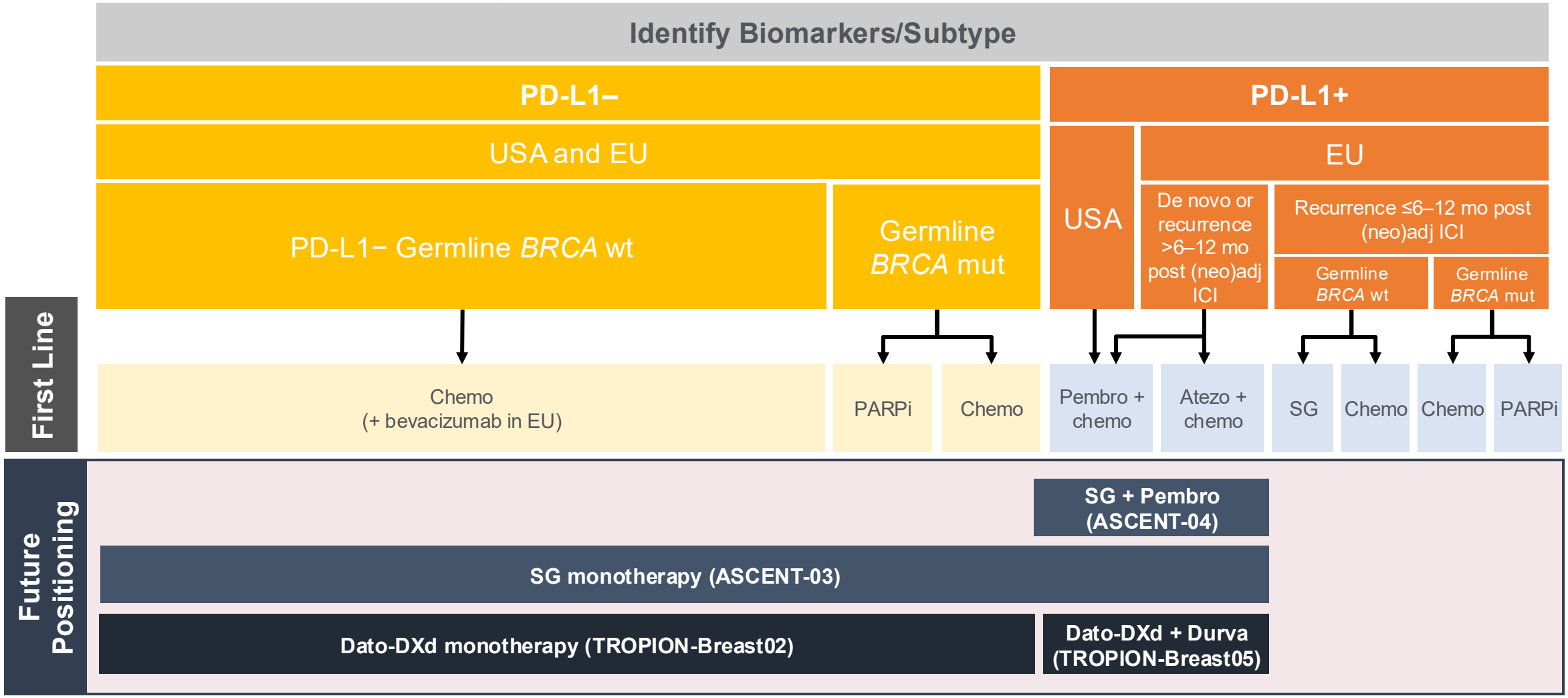
- Primary: PFS by BICR
- Secondary: OS, PFS (investigator), ORR, safety, PROs

[a]Secondary endpoints not exhaustive.

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

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

NCCN and ESMO Guidelines for 1L



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

Sacituzumab Tirumotecan (sac-TMT)

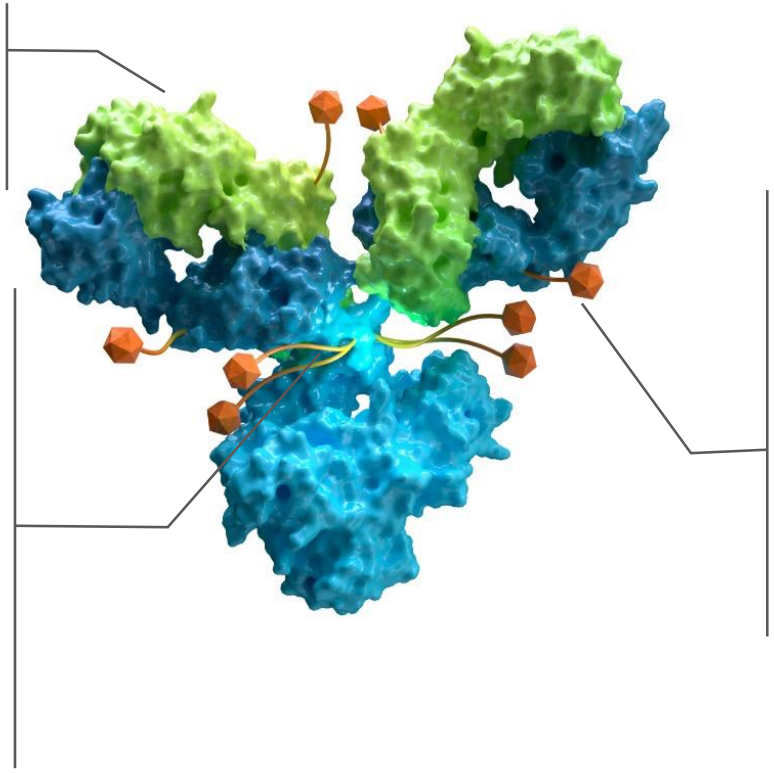
Sac-TMT is a TROP2 ADC developed with a proprietary Kthiol (pyrimidine-thiol) linker conjugated to a novel topoisomerase I inhibitor at DAR 7.4. The features of sac-TMT lead to release of the payload both in the tumor microenvironment (TME) and inside tumor cells, achieving a balance between the safety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

Antibody

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

Linker

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



Payload

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

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

OptiTROP-Breast05: Phase II 1st Line Sac-TMT

Multicenter, open-label phase II study (NCT05445908)

Key eligibility criteria

- **No prior systemic therapy for a/m TNBC**
- **PD-L1 positive or negative[a]**
- **DFI ≥6 months**
- **ECOG PS 0–1**

→ **Sac-TMT (5 mg/kg Q2W)**

N=41

→ Treatment until disease progression or unacceptable toxicity

→ **Primary endpoint[b]**

- ORR by investigator assessment

Secondary endpoints

- PFS, DOR, DCR, OS
- Safety

Tumor assessment

- Every 6 weeks for the first 18 months and every 12 weeks afterward.

Disease-free interval, n (%)	
De novo metastasis	12 (29.3)
6-12 months	8 (19.5)
≥12 months	21 (51.2)

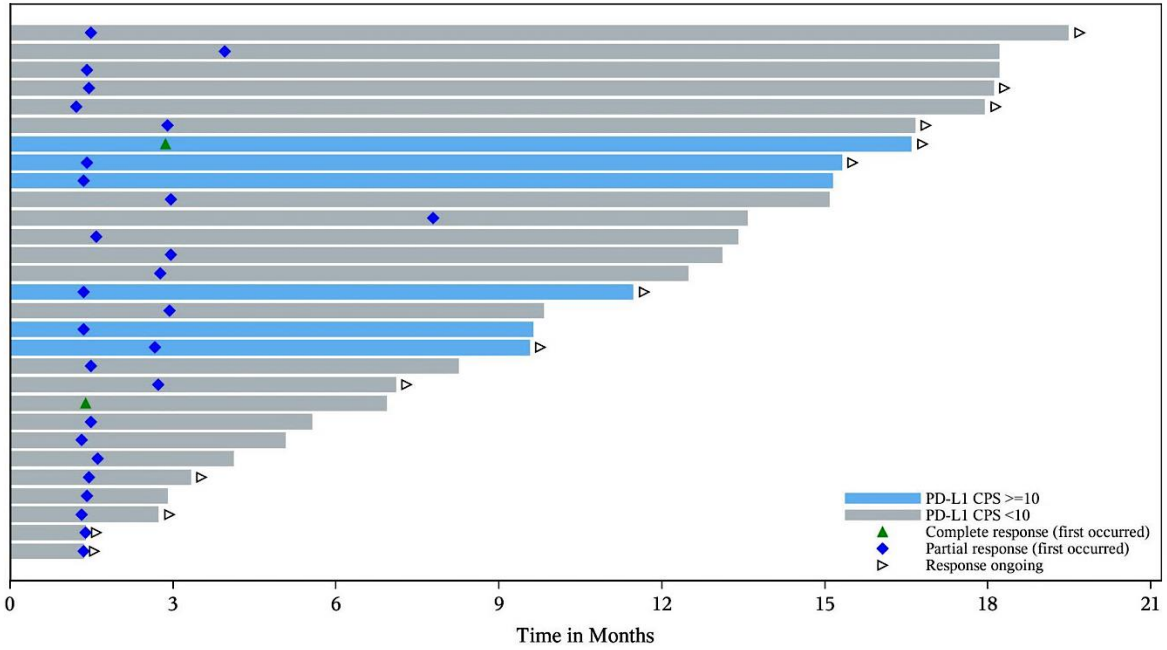
PD-L1 expression,[b] n (%)	
CPS <10	32 (78.0)
CPS ≥10	9 (22.0)

Yin Y et al, ASCO 2025;Abstract 1019

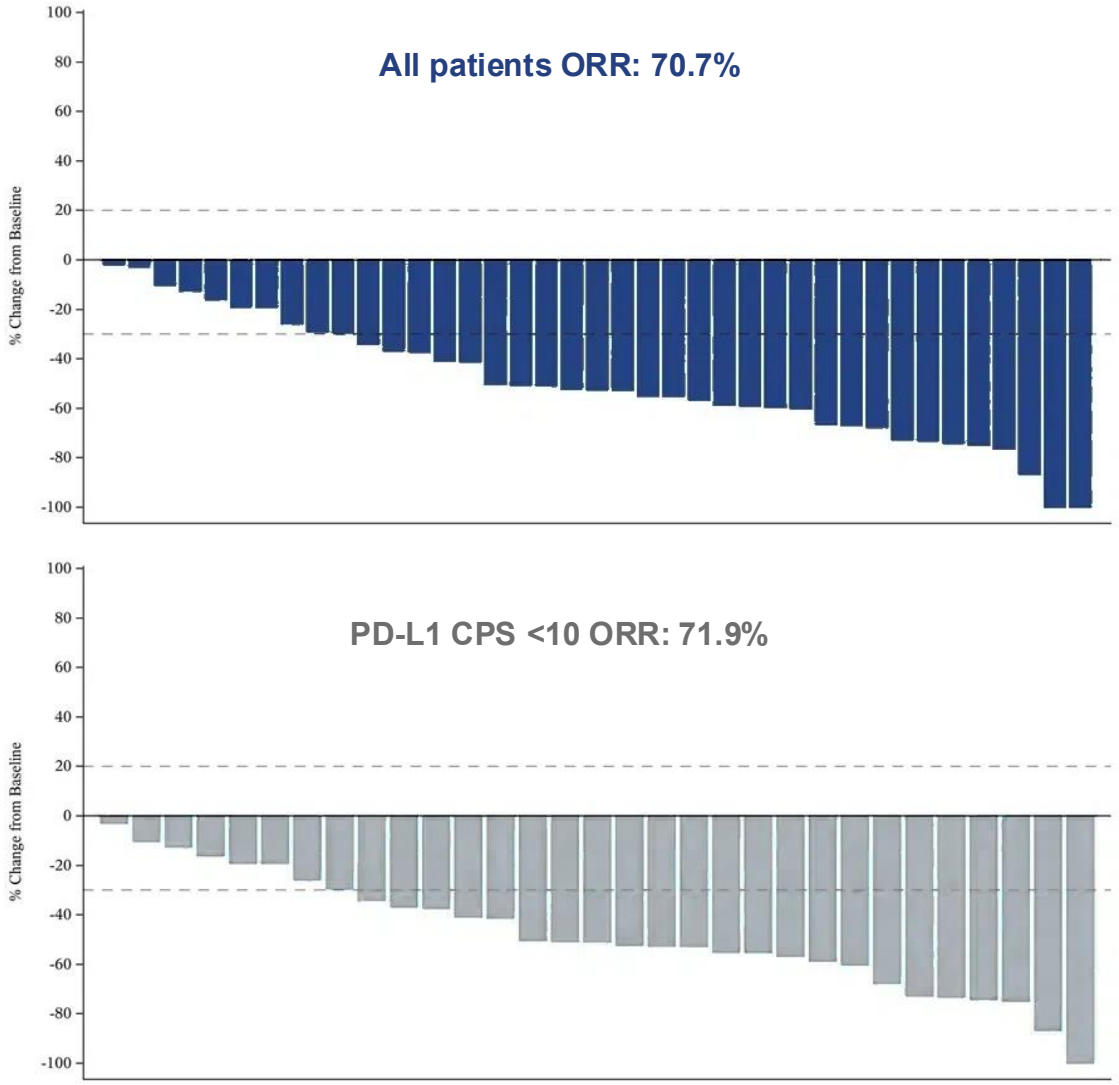
OptiTROP-Breast05: Phase II 1st Line Sac-TMT

N=41

Median DOR was 12.2 mo (range: 1.4+-18.0+) and 12-month DOR rate was 50.6% in all patients.



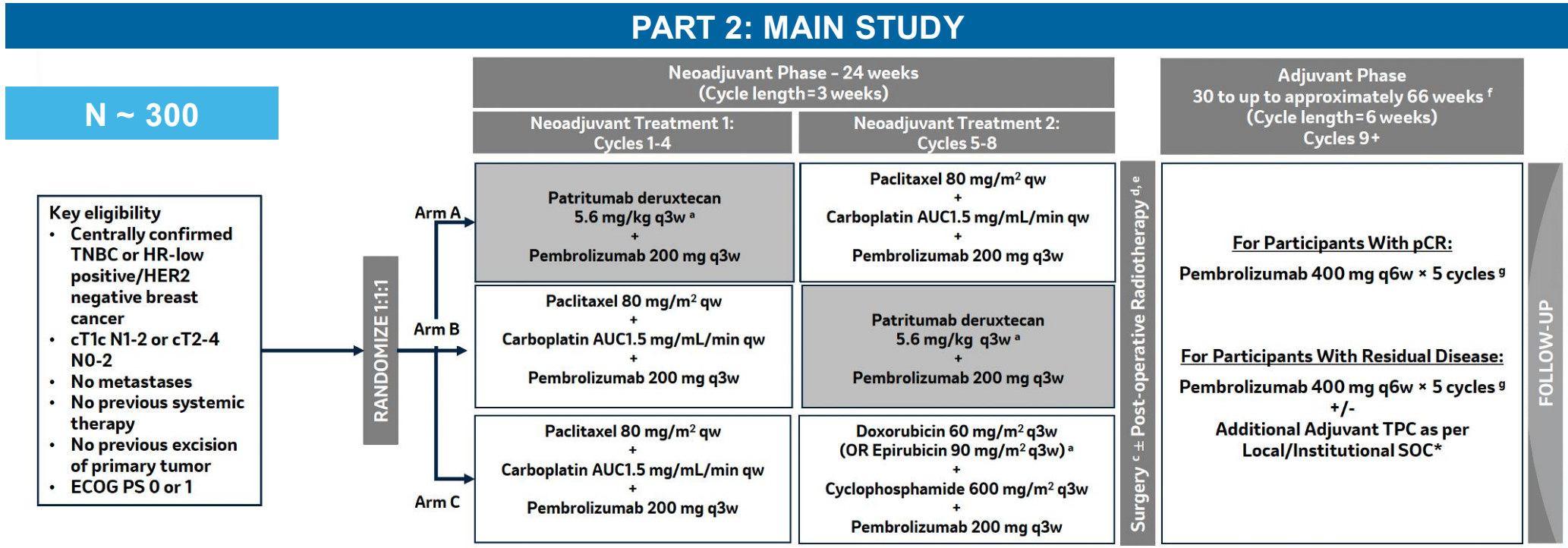
- **The most common grade ≥3 TRAEs (occurred in ≥5% of pts):**
  - Neutrophil count decreased (46.3%)
  - WBC count decreased (34.1%)
  - Anemia (12.2%)
  - Stomatitis (9.8%)
  - Lymphocyte count decreased (7.3%)
  - Fatigue (7.3%)



Median follow-up was 18.6 months.

Yin Y et al, ASCO 2025;Abstract 1019

HERTHENA-Breast03 (NCT06797635): Preoperative HER3-DXd in sequence in TNBC



Dana-Farber Cancer Institute

O'Shaughnessy J et al, ASCO 2025;Abstract TPS629

Adjuvant Olaparib Indication

As adjuvant therapy for adult patients with deleterious or suspected deleterious germline BRCA-mutant, HER2-negative high-risk localized breast cancer who have received neoadjuvant or adjuvant chemotherapy

Faculty Discussion Questions

For which patients with localized disease are you using adjuvant olaparib, and how does this correlate with the current FDA indication?

Reimbursement and regulatory issues aside, what is the optimal first-line therapy for patients with PD-L1-positive and PD-L1-negative mTNBC? How does prior treatment in the neoadjuvant and adjuvant settings affect this?

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

A CME/MOC-Accredited Live Webinar

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

Faculty

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

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!

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

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

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