The Implications of Recent Datasets for the Current and Future Management of Breast Cancer — An ASCO 2026 Review

A CME/MOC-Accredited Live Webinar

Thursday, July 30, 2026
5:00 PM – 6:30 PM ET

Faculty

Aditya Bardia, MD, MPH
Kevin Kalinsky, MD, MS, FASCO
Joyce O'Shaughnessy, MD

Moderator

Neil Love, MD

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Faculty

Aditya Bardia, MD, MPH
Program Director, Breast Medical Oncology
Assistant Chief (Translational Research)
Division of Hematology-Oncology
Director of Translational Research Integration
UCLA Health Jonsson Comprehensive Cancer Center
Professor of Medicine, Geffen School of Medicine
University of California Los Angeles
Los Angeles, California

Joyce O'Shaughnessy, MD
Celebrating Women Chair in Breast Cancer Research
Baylor University Medical Center
Director, Breast Cancer Research Program
Texas Oncology
Sarah Cannon Research Institute
Dallas, Texas

Kevin Kalinsky, MD, MS, FASCO
Professor of Medicine
Director, Division of Medical Oncology
Louisa and Rand Glenn Family Chair in Breast Cancer Research
Winship Cancer Institute at Emory University
Atlanta, Georgia

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Commercial Support

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Dr Love — Disclosures

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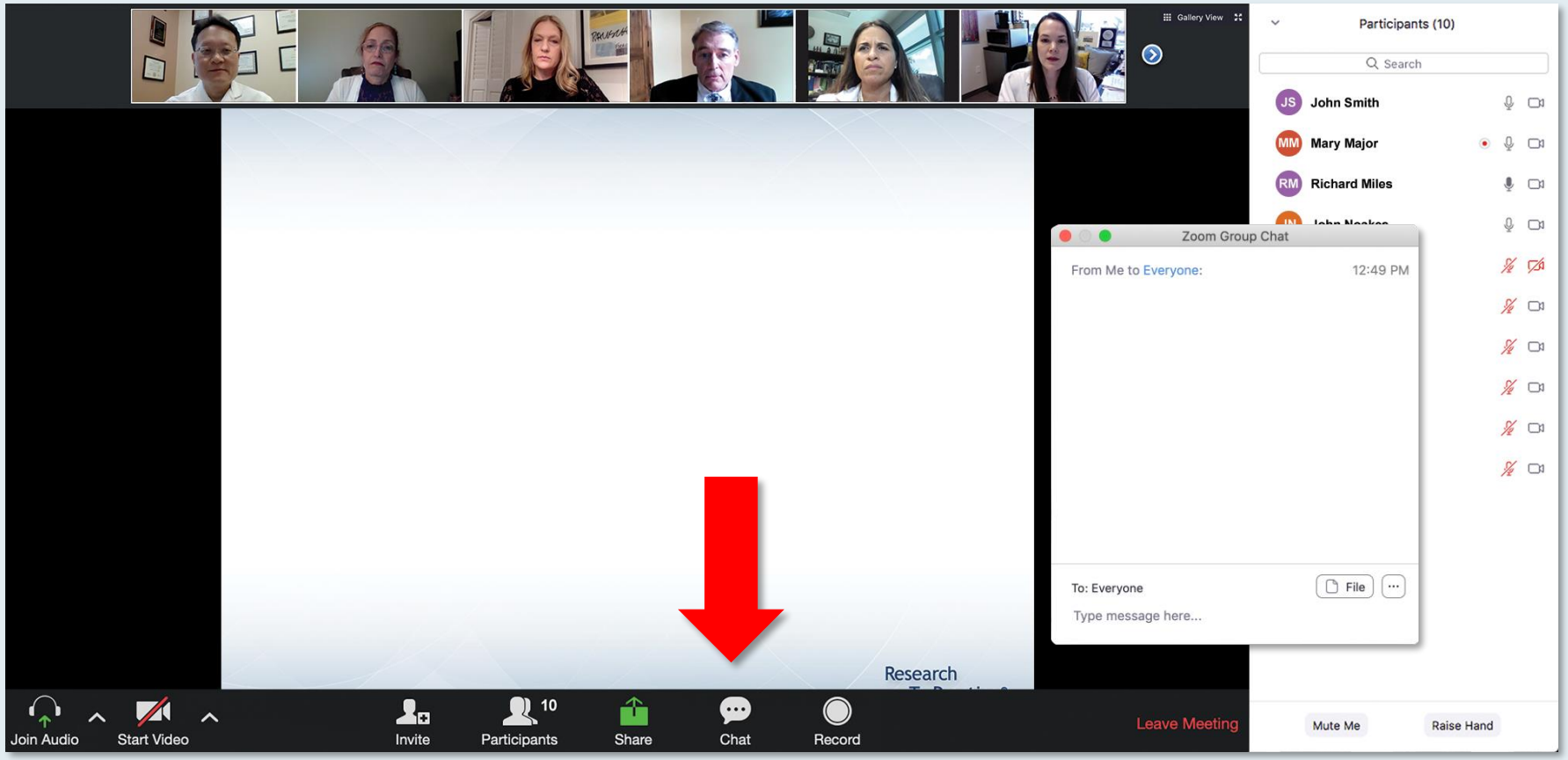

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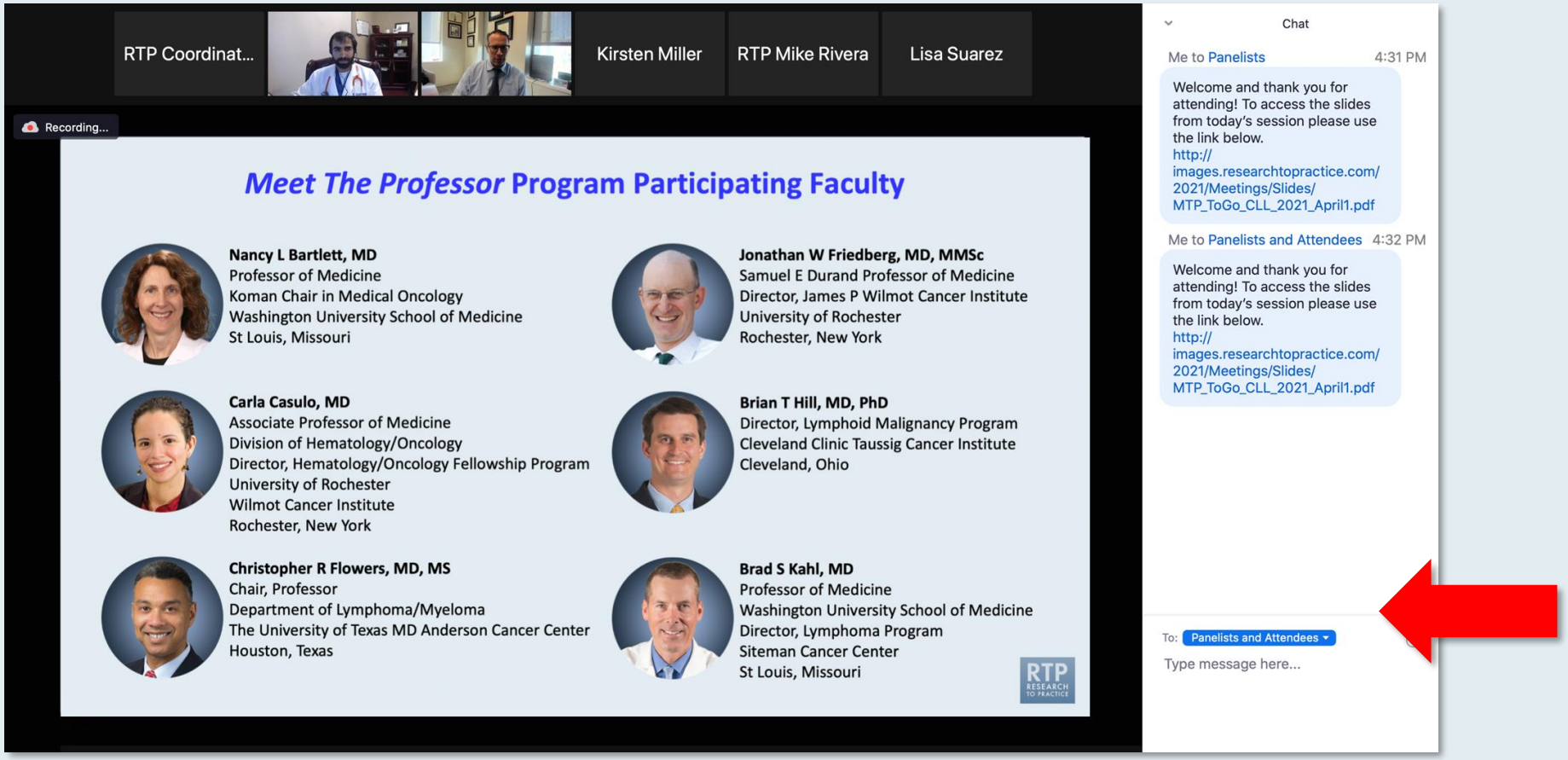

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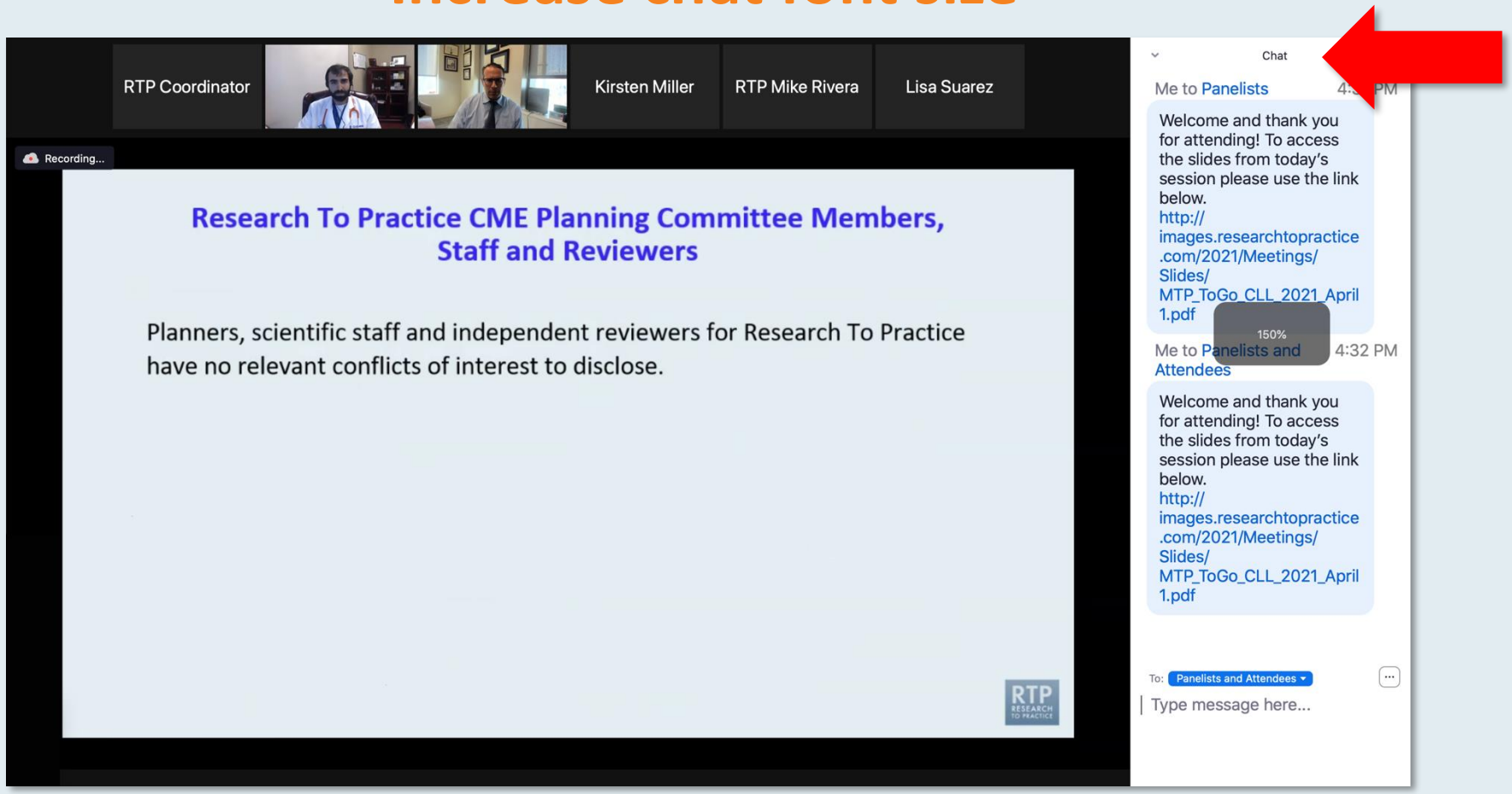

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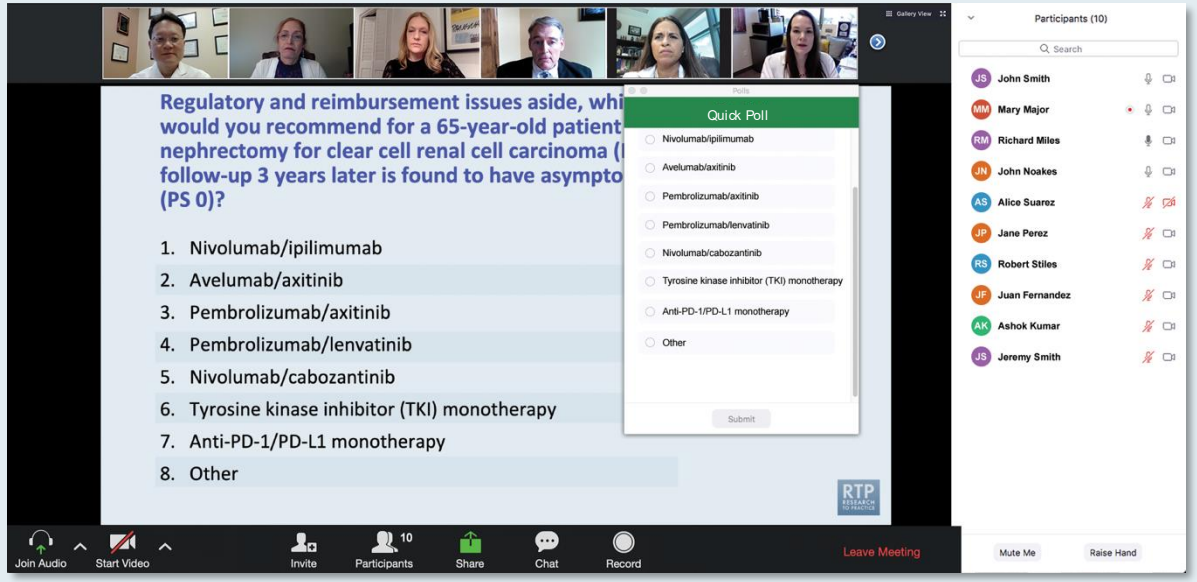

ONCOLOGY TODAY

WITH DR NEIL LOVE

Breast Cancer — Proceedings from a Session Held in Conjunction with the 2026 ASCO Annual Meeting on the Use of Oral SERDs and Agents Targeting the PI3K/AKT/mTOR Pathway

SARA A HURVITZ, MD, FACP
FRED HUTCHINSON CANCER CENTER

NICHOLAS TURNER, MD, PHD
THE INSTITUTE OF CANCER RESEARCH

ERICA MAYER, MD, MPH, FASCO
DANA-FARBER CANCER INSTITUTE

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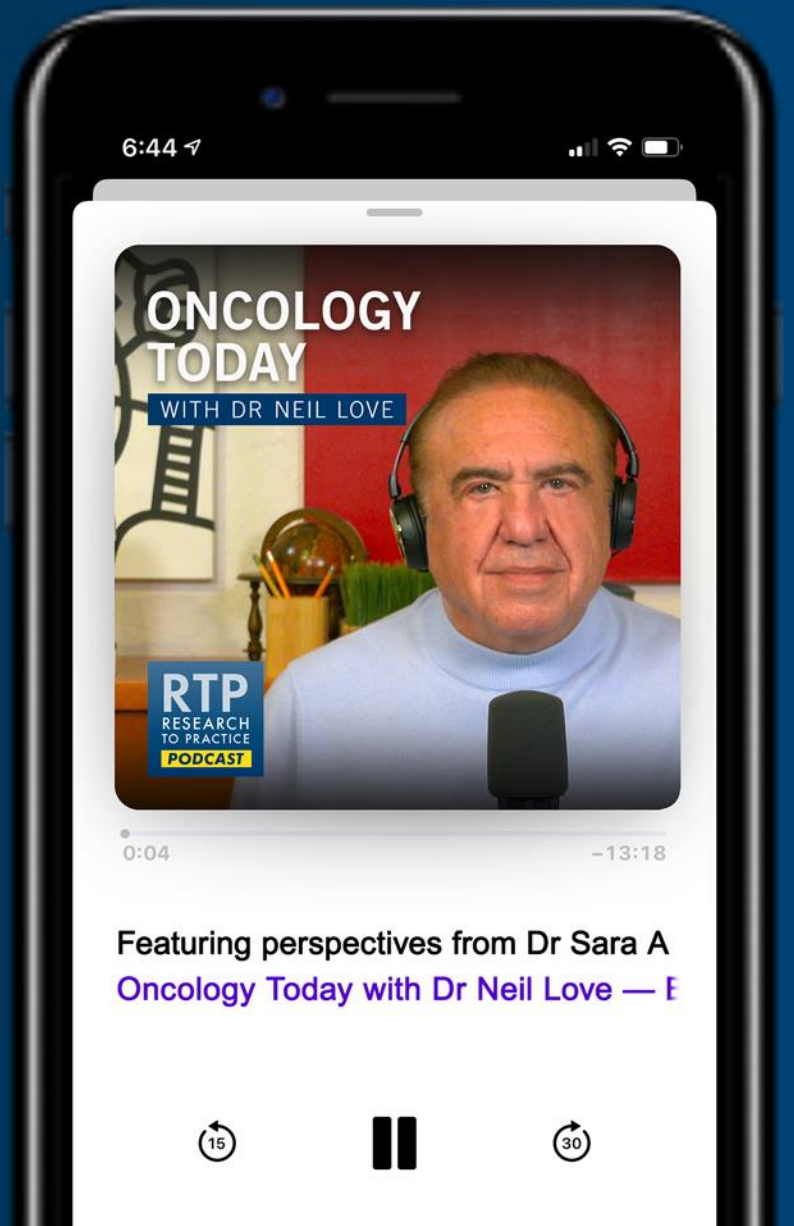
SARAH CANNON RESEARCH INSTITUTE



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Integrating New Advances into Community Oncology Practice

A Multitumor Symposium Hosted in Conjunction with the American Oncology Network

Saturday, August 22, 2026

JW Marriott Nashville | Nashville, Tennessee

Chronic Lymphocytic Leukemia
9:05 AM – 9:55 AM CT

Gastroesophageal Cancers
9:55 AM – 10:45 AM CT

Gynecologic Cancers
11:00 AM – 11:50 AM CT

Diffuse Large B-Cell Lymphoma
12:40 PM – 1:30 PM CT

Lung Cancer
1:30 PM – 2:20 PM CT

Moderator
Stephen “Fred” Divers, MD

RTP RESEARCH TO PRACTICE

The Implications of Recent Datasets for the Current and Future Management of Gynecologic Cancers — An ASCO 2026 Review

A CME/MOC-Accredited Live Webinar

Wednesday, August 26, 2026
5:00 PM – 6:00 PM ET

Faculty

Faculty to be announced

Moderator

Neil Love, MD

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Data + Perspectives: Investigators Discuss the Optimal Management of Relapsed/Refractory Multiple Myeloma

A CME-Accredited Satellite Symposium During the Society of Hematologic Oncology 2026 Annual Meeting

Wednesday, September 9, 2026
11:56 AM – 12:56 PM CT

Faculty

Noopur Raje, MD
Paul G Richardson, MD

Moderator

Robert Z Orlowski, MD, PhD

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Grand Rounds

CME/MOC-Accredited Interactive Series

Regional Activities

Three Series

Integrating Recent Advances into the Management of Gastroesophageal Cancers

Optimizing the Use of Novel Therapies for Patients with Diffuse Large B-Cell Lymphoma

Optimizing Therapy for Patients with Hormone Receptor-Positive Localized Breast Cancer

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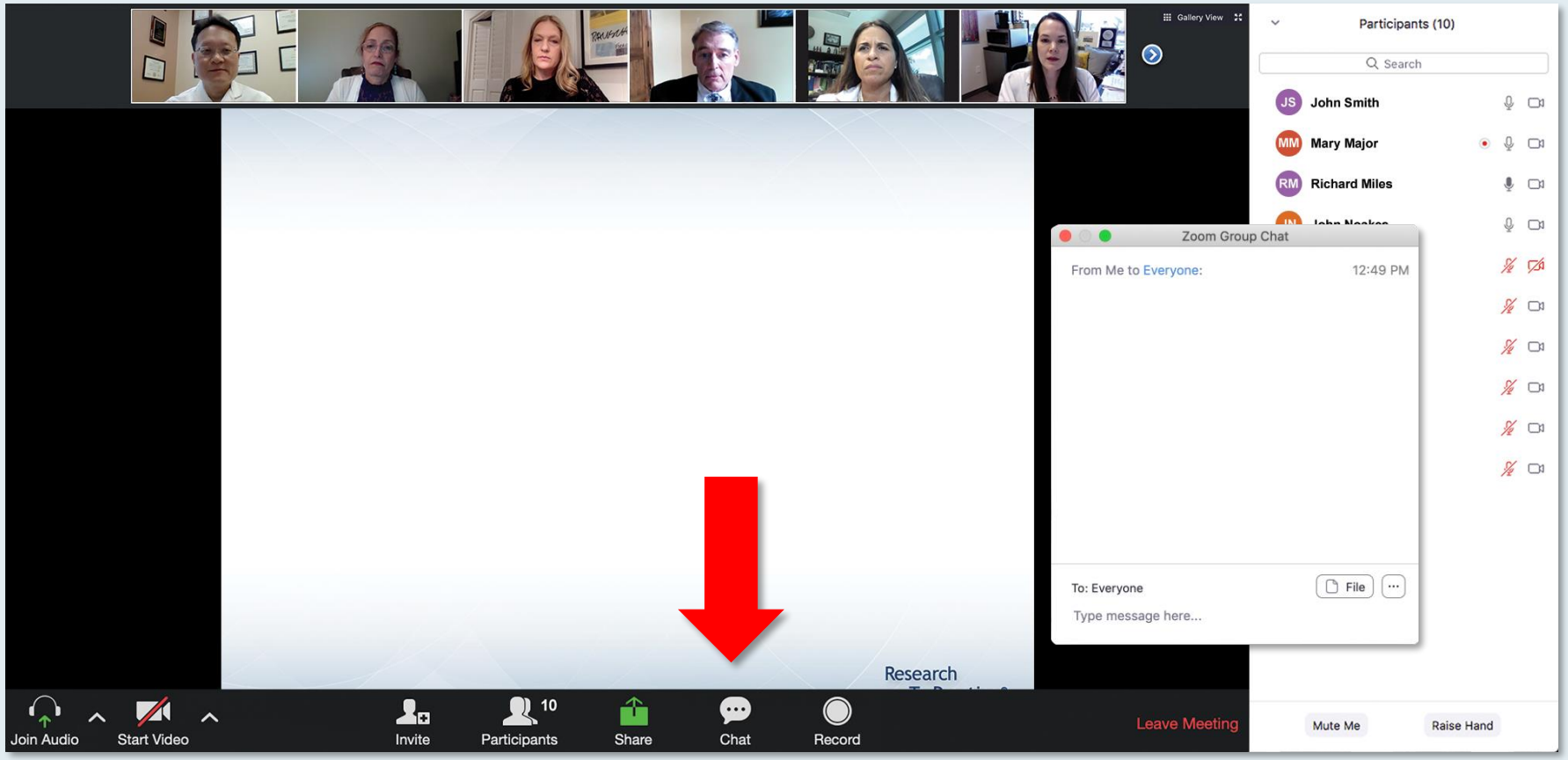

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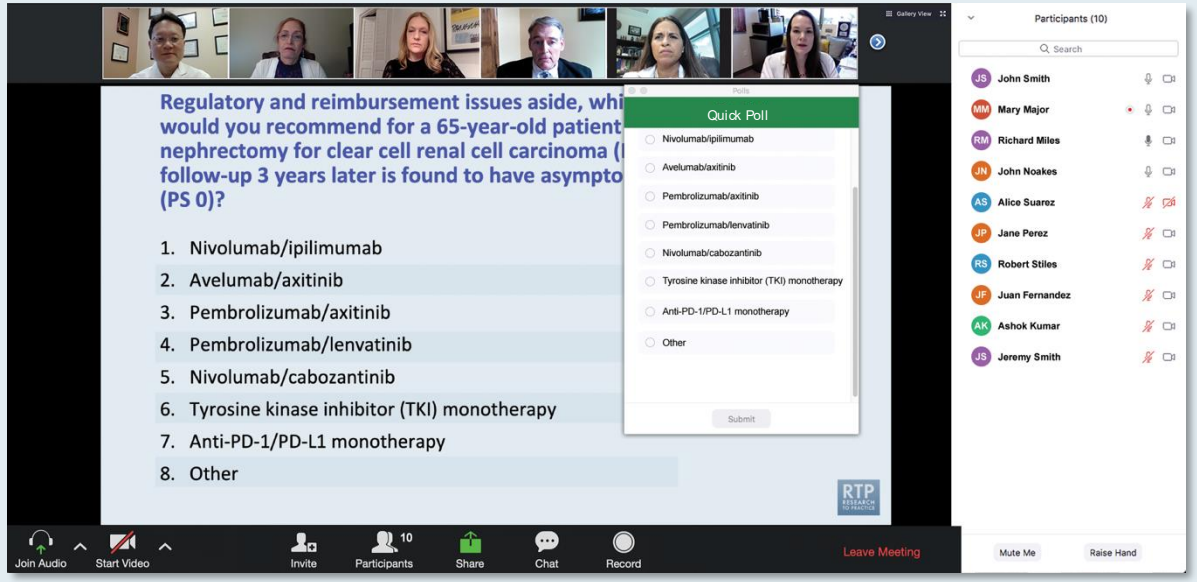

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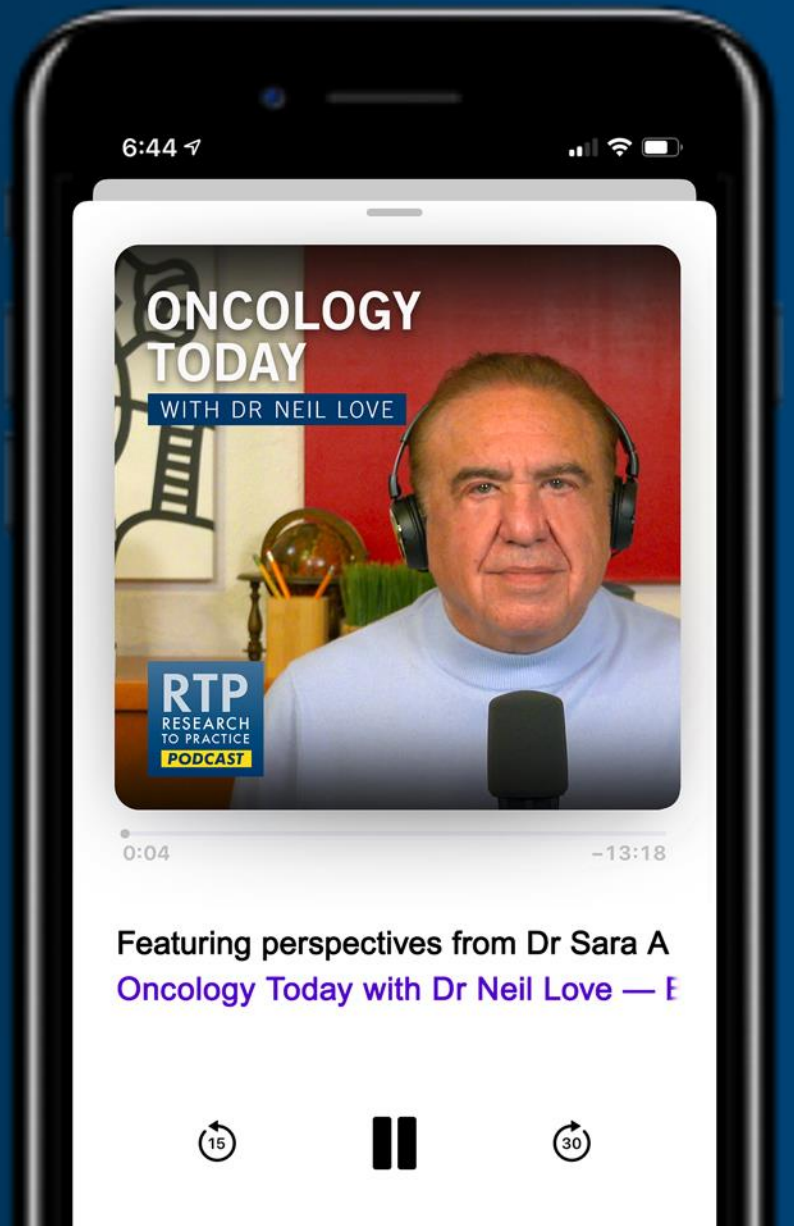

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Agenda

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

Module 2: HER2-Positive Breast Cancer — Dr Bardia

Module 3: Triple-Negative Breast Cancer — Dr O'Shaughnessy

Agenda

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

Module 2: HER2-Positive Breast Cancer — Dr Bardia

Module 3: Triple-Negative Breast Cancer — Dr O'Shaughnessy

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Advances in Hormone Receptor-Positive Breast Cancer

Kevin Kalinsky, MD, MS, FASCO

Professor of Medicine

Director, Division of Medical Oncology

Louisa and Rand Glenn Family Chair in Breast Cancer Research

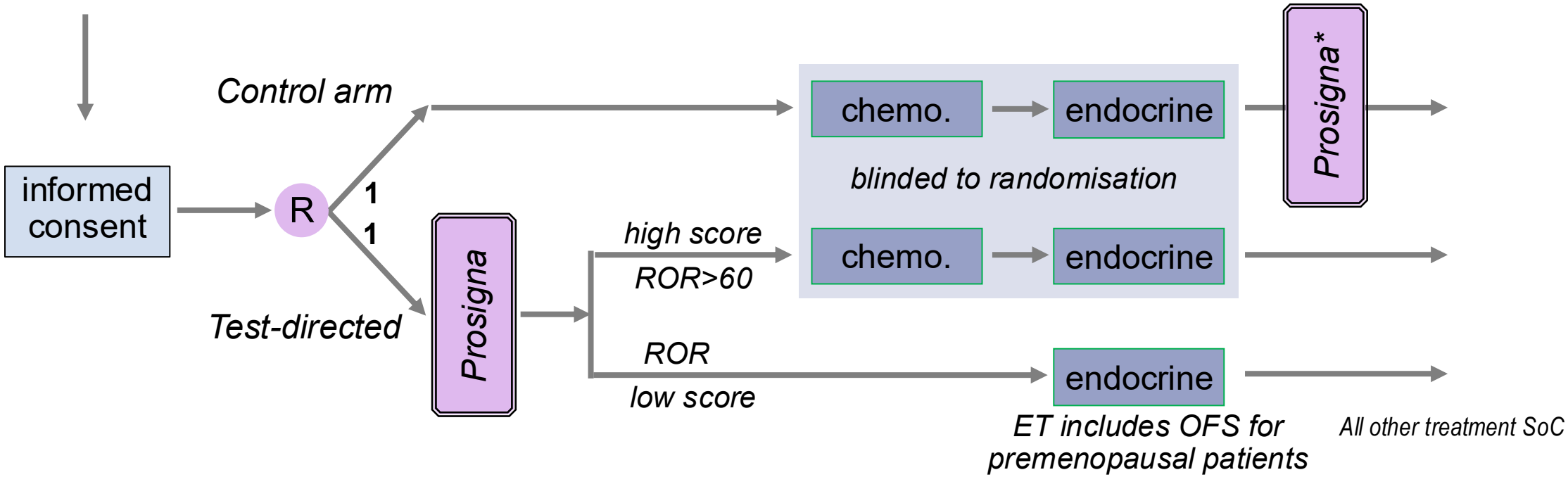
Winship Cancer Institute at Emory University

Atlanta, Georgia

OPTIMA Trial Design

Main eligibility criteria

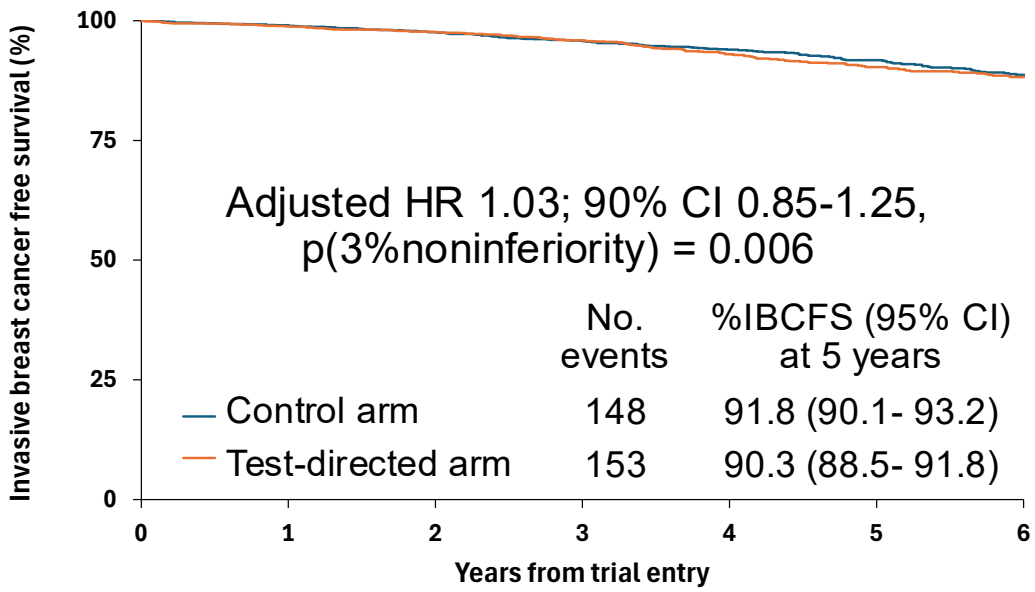
- Women & men age ≥40 with excised breast cancer
- ER-pos (IHC>10%) & HER2-neg
- Nodes: ▸0-9N+,
  ▸minimum T-size requirement if N0/ N1mi
- Neoadjuvant chemotherapy prohibited



*Control arm Prosigna testing used for analysis only. U.K. control arm testing performed following recruitment completion

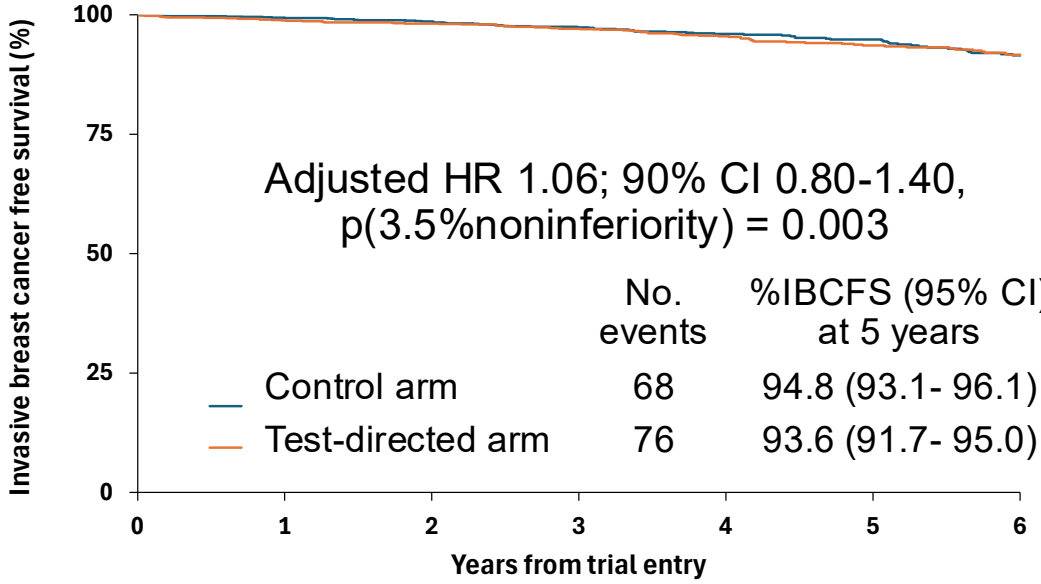
Invasive Breast Cancer Free Survival (IBCFS)

Complete Per Protocol



Number at risk:							
Control	2059	1818	1563	1283	999	741	485
Test-directed	2094	1857	1591	1303	989	724	481

ROR ≤ 60 (2/3rd)

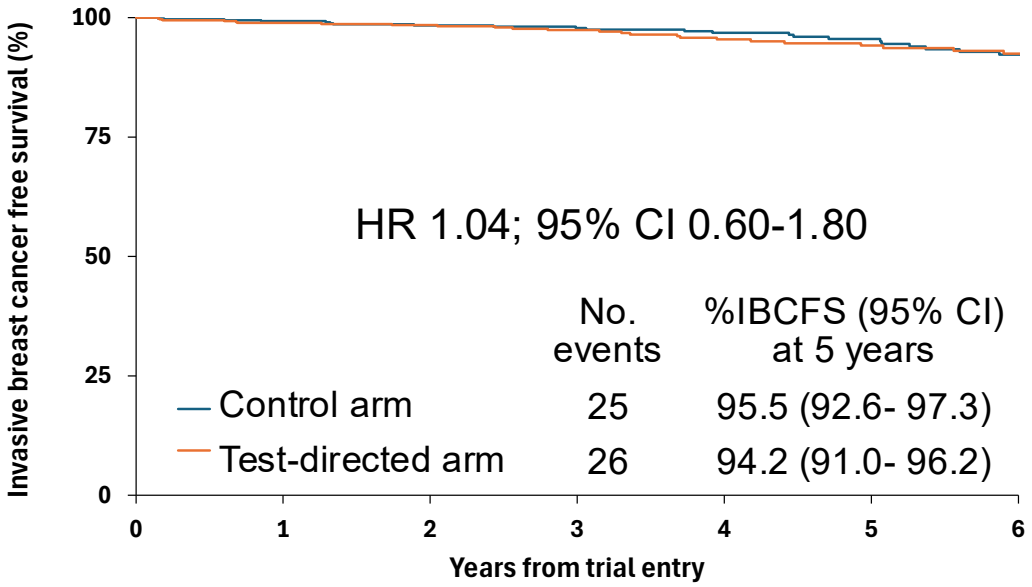


Number at risk:							
Control	1358	1207	1043	862	672	504	337
Test-directed	1421	1257	1086	905	694	503	342

Median follow-up 4.0 years: IQR 2.0-6.0 years

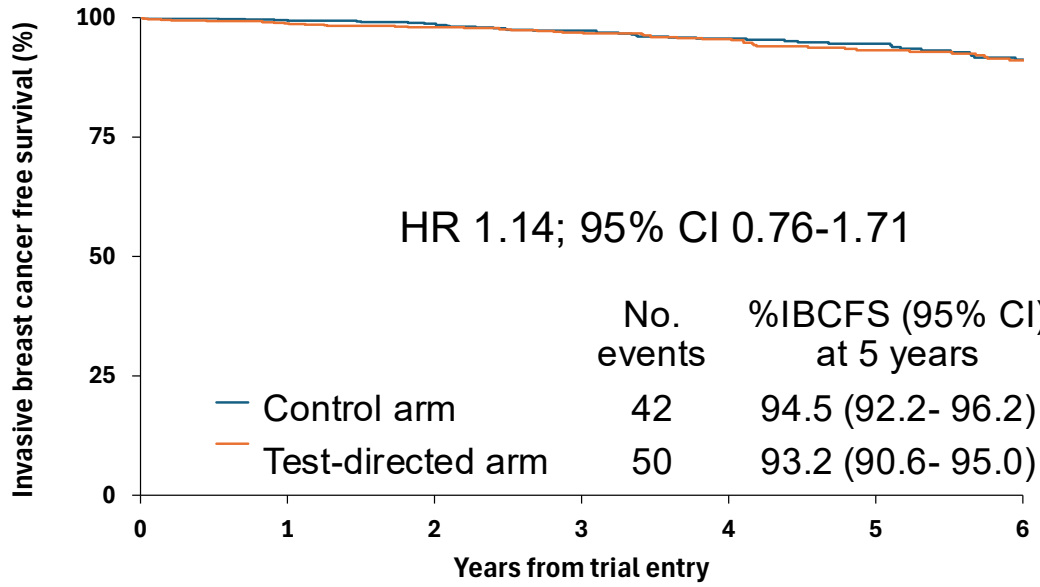
IBCFS vs menopausal status: low ROR score

Premenopausal (40%)



Number at risk:							
Control	561	481	409	338	258	200	140
Test-directed	559	487	410	347	256	195	135

Postmenopausal (60%)

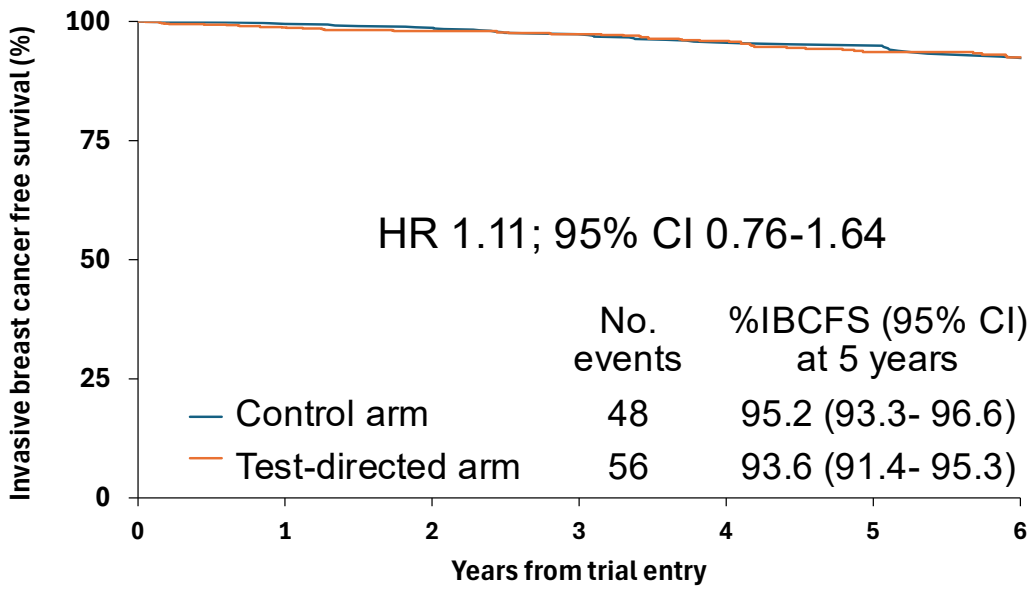


Number at risk:							
Control	791	721	631	522	414	304	197
Test-directed	858	766	673	556	437	307	207

Postmenopausal: age > 45 and LMP > 12 months; BSO; or estradiol and FSH in postmenopausal range

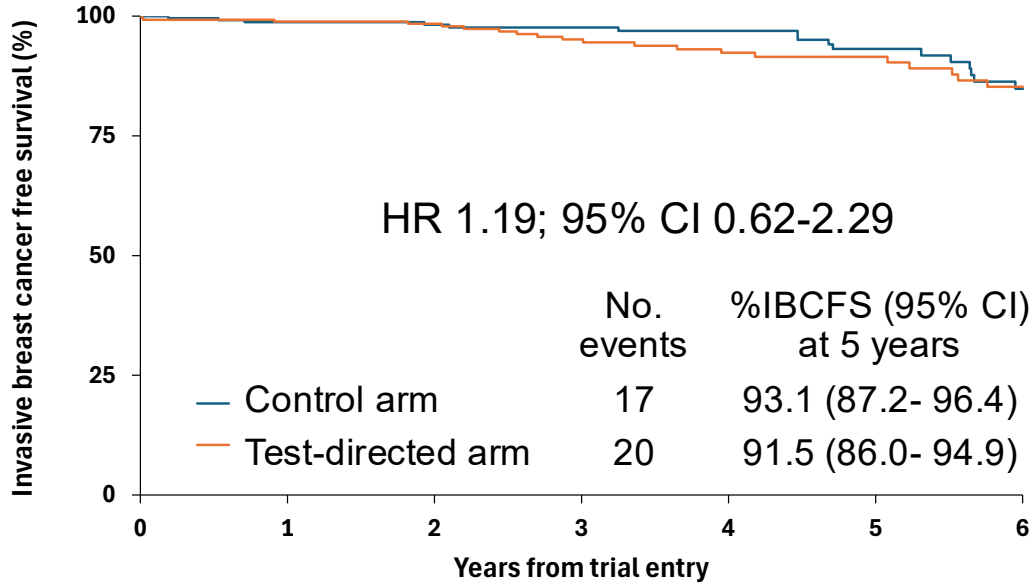
IBCFS vs menopausal status: low ROR score

N1 (1-3 LN+) (80%)



Number at risk:							
Control	1015	914	798	651	499	382	264
Test-directed	1063	953	829	700	539	389	270

N2 (4-9 LN+) (20%)



Number at risk:							
Control	243	214	181	155	125	84	48
Test-directed	269	232	197	158	118	86	49

NATALEE study design

- Adult pts with HR+/HER2− EBC
- Prior ET allowed up to 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]

Ribociclib
400 mg/day
3 weeks on/1 week off
for 3 y

+

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

NSAI
Letrozole or anastrozole[d]
for ≥ 5 y
+ 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

Exploratory end points
- Locoregional recurrence–free survival
- Gene expression and alterations in tumor and ctDNA/ctRNA samples

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

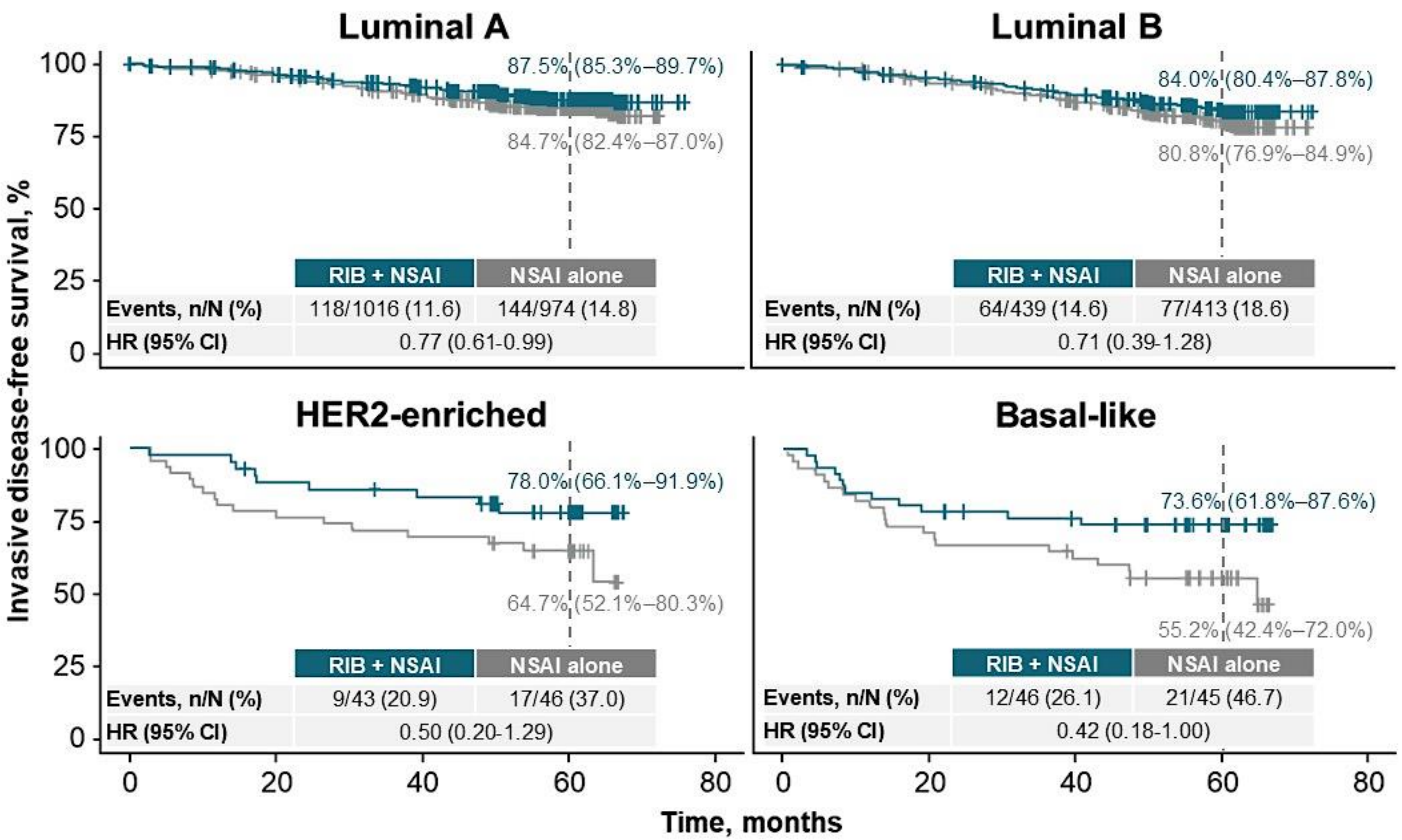
Data cutoff: May 28, 2025

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; STEEP, Standardized Definitions for Efficacy End Points in Adjuvant Breast Cancer Trials.

[a] Enrollment of patients with stage II disease was capped at 40%. [b] 5101 patients were randomized from January 10, 2019, to April 20, 2021. [c] Open-label design. [d] Per investigator choice.
Fasching PA et al. ESMO 2024. Oral LBA13.

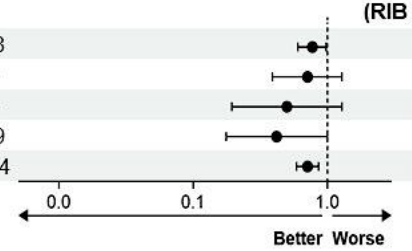
Ribociclib treatment benefit was seen across all PAM50-based intrinsic subtypes

iDFS by Intrinsic Subtype[a]



Ribociclib Treatment Benefit Across Intrinsic Subtypes[a,b]

Population	Events, n	Patients, n	*P*	HR for treatment benefit (RIB + NSAI vs NSAI alone)
Luminal A	262	1990	.038	0.77 (0.61-0.99)
Luminal B	141	852	.25	0.71 (0.39-1.28)
HER2-enriched	26	89	.15	0.50 (0.20-1.29)
Basal-like	33	91	.049	0.42 (0.18-1.00)
Biomarker	462	3022	.0004	0.72 (0.60-0.86)



- Across treatment arms, PAM50 subtypes were strongly prognostic (hazard ratio vs luminal A: luminal B, 1.39; HER2-enriched, 2.62; basal-like, 3.92[c])
- No significant interaction between subtype and treatment was observed (*P*=.34[d])

HER2, human epidermal growth factor receptor 2; HR, hazard ratio; iDFS, invasive disease–free survival; NSAI, nonsteroidal aromatase inhibitor; PAM50, Prediction Analysis of Microarray 50; RIB, ribociclib.
[a] HRs were estimated using Cox proportional hazards models stratified by the four main strata and including a term for biomarker-by-treatment interaction. [b] The p-values for treatment effects within individual biomarker subgroups are model-based nominal two-sided Wald p-values without multiplicity correction. [c] HRs were obtained from Cox proportional hazards models stratified by the four main strata and adjusted for treatment group. [d] Nominal two-sided p-value from likelihood ratio test without multiplicity correction.

lidERA BC study design

A global, randomized, open-label, multicenter, Phase III trial

Key eligibility criteria

- Participants with ER+, HER2– eBC
- Stage I–III disease (anatomic)
  - pN0 and pT > 1 cm with Grade 3, or Ki67 ≥ 20%, or high score on genomic assay,* or pT4N0
  - Node-positive
- **Pre- or post-menopausal**
- BC surgery within 12 months
- (Neo)adjuvant chemotherapy if indicated

Stratification factors

- Risk: Medium-† vs high-risk‡ Stage I–III BC
- Region: USA/Canada/Western Europe vs Asia–Pacific vs RoW
- Previous chemotherapy: No vs yes
- Menopausal status§: Pre-menopausal vs post-menopausal

Primary endpoint

- IDFS (excluding second primary non-BC)

Key secondary endpoints

- DFS, DRFI, IDFS (including second primary non-breast invasive cancer, with exception of non-melanoma skin cancers and *in situ* carcinomas of any site), LRRFI, OS, safety

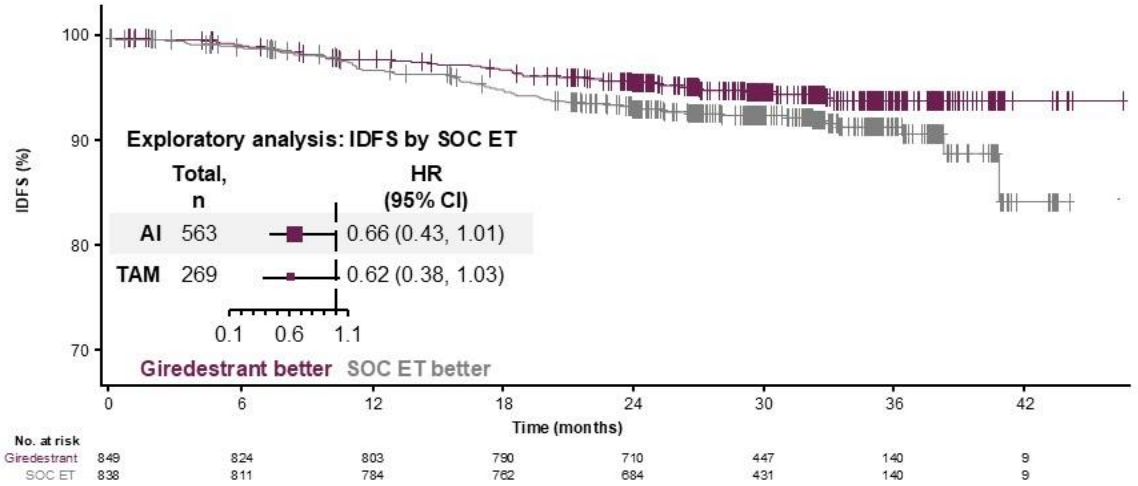
Ovarian function suppression with an approved LHRH agonist was required for all men and pre-menopausal women receiving AIs or giredestrant

ClinicalTrials.gov number, NCT04961996. Adapted from Geyer CE, *et al.* ASCO 2023 (TPS616), with permission. Enrollment: August 2021 to September 2023. Up to 12 weeks of ET ± CDK4/6i were allowed. ER+ was defined as ≥ 1% positive cells by immunohistochemistry. * Oncotype ≥ 26 or high-risk MammaPrint. † Medium risk: pN0 and primary tumor > 1 cm with high-risk biologic features (Grade 3, or Ki67 ≥ 20%, or high score on genomic assay [if available]) and pN1 with low-risk biologic features (Grade 1/2 and Ki67 < 20% and tumor ≤ 5 cm and low score on genomic assay [if available]). ‡ High risk: pT4, or pN2, or pN3 and pN1 with high-risk biologic features (Grade 3, or Ki67 ≥ 20%, or tumor > 5 cm, or high score on genomic assay [if available]). § Defined as: prior bilateral oophorectomy, or age ≥60 years, or <60 years and amenorrheic for 12 months or more. AI, aromatase inhibitor; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; DFS, disease-free survival; DRFI, distant recurrence-free interval; (e)BC, (early) breast cancer; ER+, estrogen receptor-positive; ET, endocrine therapy; HER2–, HER2-negative; IDFS, invasive disease-free survival; LHRH, luteinizing hormone-releasing hormone; LRRFI, locoregional recurrence-free interval; OS, overall survival; PO, orally; QD, once daily; R, randomization; RoW, rest of the world; SOC, standard-of-care.

IDFS by menopausal status

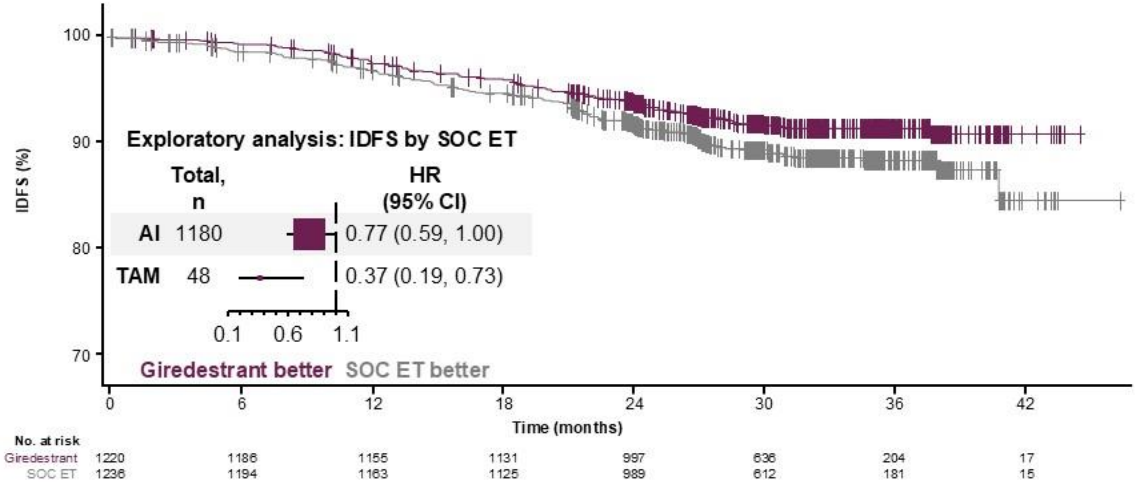
Pre-menopausal

	Giredestrant n = 849	SOC ET n = 838
Events, n (%)	44 (5.2)	66 (7.9)
3-year rate, %	94.0	91.5
HR (95% CI)	**0.65** (0.44, 0.95)	



Post-menopausal

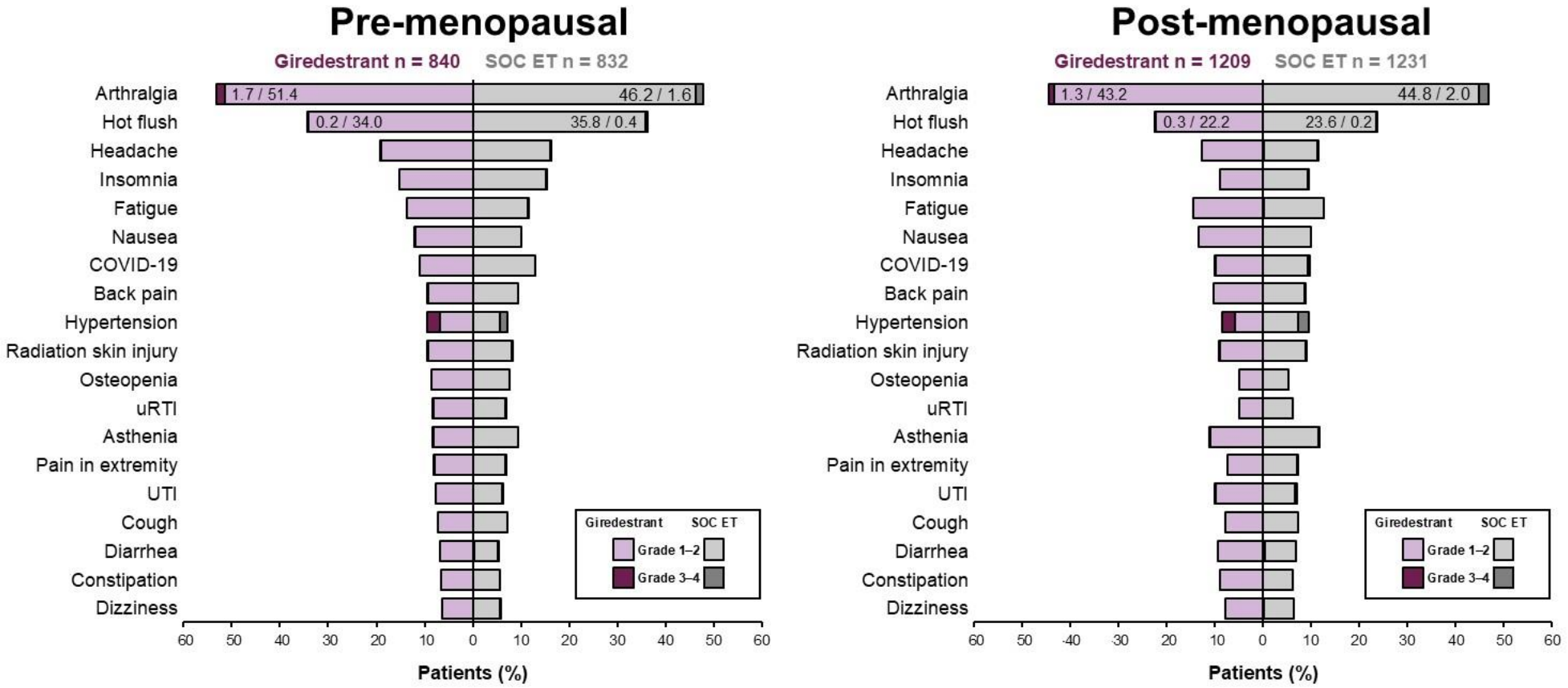
	Giredestrant n = 1220	SOC ET n = 1236
Events, n (%)	96 (7.9)	129 (10.4)
3-year rate, %	91.3	88.3
HR (95% CI)	**0.74** (0.57, 0.96)	



Giredestrant showed IDFS benefit and higher 3-year rates in both pre-menopausal and post-menopausal subgroups

Data cutoff: August 8, 2025. HR estimates are unstratified vs SOC ET.
AI, aromatase inhibitor; CI, confidence interval; ET, endocrine therapy; HR, hazard ratio; IDFS, invasive disease-free survival; SOC, standard-of-care; TAM, tamoxifen.

Common AEs



Independent of menopausal status:

- **Fewer patients** switched to alternative ET in the giredestrant vs. SOC ET arm (5.7 vs 10.1%), mainly due to AEs
- **Fewer patients** discontinued treatment due to AEs in the giredestrant vs. SOC ET arm (5.3 vs 8.2%)

Common AEs were comparable across arms and subgroups at any grade.
Arthralgia and hot flush were the most common AEs regardless of menopausal status

Data cutoff: August 8, 2025.
AE, adverse event; ET, endocrine therapy; SOC, standard-of-care; uRTI, upper respiratory tract infection; UTI, urinary tract infection.

Dr Kalinsky Case Presentation #1

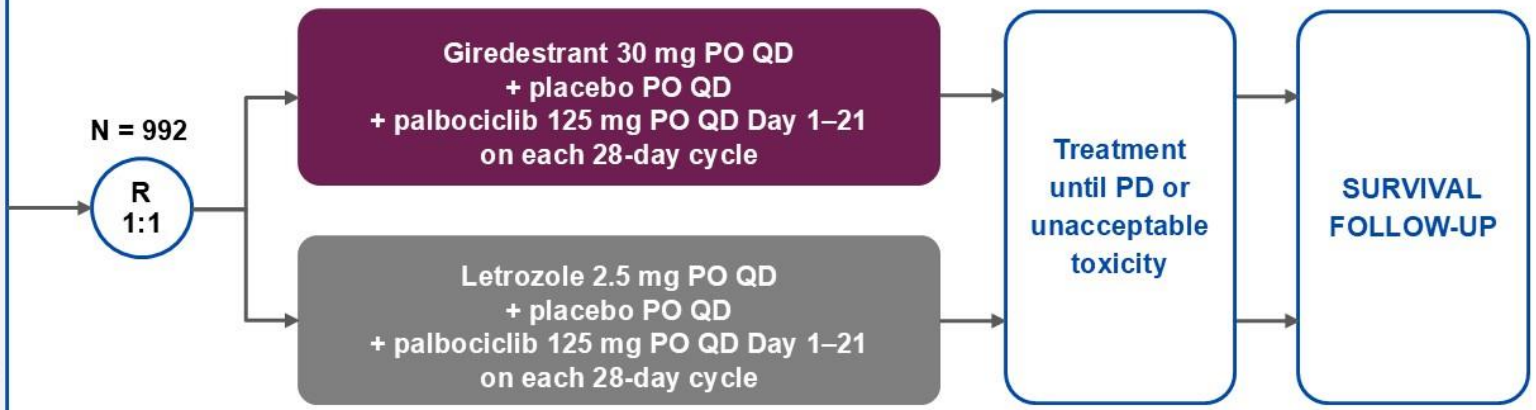
- 53 year old premenopausal F
- Right breast mastectomy, SLNB:
  - grade I 1.7 cm strongly HR+/HER2- IDC, 0/1 LN. oncotype 13
- Left breast mastectomy, SLNB
  - Grade II 3.2 cm, 1.7 cm strongly HR+/HER2- IDC, 1/3 LN. oncotype 13
- s/p CMF x 8
- s/p XRT
- Hx of pulmonary embolus. Concern with tamoxifen
- On leuprolide acetate + ribo/letrozole since 6/6/24

persevERA BC study design

A Phase III, randomized, double-blind, placebo-controlled, multicenter trial in 1L LA/mBC

Key eligibility criteria:

- 1L ER+, HER2– LA/mBC*
- Locally confirmed histologic/cytologic diagnosis
- No prior treatment for advanced disease
- No prior treatment with a SERD
- Disease recurrence > 12 months from completing prior (neo)adjuvant tamoxifen/AI
- Disease recurrence ≤ 12 months for patients receiving (neo)adjuvant tamoxifen (protocol v1)
- No active cardiac disease or history of cardiac dysfunction



* Patients with *de novo* mBC were capped at 20%

Stratification factors:

- Site of disease: Visceral vs non-visceral
- Menopausal status: Post-menopausal vs pre-menopausal/male
- Region: North America vs Western Europe vs Asia–Pacific vs other
- TFI since the end of prior (neo)adjuvant therapy: *De novo* metastatic vs ≤ 12 months vs > 12 months

Primary endpoint:

- Investigator-assessed PFS (INV-PFS) per RECIST v1.1

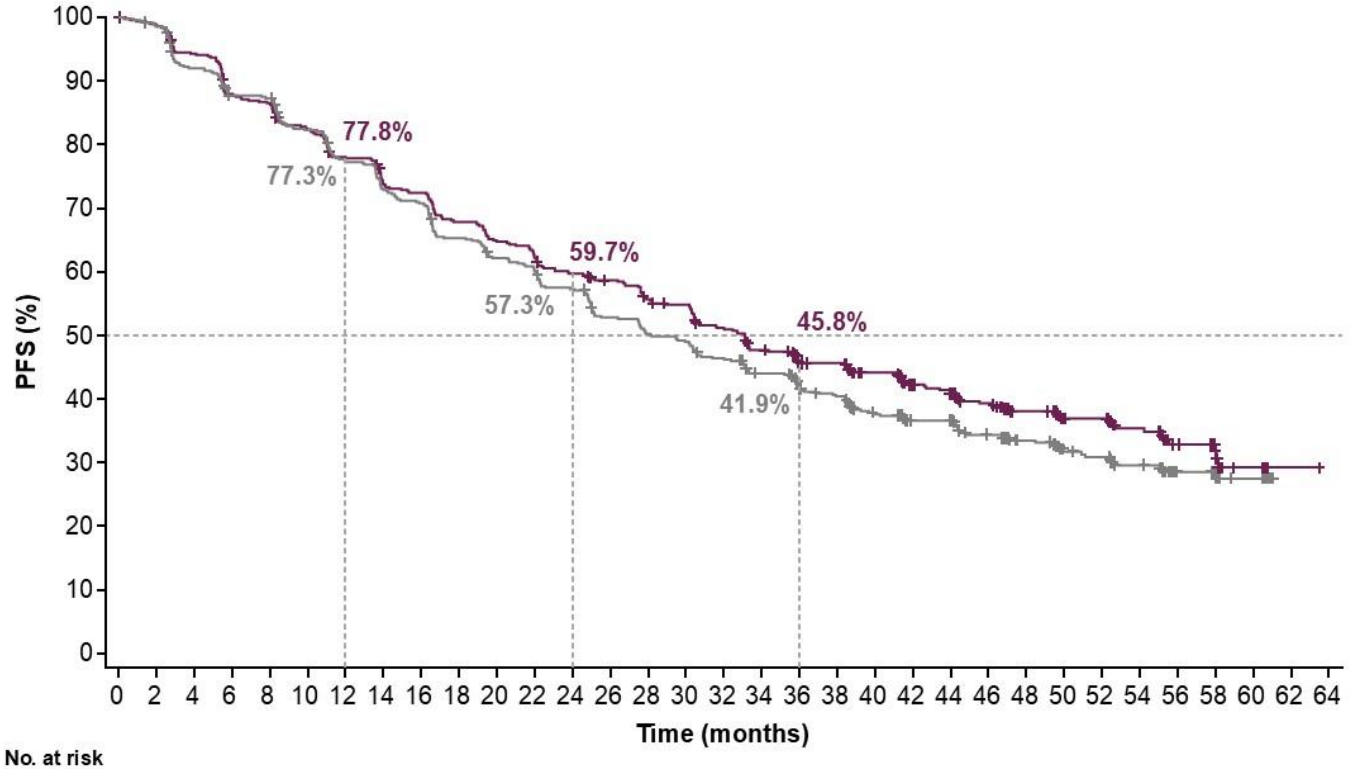
Secondary endpoints:

- OS, ORR, CBR, DoR, safety, PROs (TTD of pain, physical functioning, role functioning, GHS/QoL)

Enrollment: October 9, 2020, to March 27, 2023. ER+ was defined as ≥ 1% positive cells by immunohistochemistry. Pre-menopausal women, and men, also received ovarian function suppression with an approved luteinizing hormone-releasing hormone agonist. 1L, first line; AI, aromatase inhibitor; CBR, clinical benefit rate; DoR, duration of response; ER+, estrogen receptor-positive; GHS/QoL, global health status/quality of life; HER2–, HER2-negative; (LA/m)BC, (locally advanced/metastatic) breast cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PO, orally; PRO, patient-reported outcome; QD, once daily; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumours; SERD, selective estrogen receptor antagonist and degrader; TFI, treatment-free interval; TTD, time to deterioration.
ClinicalTrials.gov number, NCT04546009. Adapted from Turner NC, *et al.* ASCO 2021 (TPS1103), with permission.

Turner NC et al. ASCO 2026;Abstract LBA1006

Primary endpoint: INV-PFS



No. at risk

Giredestrant + palbociclib	495	484	461	429	422	399	375	353	347	325	310	298	285	276	261	255	236	217	195	190	170	149	142	130	108	88	86	65	42	27	14	1
Letrozole + palbociclib	497	484	449	424	422	394	369	349	338	311	295	286	271	248	236	230	217	200	186	176	156	141	139	119	103	78	75	62	36	27	11	

	Giredestrant + palbociclib n = 495	Letrozole + palbociclib n = 497
Events, n (%)	300 (60.6)	323 (65.0)
Median, months (95% CI)	**33.1** (30.2, 38.3)	**28.2** (25.0, 33.1)
Stratified HR (95% CI)	**0.89** (0.76, 1.05); p = 0.1553	

Median follow-up
Giredestrant arm: 52.2 months (range: 0.4–63.5)
Letrozole arm: 52.1 months (range: 0.3–62.6)

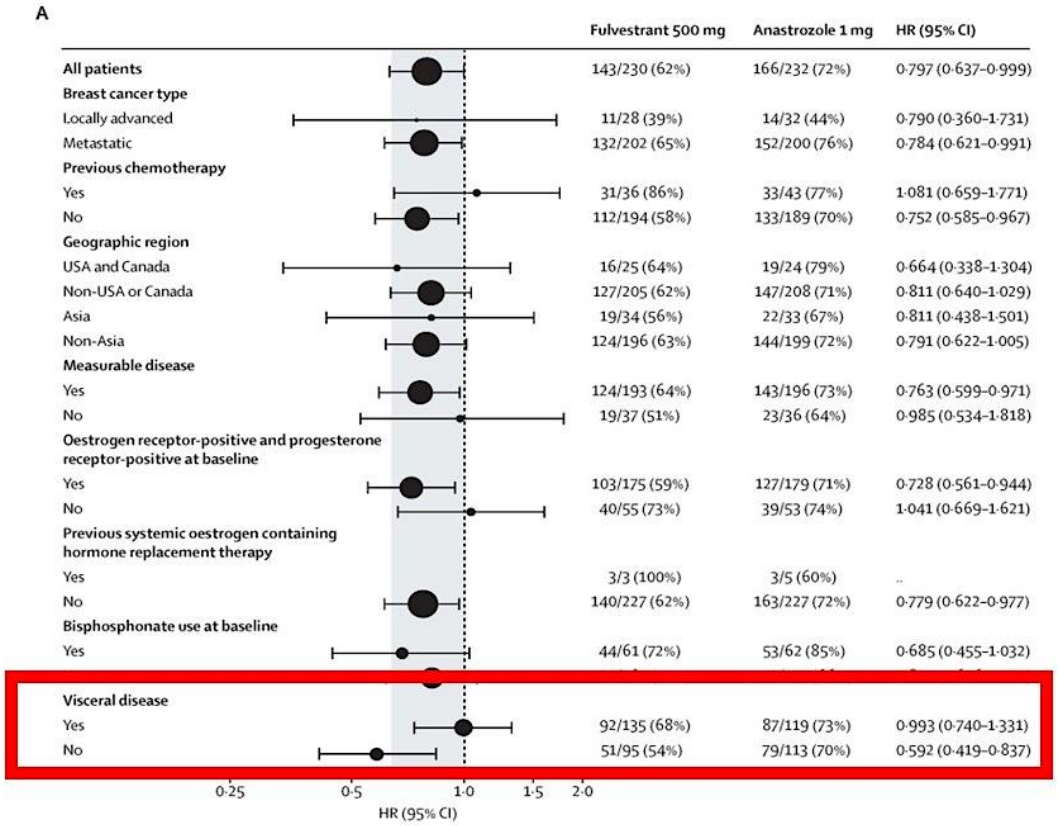
Giredestrant + palbociclib demonstrated a numerical improvement in INV-PFS vs letrozole + palbociclib, despite the lack of statistical significance

Turner NC et al.
ASCO 2026;Abstract LBA1006

Data cutoff: January 30, 2026. The boundary for statistical significance was HR 0.85; 2-sided p < 0.0456.
CI, confidence interval; HR, hazard ratio; (INV-)PFS, (investigator-assessed) progression-free survival.

Outcomes in FALCON and PersevERA by Visceral/non-Visceral Status

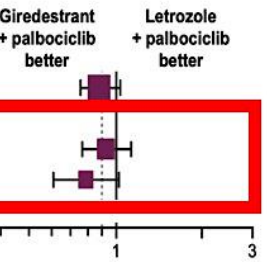
48% of FALCON patients had non-visceral mets



HR 0.59 (0-42-0.84) vs. 0.99 (0-74-1-33)

39% of PersevERA patients had non-visceral mets

Baseline risk factors	Total n	Giredestrant + palbociclib n = 495 n	Median (months)	Letrozole + palbociclib n = 497 n	Median (months)	HR	95% Wald CI
All patients	992	495	33.1	497	28.2	0.89	(0.76, 1.04)
Site of disease							
Visceral	599	301	27.9	298	25.2	0.94	(0.77, 1.15)
Non-Visceral	393	194	44.0	199	32.0	0.80	(0.62, 1.04)



HR 0.80 (0-62-1.04) vs. HR 0.94 (0-77-1.15)

Hypothesis: Patients with non-visceral disease (e.g. bone) may be:

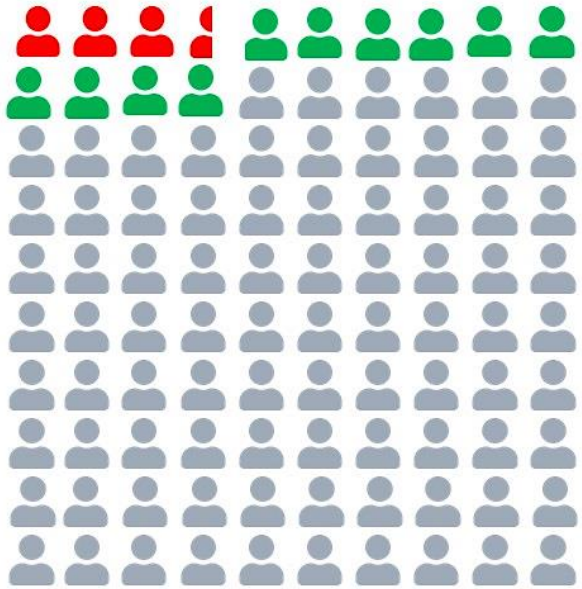
1) More likely to derive benefit from SERDs vs AIs
2) More likely to develop *ESR1* mutations[1]

PADA-1 Cabel et al *Annals of Oncology* 2025

SERENA 6 Consort Diagram (Strategy)

SERENA-6
***ESR1* Mutation Screening every 2-3 months for years**

3256 Patients tested



548 with an *ESR1* Mutation
Cumulative incidence of *ESR1* mutations approx. 20% at 2 years[1]

117 had an *ESR1* mutation and radiographic progression.
These patients went off study

315 had an *ESR1* mutation without radiographic progression and eligible for randomization

R

Switch to camizestrant and continue CDK 4/6

mPFS: 16.8 months

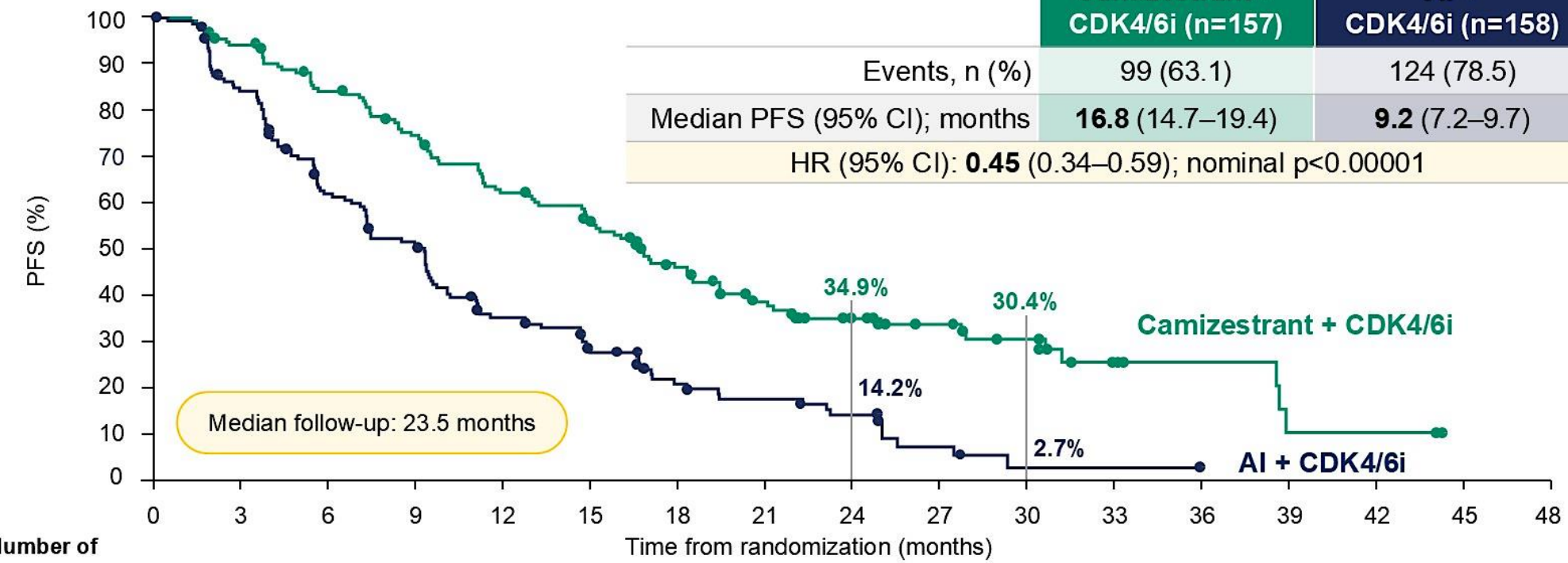
Continue SOC (AI plus CDK 4/6i)

mPFS: 9.2 months

Updated PFS (primary endpoint, investigator-assessed)

With longer follow-up, median PFS improvement with camizestrant + CDK4/6i is 7.6 months

	Camizestrant + CDK4/6i (n=157)	AI + CDK4/6i (n=158)
Events, n (%)	99 (63.1)	124 (78.5)
Median PFS (95% CI); months	**16.8** (14.7–19.4)	**9.2** (7.2–9.7)
HR (95% CI): **0.45** (0.34–0.59); nominal p<0.00001		



Number of patients at risk

Camizestrant + CDK4/6i	157	143	125	109	90	78	57	42	31	23	17	7	5	2	2	0	
AI + CDK4/6i	158	127	90	73	48	35	20	16	12	4	1	1	0	0	0	0	

DCO3 (Jan 02, 2026). At DCO3, 45 patients in the camizestrant + CDK4/6i arm and 12 patients in the AI + CDK4/6i arm were still receiving study treatments. The p value is based on the stratified log-rank test, stratified by disease site (visceral vs non-visceral), timing of *ESR1*m detected (first vs subsequent test), and time from initiation of AI + CDK4/6i to randomization (<18 months vs ≥18 months).

Bidard FC et al. ASCO 2026;Abstract LBA1007

First subsequent therapy

	Patients who received a first subsequent therapy at DCO3	
	Camizestrant + CDK4/6i (n=87)	AI + CDK4/6i (n=117)
Endocrine-based therapy	**48 (55.2%)**	**78 (66.7%)**
SERD or novel ET* ± targeted therapy	24 (27.6%)	57 (48.7%)
Fulvestrant ± targeted therapy	22 (25.3%)	42 (35.9%)
Oral SERD or novel ET* ± targeted therapy	2 (2.3%)	15 (12.8%)
Other endocrine regimens† ± targeted therapy	24 (27.6%)	21 (17.9%)
Cytotoxic therapy	**38 (43.7%)**	**36 (30.8%)**
Oral chemotherapy	22 (25.3%)	12 (10.3%)
IV regimen	16 (18.4%)	24 (20.5%)
Chemotherapy	14 (16.1%)	14 (12.0%)
Antibody–drug conjugate	2 (2.3%)	10 (8.5%)
Other§	**1 (1.1%)**	**3 (2.6%)**

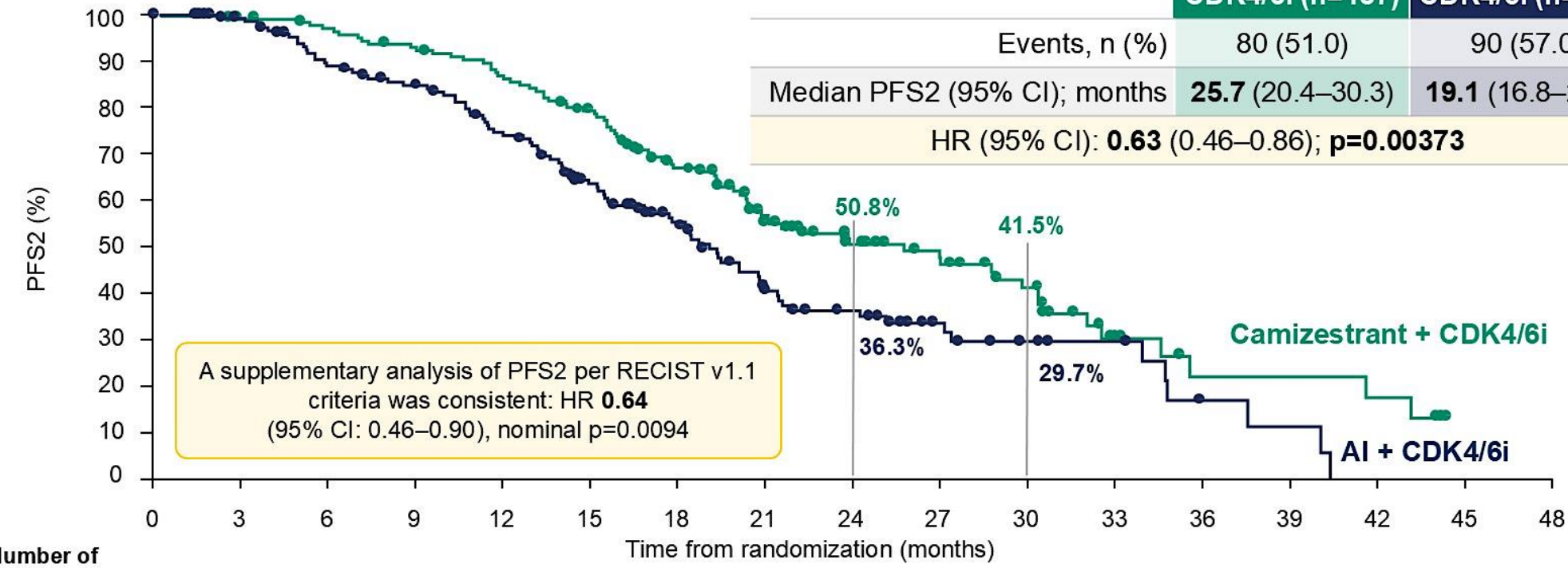
Rate of visceral disease at progression was balanced between arms (supplemental slides)
Approximately half of the patients in the control arm received SERD or novel ET ± targeted therapy

DCO3 (Jan 02, 2026). *"Novel ET" subgroup includes the following terms – elacestrant, imlunestrant, camizestrant, vepdegestrant, lasofoxifene, and palazestrant. Oral SERDs included elacestrant, imlunestrant, camizestrant, and palazestrant. †'Other' endocrine regimens include AI or tamoxifen. §"Other" included PARPi (olaparib, talazoparib) or androgen receptor modulator (enobosarm). Novel ET was used in any subsequent line of therapy in 2/87 (2.3%) patients in the camizestrant+CDK4/6i arm and 23/117 (19.7%) patients in the AI+CDK4/6i arm. ET, endocrine therapy; IV, intravenous; SERD, selective estrogen receptor degraders.

Final second progression-free survival (PFS2)

Camizestrant + CDK4/6i significantly extended time to second progression or death, demonstrating PFS benefit is sustained beyond first progression

	Camizestrant + CDK4/6i (n=157)	AI + CDK4/6i (n=158)
Events, n (%)	80 (51.0)	90 (57.0)
Median PFS2 (95% CI); months	**25.7** (20.4–30.3)	**19.1** (16.8–21.0)
HR (95% CI): **0.63** (0.46–0.86); **p=0.00373**		



Number of patients at risk

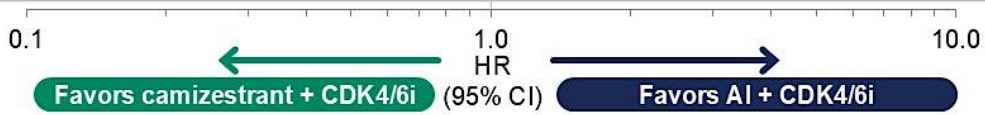
Camizestrant + CDK4/6i	157	150	145	138	127	113	86	63	42	32	24	10	5	5	4	0	
AI + CDK4/6i	158	149	129	120	102	82	60	40	30	17	12	8	3	2	0	0	

DCO3 (Jan 02, 2026). PFS2, defined in a standard manner (assessed by the investigator according to local standard clinical practice) as the time from randomisation to the earliest of disease progression after first subsequent therapy or death in the primary analysis. The p value is based on the stratified log-rank test, stratified by disease site (visceral vs non-visceral), timing of *ESR1*m detected (first vs subsequent test), and time from initiation of AI+CDK4/6i to randomization (<18 months vs ≥18 months).

Updated patient reported outcomes

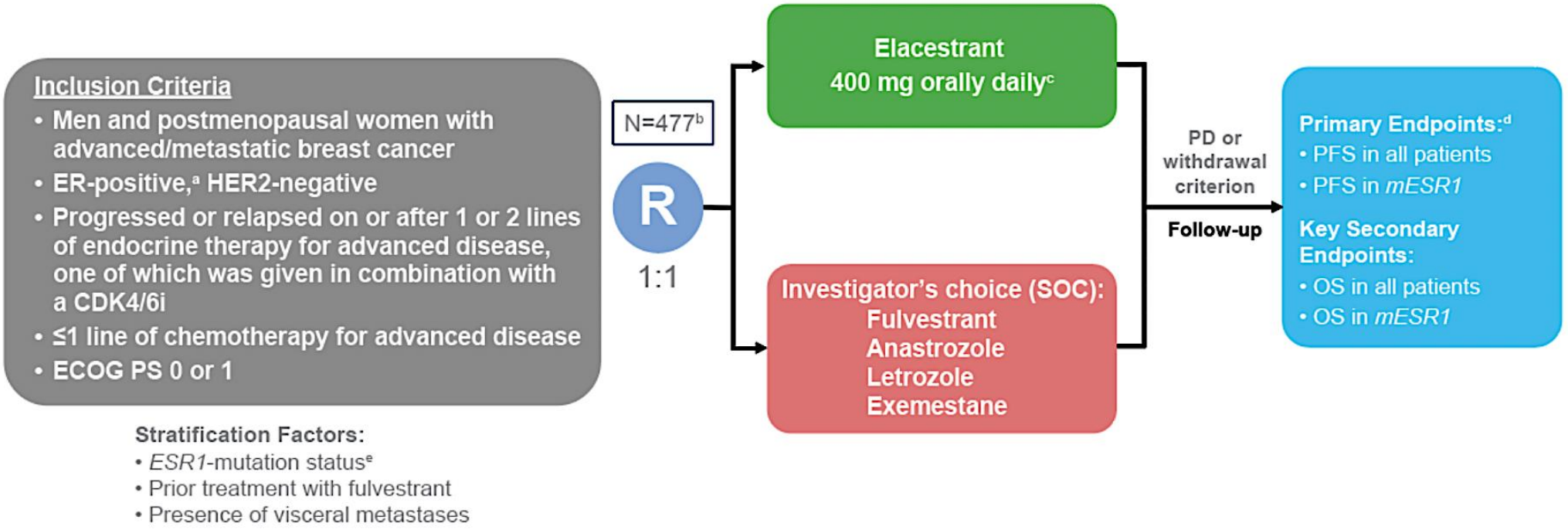
Camizestrant + CDK4/6i reduced the risk of deterioration in patient-reported cancer symptoms and functioning

		Deterioration events, n/N		Hazard ratio (95% CI)
		Camizestrant + CDK4/6i	AI + CDK4/6i	
EORTC QLQ-C30	GHS/QOL	37/107	49/95	0.48 (0.31–0.76)
	Physical functioning*	38/108	36/95	0.68 (0.43–1.08)
	Role functioning	53/108	52/94	0.69 (0.47–1.03)
	Cognitive functioning	39/107	33/95	0.87 (0.55–1.40)
	Emotional functioning	29/107	33/95	0.55 (0.33–0.91)
	Social functioning	39/107	41/95	0.66 (0.42–1.03)
	Pain*	48/106	53/94	0.54 (0.36–0.81)
	Shortness of breath/ dyspnoea	25/105	36/94	0.41 (0.23–0.70)
	Fatigue	35/104	37/91	0.68 (0.42–1.10)
EORTC QLQ-BR23	Breast symptoms*	19/103	17/92	0.64 (0.32–1.28)
	Arm symptoms*	19/101	18/90	0.79 (0.41–1.55)



DCO3 (Jan 02, 2026). Time to deterioration defined as time from randomization to deterioration based on meaningful change thresholds (16.6 for GHS/QoL, role, emotional, cognitive, social functioning, pain and breast symptoms, 22.2 for fatigue and arm symptoms, 13.3 for physical functioning, and 10 for dyspnoea). *Time to deterioration in pain, physical functioning, breast symptoms, and arm symptoms were pre-defined secondary endpoints.
EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; EORTC QLQ-BR23, EORTC QLQ breast cancer-specific supplement; GHS, global health status; QoL, quality of life.

Phase III EMERALD Study Design

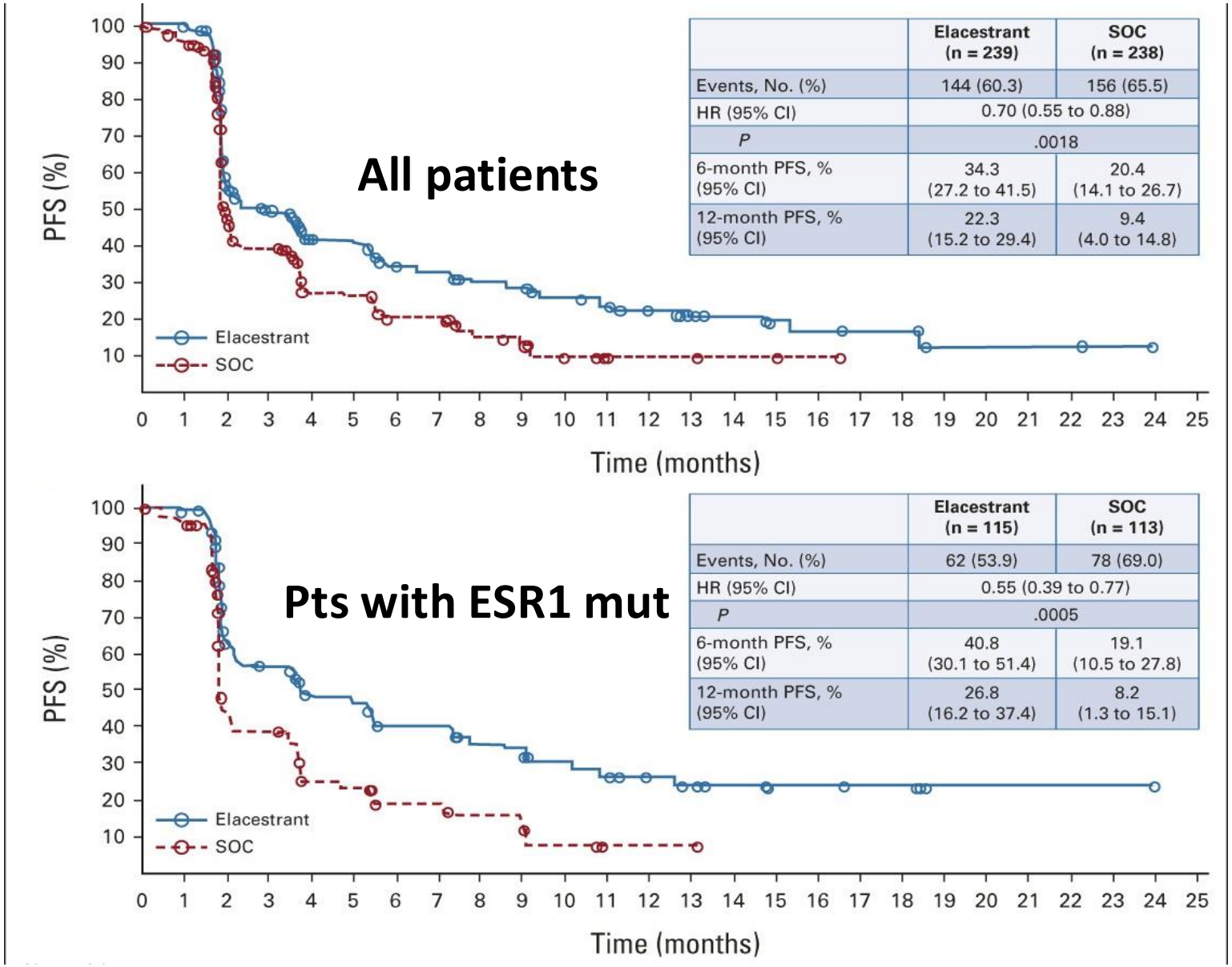


[a]Documentation of ER-positive tumor with ≥1% staining by immunohistochemistry; [b]Recruitment from February 2019 to October 2020; [c]Protocol-defined dose reductions permitted; [d]Blinded independent central review. [e]*ESR1*-mutation status was determined by cell-free circulating DNA analysis using Guardant360® CDx (Guardant Health, Redwood City, CA)

CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; m*ESR1*, *ESR1*-mutant breast cancer population; PFS, progression-free survival; R, randomized; SOC, standard of care.

Bidard FC et al. *J Clin Oncol* 2022 October 1;40(28):3246-56.

Phase III EMERALD: PFS (Primary Endpoint)



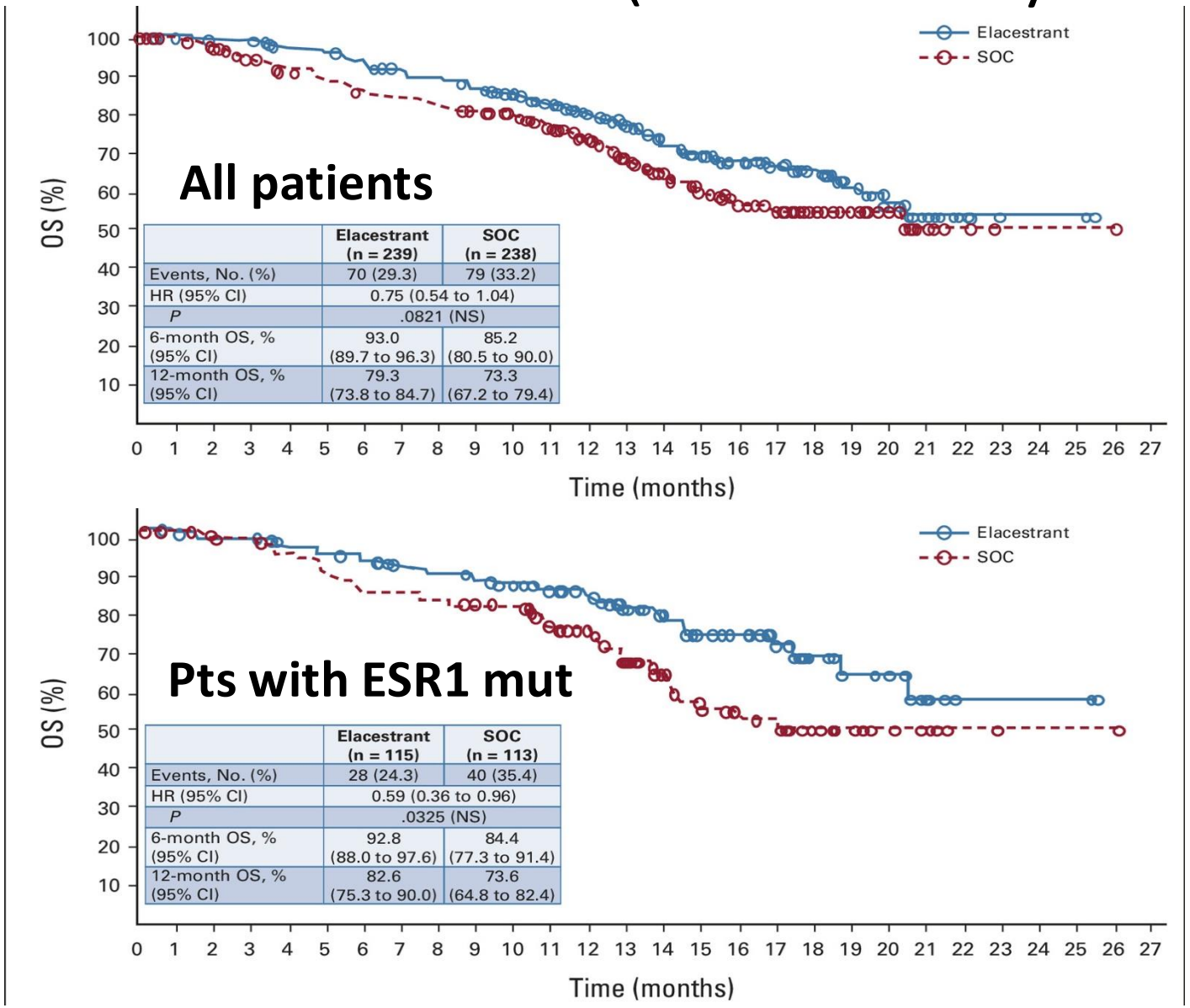
	Elacestrant (n = 239)	SOC (n = 238)
Events, No. (%)	144 (60.3)	156 (65.5)
HR (95% CI)	0.70 (0.55 to 0.88)	
P	.0018	
6-month PFS, % (95% CI)	34.3 (27.2 to 41.5)	20.4 (14.1 to 26.7)
12-month PFS, % (95% CI)	22.3 (15.2 to 29.4)	9.4 (4.0 to 14.8)

	Elacestrant (n = 115)	SOC (n = 113)
Events, No. (%)	62 (53.9)	78 (69.0)
HR (95% CI)	0.55 (0.39 to 0.77)	
P	.0005	
6-month PFS, % (95% CI)	40.8 (30.1 to 51.4)	19.1 (10.5 to 27.8)
12-month PFS, % (95% CI)	26.8 (16.2 to 37.4)	8.2 (1.3 to 15.1)

Bidard FC et al. *J Clin Oncol* 2022 October 1;40(28):3246-56.

PFS = progression-free survival; SOC = standard of care

Phase III EMERALD: OS (Secondary Endpoint)



All patients

	Elacestrant (n = 239)	SOC (n = 238)
Events, No. (%)	70 (29.3)	79 (33.2)
HR (95% CI)	0.75 (0.54 to 1.04)	
P	.0821 (NS)	
6-month OS, % (95% CI)	93.0 (89.7 to 96.3)	85.2 (80.5 to 90.0)
12-month OS, % (95% CI)	79.3 (73.8 to 84.7)	73.3 (67.2 to 79.4)

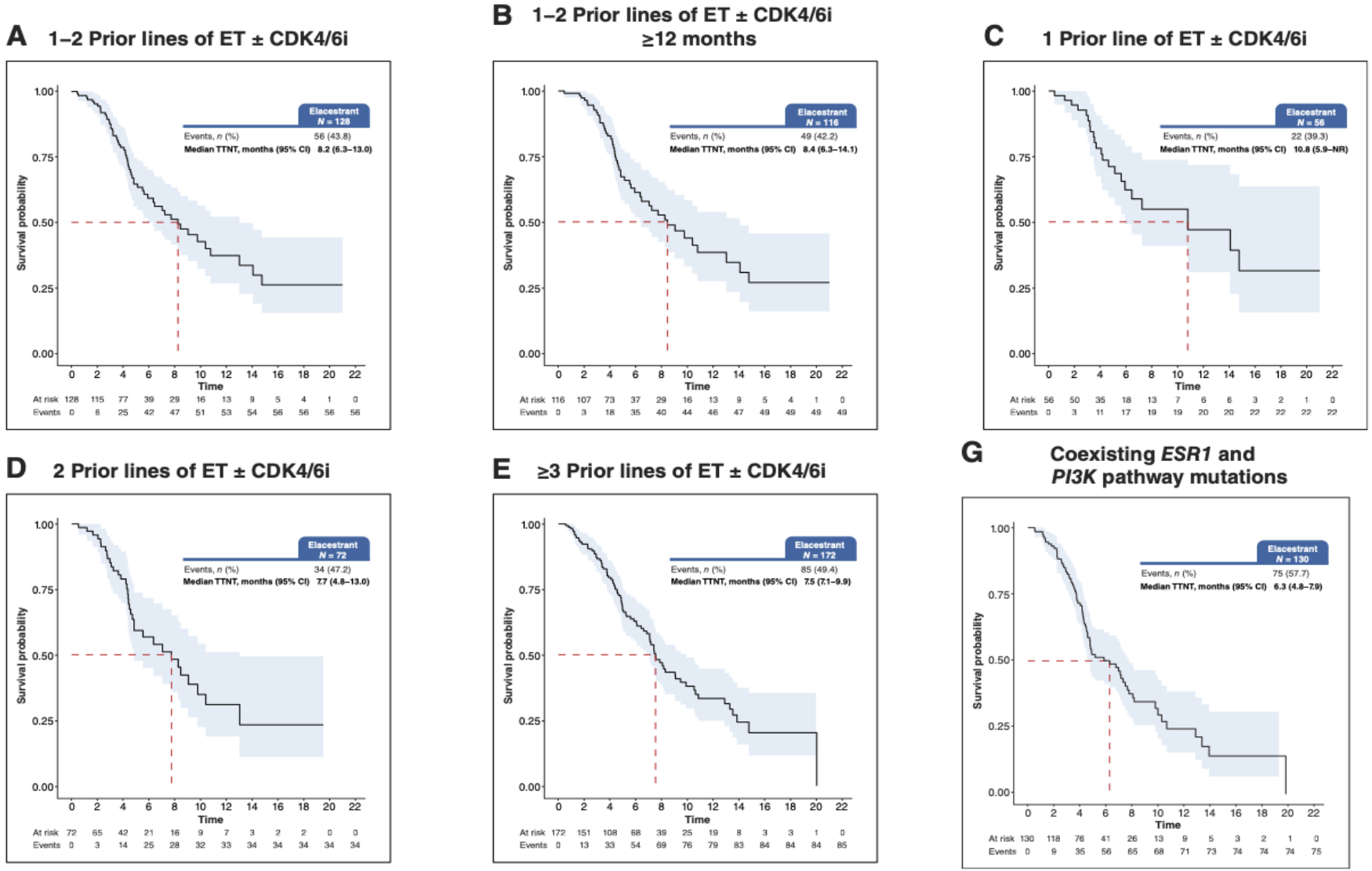
Pts with ESR1 mut

	Elacestrant (n = 115)	SOC (n = 113)
Events, No. (%)	28 (24.3)	40 (35.4)
HR (95% CI)	0.59 (0.36 to 0.96)	
P	.0325 (NS)	
6-month OS, % (95% CI)	92.8 (88.0 to 97.6)	84.4 (77.3 to 91.4)
12-month OS, % (95% CI)	82.6 (75.3 to 90.0)	73.6 (64.8 to 82.4)

Bidard FC et al. *J Clin Oncol* 2022 October 1;40(28):3246-56.

OS = overall survival

Real-World Outcomes with Elacestrant: Median Time to Next Treatment



Rugo HS et al. *Clin Cancer Res* 2026 January 6;32(1):179-87.

ASCO 2026 Abstracts of Interest: Elacestrant

Bardia A et al. ELEGANT: Elacestrant versus standard endocrine therapy (ET) in women and men with node-positive, estrogen receptor–positive (ER+), HER2-negative (HER2−), early breast cancer (eBC) with high risk of recurrence in a global, multicenter, randomized, open-label phase 3 study. ASCO 2026;Abstract TPS1153.

Llombart-Cussac A et al. ADELA: A double-blind, placebo-controlled, randomized phase 3 trial of elacestrant (Ela) + everolimus (EVE) versus elacestrant + placebo in ER+/HER2− advanced breast cancer (aBC) patients with ESR1-mutated tumors progressing on endocrine therapy (ET) + CDK4/6i. ASCO 2026;Abstract TPS1154.

Ibrahim N et al. ELECTRA: An open-label, multicenter, phase 1b/2 study of elacestrant in combination with abemaciclib in patients with brain metastasis from ER+/HER2− breast cancer. ASCO 2026;Abstract TPS1155.

CAPELA: A phase II multicenter open-label randomized study of capecitabine in combination with elacestrant versus capecitabine alone in advanced estrogen receptor (ER)-positive breast cancer (TBCRC 070). ASCO 2026;Abstract TPS1156.

McHayleh W et al. Elacestrant in combination with capivasertib in patients with ER+/HER2− advanced breast cancer: Update from ELEVATE, a phase 1b/2, open-label, umbrella study. ASCO 2026;Abstract 1098.

EMBER-3 Study Design

ER+, HER2- ABC

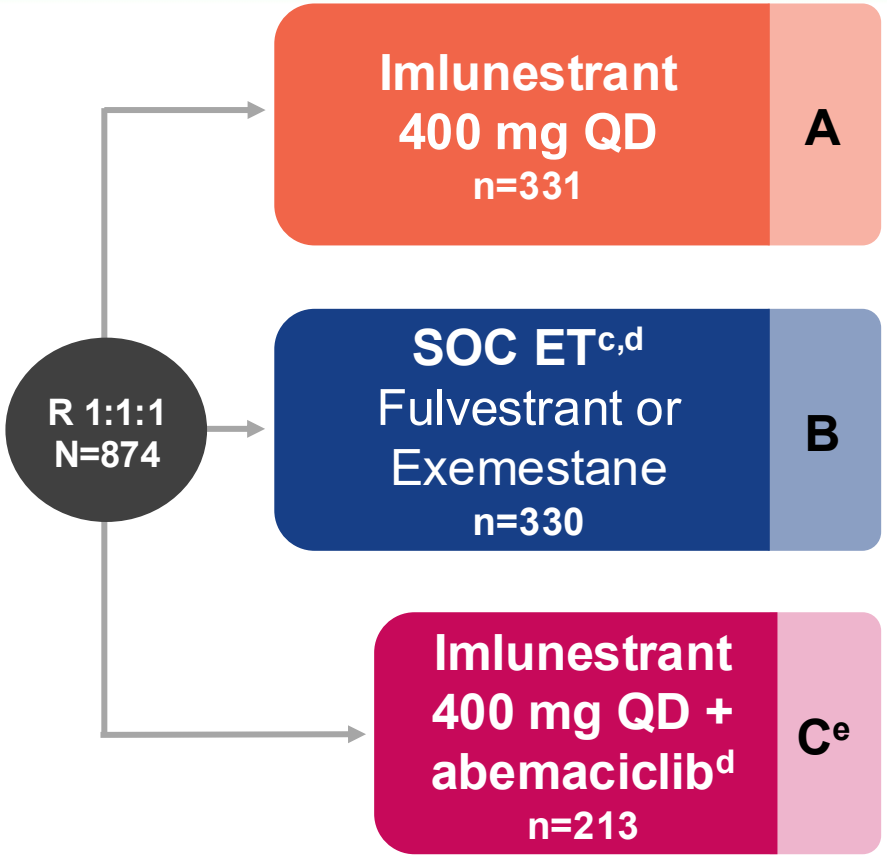
Men and pre-[a]/post-menopausal women

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

Stratification Factors:

- Prior CDK4/6i therapy (Y/N)
- Visceral metastases (Y/N)
- Region[b]



Primary Endpoints

Investigator-assessed PFS for[f]:

- A vs B in patients with *ESR1*m[g]
- A vs B in all patients
- C vs A in all patients[h]

Key Secondary Endpoints

- OS, PFS by BICR, and ORR
- Safety

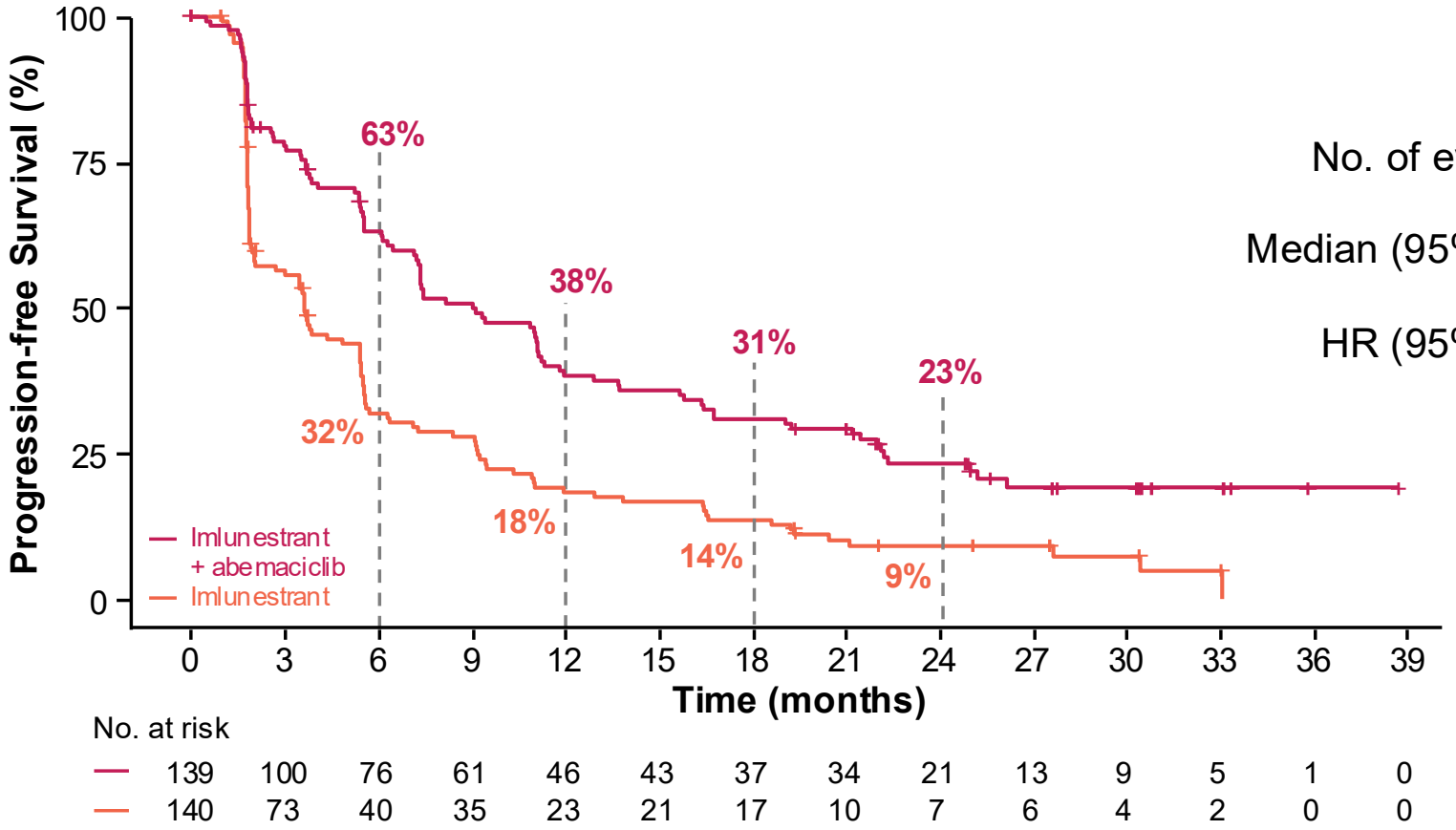
Exploratory Endpoints

- TTC[i], CFS[j], PFS2[k]

[a]A GnRH agonist was required in men and premenopausal women. [b]East Asia vs United States/European Union vs others; [c]Investigator's choice. [d]Labeled dose. [e]Enrollment into Arm C started with Protocol Amendment A (at which point 122 patients had been randomized across Arms A and B). [f]Scans every 8 weeks for the first 12 months, then every 12 weeks. [g]*ESR1*m status was centrally 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 concurrently randomized patients. [i]Defined as the time from randomization to start of first chemotherapy (censoring patients who died prior to initiation of chemotherapy). [j]Defined as the time from randomization to initiation of first chemotherapy or death, whichever occurred first. [k]Defined as the time from randomization to progression on the next line of therapy or death from any cause. Note: Patients were enrolled from October 2021 to November 2023 across 195 sites in 22 countries. *ABC, advanced breast cancer; AI, aromatase inhibitor; BICR, blinded independent central review; CDK4/6i, cyclin-dependent kinase 4 and 6 inhibitor; CFS, chemotherapy-free survival; ER, estrogen receptor; ESR1m, estrogen receptor 1 gene mutation; GnRH, gonadotropin releasing hormone; HER2, human endothelial growth factor receptor 2; N, no; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; QD, once daily; R, randomized; SOC ET, standard of care endocrine therapy; TTC, time to chemotherapy; Y, yes.*

Jhaveri K et al. SABCS 2025;Abstract GS3-08

Subgroup Analysis: PFS of Imlunestrant + Abemaciclib vs Imlunestrant in CDK4/6i Pretreated Patients



	Imlunestrant + abemaciclib n=139	Imlunestrant n=140
No. of events	97	120
Median (95% CI)	**9.1** (7.2-11.3)	**3.7** (2.1-5.5)
HR (95% CI)	**0.53 (0.40-0.69)**	
	Nominal *p*-value < 0.0001	

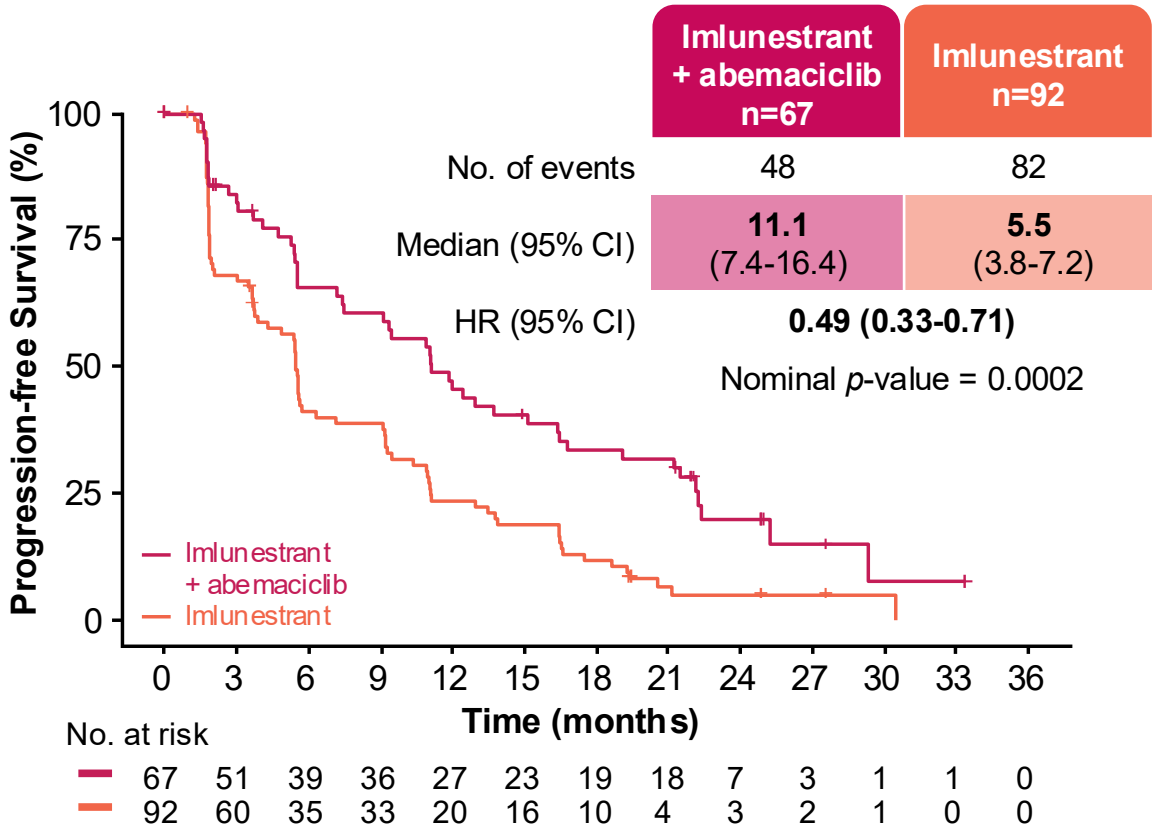
Consistent benefit of imlunestrant + abemaciclib maintained in patients previously treated with a CDK4/6i

CDK4/6i, cyclin-dependent kinase 4 and 6 inhibitor; CI, confidence interval; HR, hazard ratio; PFS, progression-free survival.

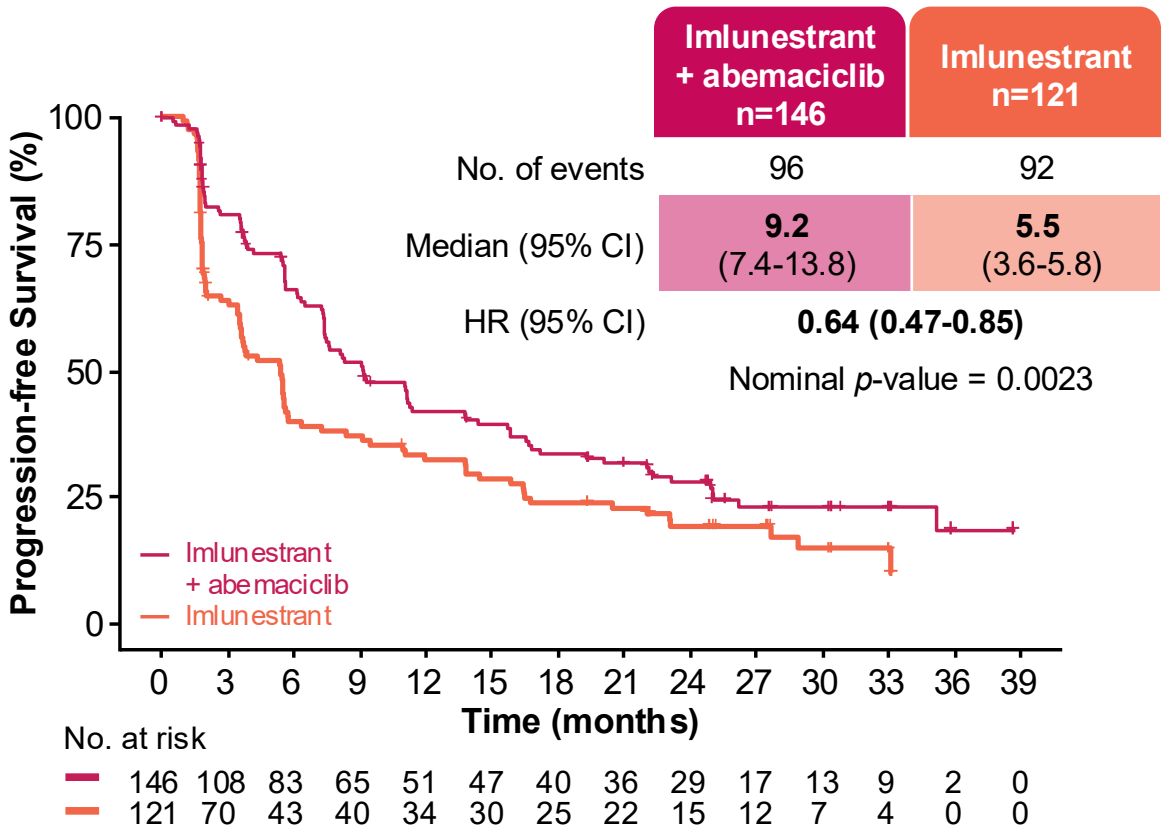
Jhaveri K et al. SABCS 2025;Abstract GS3-08

Subgroup Analysis: PFS of Imlunestrant + Abemaciclib vs Imlunestrant by *ESR1*m Status

Patients With *ESR1*m



Patients Without *ESR1*m



Consistent benefit of imlunestrant + abemaciclib maintained regardless of *ESR1*m status

CI, confidence interval; ESR1m, estrogen receptor 1 gene mutation; HR, hazard ratio; PFS, progression-free survival.

Jhaveri K et al. SABCS 2025;Abstract GS3-08

evERA BC study design

A global, randomized, open-label, Phase III trial

Key eligibility criteria*

- ER+, HER2– aBC (1–3L of therapy)
- ≤ 2 prior lines of ET in the aBC setting
- PD or relapse during/post-CDK4/6i + ET†
- No prior chemotherapy in the aBC setting
- Measurable disease per RECIST v1.1 or evaluable bone metastases

Enrollment period: August 2022 to October 2024

N = 373*

R 1:1

Giredestrant 30 mg PO QD + everolimus 10 mg‡

SOC ET§ + everolimus 10 mg‡

§ Exemestane/fulvestrant/tamoxifen

Until PD or unacceptable toxicity

‡ Alcohol-free dexamethasone mouthwash (0.5 mg/5 mL) prophylaxis and treatment of stomatitis was strongly recommended (10 mL swished for 2 minutes and spat QID) starting concurrently with study treatment for 8 weeks, and then reactively thereafter with the first appearance of symptoms[1]

* Trial was enriched to 55% of patients with *ESR1*m tumors at baseline (centrally tested via circulating tumor DNA)
† Patients had to receive ≥ 6 months of CDK4/6i + ET in the aBC setting to be eligible for enrollment; prior fulvestrant was allowed

Stratification factors

- Prior treatment with fulvestrant (yes vs no)
- *ESR1*m tumor (yes vs no/indeterminate)
- Site of disease (visceral [lung and/or liver involvement] vs non-visceral)

Co-primary endpoints (RECIST v1.1)

- INV-PFS in patients with *ESR1*m tumors
- INV-PFS in the overall study population

Key secondary endpoints

- OS
- INV-ORR, DoR

Exploratory endpoints

- PFS2‖
- Chemotherapy-free survival¶
- Post-progression treatment

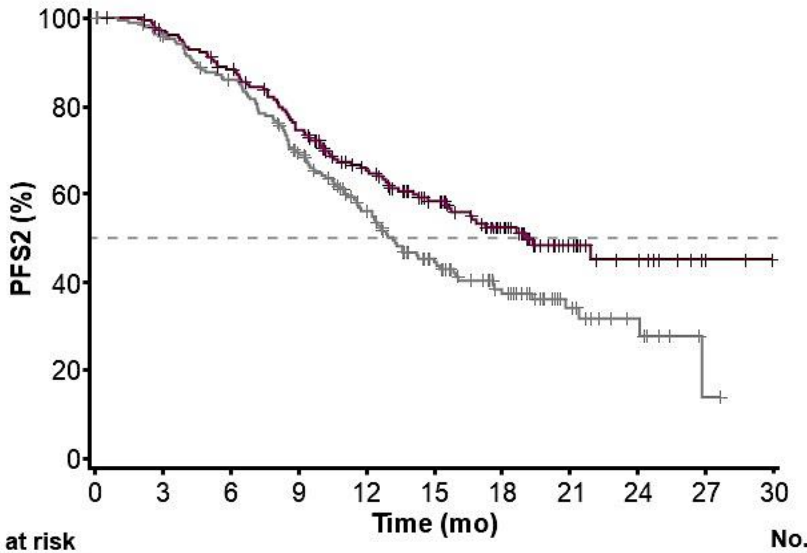
ClinicalTrials.gov number, NCT05306340. Adapted from Mayer EL, *et al*. ESMO 2025 (oral LBA16), with permission. ‖ Defined as the time from randomization to first progression on next-line therapy or death. ¶ Defined as the time from randomization to the start of the first chemotherapy and/or antibody–drug conjugate or death from any cause, whichever occurred first. 1–3L, first to third line; (a)BC, (advanced) breast cancer; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; DoR, duration of response; ER+, estrogen receptor-positive; *ESR1*m, *ESR1*-mutated; ET, endocrine therapy; HER2–, HER2-negative; INV, investigator-assessed; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PFS2, progression-free survival 2; PO, orally; QD, once daily; QID, four times daily; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumours; SOC, standard-of-care.

1. Rugo HS, *et al. Lancet Oncol* 2017; **18**:654–662.

PFS2 in the overall study, *ESR1*m, and *ESR1*m not detected populations

Overall study

	Giredestrant + everolimus n = 183	SOC ET + everolimus n = 190
Events, n (%)	81 (44.3)	108 (56.8)
Median, mo (95% CI)	**19.02** (15.51, NE)	**13.17** (11.70, 15.87)
HR (95% CI)	**0.69** (0.51, 0.92)	

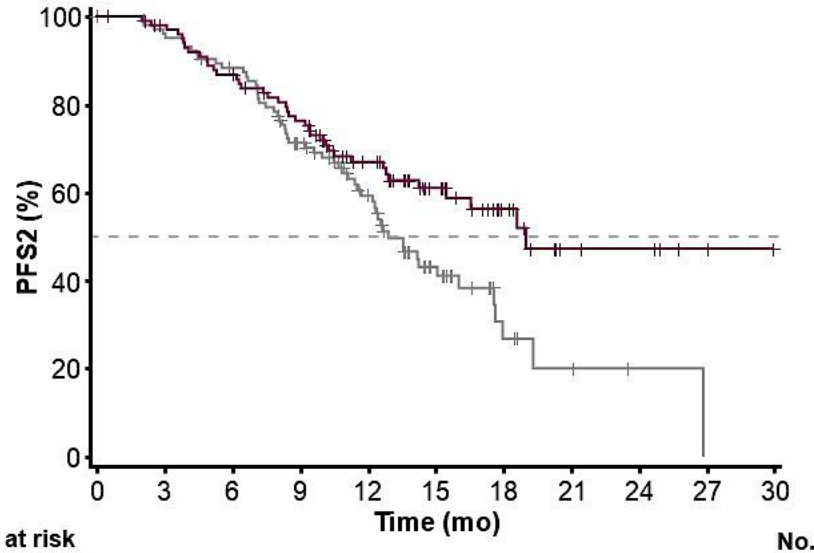


No. at risk

Giredestrant + everolimus	183	173	156	129	100	74	48	21	11	3
SOC ET + everolimus	190	177	157	121	87	58	38	18	8	1

*ESR1*m

	Giredestrant + everolimus n = 102	SOC ET + everolimus n = 105
Events, n (%)	39 (38.2)	57 (54.3)
Median, mo (95% CI)	**19.02** (15.51, NE)	**12.94** (11.76, 17.61)
HR (95% CI)	**0.61** (0.40, 0.93)	

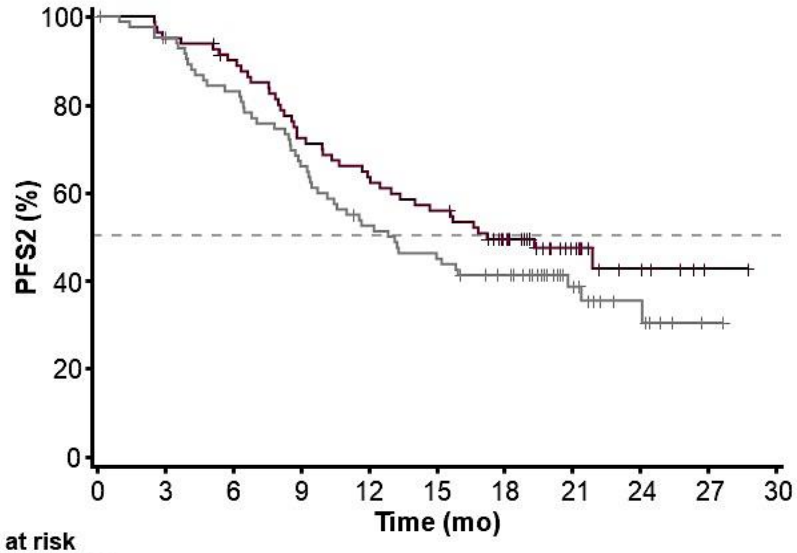


No. at risk

Giredestrant + everolimus	102	96	85	72	50	30	15	6	5	2
SOC ET + everolimus	105	99	89	66	45	21	8	3	1	

*ESR1*m not detected

	Giredestrant + everolimus n = 81	SOC ET + everolimus n = 85
Events, n (%)	42 (51.9)	51 (60.0)
Median, mo (95% CI)	**17.25** (13.01, NE)	**12.88** (9.76, 20.83)
HR (95% CI)	**0.77** (0.51, 1.17)	



No. at risk

Giredestrant + everolimus	81	77	71	57	50	44	33	15	6	1
SOC ET + everolimus	85	78	68	55	42	37	30	15	7	1

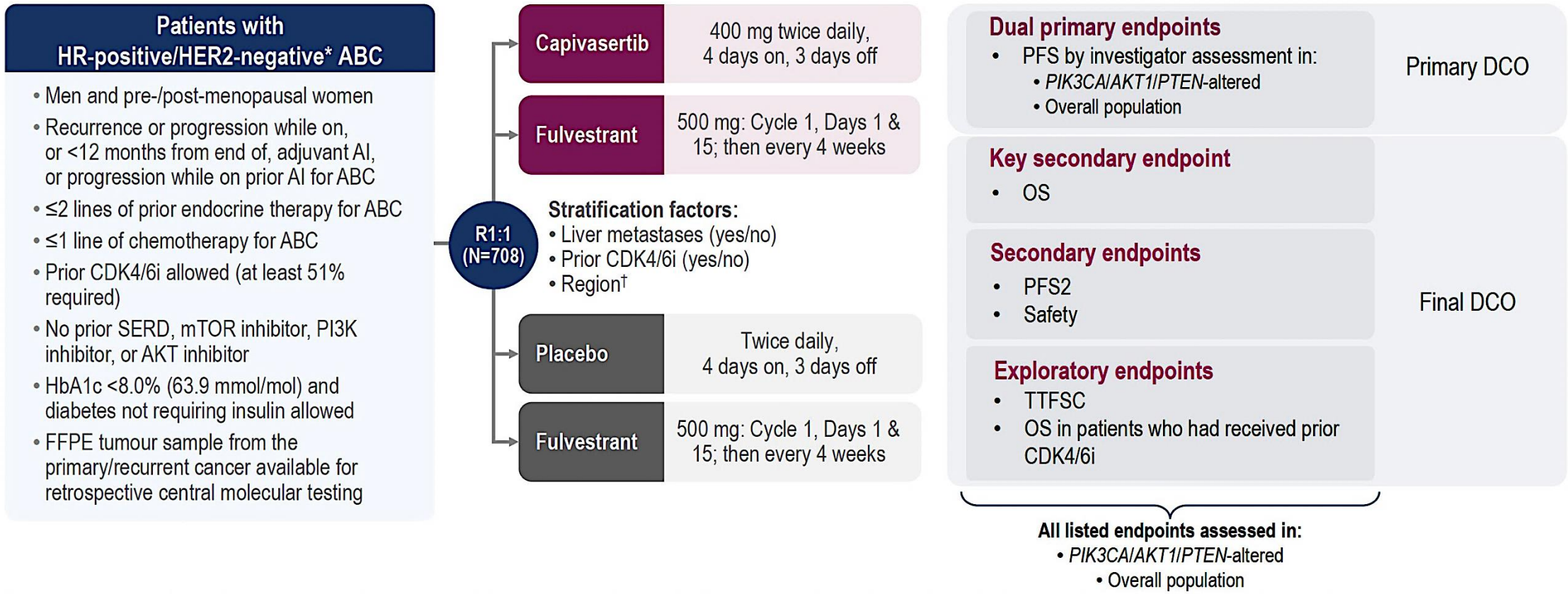
Data cutoff: July 16, 2025. Median follow-up: 18.4 mo (giredestrant + everolimus); 18.7 mo (SOC ET + everolimus). HR estimates are stratified. PFS2 was defined as the time from randomization to first progression on next-line therapy or death.
CI, confidence interval; *ESR1*m, *ESR1* mutation; ET, endocrine therapy; HR, hazard ratio; mo, months; NE, not evaluable; PFS2, progression-free survival 2; SOC, standard-of-care.

Dr Kalinsky Case Presentation #2

- 69 yo F, biopsy of left mass showed atypical papillary proliferation with DCIS, and Invasive ductal carcinoma at 8 o'clock. , ER 100% positive, PR 80% positive, Her -2 negative, Ki67 20%
- Excisional biopsy with sentinel node biopsy: 0.8cm invasive ductal carcinoma, no lymph node involved (0/4 positive)
- Left mastectomy, pathology no invasive component. No chemotherapy, No XRT
- Anastrozole: 12/31/21: Completed endocrine therapy x 10
- 11/9/22 Repeat R ilium biopsy confirmed +mets, ER 94%, PR 33%, HER2 equivocal 2+, *HER2* FISH neg
- Guardant testing: +ESR1 mutation, no PIK3CA mutation
- Palbociclib/Fulvestrant x 2 years
- Switched to Elacestrant x 1 yr, tolerated therapy well

Phase III CAPItello-291 Study Design

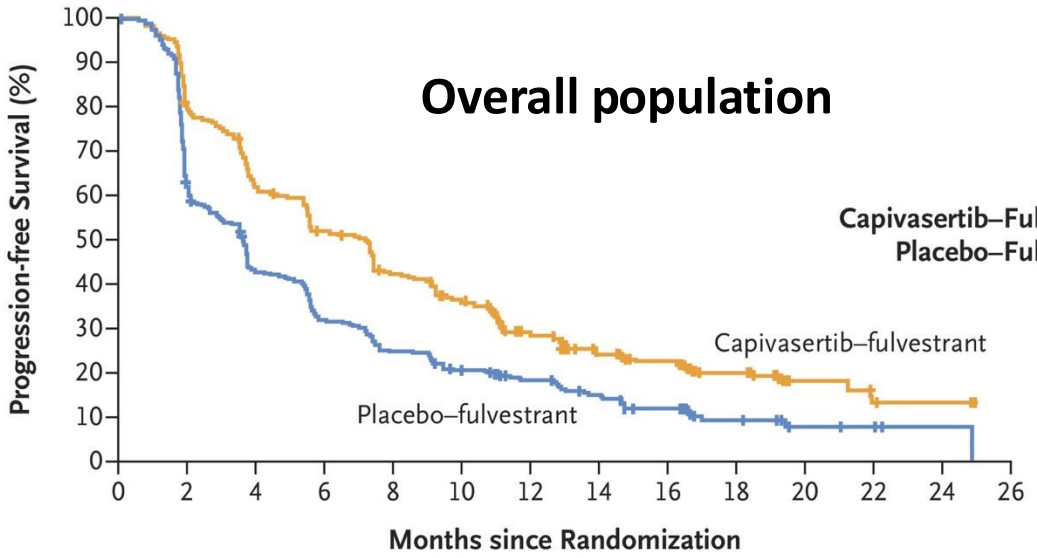
Phase 3, randomised, double-blind, placebo-controlled study (NCT04305496)



Pre- or peri-menopausal women also received a luteinising hormone-releasing hormone agonist for the duration of the study treatment. *HER2-negative was defined as IHC 0 or 1+, or IHC 2+/ISH–. †Region 1: United States, Canada, Western Europe, Australia and Israel, Region 2: Latin America, Eastern Europe and Russia vs Region 3: Asia. AI, aromatase inhibitor; DCO, data cut-off; FFPE, formalin-fixed paraffin-embedded; IHC, immunohistochemistry; ISH, *in situ* hybridisation; mTOR, mechanistic target of rapamycin; OS, overall survival; PFS, progression-free survival; PFS2, time from randomisation until second progression or death due to any cause; R, randomised; SERD, selective oestrogen receptor degrader; TTFSC, time to first subsequent chemotherapy.

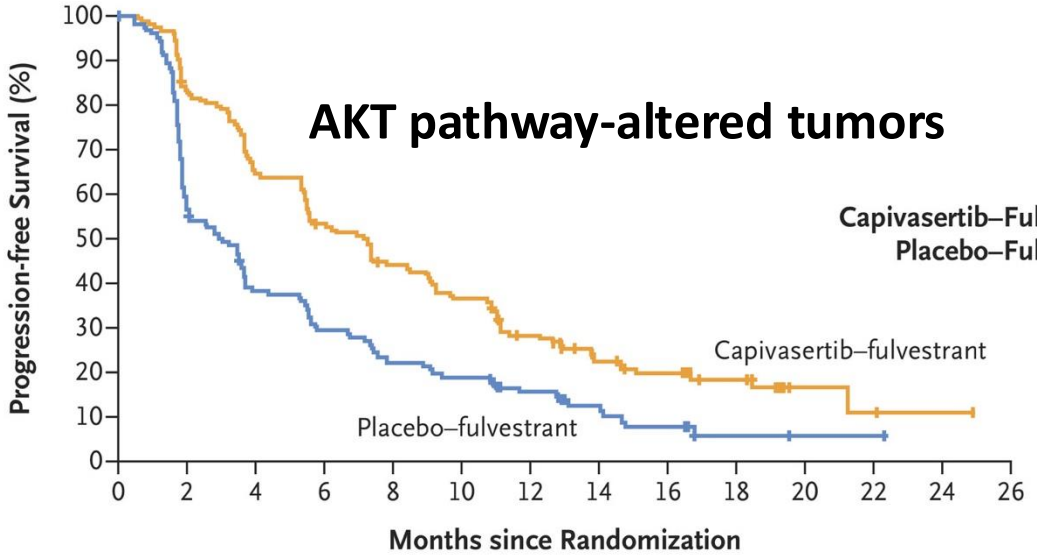
Rugo HS et al. ESMO Breast 2026;Abstract 417O.

Phase III CAPItello-291: Progression-Free Survival (Dual Primary Endpoints)



	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



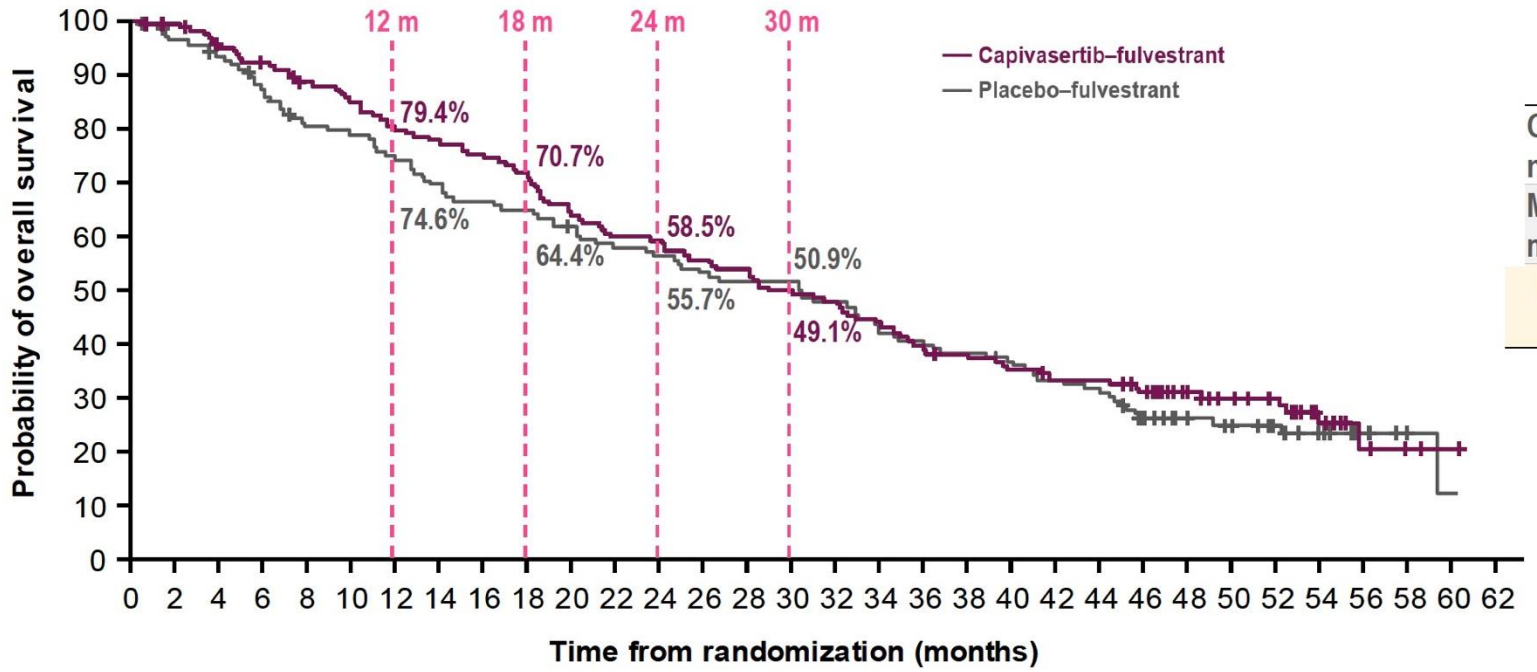
	No. of Patients	No. of Events	Median Progression-free Survival (95% CI)
			mo
Capivasertib–Fulvestrant	155	121	7.3 (5.5–9.0)
Placebo–Fulvestrant	134	115	3.1 (2.0–3.7)

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 Med* 2023 June 1;388(22):2058-70.

Phase III CAPItello-291: Overall Survival (Altered Population)

There was a numerical trend in hazard ratio favouring capivasertib–fulvestrant vs placebo–fulvestrant for the *PIK3CA/AKT1/PTEN*-altered population, but the analysis was underpowered and statistical significance was not reached

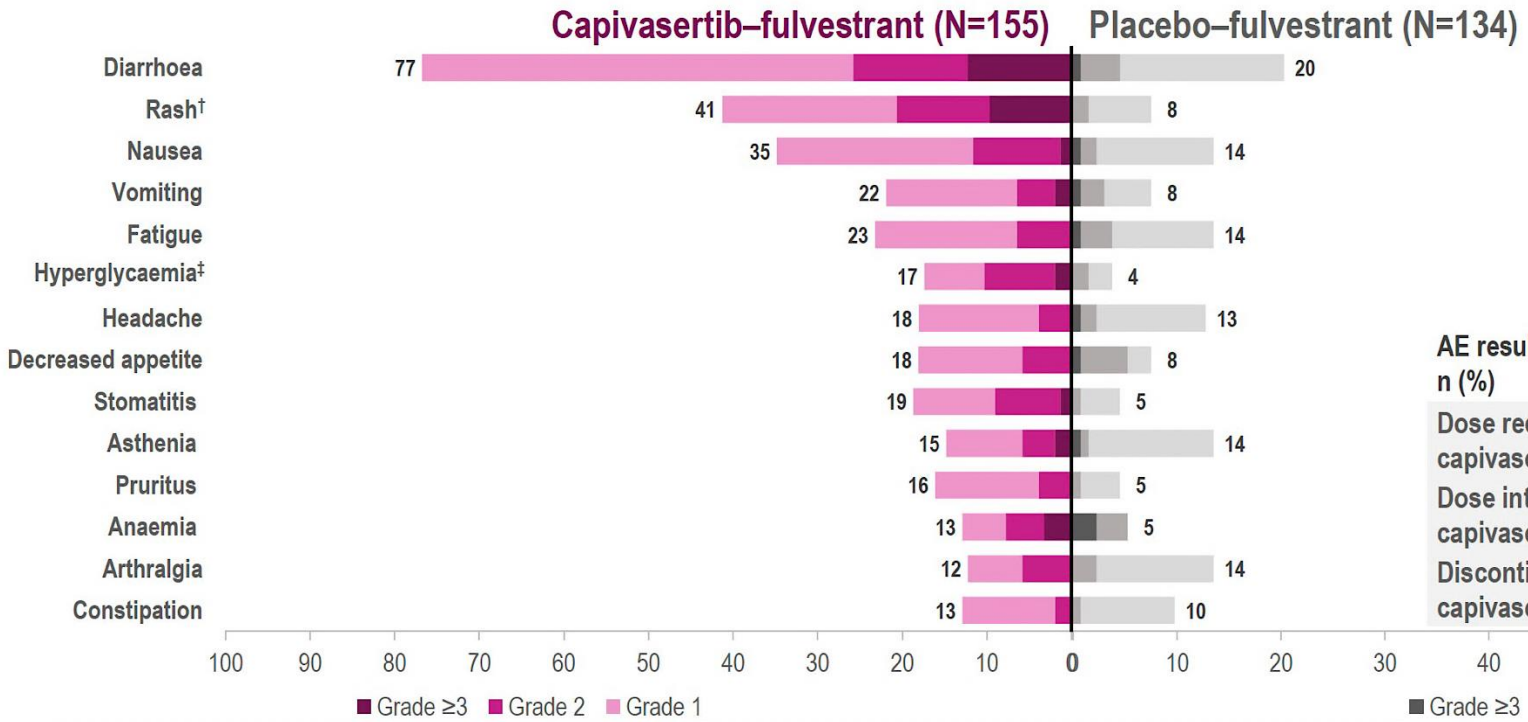


	Capivasertib –fulvestrant (N=155)	Placebo –fulvestrant (N=134)
OS events, n (%)	109 (70.3)	98 (73.1)
Median OS, months	28.5	30.4
Hazard ratio (95% CI): **0.83** (0.63–1.10); p=0.201		

Rugo HS et al. ESMO Breast 2026;Abstract 417O.

Phase III CAPItello-291: Safety

The safety profile of capivasertib–fulvestrant was consistent with the primary analysis; no new safety signals were identified since the primary data cut-off



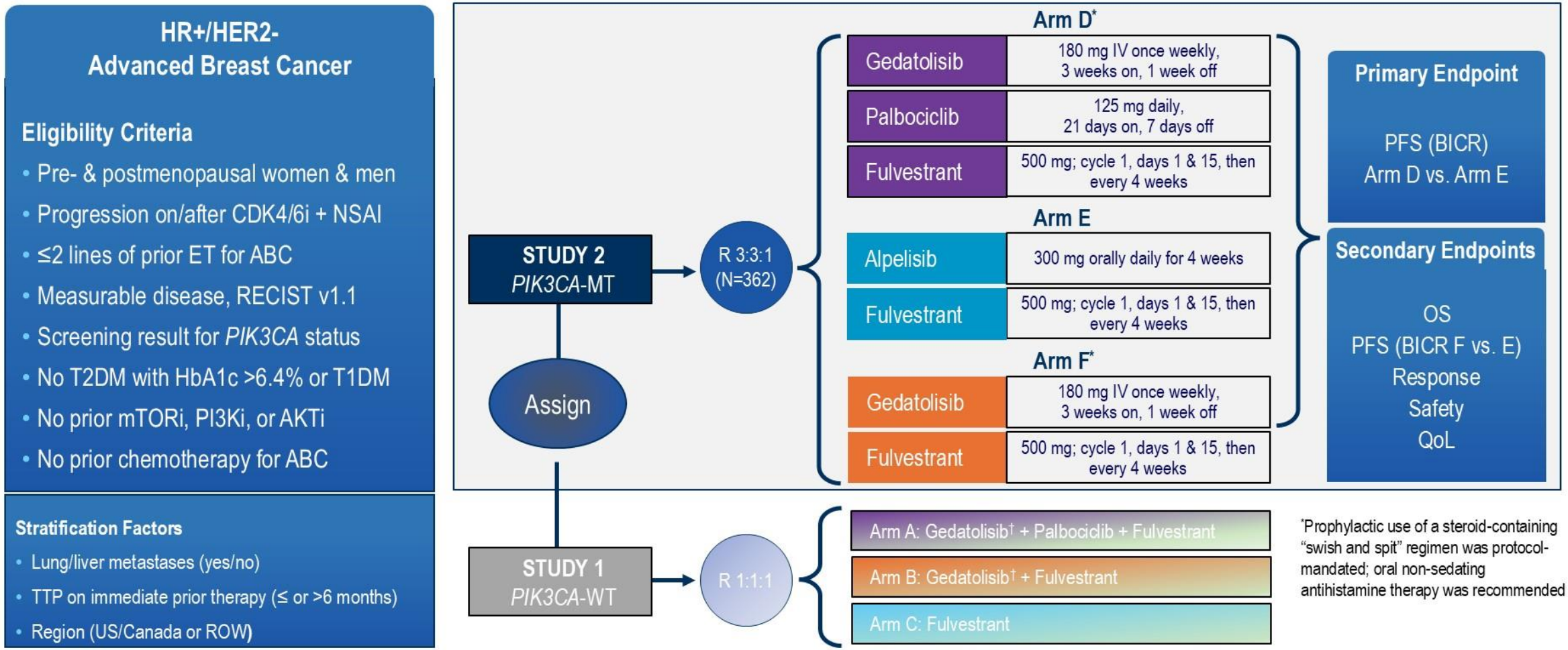
AE resulting in, n (%)	Capivasertib–fulvestrant (N=155)	Placebo–fulvestrant (N=134)
Dose reduction of capivasertib/placebo	34 (21.9)	1 (0.8)
Dose interruption of capivasertib/placebo	60 (38.7)	15 (11.3)
Discontinuation of capivasertib/placebo	10 (6.5)	1 (0.8)

At final analysis in the altered population, there were 6 (3.9%) patients in the capivasertib–fulvestrant arm and 4 (3.0%) in the placebo–fulvestrant arm still receiving study treatment

Number in bold indicates percentage total. *The listed events were reported as a single term in >10% of the patients for any grade in either group. AEs are reported regardless of the relationship to the study drugs. †Group term of rash includes the preferred terms of rash, rash macular, maculopapular rash, rash papular and rash pruritic. ‡Group term of hyperglycaemia includes the preferred terms of blood glucose increased and hyperglycaemia. AE, adverse event.

Rugo HS et al. ESMO Breast 2026;Abstract 417O.

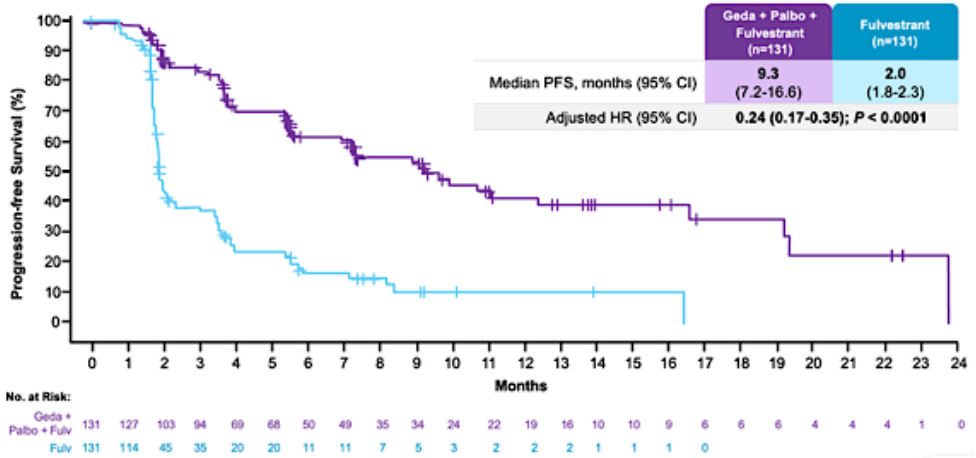
VIKTORIA-1 Study Design



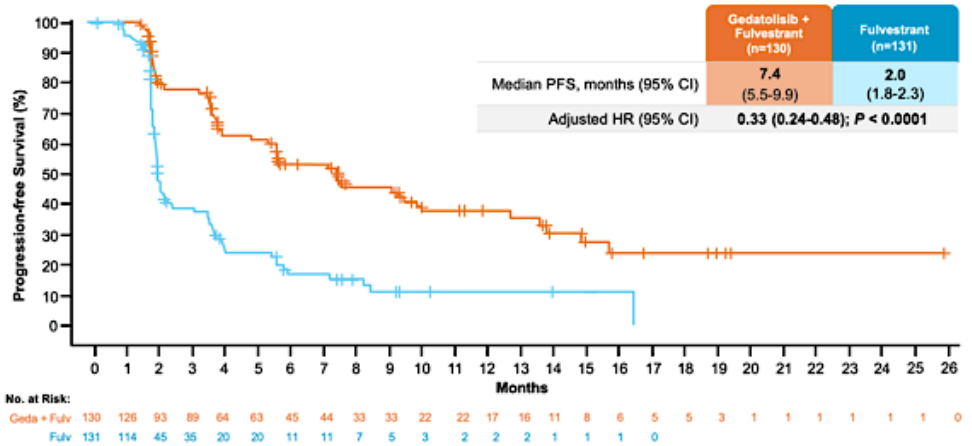
Abbreviations: ABC, advanced breast cancer; AKTi, protein kinase B inhibitor; BICR, blinded independent central review; CDK4/6i, cyclin-dependent kinase 4 and 6 inhibitor; ET, endocrine therapy; HbA1c, hemoglobin A1c; HER2-, human epidermal growth factor receptor 2-negative; HR+, hormone receptor-positive; IV, intravenous; MT, mutant; mTORi, mechanistic target of rapamycin inhibitor; NSAI, non-steroidal aromatase inhibitor; OS, overall survival; PFS, progression-free survival; PI3Ki, phosphatidylinositol 3-kinase inhibitor; QoL, quality of life; R, randomization; ROW, rest of world; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; TTP, time to progression; WT, wild-type

VIKTORIA-1 Study 1 results for PI3K WT

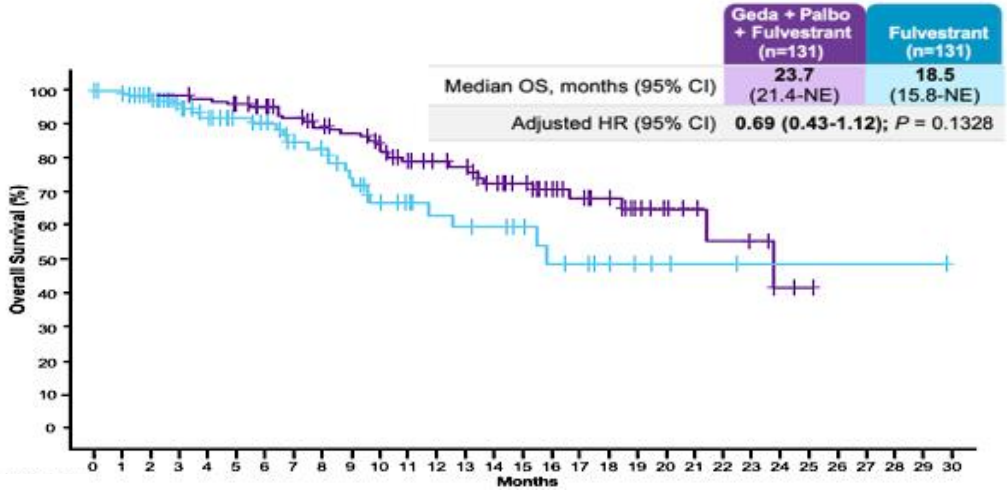
PFS Gedatolisib Triplet vs. Fulvestrant



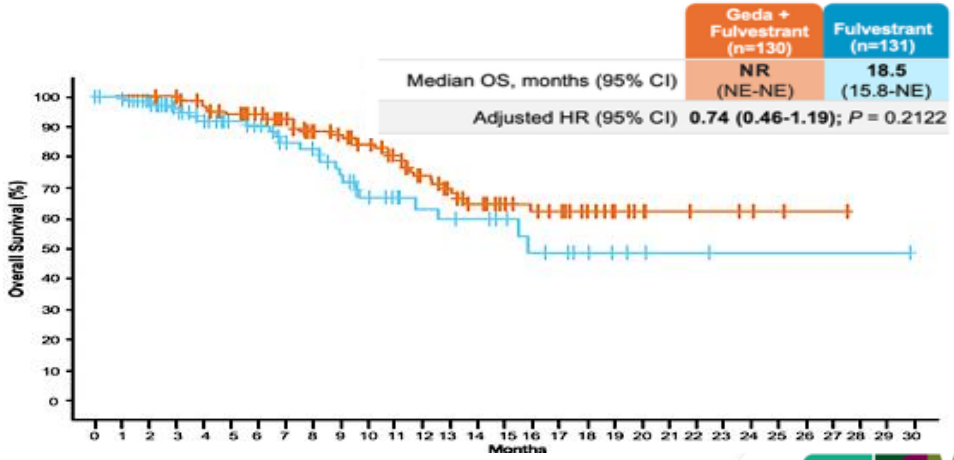
PFS Gedatolisib Doublet vs. Fulvestrant



Interim OS Censored at Cross-Over Gedatolisib Triplet vs. Fulvestrant



Interim OS Censored at Cross-Over Gedatolisib Doublet vs. Fulvestrant

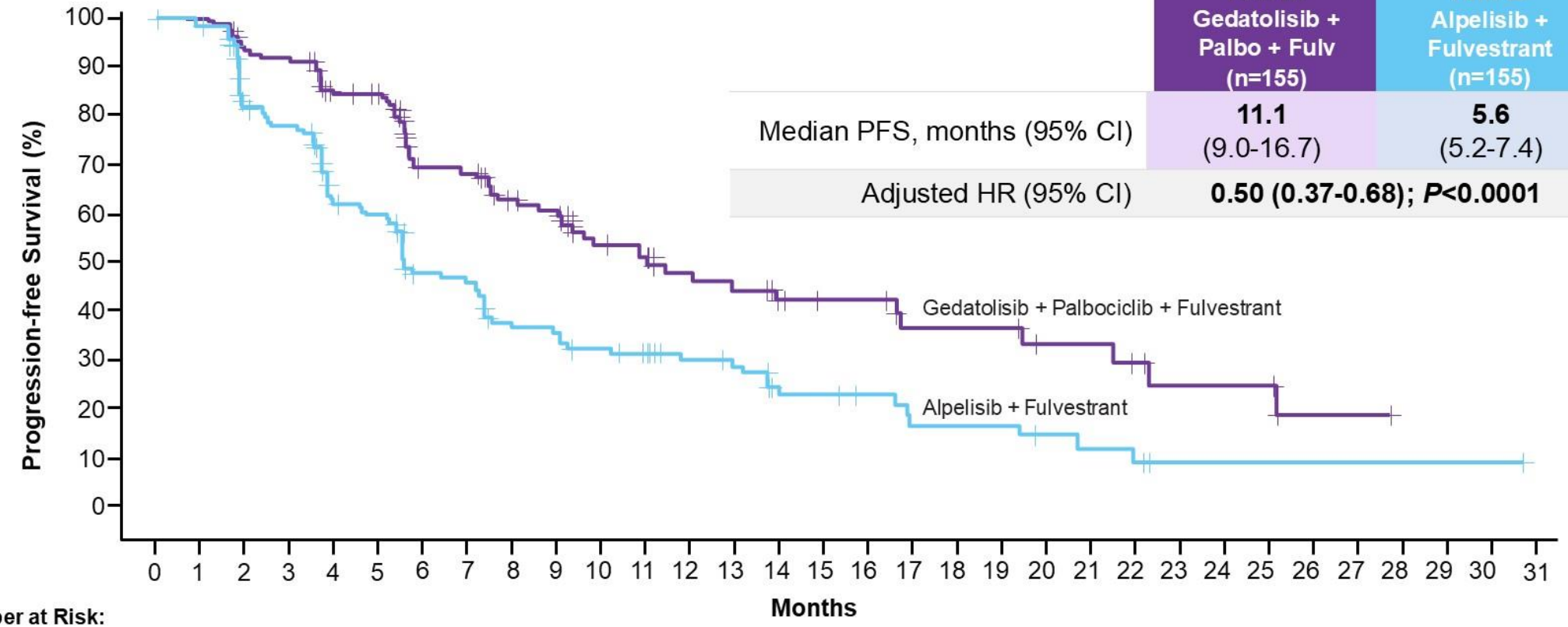


Hurvitz SA et al, ESMO 2025.

Primary Endpoint: Progression-Free Survival (BICR)

Gedatolisib Triplet vs. Alpelisib + Fulvestrant in VIKTORIA-1 Study 2

	Arm D: Gedatolisib + Palbo + Fulv (n=155)	Arm E: Alpelisib + Fulvestrant (n=155)
Median PFS, months (95% CI)	**11.1** (9.0-16.7)	**5.6** (5.2-7.4)
Adjusted HR (95% CI)	**0.50 (0.37-0.68); *P*<0.0001**	

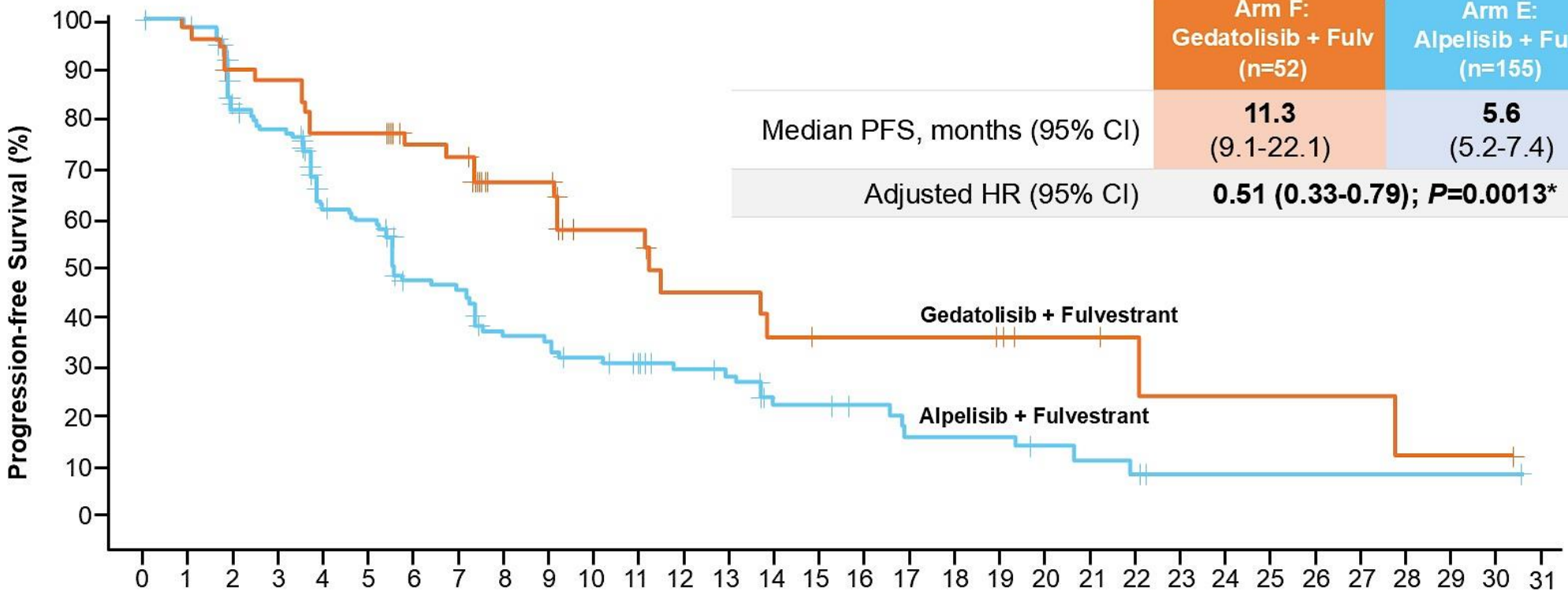


Number at Risk:

Geda + Palbo + Fulv	155	150	134	131	110	107	77	76	62	57	42	38	27	25	20	16	16	12	12	12	9	9	7	5	5	5	2	2	0
Alpelisib + Fulv	155	148	116	107	78	74	53	51	35	34	30	27	22	20	13	13	11	8	8	8	5	4	3	1	1	1	1	1	1	1	1	0

Secondary Endpoint: Progression-Free Survival (BICR)

Gedatolisib Doublet vs. Alpelisib + Fulvestrant in VIKTORIA-1 Study 2



	Arm F: Gedatolisib + Fulv (n=52)	Arm E: Alpelisib + Fulv (n=155)
Median PFS, months (95% CI)	**11.3** (9.1-22.1)	**5.6** (5.2-7.4)
Adjusted HR (95% CI)	**0.51 (0.33-0.79); *P*=0.0013***	

Number at Risk:

Gedatolisib + Fulv	52	48	42	41	36	36	31	30	23	23	15	15	10	10	8	7	7	7	7	6	4	4	3	2	2	2	2	2	1	1	1	0
Alpelisib + Fulv	155	148	116	107	78	74	53	51	35	34	30	27	22	20	13	13	11	8	8	8	5	4	3	1	1	1	1	1	1	1	1	0

*Arm F vs. E analysis was not part of the primary efficacy analysis in the hierarchical order.

Dr Kalinsky Case Presentation #3

- 60 yo F
- 2/17/05: s/p right lumpectomy + SLNB: IDC, grade 2 (0.5 cm in greatest dimension), 1/7 LNs, ER+/PR+/HER2 2+, FISH negative.
- Received adjuvant chemotherapy with FEC x3 cycles followed by docetaxel x3 cycles, s/p XRT and endocrine therapy x 11 years (Tam, AI)
- 5/27/21: CT-biopsy of left iliac bone lesion confirmed metastatic carcinoma consistent with breast primary, ER+/PR-/HER2 2+, FISH negative. Ki-67 24%.
- Anastrozole + Abemaciclib x 2 years
- Fulvestrant + everolimus x 1.5 years
- Carbo x 6 months (somatic BRCA, no other mutations)
- Capecitabine x 1 year
- Recently started T-DXD

Agenda

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

Module 2: HER2-Positive Breast Cancer — Dr Bardia

Module 3: Triple-Negative Breast Cancer — Dr O'Shaughnessy

RTP RESEARCH TO PRACTICE

Updates from ASCO 2026: HER2-Positive Breast Cancer

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HER2-Positive Breast Cancer

EBC:

- **Stage II-III (high risk)**
  - **Neoadjuvant (DESTINY-B 11)**
  - **Adjuvant (DESTINY-B05)**

- **MBC:**
  - **T-DXd upfront (DESTINY-B09)**
  - **T-DXd and Durvalumab (DESTINY-B07)**

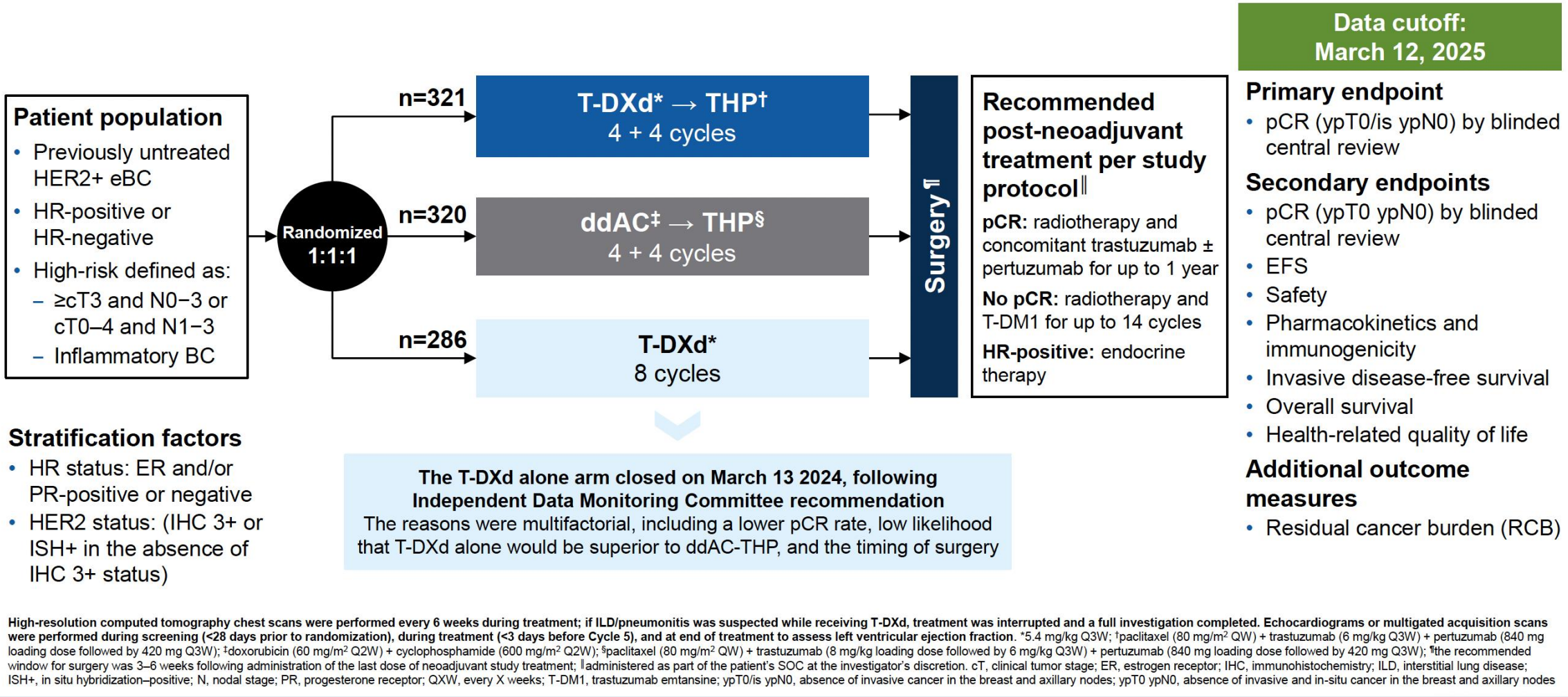
Dr Bardia – Case #1: 35F

Noted palpable mass in left breast. Diagnostic US demonstrated irregular mass measuring 29 * 13 mm seen in the left breast at 3 o'clock located 1 centimeter from the nipple, and prominent axillary lymph node measuring 3.9 mm in the left axilla. Biopsy confirmed IDC, poorly differentiated grade 3, ER+/PR-/HER2+ (both breast and LN), Ki67 = 40%.

What would you consider next?

a. **Taxane + Carboplatin + Trastuzumab + Pertuzumab (TCHP)**
b. **Trastuzumab and Pertuzumab and Taxane (THP)**
c. **Trastuzumab deruxtecan (T-DXd) followed by THP**
d. **Doxorubicin + Cyclophosphamide (AC) followed by THP**

Phase III DESTINY-Breast11 Study Design



High-resolution computed tomography chest scans were performed every 6 weeks during treatment; if ILD/pneumonitis was suspected while receiving T-DXd, treatment was interrupted and a full investigation completed. Echocardiograms or multigated acquisition scans were performed during screening (<28 days prior to randomization), during treatment (<3 days before Cycle 5), and at end of treatment to assess left ventricular ejection fraction. *5.4 mg/kg Q3W; †paclitaxel (80 mg/m^2 QW) + trastuzumab (6 mg/kg Q3W) + pertuzumab (840 mg loading dose followed by 420 mg Q3W); ‡doxorubicin (60 mg/m^2 Q2W) + cyclophosphamide (600 mg/m^2 Q2W); §paclitaxel (80 mg/m^2 QW) + trastuzumab (8 mg/kg loading dose followed by 6 mg/kg Q3W) + pertuzumab (840 mg loading dose followed by 420 mg Q3W); ¶the recommended window for surgery was 3–6 weeks following administration of the last dose of neoadjuvant study treatment; ‖administered as part of the patient's SOC at the investigator's discretion. cT, clinical tumor stage; ER, estrogen receptor; IHC, immunohistochemistry; ILD, interstitial lung disease; ISH+, in situ hybridization–positive; N, nodal stage; PR, progesterone receptor; QXW, every X weeks; T-DM1, trastuzumab emtansine; ypT0/is ypN0, absence of invasive cancer in the breast and axillary nodes; ypT0 ypN0, absence of invasive and in-situ cancer in the breast and axillary nodes

eBC = early breast cancer; THP = paclitaxel with trastuzumab and pertuzumab; ddAC = dose-dense doxorubicin and cyclophosphamide; pCR = pathologic complete response; EFS = event-free survival

Harbeck N et al. ESMO 2025;Abstract 291O.

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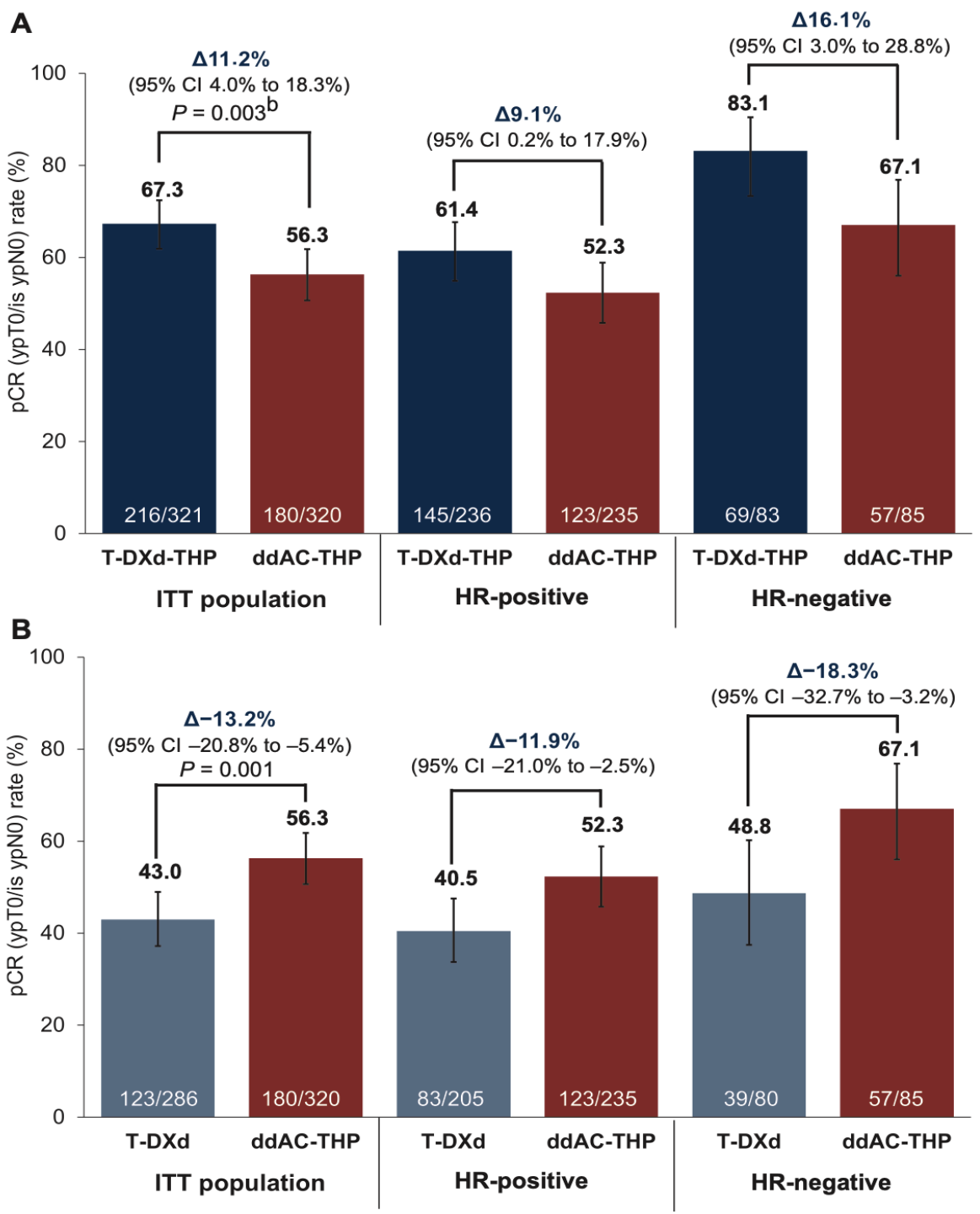
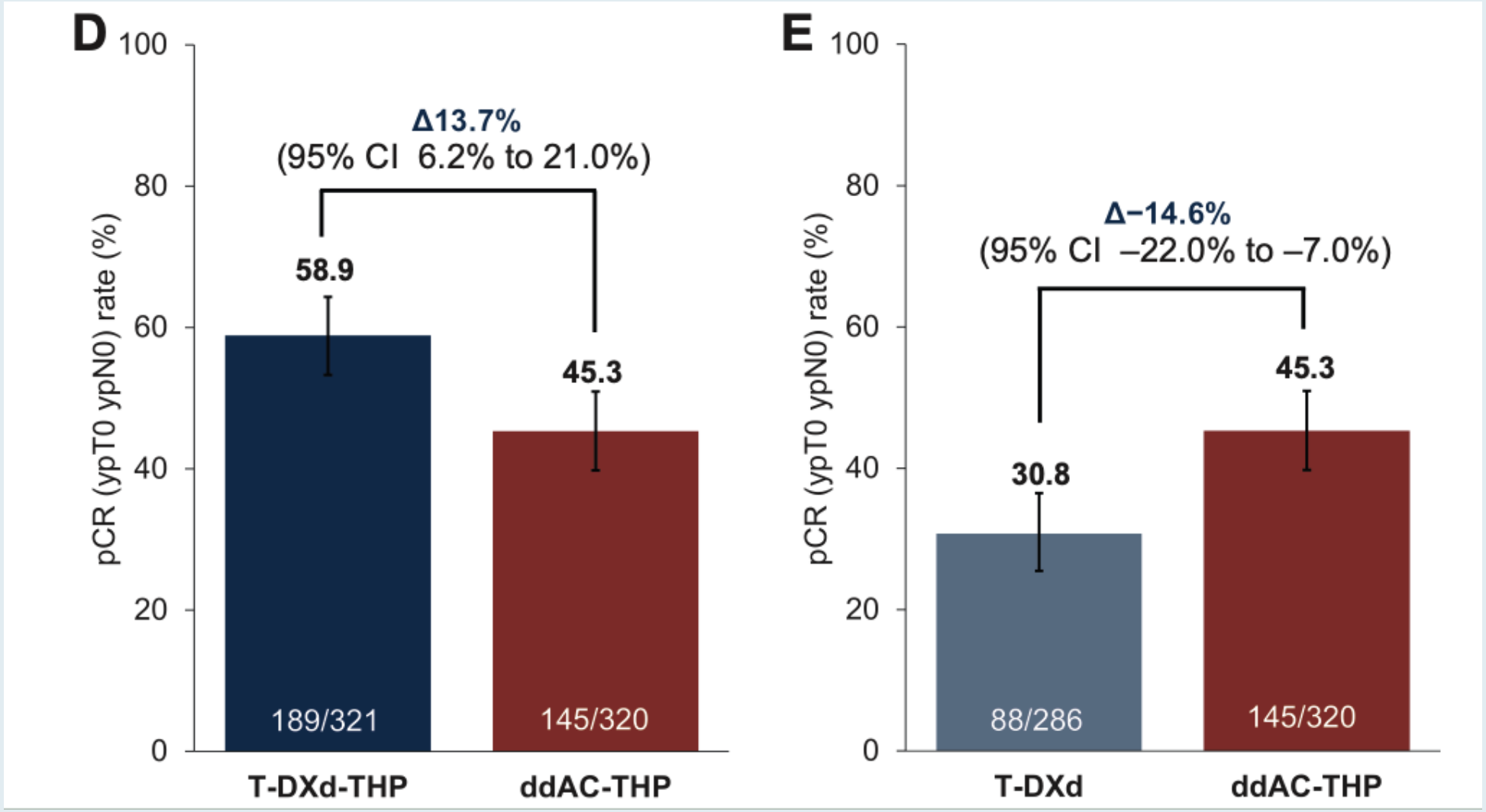
Phase III DESTINY-Breast11: pCR (Primary Endpoint)



ITT = intention-to-treat

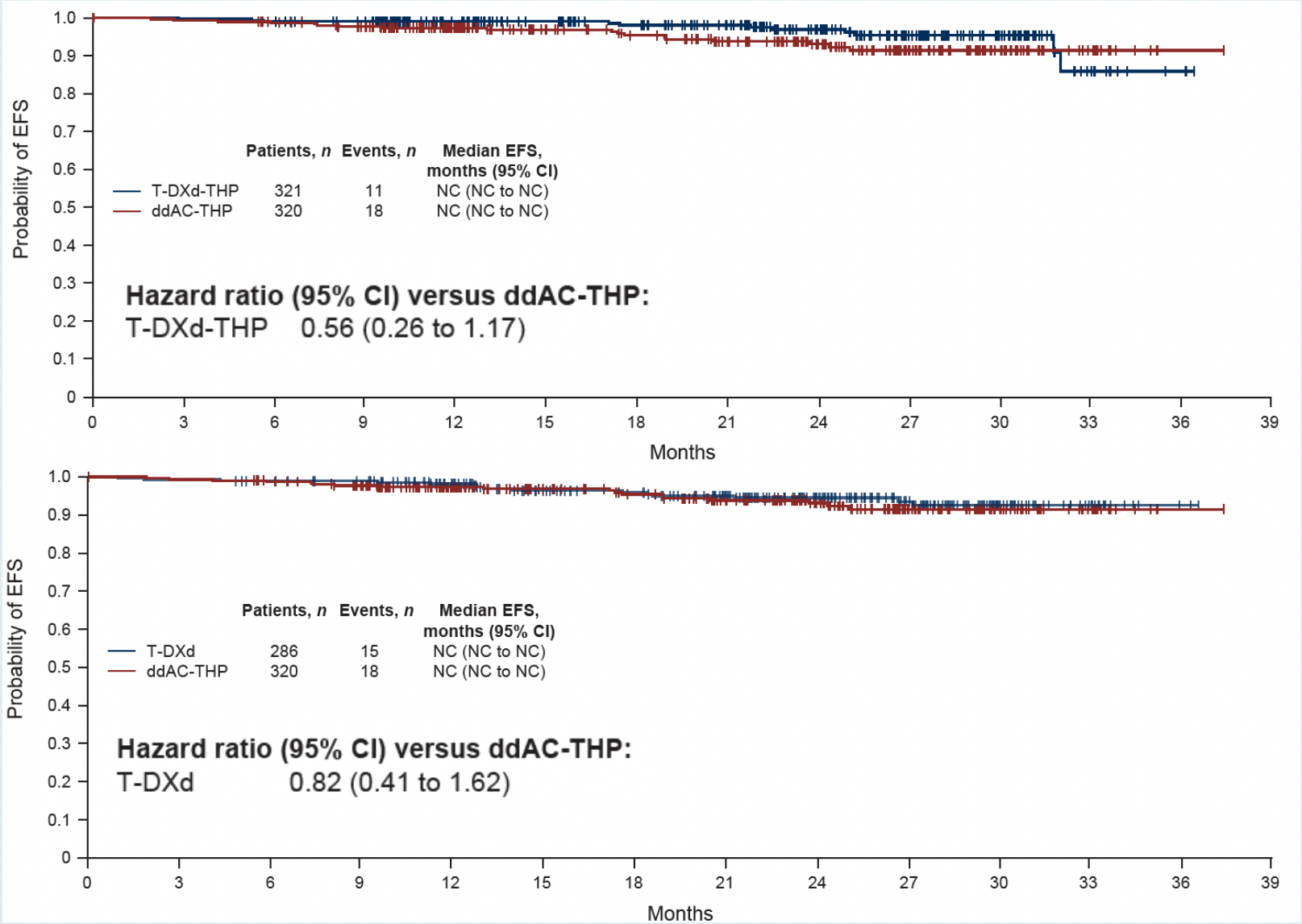
Harbeck N et al. *Ann Oncol* 2026 February;37(2):166-79.

Phase III DESTINY-Breast11: pCR (Secondary Endpoint)



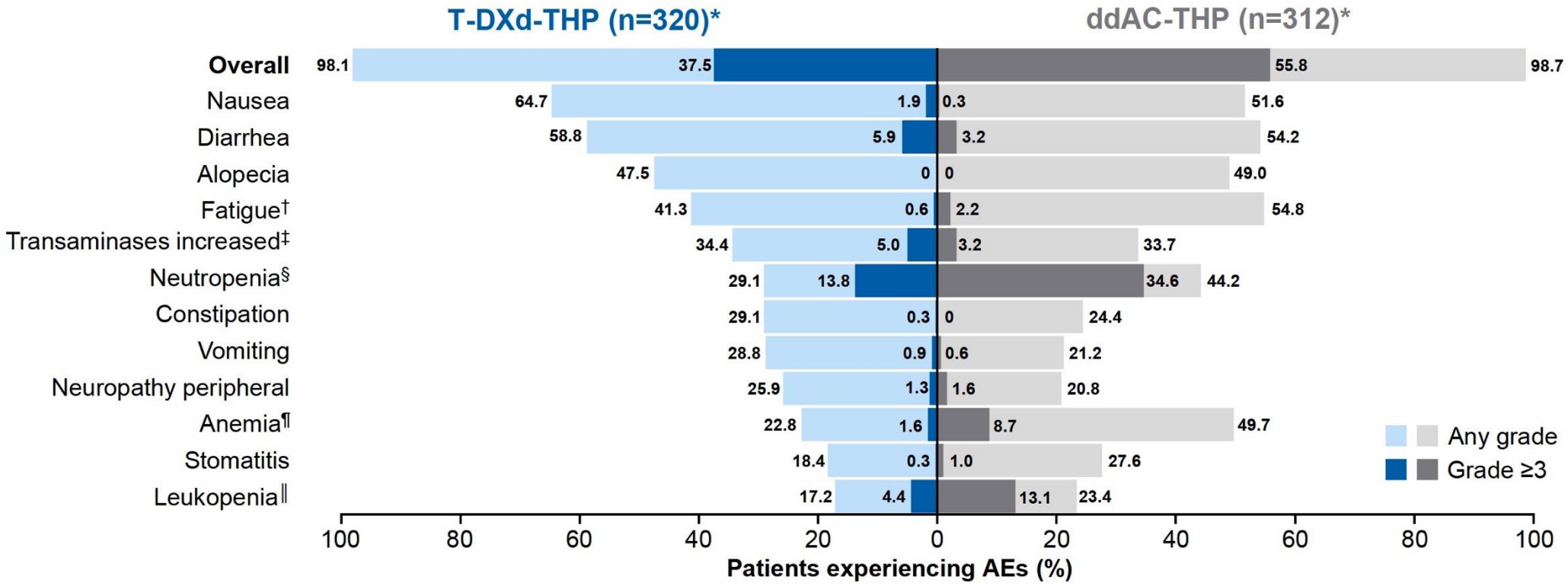
Harbeck N et al. *Ann Oncol* 2026 February;37(2):166-79.

Phase III DESTINY-Breast11: EFS (Secondary Endpoint)



Harbeck N et al. *Ann Oncol* 2026 February;37(2):166-79.

Phase III DESTINY-Breast11: Common AEs



T-DXd-THP had fewer any-grade and Grade ≥3 hematological and fatigue events than ddAC-THP
Aside from nausea, gastrointestinal toxicity was comparable between arms

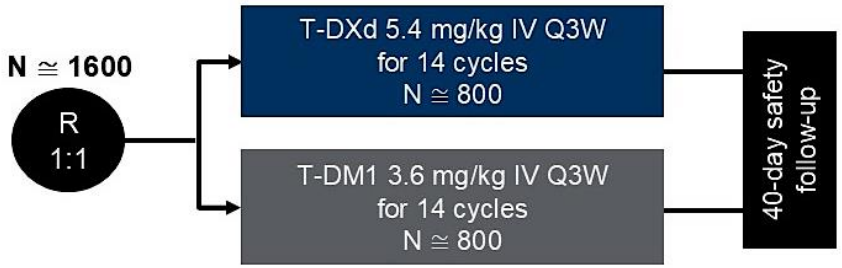
*Safety analyses included all patients who received at least one dose of any study treatment; †grouped term: fatigue, asthenia, malaise, and lethargy; ‡grouped term: transaminases increased, aspartate transaminase increased, alanine transaminase increased, gamma-glutamyl transferase increased, liver function test abnormal, hypertransaminasemia, hepatic function abnormal, and liver function test increased; §grouped term: neutrophil count decreased and neutropenia; ¶grouped term: hemoglobin decreased, red blood cell count decreased, and anemia and hematocrit decreased; ‖grouped term: white blood cell count decreased and leukopenia. TEAE, treatment-emergent adverse event

Harbeck N et al. ESMO 2025;Abstract 291O.

Phase III DESTINY-Breast05: Study Design and Summary

Key Eligibility Criteria

- **Residual invasive disease in the breast and/or axillary lymph nodes** after neoadjuvant chemotherapy with HER2-directed therapy (NAT)[a]
- **High risk of recurrence**[b]
- **Centrally confirmed HER2+** (IHC 3+ or ISH+) eBC
- ECOG PS 0 or 1



If administered, RT could be initiated concurrent (CC) with study therapy or completed prior to initiation of study therapy (sequential; SEQ) per investigator

Primary endpoint: IDFS

Key secondary endpoint: DFS

Other secondary endpoints: OS, BMFI, Safety, DRFI

DCO: July 2, 2025

Efficacy

T-DXd is approved in the US based on the primary results of DESTINY-Breast05,[2] in which T-DXd demonstrated superior efficacy versus T-DM1 in patients with HER2+ eBC with residual invasive disease after NAT and high risk of recurrence (IDFS events hazard ratio, 0.47 [95% CI, 0.34-0.66]; $P < 0.001$) — a population in which RT is broadly used

Safety

In both treatment arms, >72% of patients had completed 14 treatment cycles[c]; treatment had concluded for all patients in the study

Most cases of adjudicated drug-related **ILD were grade 1 or 2**

Rates of investigator-reported **RP**, most of which were **grade 1**, were similar between the T-DXd and T-DM1 arms

Timing of aRT showed no impact on the rates of ILD or RP whether administered SEQ or CC

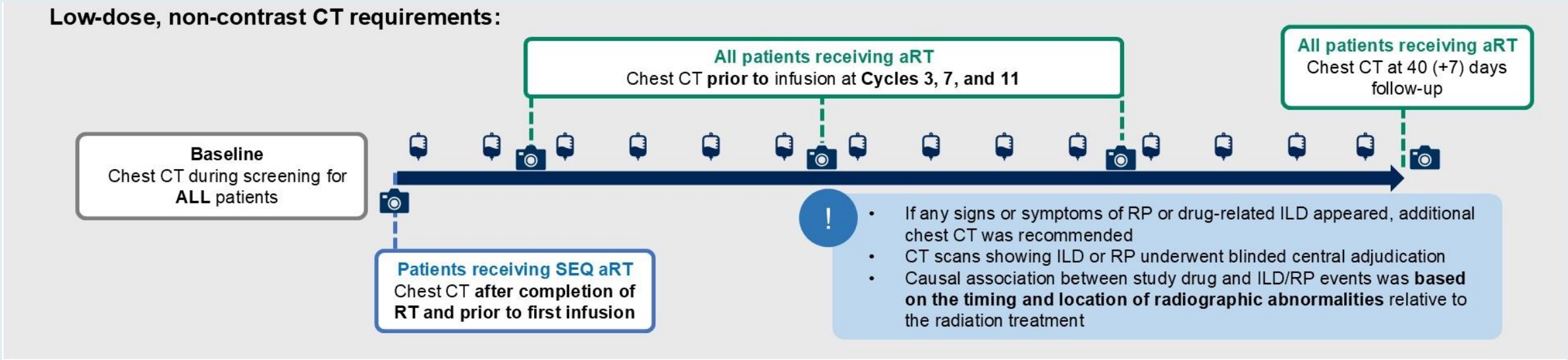
1. Loibl S et al. *New Eng J Med.* 2026;394(9):845-857. 2. Daiichi Sankyo. ENHERTU® Prescribing Information. May 2026.

[a]NAT is defined as ≥16 weeks' NAT, with ≥9 weeks of trastuzumab ± pertuzumab therapy and ≥9 weeks of taxane-based chemotherapy. [b]High risk defined as inoperable eBC (cT4, N0-3, M0 or cT1-3, N2-3, M0) or operable eBC (cT1-3, N0-1, M0) with axillary node–positive disease (ypN1-3) after NAT. [c]Median study treatment duration: T-DXd, 9.8 months; T-DM1, 9.7 months.

aRT, adjuvant radiotherapy; BMFI, brain metastasis–free interval; CC, concurrent; CI, confidence interval; DCO, data cutoff; DFS, disease-free survival; DRFI, distant recurrence–free interval; eBC, early breast cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; IDFS, invasive disease–free survival; IHC, immunohistochemistry; ILD, interstitial lung disease; ISH, in situ hybridization; IV, intravenous; NAT, neoadjuvant therapy; OS, overall survival; Q3W, every 3 weeks; R, randomization; RP, radiation pneumonitis; RT, radiotherapy; SEQ, sequential; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; ypN, post-NAT pathologic nodal stage.

Untch M et al. ASCO 2026;Abstract 516.

Phase III DESTINY-Breast05 Secondary Safety Analysis: Guidance on CT Requirements for Identifying ILD and RP



Treatment management guidelines:

Grade 1
- **Drug-related ILD: Interrupt** T-DXd for grade 1 and consider steroids; restart T-DXd only after full resolution (grade 0[a])
- **Radiation-related pulmonary toxicity: Maintain** dose for grade 1 cases

Grade 2
- **Drug-related ILD:** Permanently **discontinue** T-DXd and initiate steroids (symptomatic with radiographic abnormalities)
- **Radiation-related pulmonary toxicity: Interrupt** and manage per standard of care (eg, steroids) until recovery to grade ≤1 (asymptomatic)

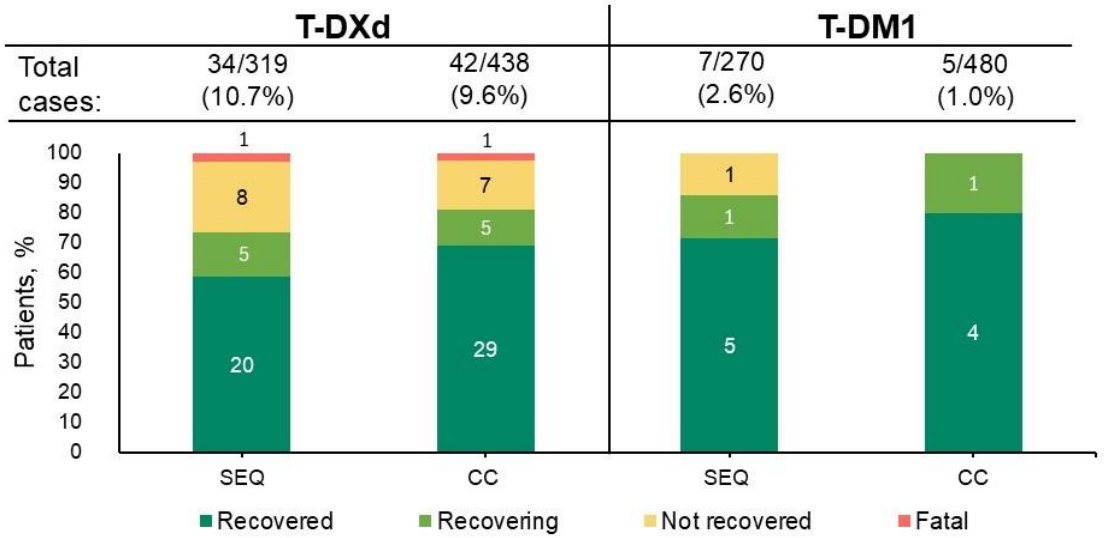
Grade 3-4
Discontinue study treatment and initiate steroids

[a]If resolved in ≤28 days from day of onset, maintain dose. If resolved in >28 days from day of onset, reduce dose 1 level. However, if the event grade 1 ILD/pneumonitis has not resolved within 126 days from the last infusion, T-DXd should be discontinued. aRT, adjuvant radiotherapy; CC, concurrent; CT, computed tomography; ILD, interstitial lung disease; RP, radiation pneumonitis; RT, radiotherapy; SEQ, sequential; T-DXd, trastuzumab deruxtecan

Untch M et al. ASCO 2026;Abstract 516.

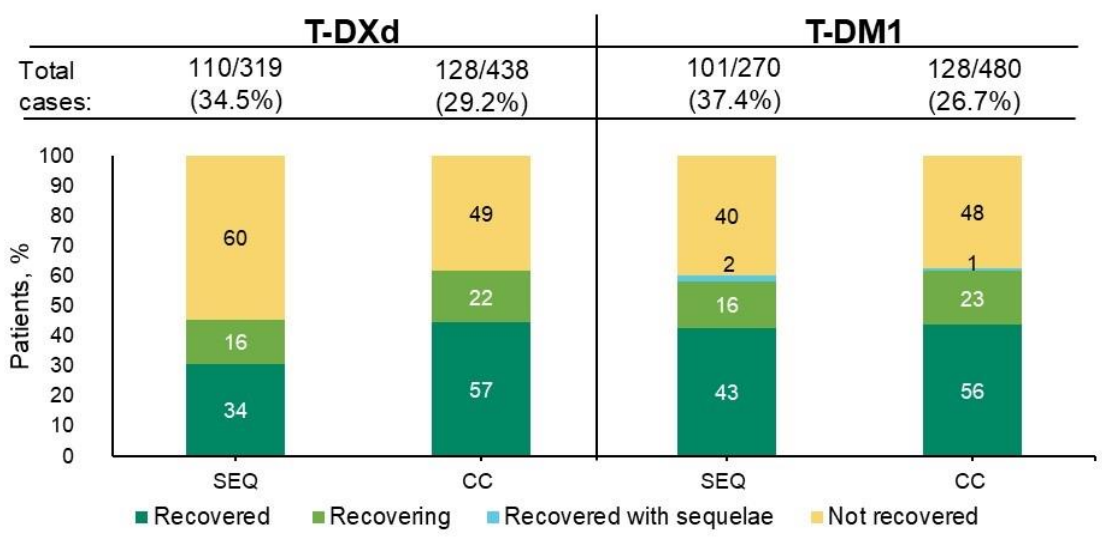
Phase III DESTINY-Breast05 Secondary Safety Analysis: Drug-Related ILD and Investigator-Reported RP (Outcomes at DCO)

Adjudicated drug-related ILD[a]



- **Most ILD** events were **grade 1 or 2; most** patients with **ILD** had **recovered[c]** by DCO (T-DXd, 64.9% [50/77]; T-DM1, 76.9% [10/13]), with **consistent rates across aRT timing**
- Median duration of ILD[d] events in the T-DXd arm was 77.0 days and 67.0 days for SEQ and CC aRT, respectively; in the T-DM1 arm, median durations were 114.0 and 142.0 days, respectively

Investigator-reported RP[b]



- Most **RP** events were **grade 1;** 38.2% (91/238) of patients with RP who received T-DXd and 43.2% (99/229) of T-DM1 patients had **recovered[c]**
- Median duration of RP[e] events in the T-DXd arm was 13.5 months and 9.6 months for SEQ and CC aRT, respectively; in the T-DM1 arm, median durations were 10.1 months and 9.8 months, respectively

Stacked bars show percentages of patients; numbers inside bars are counts (n).
[a]The outcome of the worst ILD event denominator is based on the number of patients with adjudicated drug-related ILD events. [b]RP grouped terms include the following MedDRA preferred terms: pulmonary radiation injury, radiation alveolitis, radiation bronchitis, radiation fibrosis - lung, radiation pneumonitis. [c]Recovery/resolution is defined as grade 0 (no radiographic abnormalities). Recovery of RP to grade 0 may take up to 1 year. [d]Duration of first ILD = investigator-reported end date – investigator-reported onset date + 1. End date will be censored for ongoing ILDs. [e]Duration of first investigator-reported RP = investigator-reported end date – investigator-reported onset date + 1. End date will be censored for ongoing events. aRT, adjuvant radiotherapy; CC, concurrent; CT, computed tomography; DCO, data cutoff; ILD, interstitial lung disease; RP, radiation pneumonitis; SEQ, sequential; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

Untch M et al. ASCO 2026;Abstract 516.

Phase III DESTINY-Breast05 Secondary Safety Analysis: Drug-Related ILD and Investigator-Reported RP by Subgroup

Japan vs non-Japan

	T-DXd			T-DM1		
n (%)	Japan (n = 87)	Asia (excludes Japan) (n = 301)	Global (excludes Japan) (n = 719)	Japan (n = 60)	Asia (excludes Japan) (n = 315)	Global (excludes Japan) (n = 741)
Adjudicated drug-related ILD	13 (14.9)	25 (8.3)	64 (8.9)	4 (6.7)	4 (1.3)	9 (1.2)
Investigator-reported RP[a]	41 (47.1)	116 (38.5)	197 (27.4)	27 (45.0)	122 (38.7)	202 (27.3)

- In both treatment arms, higher rates of adjudicated drug-related ILD and RP were observed in patients from Japan versus outside Japan and the rest of Asia
  - Patients from Japan who received CC aRT had higher rates of RP compared with those who received SEQ aRT, although sample size was small

Baseline renal function

	T-DXd (n = 806)			T-DM1 (n = 801)		
n (%)	Normal (n = 506)	Mild Impairment (n = 258)	Moderate Impairment (n = 42)	Normal (n = 486)	Mild Impairment (n = 274)	Moderate Impairment (n = 40)
Adjudicated drug-related ILD	49 (9.7)	22 (8.5)	6 (14.3)[b]	5 (1.0)	6 (2.2)	2 (5.0)[c]
Investigator-reported RP[a]	133 (26.3)	95 (36.8)	10 (23.8)	131 (27.0)	86 (31.4)	11 (27.5)

- Across treatment arms, adjudicated drug-related ILD rates were higher in patients with moderate renal impairment versus mild impairment and normal renal function

Normal renal function defined as creatinine clearance ≥90 mL/min; mild impairment defined as creatinine clearance ≥60 and <90 mL/min; moderate impairment defined as creatinine clearance ≥30 and <60 mL/min.
[a]Grouped term. Includes the MedDRA preferred terms of pulmonary radiation injury, radiation bronchitis, radiation alveolitis, radiation fibrosis - lung, and radiation pneumonitis. [b]Among patients with baseline moderate renal impairment who developed adjudicated drug-related ILD in the T-DXd arm, 5 of 6 had grade 2 ILD (all recovered at DCO) and 1 of 6 had grade 3 ILD (not recovered at DCO). [c]Both patients with baseline moderate renal impairment who developed adjudicated drug-related ILD in the T-DM1 arm had grade 2 ILD and had recovered at DCO.
aRT, adjuvant radiotherapy; CC, concurrent; DCO, data cutoff; ILD, interstitial lung disease; RP, radiation pneumonitis; SEQ, sequential; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

Untch M et al. ASCO 2026;Abstract 516.

HER2-Positive Breast Cancer

EBC:

- ***Stage II-III (high risk)***
  - ***Neoadjuvant T-DXd (DESTINY-B 11)***
  - ***Adjuvant T-DXd (DESTINY-B05)***

- **MBC:**
  - **T-DXd upfront (DESTINY-B09)**
  - **T-DXd and Durvalumab (DESTINY-B07)**

Dr Bardia – Case #2: 45F

Received neoadjuvant TCHP (*6 cycles) for cT2N1Mx HR+/HER2+ Breast Cancer Underwent lumpectomy. Surgical path yT1aN0MX.
Received adjuvant T-DM1 (and radiation therapy)
3 years later diagnosed with hepatic metastasis, HR+/HER2+

What would you consider next?

a. Trastuzumab and Pertuzumab and Taxane (THP) for 6 cycles followed by HP + ET + Palbociclib
b. Trastuzumab and Pertuzumab and Taxane (THP) for 6 cycles followed by HP + Tucatinib
c. Trastuzumab deruxtecan (T-DXd)
d. Tucatinib with capecitabine and trastuzumab
e. T-DM1

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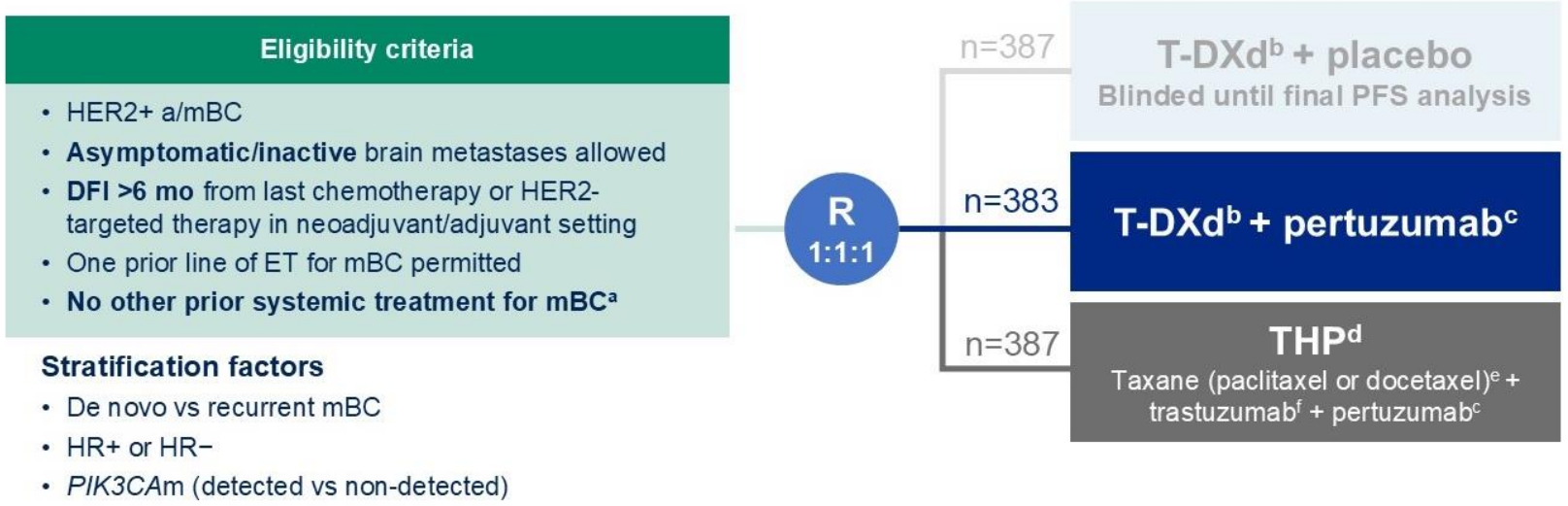
Phase III DESTINY-Breast09: Study Design



At the prespecified interim analysis, T-DXd + P met its primary endpoint (DCO: Feb 26, 2025; presented at ASCO 2025)[1,2]:

Efficacy

- **Median PFS:** 40.7 vs 26.9 mo with T-DXd + P vs THP, respectively (*P*<0.00001)[1g]
- **Confirmed ORR:** 85.1%[h] vs 78.6%[i] with T-DXd + P vs THP, respectively[1]
- **CRs nearly doubled** in the T-DXd + P vs THP arm (15.1% vs 8.5%, respectively)[1]

Safety

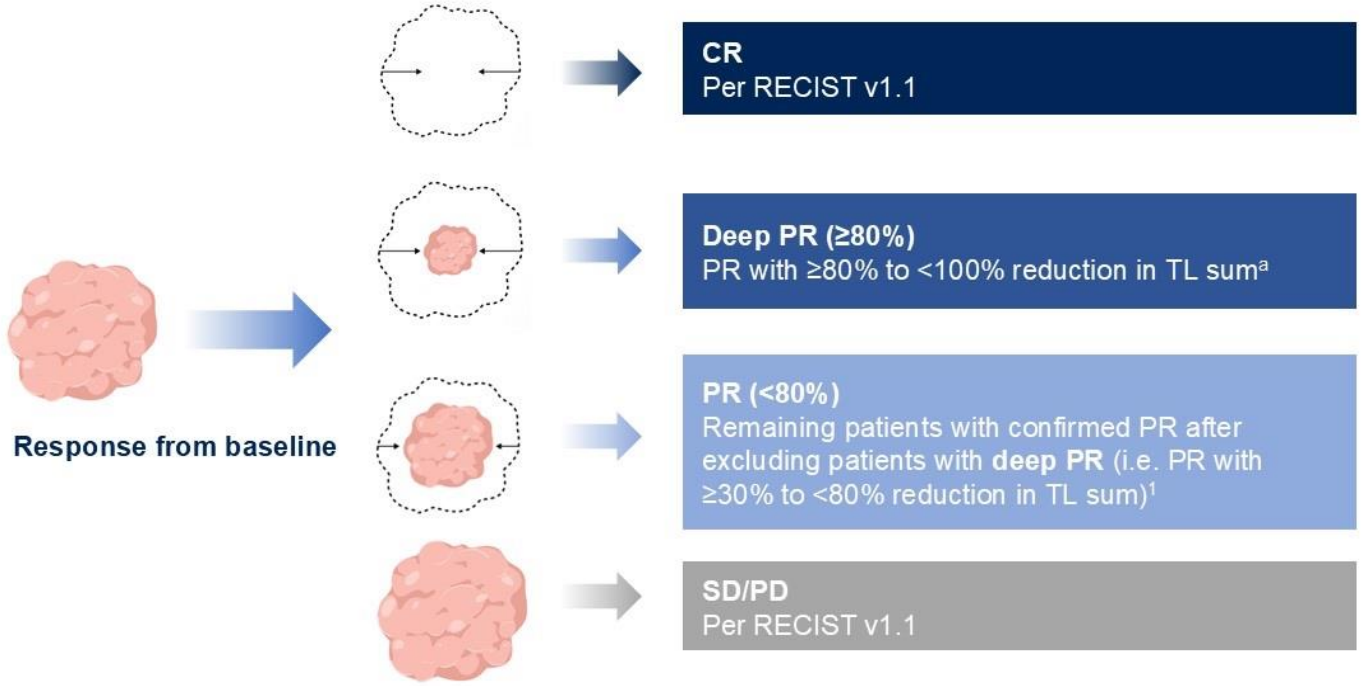
T-DXd + P safety data were **consistent** with the **known profiles** of individual treatments

The aim of this exploratory analysis was to evaluate the **association between depth of response to T-DXd + P treatment and long-term clinical benefit**

[a]HER2-targeted therapy or chemotherapy. [b]5.4 mg/kg Q3W. [c]840 mg loading dose, then 420 mg Q3W. [d]Open label for THP arm. Double-blinded for pertuzumab in experimental arms. [e]Paclitaxel 80 mg/m² QW or 175 mg/m² Q3W, or docetaxel 75 mg/m² Q3W for ≤6 cycles or intolerable toxicity. [f]8 mg/kg loading dose, then 6 mg/kg Q3W. [g]Hazard ratio, 0.56 (95% CI, 0.44, 0.71). [h]95% CI: 81.2, 88.5. [i]95% CI: 74.1, 82.5.
a/mBC, advanced/metastatic breast cancer; BICR, blinded independent central review; CI, confidence interval; DCO, data cutoff; DFI, disease-free interval; DOR, duration of response; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HER2+, HER2-positive; HR+/−, hormone receptor–positive/–negative; INV, investigator; mo, months; OS, overall survival; ORR, objective response rate; 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; THP, taxane + trastuzumab + pertuzumab. NCT04784715. Available from: https://clinicaltrials.gov/study/NCT04784715 (Accessed March 13, 2026).
1. Tolaney SM, et al. *J Clin Oncol*. 2025;43(17 Suppl):LBA 1008. 2. Tolaney SM, et al. *N Engl J Med*. 2026;394:551–562.

Park YH et al. ASCO 2026;Abstract 1021.

Phase III DESTINY-Breast09: Exploratory Analysis of Response



CR
Per RECIST v1.1

Deep PR (≥80%)
PR with ≥80% to <100% reduction in TL sum[a]

PR (<80%)
Remaining patients with confirmed PR after excluding patients with **deep PR** (i.e. PR with ≥30% to <80% reduction in TL sum)[1]

SD/PD
Per RECIST v1.1

Endpoints evaluated in DESTINY-Breast09 response subgroups[b]:

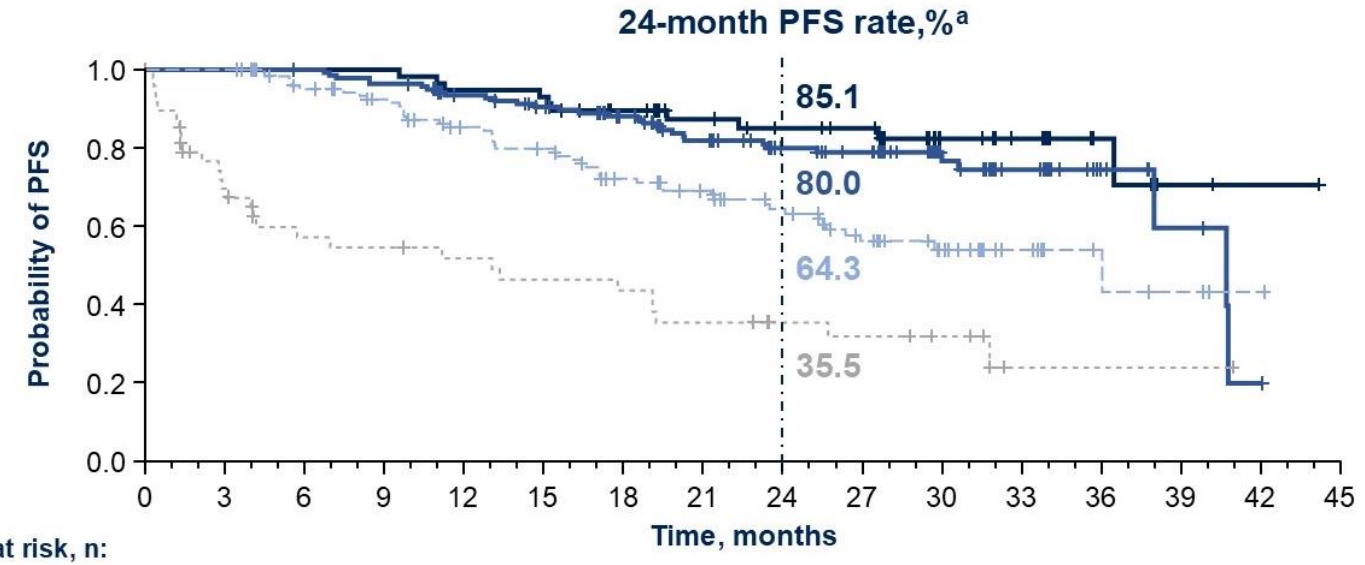
- Time to best response
- Duration of response
- Progression-free survival
- Safety (including TEAEs and adjudicated drug-related ILD/pneumonitis)

Analyses were not pre-defined to allow comparisons between the T-DXd + P and THP arms

[a]PR with ≥80% to <100% reduction in TL sum and CR or non-CR/non-PD in non-TLs, or CR in TL and non-CR/non-PD in non-TLs. [b]Data cut-off date: February 26, 2025. Endpoints were analyzed by the best confirmed response by BICR of CT or MRI every 6 weeks from randomization for 48 weeks and then every 9 weeks until disease progression.
CT, computed tomography; ILD, interstitial lung disease; MRI, magnetic resonance imaging; PD, progressive disease; RECIST, Response Evaluation in Solid Tumors; SD, stable disease; TEAE, treatment-emergent adverse event; TL, target lesion.
1. Hamilton E, et al. Poster presented at the European Society for Medical Oncology Breast Cancer (ESMO BC) Annual Meeting; May 14-17, 2026; Munich, Germany.

Park YH et al. ASCO 2026;Abstract 1021.

Phase III DESTINY-Breast09: PFS by Response Subgroup (T-DXd with Pertuzumab Arm)



Patients at risk, n:

CR	58	58	58	58	55	54	47	39	35	33	21	16	7	2	1	0
Deep PR[b]	141	141	140	135	125	117	105	91	77	72	34	22	8	4	1	0
PR (<80%)	127	127	113	105	92	85	72	63	52	38	20	10	5	3	1	0
SD/PD	51	30	22	21	19	17	16	13	10	9	7	1	1	1	0	0

CR – Deep PR =

Δ 5.1%

Deep PR – PR (<80%) =

Δ 15.7%

Achieving CR and deep PR was associated with similar durable PFS outcomes

[a]95% CIs for 24-mo PFS rates: CR: 72.2, 92.3; deep PR: 71.7, 86.1; PR (<80%): 54.3, 72.8; SD/PD: 21.1, 50.2. [b]PR with ≥80% to <100% reduction in TL sum and CR or non-CR/non-PD in non-TLs, or CR in TL and non-CR/non-PD in non-TLs.

Park YH et al. ASCO 2026;Abstract 1021.

Phase III DESTINY-Breast09: Response Characteristics (T-DXd with Pertuzumab Arm)

	CR (n=58)	Deep PR[a] (n=141)	PR (<80%) (n=127)	SD/PD (n=51)
Time to best response (median, mo) [95% CI]	8.4 [5.6, 11.1]	9.6 [6.8, 11.0]	1.5 [1.4, 2.0]	NA
Duration of best response (median, mo) [95% CI]	NC [35.1, NC]	39.2 [35.3, NC]	34.8 [22.8, NC]	NA
Patients remaining in best response, % [95% CI]				
12 mo	94.8 [84.8, 98.3]	91.3 [85.1, 95.0]	78.9 [70.1, 85.3]	NA
24 mo	85.0 [72.1, 92.3]	78.9 [70.4, 85.2]	60.4 [50.0, 69.3]	NA
Total treatment duration, (median, mo) [range][b]	28.0 [4.8–44.5]	25.4 [3.4–42.7]	20.6 [2.8–41.8]	4.4 [0.3–37.2]
PFS at 24 mo, % [95% CI]	85.1 [72.2, 92.3]	80.0 [71.7, 86.1]	64.3 [54.3, 72.8]	35.5 [21.1, 50.2]

80% of patients (ITT) achieved **maximal tumor reduction** by **24 months**

Patients who achieved CR and deep PR had the longest treatment duration, with responses deepening over time

[a]PR with ≥80% to <100% reduction in TL sum and CR or non-CR/non-PD in non-TLs, or CR in TL and non-CR/non-PD in non-TLs. [b]Per protocol, a small proportion of patients in each group transitioned to trastuzumab (CR, 8 [13.8%]; deep PR, 11 [7.8%]; PR(<80%), 10 [6.9%]; SD/PD, 5 [10.0%]).
ITT, intention to treat; NA, not applicable; NC, not calculable.

Park YH et al. ASCO 2026;Abstract 1021.

Phase III DESTINY-Breast09: Safety Summary (T-DXd with Pertuzumab Arm)

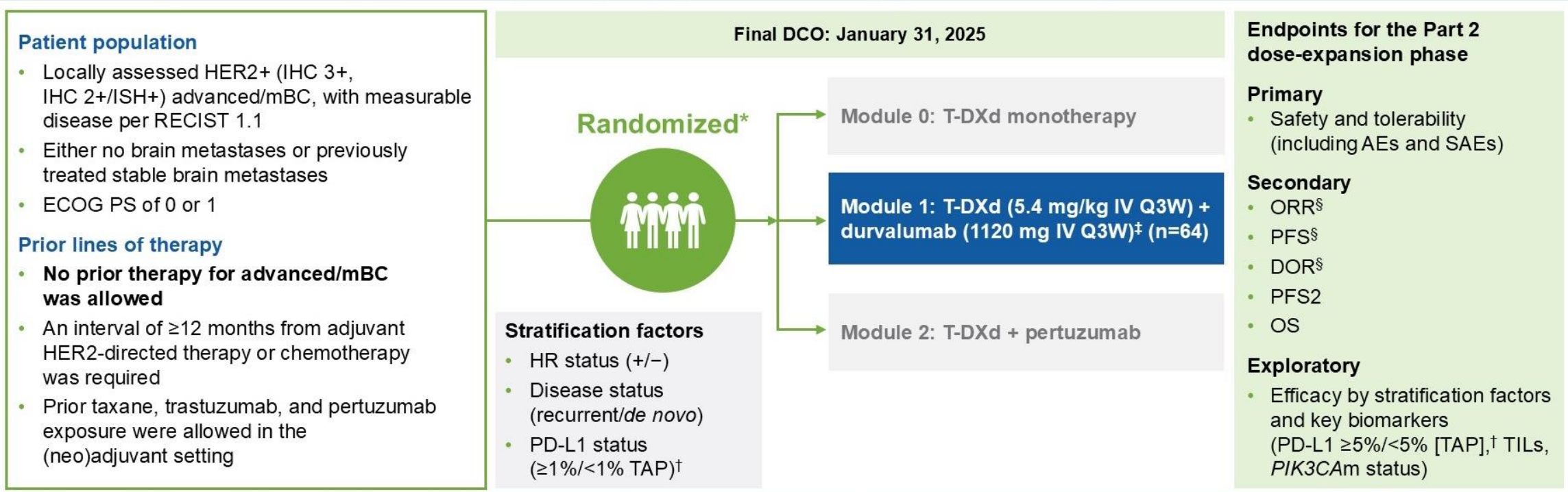
	CR (n=58)	Deep PR[b] (n=142)	PR (<80%) (n=128)	SD/PD (n=49)
Possibly treatment-related TEAEs[c], n (%)	37 (63.8)	77 (54.2)	68 (53.1)	25 (51.0)
Grade ≥3				
EAIRs of drug-related grade ≥3 AEs, per patient-year	0.30	0.28	0.32	0.57
Serious TEAEs, n (%)	16 (27.6)	35 (24.6)	36 (28.1)	13 (26.5)
TEAEs associated with any treatment discontinuation, n (%)	18 (31.0)[d]	26 (18.3)	27 (21.1)	7 (14.3)
EAIRs of TEAEs associated with any study drug discontinuation, per patient-year	0.14	0.10	0.13	0.16
TEAEs associated with any dose interruptions, n (%)	45 (77.6)	106 (74.6)	85 (66.4)	24 (49.0)
TEAEs associated with any dose reductions, n (%)	33 (56.9)	72 (50.7)	52 (40.6)	16 (32.7)
Possibly treatment-related TEAEs associated with an outcome of death, n (%)	0	1 (0.7)	1 (0.8)	3 (6.1)
Adjudicated drug-related ILD/pneumonitis, n (%)	7 (12.1)	22 (15.5)	10 (7.8)	6 (12.2)
Grade ≥3	0	0	0	2 (4.1)
Left ventricular dysfunction, n (%)	8 (13.8)	15 (12.0)	14 (9.7)	4 (8.2)
Grade ≥3	2 (3.4)	4 (2.8)	1 (0.8)	1 (2.0)

EAIRs for drug-related grade ≥3 AEs were similar across different responder subgroups, with no new safety signals identified

Note: Data for the THP arm are available at the QR code shared at the end of the presentation. [a]Total treatment duration (median, mo): CR, 28.0; Deep PR, 25.4; PR (<80%), 20.6; SD/PD, 4.4. [b]PR with ≥80% to <100% reduction in TL sum and CR or non-CR/non-PD in non-TLs, or CR in TL and non-CR/non-PD in non-TLs. [c]Investigator assessed. [d]17/18 were T-DXd discontinuations.
EAIR, exposure-adjusted incidence rate.

Park YH et al. ASCO 2026;Abstract 1021.

Phase Ib/II DESTINY-Breast07 Study Design



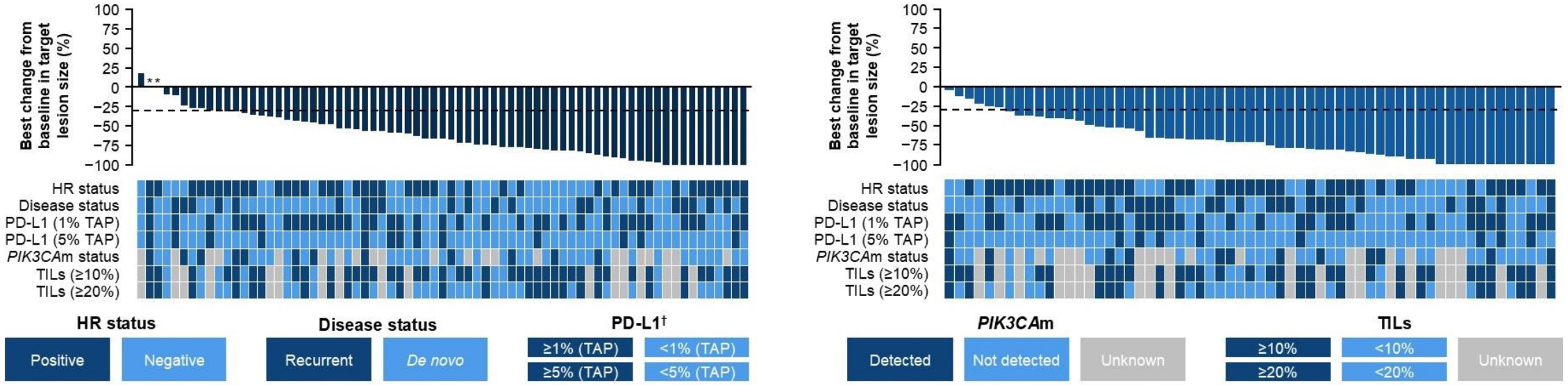
Results reported here are from the final analysis of the Part 2 dose-expansion phase for Module 1.
Primary results for Modules 0 and 2 were presented previously[2]

*For Modules 1 and 2, randomization began after determination of the RP2D. For all modules, a dynamically changing randomization ratio was employed to account for fluctuation in the number of treatment arms open for enrollment over the course of the study; †VENTANA PD-L1 (SP263) Assay (investigational use only); Roche Diagnostics; ‡RP2D for Module 1 was determined by the DESTINY-Breast07 Safety Review Committee based on data from the BEGONIA study;[3] §evaluated by investigator per RECIST 1.1. AE, adverse event; DCO, data cutoff; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; HER2+, human epidermal growth factor receptor 2–positive; HR, hormone receptor; IHC, immunohistochemistry; ISH+, in situ hybridization–positive; IV, intravenous; mBC, metastatic breast cancer; ORR, objective response rate; OS, overall survival; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; PFS2, second progression-free survival; *PIK3CA*m, *PIK3CA* mutation; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumours; RP2D, recommended Phase 2 dose; SAE, serious adverse event; TAP, tumor area positivity; T-DXd, trastuzumab deruxtecan; TIL, tumor-infiltrating lymphocyte. 1. NCT04538742. Updated. December 8, 2025. Available from: https://clinicaltrials.gov/study/NCT04538742 (Accessed May 07, 2026); 2. André F, et al. *Clin Cancer Res.* 2026;32(Suppl. 4):PS5-01-14; 3. Schmid P, et al. *J Clin Oncol.* 2021;39(Suppl. 15):1023 (Abstract)

Loi S et al. ASCO 2026;Abstract 1012.

Phase Ib/II DESTINY-Breast07: Responses

	T-DXd[1] (N=75)	T-DXd + durvalumab (N=64)
cORR, n (%) [80% CI; 95% CI]	**59 (78.7)** [71.4, 84.7; 67.7, 87.3]	**53 (82.8)** [75.2, 88.8; 71.3, 91.1]
BOR, n (%)		
CR	7 (9.3)	10 (15.6)
PR	52 (69.3)	43 (67.2)
Median DOR, months (Q1, Q3)	NE (19.5, NE)	36.1 (23.3, NE)

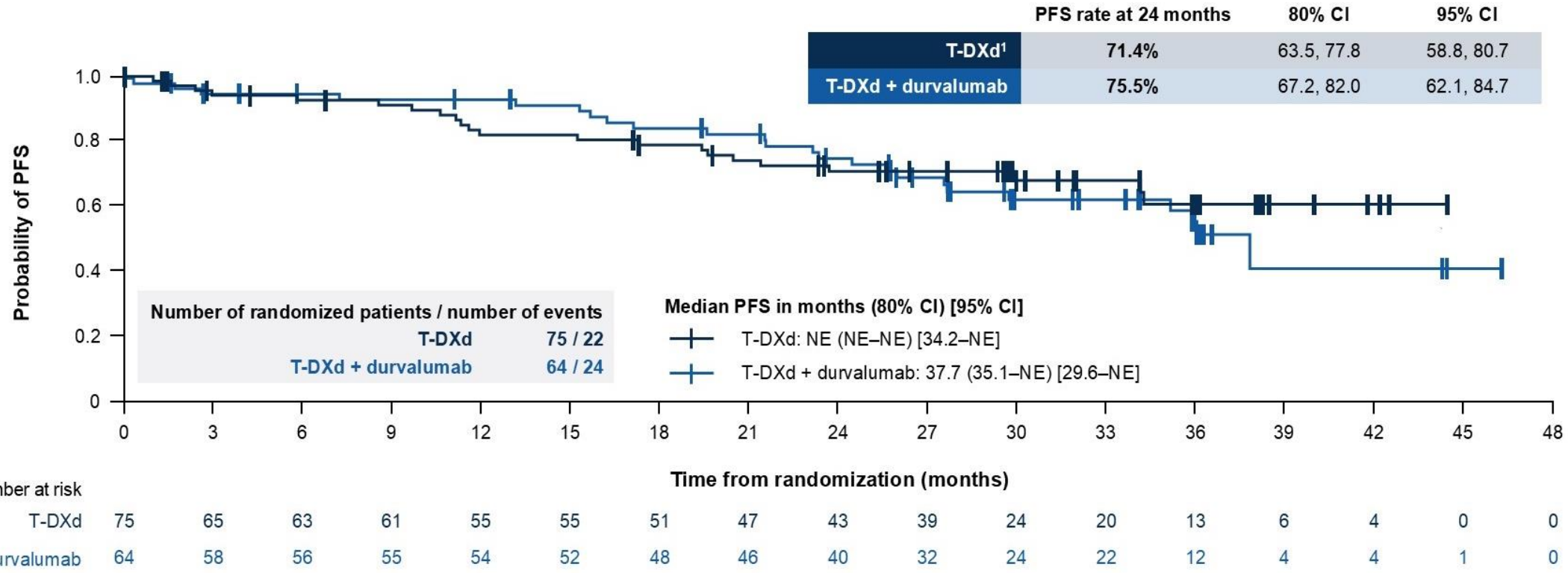


As with T-DXd monotherapy,[1] robust and deep responses were seen with T-DXd + durvalumab

Dashed reference line at −30% indicates the threshold for partial response. Data shown where response data available (T-DXd, n=71; T-DXd + durvalumab, n=61)
'*' symbols indicate patients with no change; †VENTANA PD-L1 (SP263) Assay (investigational use only); Roche Diagnostics. BOR, best overall response; CI, confidence interval; cORR, confirmed objective response rate; CR, complete response; DOR, duration of response; HR, hormone receptor; NE, not evaluable; PD-L1, programmed cell death ligand 1; *PIK3CA*m, *PIK3CA* mutation; PR, partial response; Q, quartile; RECIST, Response Evaluation Criteria in Solid Tumours; TAP, tumor area positivity; T-DXd, trastuzumab deruxtecan; TIL, tumor-infiltrating lymphocyte. 1. André F, et al. Poster presented at SABCS 2025 (Abstract PS5-01-14)

Loi S et al. ASCO 2026;Abstract 1012.

Phase Ib/II DESTINY-Breast07: PFS

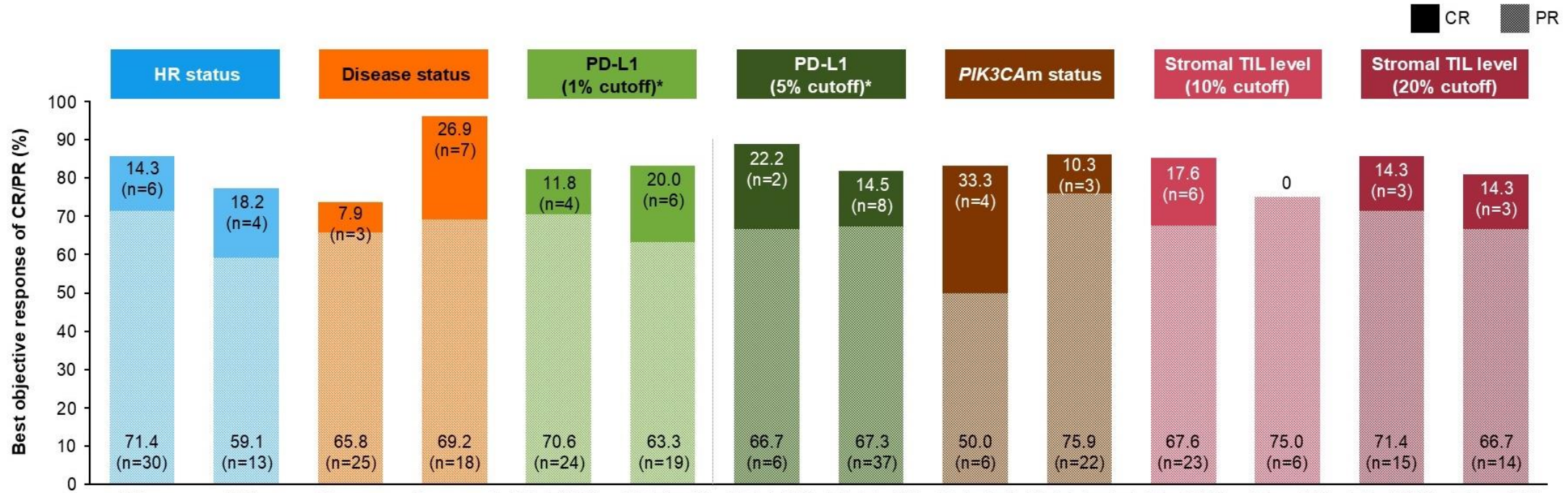


Strong first-line efficacy was seen across both T-DXd arms:[1]
T-DXd + durvalumab was observed to have a PFS rate at 24 months of 75.5% and a median PFS of 37.7 months

Median duration of follow up for T-DXd module: 31.4 months (range: 1.1–44.8); median duration of follow up for T-DXd + durvalumab module: 30.1 months (range: 0.3–47.5). At final DCO, overall survival was not evaluable in the T-DXd and in the T-DXd + durvalumab modules
CI, confidence interval; DCO, data cutoff; NE, not evaluable; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours; T-DXd, trastuzumab deruxtecan
1. André F, et al. Poster presented at SABCS 2025 (Abstract PS5-01-14)

Loi S et al. ASCO 2026;Abstract 1012.

Phase Ib/II DESTINY-Breast07: Biomarker Analysis



	HR+	HR−	*De novo*	Recurrent	PD-L1 ≥1%	PD-L1 <1%	PD-L1 ≥5%	PD-L1 <5%	Detected	Not detected	TILs ≥10%	TILs <10%	TILs ≥20%	TILs <20%
Patients, n	42	22	38	26	34	30	9	55	12	29	34	8	21	21
cORR, n (%)	36 (**85.7**)	17 (**77.3**)	28 (**73.7**)	25 (**96.2**)	28 (**82.4**)	25 (**83.3**)	8 (**88.9**)	45 (**81.8**)	10 (**83.3**)	25 (**86.2**)	29 (**85.3**)	6 (**75.0**)	18 (**85.7**)	17 (**81.0**)
80% CI	76.3, 92.3	61.9, 88.5	62.4, 83.0	85.8, 99.6	71.1, 90.5	71.3, 91.7	63.2, 98.8	73.4, 88.4	61.4, 95.5	74.3, 93.8	74.4, 92.7	46.2, 93.1	70.9, 94.6	65.5, 91.4

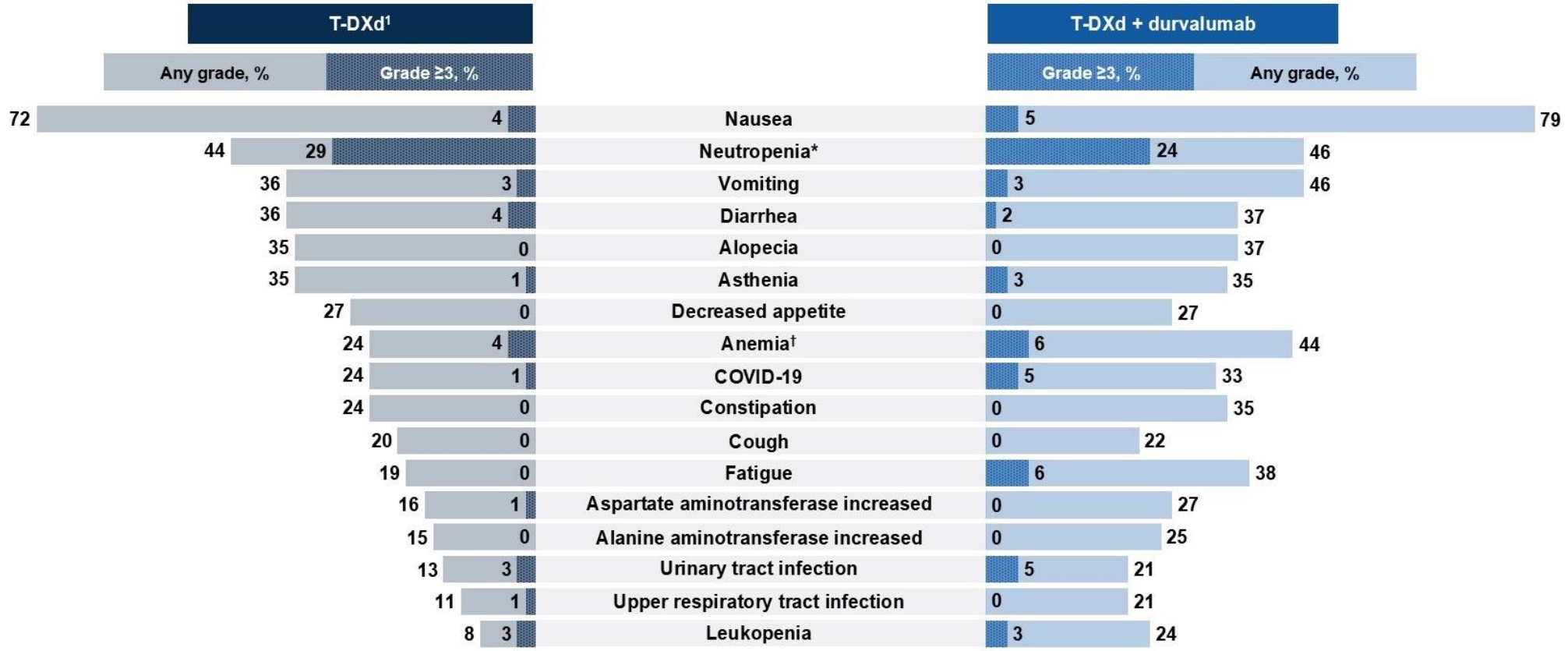
High response rates for T-DXd + durvalumab were seen across stratification factor and key biomarker subgroups

Results in subgroups should be interpreted with caution owing to the small patient numbers in each group. Standard endocrine therapy (aromatase inhibitor or tamoxifen) administered concurrently with study treatment was allowed after 8 cycles of T-DXd for patients with HR-positive tumors, as per local practice

*VENTANA PD-L1 (SP263) Assay (investigational use only); Roche Diagnostics. CI, confidence interval; cORR, confirmed objective response rate; CR, complete response; HR, hormone receptor; PD-L1, programmed cell death ligand 1; *PIK3CA*m, *PIK3CA* mutation; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours; T-DXd, trastuzumab deruxtecan; TIL, tumor-infiltrating lymphocyte

Loi S et al. ASCO 2026;Abstract 1012.

Phase Ib/II DESTINY-Breast07: Common AEs



Safety findings for T-DXd monotherapy[1] and T-DXd + durvalumab were consistent with the known profile of each therapy[2,3]

Included AEs that occurred having been absent before the first dose of the study treatment or that had worsened in severity or seriousness after initiation of study treatment until 47 days (97 days for T-DXd + durvalumab) after the last dose of study treatment or before the initiation of first subsequent cancer therapy (whichever occurred first)

*Grouped term includes febrile neutropenia, neutropenia, and neutrophil count decreased; †grouped term includes anemia and hematocrit decreased. AE, adverse event; T-DXd, trastuzumab deruxtecan

1. André F, et al. Poster presented at SABCS 2025 (Abstract PS5-01-14); 2. Cortés J, et al. *N Engl J Med.* 2022;386:1143–54; 3. Antonia SJ, et al. *N Engl J Med.* 2017;377:1919–29

Loi S et al. ASCO 2026;Abstract 1012.

HER2-Positive Breast Cancer

EBC:

- ***Stage II-III (high risk):***
  - ***Neoadjuvant (DESTINY-B 11)***
  - ***Adjuvant (DESTINY-B05)***

- ***MBC***
  - ***T-DXd upfront (DESTINY-B09)***
  - ***T-DXd and Durvalumab (DESTINY-B07)***

Agenda

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

Module 2: HER2-Positive Breast Cancer — Dr Bardia

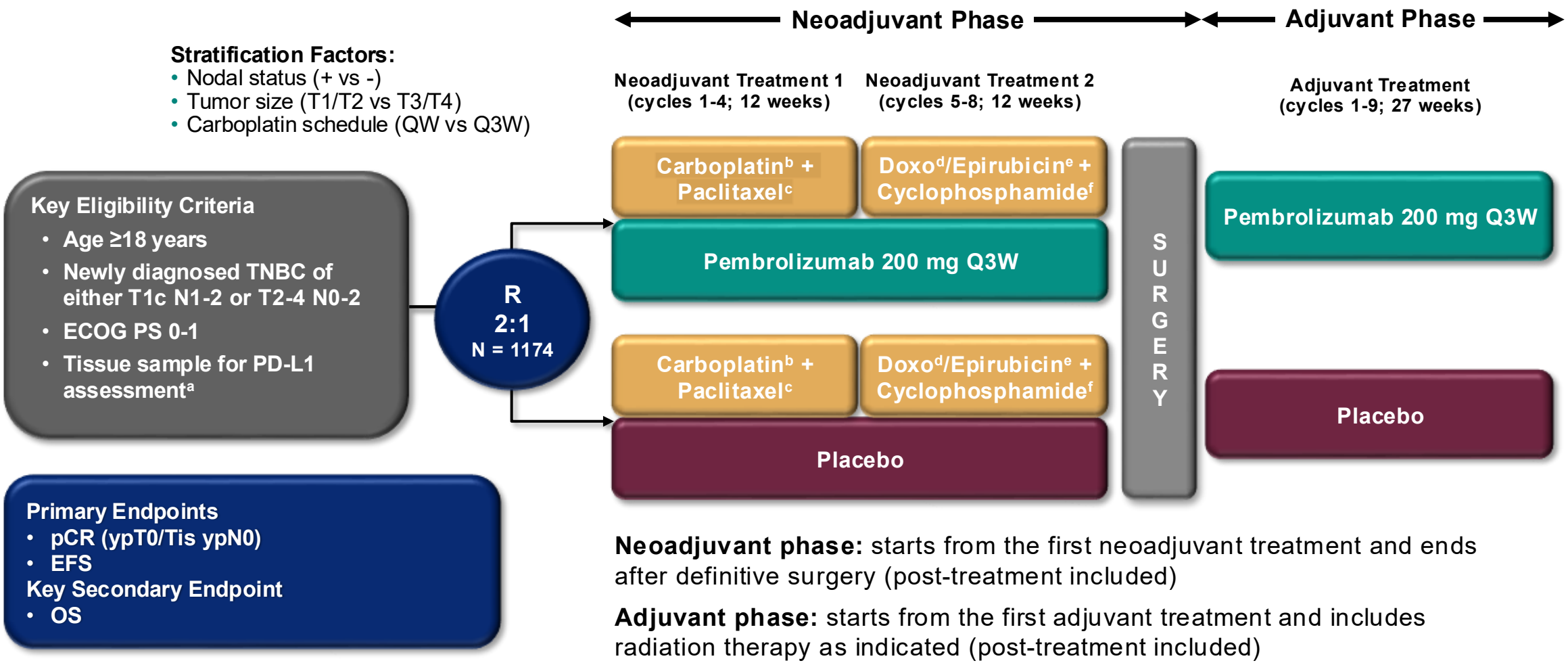
Module 3: Triple-Negative Breast Cancer — Dr O'Shaughnessy

RTP RESEARCH TO PRACTICE

Advances in Metastatic Triple Negative Breast Cancer ASCO 2026

Joyce O'Shaughnessy, MD
Baylor University Medical Center
Texas Oncology
Sarah Cannon Research Institute
Dallas TX

KEYNOTE-522 Study Design (NCT03036488)



Neoadjuvant phase: starts from the first neoadjuvant treatment and ends after definitive surgery (post-treatment included)

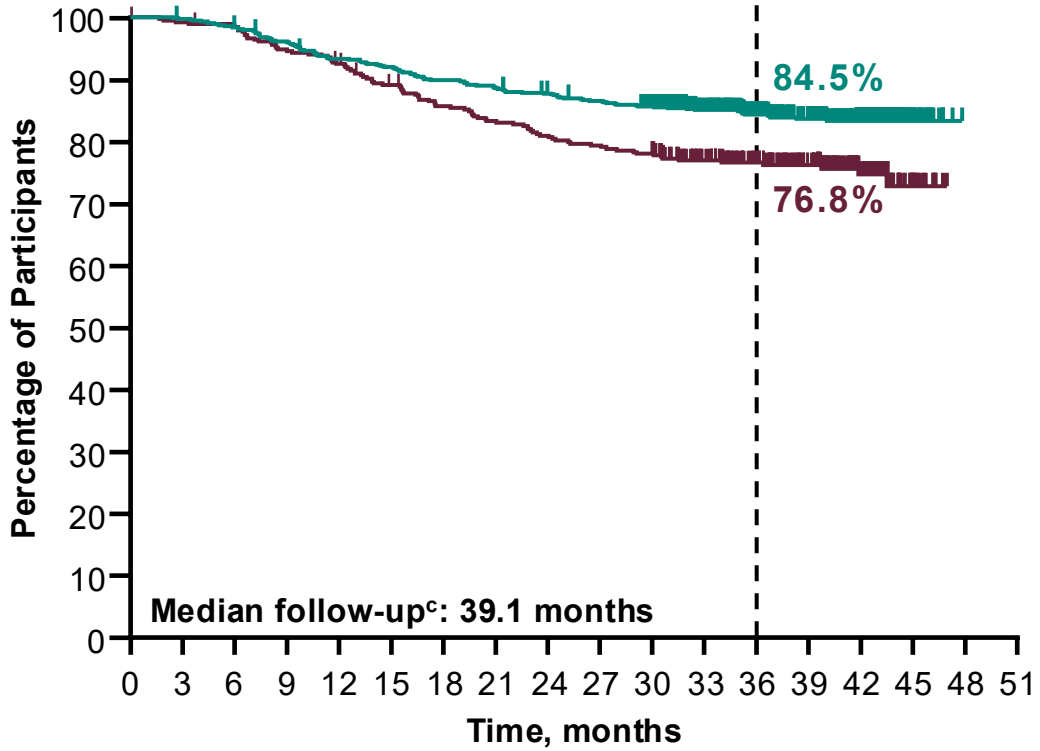
Adjuvant phase: starts from the first adjuvant treatment and includes radiation therapy as indicated (post-treatment included)

[a]Must consist of at least 2 separate tumor cores from the primary tumor. [b]Carboplatin dose was AUC 5 Q3W or AUC 1.5 QW. [c]Paclitaxel dose was 80 mg/m^2 QW. [d]Doxorubicin dose was 60 mg/m^2 Q3W. [e]Epirubicin dose was 90 mg/m^2 Q3W. [f]Cyclophosphamide dose was 600 mg/m^2 Q3W.

Schmid P, et al. ASCO 2026; Abstract 507

Event-Free Survival

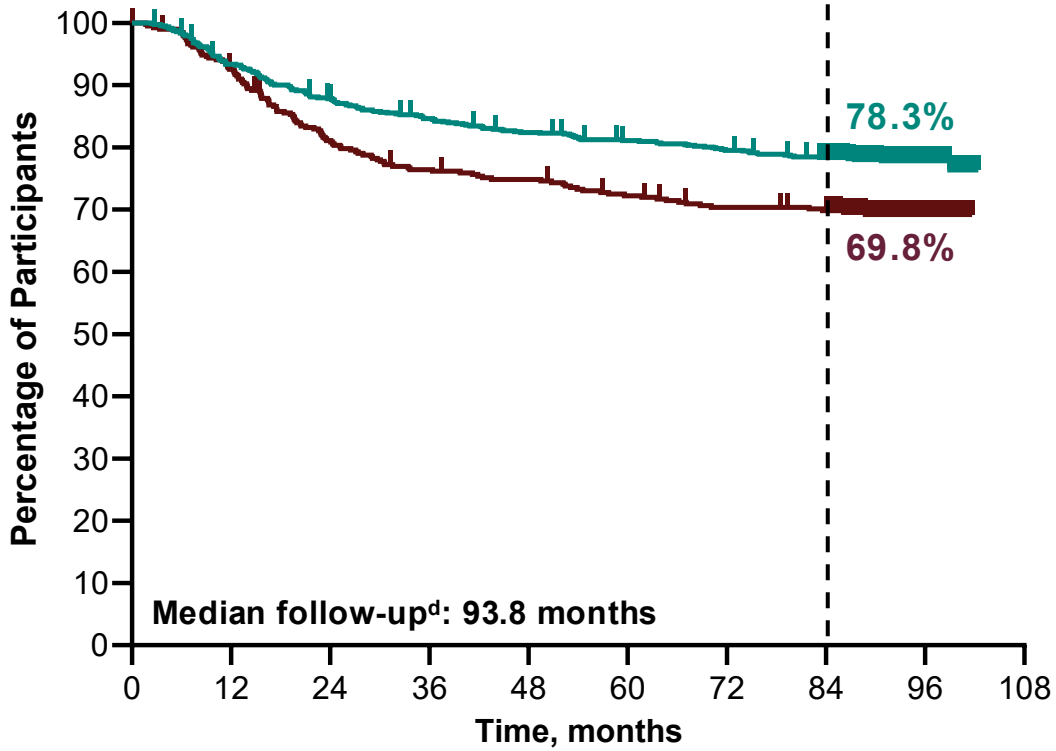
IA4	Events	HR (95% CI)	*P*-value
Pembro + Chemo/Pembro	15.7%	0.63[a] (0.48-0.82)	0.00031[b]
Placebo + Chemo/Placebo	23.8%		



No. at risk

784	781	769	751	728	718	702	692	681	671	652	551	433	303	165	28	0	0
390	386	382	368	358	342	328	319	310	304	297	250	195	140	83	17	0	0

FA	Events	HR (95% CI)
Pembro + Chemo/Pembro	21.9%	0.68[a] (0.54-0.86)
Placebo + Chemo/Placebo	30.3%	



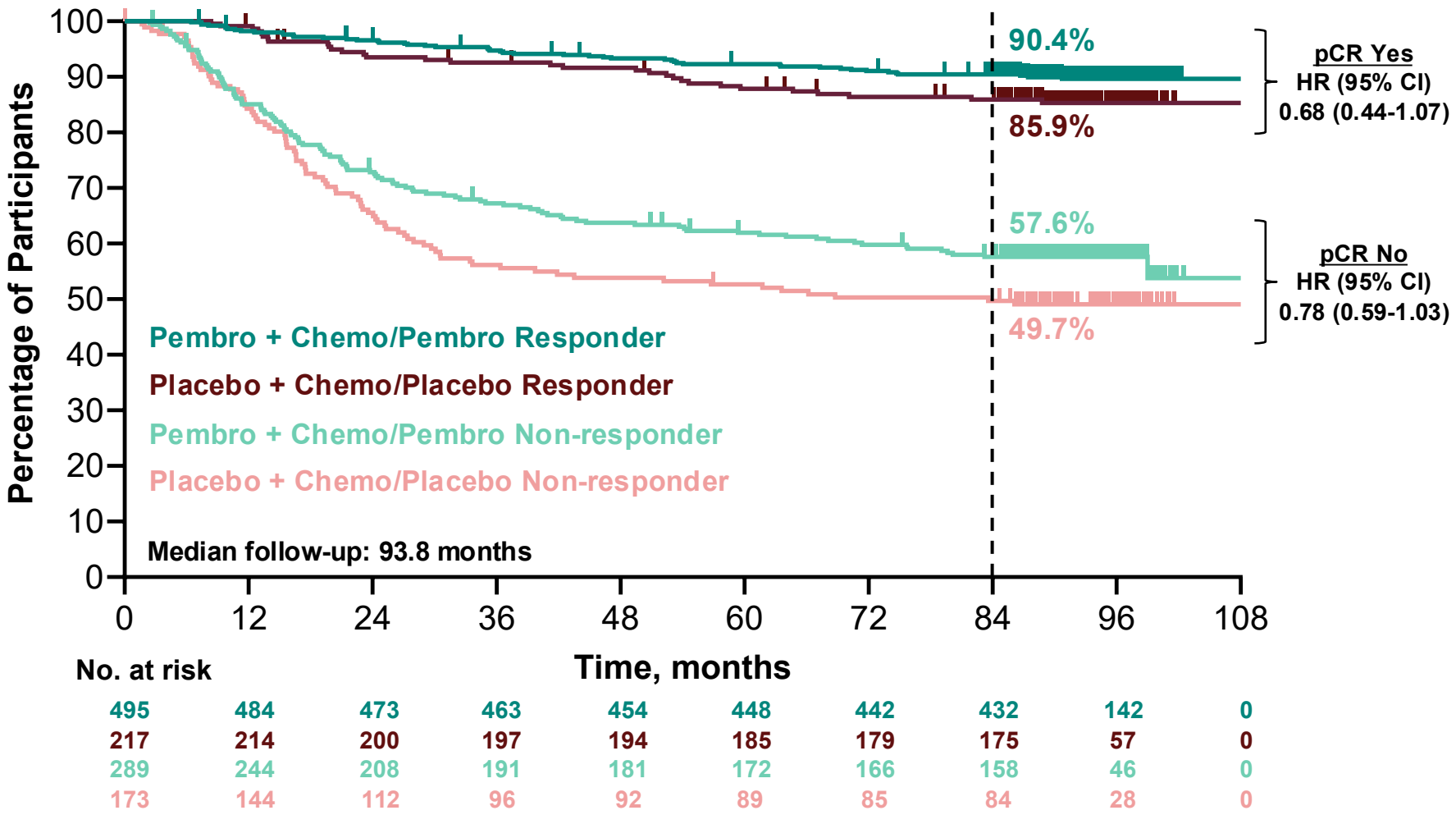
No. at risk

784	728	681	654	635	620	608	590	188	0
390	358	312	293	286	274	264	259	85	0

[a]Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. [b]Prespecified *P*-value boundary of 0.00517 was crossed.
[c]Defined as the time from randomization to the data cutoff date of March 23, 2021. [d]Defined as the time from randomization to the data cutoff date of October 14, 2025.

Schmid P, et al. ASCO 2026; Abstract 507

Event-Free Survival by Pathological Complete Response (ypT0/Tis ypN0) at FA

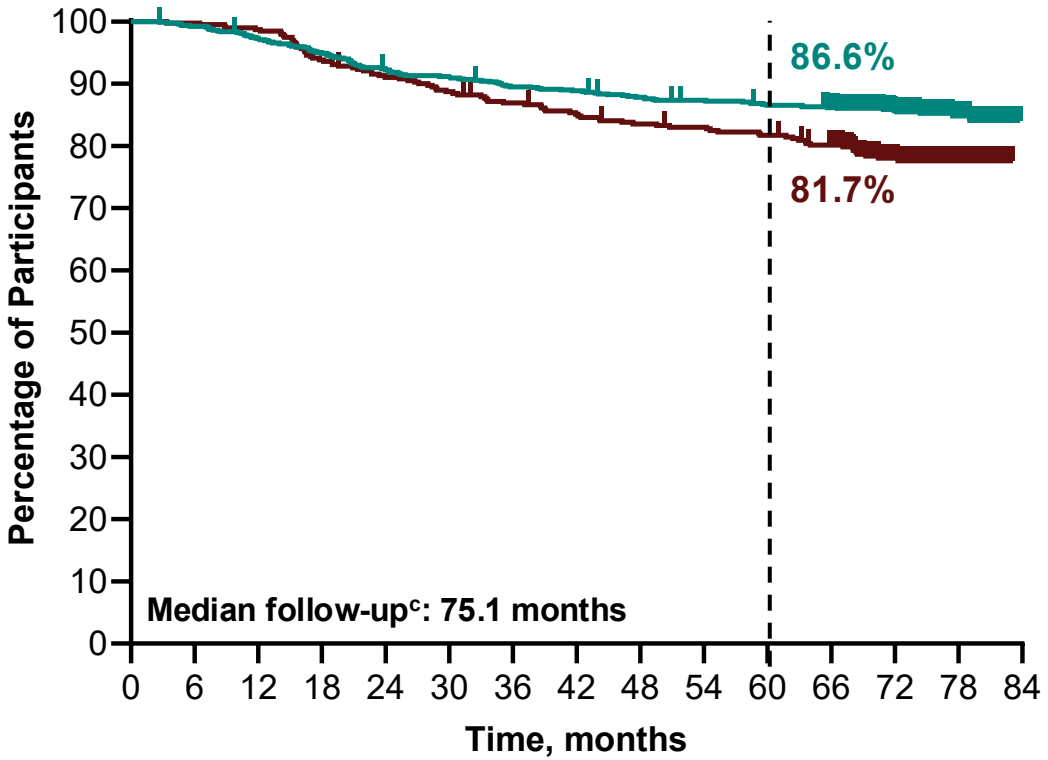


This is a non-randomized subgroup analysis based on the post-treatment outcome of pCR; HRs should be interpreted with caution. Data cutoff date: October 14, 2025.

Schmid P, et al. ASCO 2026; Abstract 507

Overall Survival

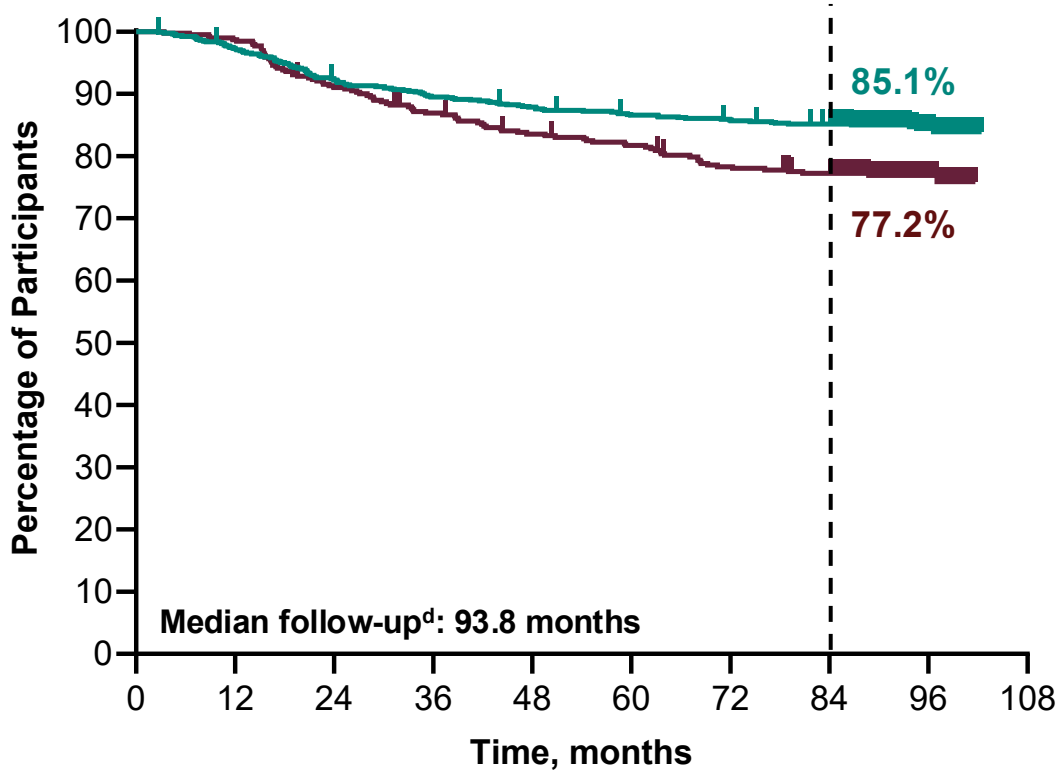
IA7	Events	HR (95% CI)	*P*-value
Pembro + Chemo/Pembro	14.7%	0.66[a] (0.50-0.87)	0.00150[b]
Placebo + Chemo/Placebo	21.8%		



No. at risk

784	777	760	742	720	712	698	693	683	677	670	656	448	176	0
390	389	385	366	354	345	336	328	321	318	313	300	199	82	0

FA	Events	HR (95% CI)
Pembro + Chemo/Pembro	15.3%	0.64[a] (0.49-0.85)
Placebo + Chemo/Placebo	23.1%	

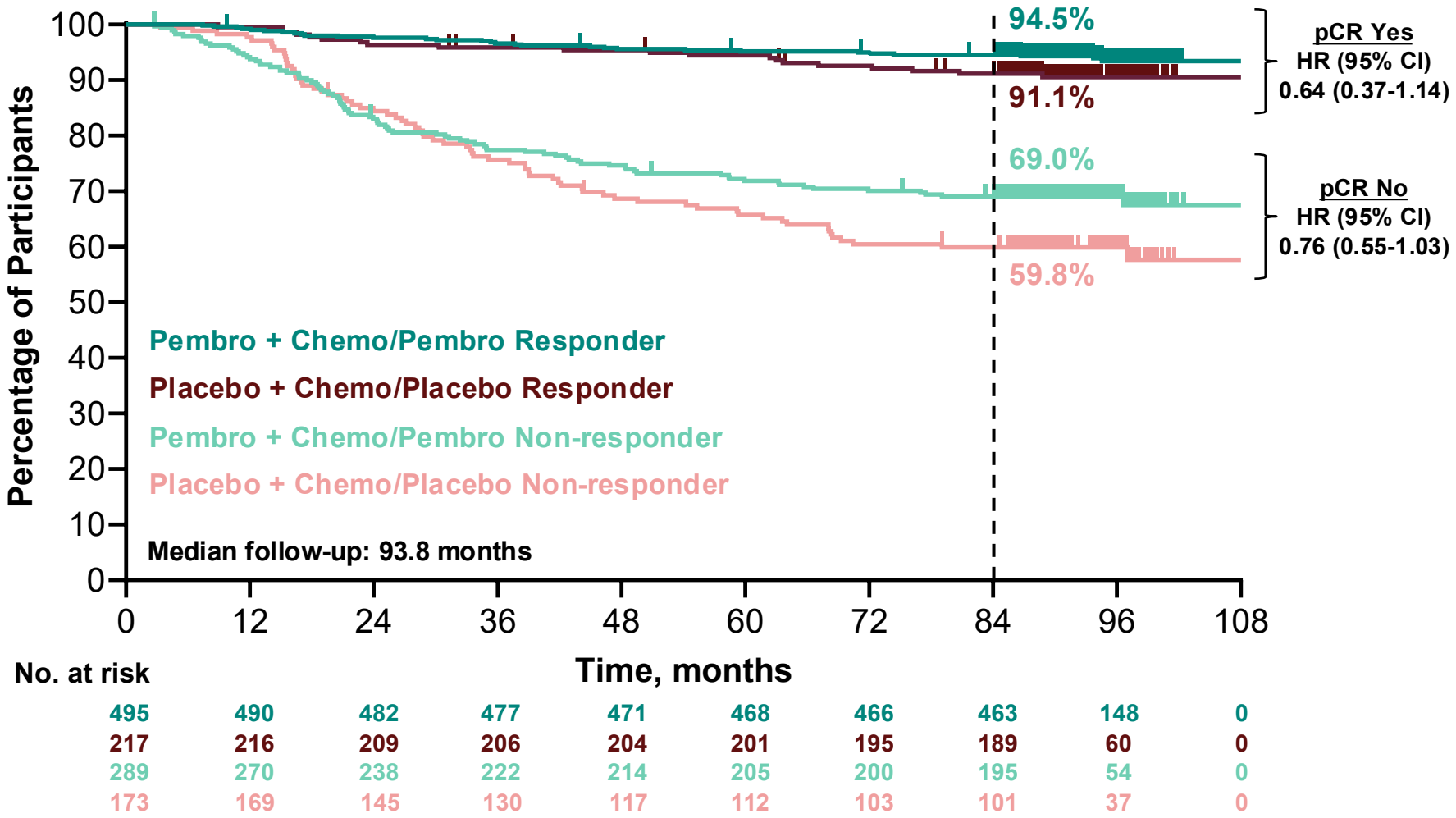


No. at risk

784	760	720	699	685	673	666	658	202	0
390	385	354	336	321	313	298	290	97	0

[a]Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. [b]Prespecified *P*-value boundary of 0.00503 was crossed.
[c]Defined as the time from randomization to the data cutoff date of March 22, 2024. [d]Defined as the time from randomization to the data cutoff date of October 14, 2025.

Overall Survival by Pathological Complete Response (ypT0/Tis ypN0) at FA



This is a non-randomized subgroup analysis based on the post-treatment outcome of pCR; HRs should be interpreted with caution. Data cutoff date: October 14, 2025.

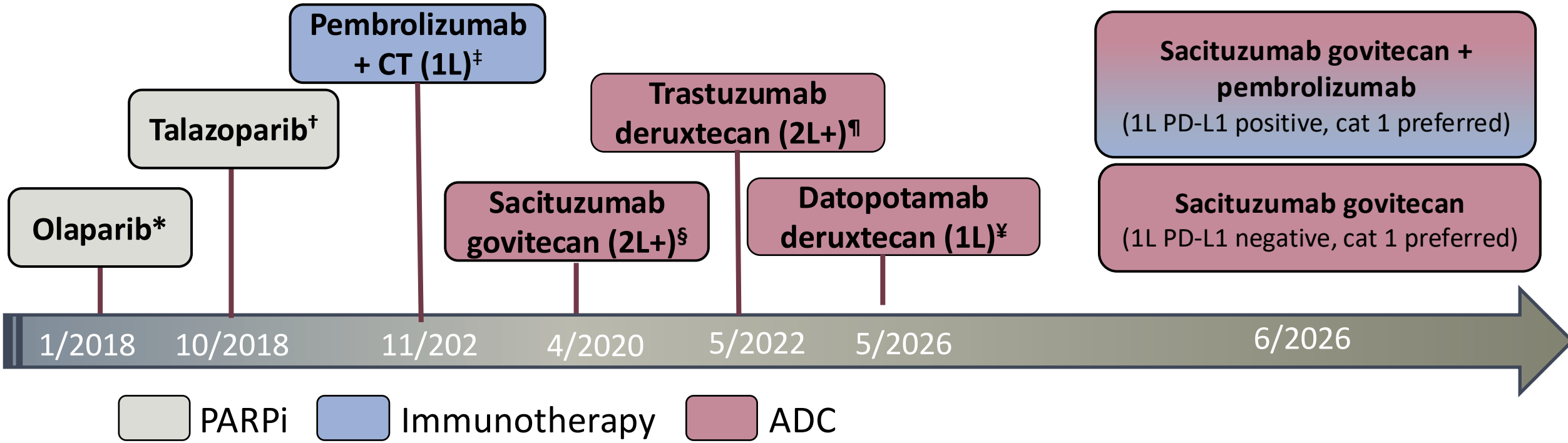
Schmid P, et al. ASCO 2026; Abstract 507

Dr O’Shaughnessy Case Presentation #1

- 48 yo physician presented with a 4 cm left breast mass and palpable axillary LN
- Biopsies showed grade 3 TNBC
- PET CT showed 1 axillary LN only and no other metastases
- She was treated with KN-522 regimen with rapid clinical CR
- Her psoriasis flared requiring treatment with anti-IL-23 MAb
- At mastectomy she had pCR in breast and LNs
- PMRT was not recommended
- She did not receive adjuvant pembrolizumab due to psoriasis which returned to her baseline post-op
- She proceeded with DIEP reconstruction

Novel and Emerging Therapies in mTNBC

FDA-Approved



*FDA-approved for patients with deleterious or suspected deleterious germline BRCA-mutated, HER2-negative metastatic breast cancer who have been treated with CT in the neoadjuvant, adjuvant, or metastatic setting

†FDA-approved for patients with deleterious or suspected deleterious germline BRCA-mutated, HER2-negative locally advanced or metastatic breast cancer

‡FDA-approved for patients with locally recurrent unresectable or metastatic TNBC whose tumors express PD-L1 (CPS ≥10). See appendix for subcutaneous formulations.

§FDA-approved for patients with unresectable locally advanced or metastatic HR+/HER2- breast cancer who have received endocrine-based therapy and ≥2 additional systemic therapies in metastatic setting

¶FDA-approved for patients with unresectable/metastatic HER2-low BC who have received prior CT in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant CT

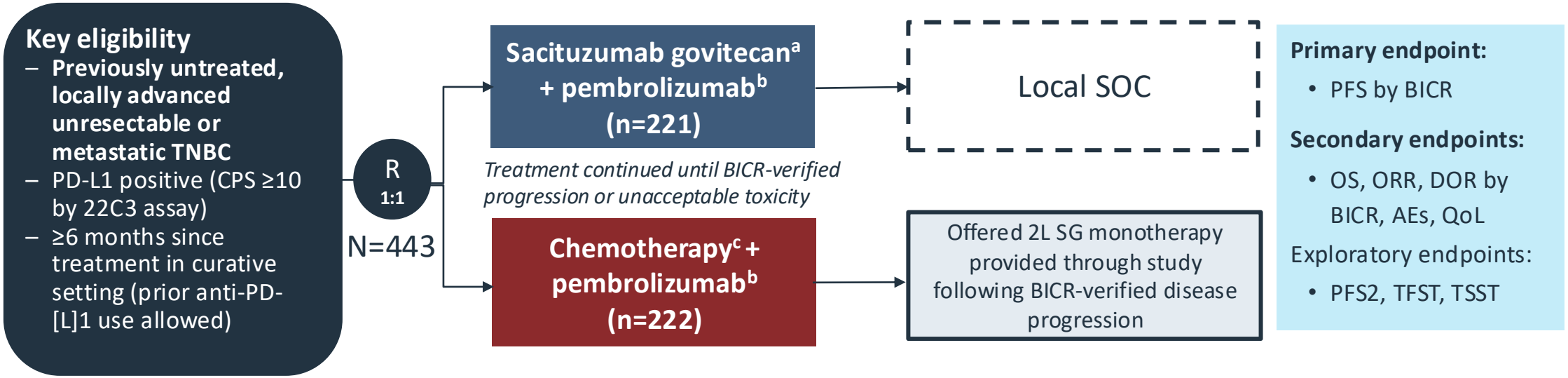
¥ FDA-approved for patients with unresectable/metastatic HR+/HER2- breast cancer who have received prior ET and CT; patients with unresectable/metastatic TNBC who are not candidates for PD-1/PD-L1 inhibitor therapy.

mTNBC = metastatic Triple-Negative Breast Cancer; ADC = Antibody-Drug Conjugate; PARPi = Poly (ADP-Ribose) Polymerase Inhibitors; 1L = First-Line Therapy; 2L = Subsequent-Line Therapy; Cat = Category.

FDA website. https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancerhematologic-malignancies-approval-notifications. Accessed 05/26;

Xiao T et al. *Curr Oncol*. 2023;30(7):6447-6461. NCCN Clinical Practice Guidelines. Breast Cancer. Version 3.2026. www.nccn.org. Accessed 5/13/26.

ASCENT-04: Untreated PD-L1+ metastatic TNBC treated with sacituzumab govitecan + pembrolizumab vs chemo + pembro



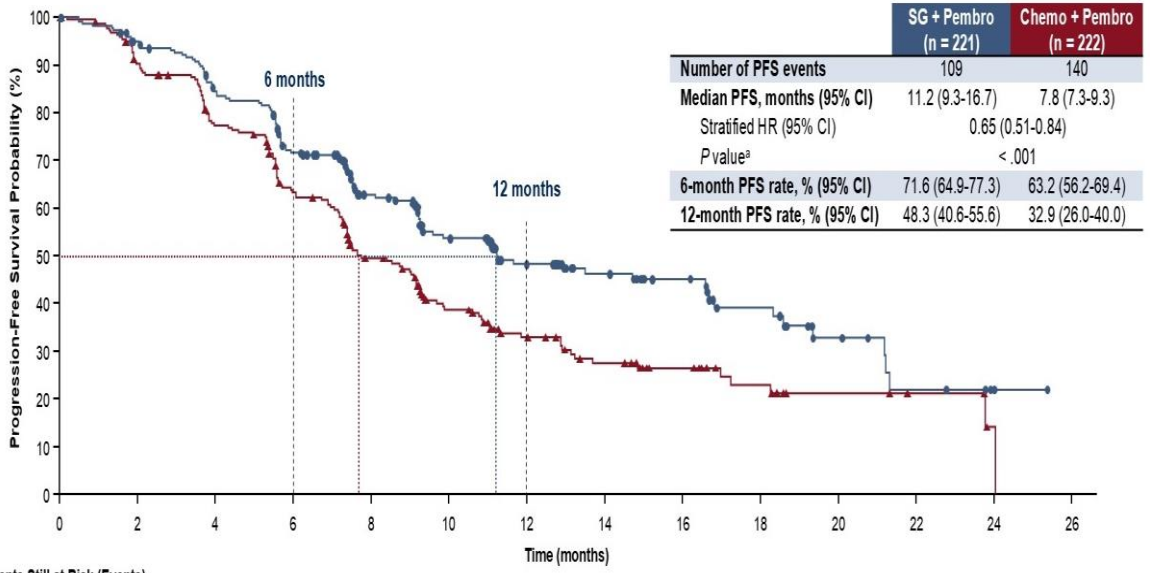
- Data cut-off: March 3, 2025
- At data cut-off, median follow-up (range): 14.0 mo (0.1–28.6)
- PFS2: Time from randomization to first documented progression on next-line therapy per investigator assessment, or death due to any cause, whichever occurred first

Participant Disposition, n (%)	SG + Pembro (n = 221)	Chemo + Pembro (n = 222)
Remaining on study treatment	95 (43)	52 (23)
Discontinued treatment[a]	125 (57)	170 (77)
Progressive disease[b]	84 (67)	138 (81)

[a]10mg/kg IV, Days 1, 8 of 21-day cycles. [b]200mg, Day 1 of 21-day cycles. [c]Paclitaxel or nab-paclitaxel or gemcitabine + carboplatin.
Kalinsky K, et al. ASCO 2026; Abstract LBA1000

ASCENT-04: Efficacy, PFS, and PFS2

PFS by BICR

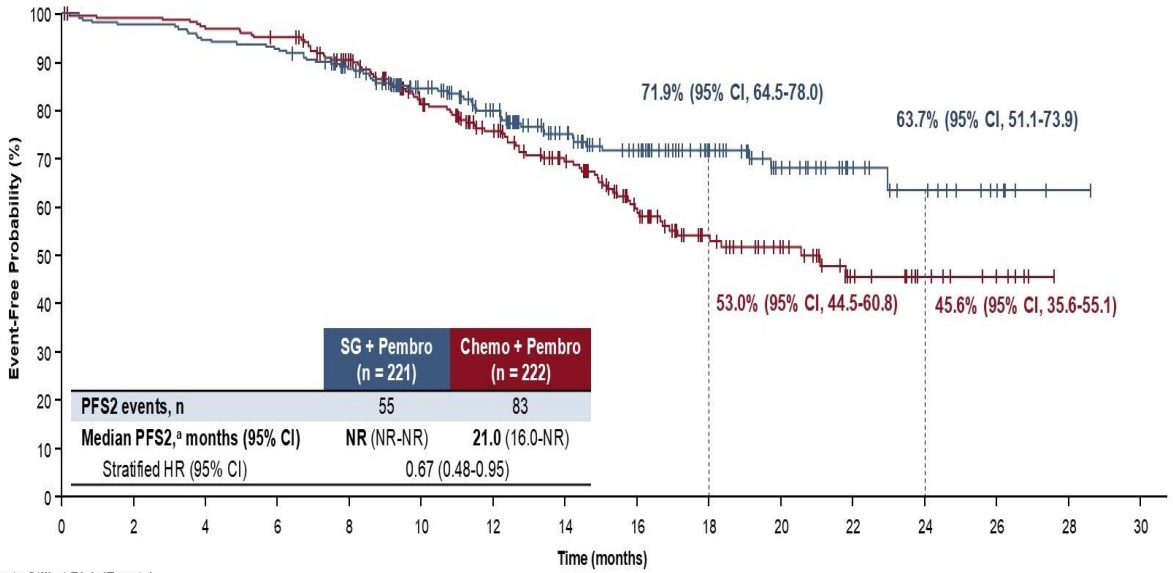


	SG + Pembro (n = 221)	Chemo + Pembro (n = 222)
Number of PFS events	109	140
Median PFS, months (95% CI)	11.2 (9.3-16.7)	7.8 (7.3-9.3)
Stratified HR (95% CI)	0.65 (0.51-0.84)	
P value[a]	< .001	
6-month PFS rate, % (95% CI)	71.6 (64.9-77.3)	63.2 (56.2-69.4)
12-month PFS rate, % (95% CI)	48.3 (40.6-55.6)	32.9 (26.0-40.0)

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)

PFS2



	SG + Pembro (n = 221)	Chemo + Pembro (n = 222)
PFS2 events, n	55	83
Median PFS2,[a] months (95% CI)	**NR** (NR-NR)	**21.0** (16.0-NR)
Stratified HR (95% CI)	0.67 (0.48-0.95)	

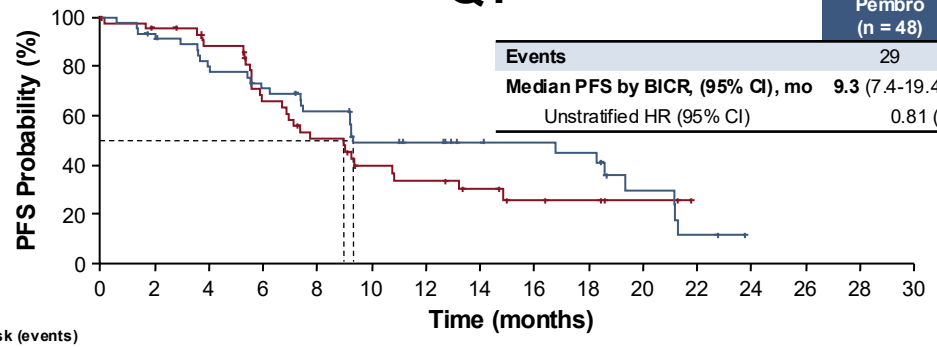
No. of Patients Still at Risk (Events)

SG + pembro	221 (0)	216 (5)	209 (12)	205 (16)	186 (25)	154 (33)	128 (41)	97 (48)	76 (52)	48 (52)	31 (54)	17 (54)	12 (55)	5 (55)	1 (55)	0 (55)
Chemo + pembro	222 (0)	218 (2)	213 (7)	208 (11)	186 (21)	154 (39)	129 (49)	101 (59)	70 (74)	46 (79)	32 (80)	16 (83)	10 (83)	5 (83)	0 (83)	

Kalinsky K, et al. ASCO 2026; Abstract LBA1000

PFS by Trop-2 H-Score Quartiles[a]

Q1

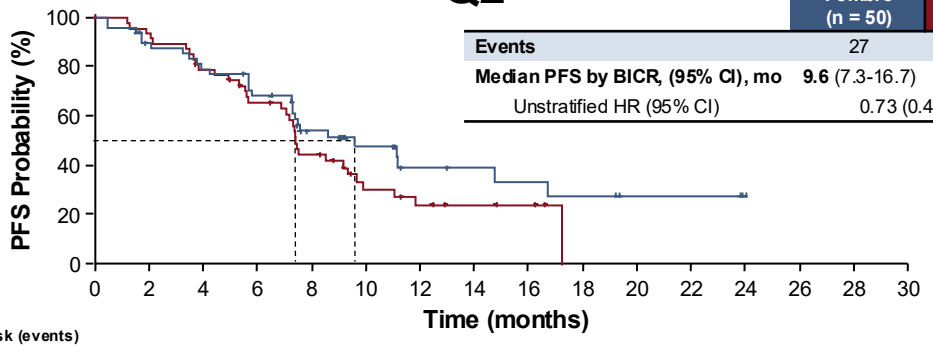


	SG + Pembro (n = 48)	Chemo + Pembro (n = 47)
Events	29	28
Median PFS by BICR, (95% CI), mo	**9.3** (7.4-19.4)	**9.0** (6.0-10.9)
Unstratified HR (95% CI)	0.81 (0.48-1.36)	

No. at risk (events)

SG + pembro	48 (0)	43 (3)	36 (9)	31 (13)	26 (17)	19 (22)	17 (22)	13 (22)	12 (22)	11 (23)	5 (26)	2 (29)	0 (29)
Chemo + pembro	47 (0)	42 (2)	37 (5)	26 (14)	19 (20)	13 (24)	11 (26)	8 (27)	5 (28)	4 (28)	2 (28)	0 (28)	

Q2

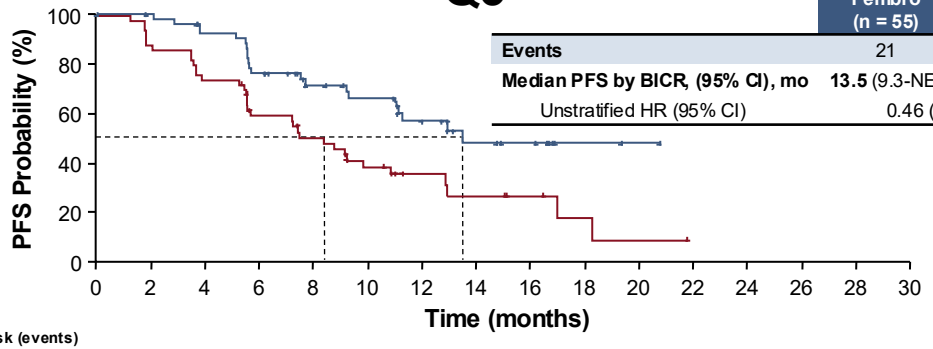


	SG + Pembro (n = 50)	Chemo + Pembro (n = 50)
Events	27	33
Median PFS by BICR, (95% CI), mo	**9.6** (7.3-16.7)	**7.4** (6.9-9.7)
Unstratified HR (95% CI)	0.73 (0.44-1.22)	

No. at risk (events)

SG + pembro	50 (0)	42 (5)	37 (10)	31 (15)	20 (21)	13 (23)	8 (25)	7 (25)	6 (26)	5 (27)	3 (27)	3 (27)	1 (27)	0 (27)
Chemo + pembro	50 (0)	45 (3)	37 (10)	29 (16)	19 (25)	10 (30)	7 (32)	5 (32)	4 (32)	0 (33)				

Q3

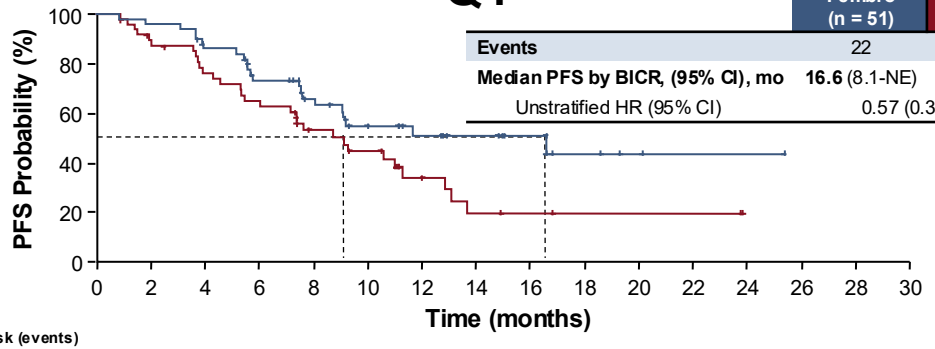


	SG + Pembro (n = 55)	Chemo + Pembro (n = 50)
Events	21	34
Median PFS by BICR, (95% CI), mo	**13.5** (9.3-NE)	**8.4** (5.6-10.8)
Unstratified HR (95% CI)	0.46 (0.27-0.80)	

No. at risk (events)

SG + pembro	55 (0)	52 (0)	46 (4)	38 (12)	28 (14)	24 (16)	17 (19)	10 (21)	7 (21)	2 (21)	1 (21)	0 (21)	
Chemo + pembro	50 (0)	44 (6)	37 (13)	27 (20)	22 (24)	15 (29)	8 (30)	6 (32)	4 (32)	2 (33)	1 (34)	0 (34)	

Q4



	SG + Pembro (n = 51)	Chemo + Pembro (n = 49)
Events	22	30
Median PFS by BICR, (95% CI), mo	**16.6** (8.1-NE)	**9.2** (5.5-11.3)
Unstratified HR (95% CI)	0.57 (0.33-0.99)	

No. at risk (events)

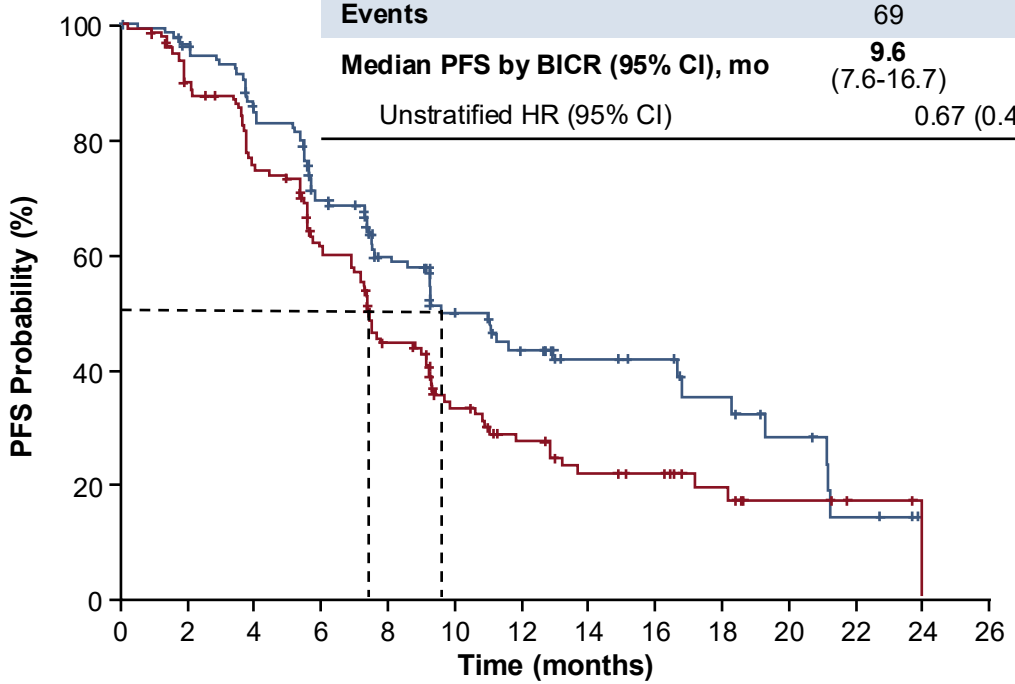
SG + pembro	51 (0)	49 (2)	42 (7)	33 (13)	25 (16)	18 (20)	13 (21)	10 (21)	8 (21)	4 (22)	2 (22)	1 (22)	1 (22)	0 (22)
Chemo + pembro	49 (0)	41 (5)	34 (11)	29 (16)	19 (21)	15 (24)	8 (27)	4 (30)	3 (30)	2 (30)	2 (30)	2 (30)	0 (30)	

SG + pembro treatment was associated with consistently improved PFS vs chemo + pembro across Trop-2 expression quartiles, with trends toward greater separation of KM curves in Q3 and Q4

[a]Trop-2 H-score quartiles: Q1, 0-224; Q2, 225-279; Q3, 280-298; Q4, 299-300.
BICR, blinded independent central review; **chemo**, chemotherapy; **HR**, hazard ratio; **KM**, Kaplan-Meier; **mo**, months; **NE**, not estimable; **pembro**, pembrolizumab; **PFS**, progression-free survival; **Q**, quartile; **SG**, sacituzumab govitecan.

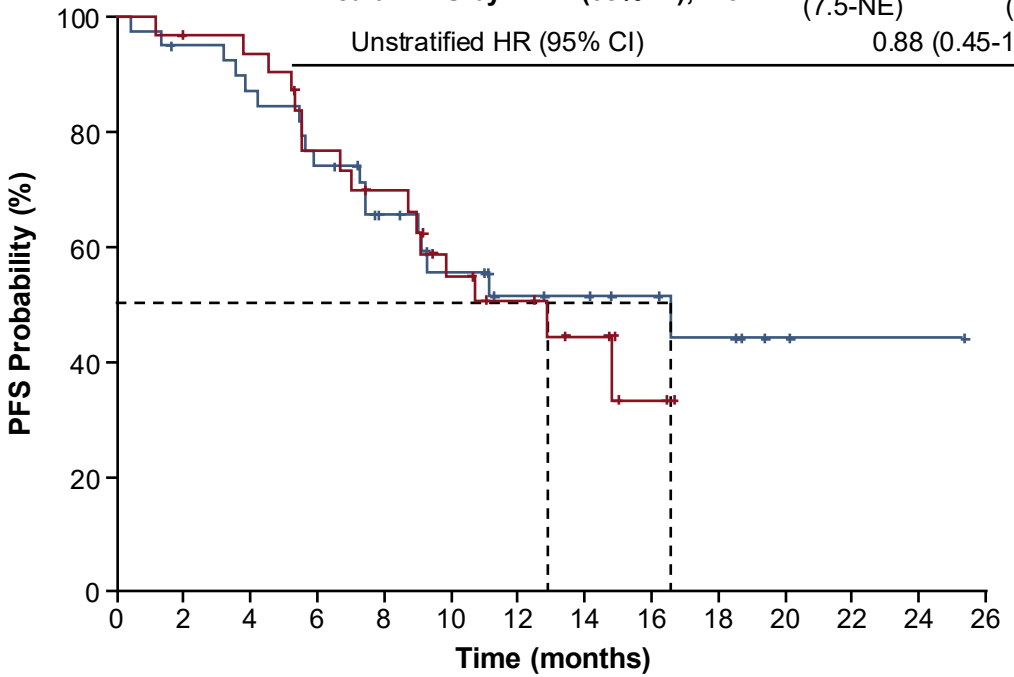
PFS by tBRCA Subgroups

	WT	
	SG + Pembro (n = 130)	Chemo + Pembro (n = 131)
Events	69	90
Median PFS by BICR (95% CI), mo	**9.6** (7.6-16.7)	**7.4** (6.9-9.2)
Unstratified HR (95% CI)	0.67 (0.49-0.91)	



No. at risk														
WT, SG + pembro	130	119	100	78	58	42	30	19	17	11	7	3	0	0
WT, Chemo + pembro	131	113	92	71	47	30	21	15	13	8	4	2	1	0

	Mut	
	SG + Pembro (n = 39)	Chemo + Pembro (n = 32)
Events	18	16
Median PFS by BICR (95% CI), mo	**16.6** (7.5-NE)	**12.9** (7.1-NE)
Unstratified HR (95% CI)	0.88 (0.45-1.74)	



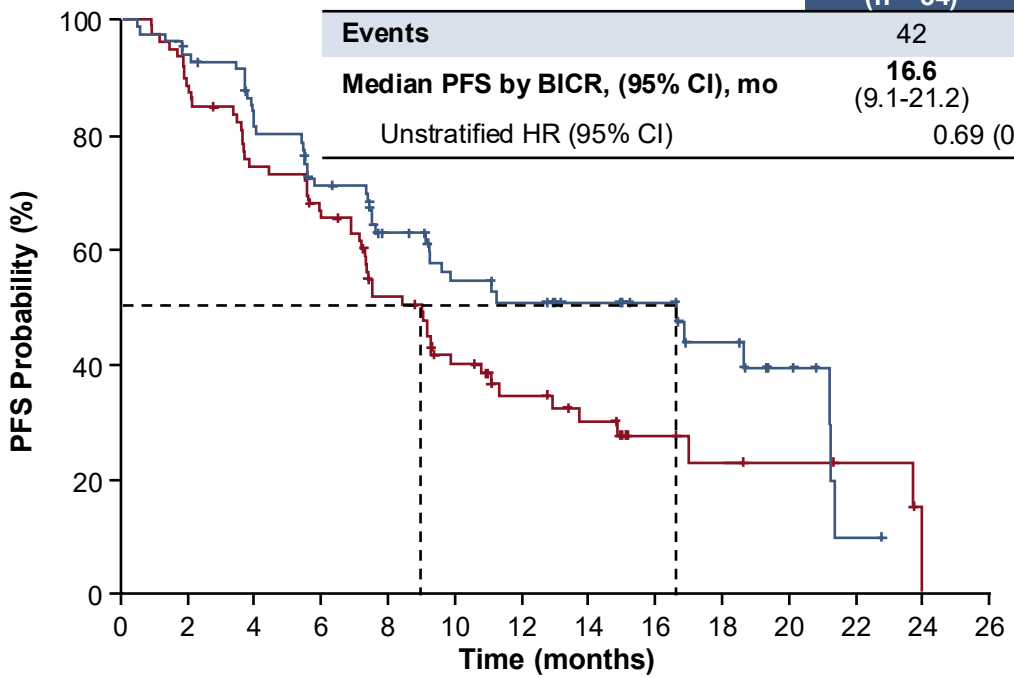
No. at risk														
Mut, SG + pembro	39	36	33	28	21	16	11	10	8	6	2	1	1	0
Mut, Chemo + pembro	32	30	29	22	19	14	9	6	2	0	0	0	0	0

PFS improvement with SG + pembro vs chemo + pembro was observed across tBRCA subgroups

BICR, blinded independent central review; **chemo**, chemotherapy; **HR**, hazard ratio; mBC, metastatic breast cancer; **mo**, months; **mut**, mutant; **NE**, not estimable; **pembro**, pembrolizumab; **PFS**, progression-free survival; **SG**, sacituzumab govitecan; **tBRCA**, tumor BRCA; **WT**, wild-type.

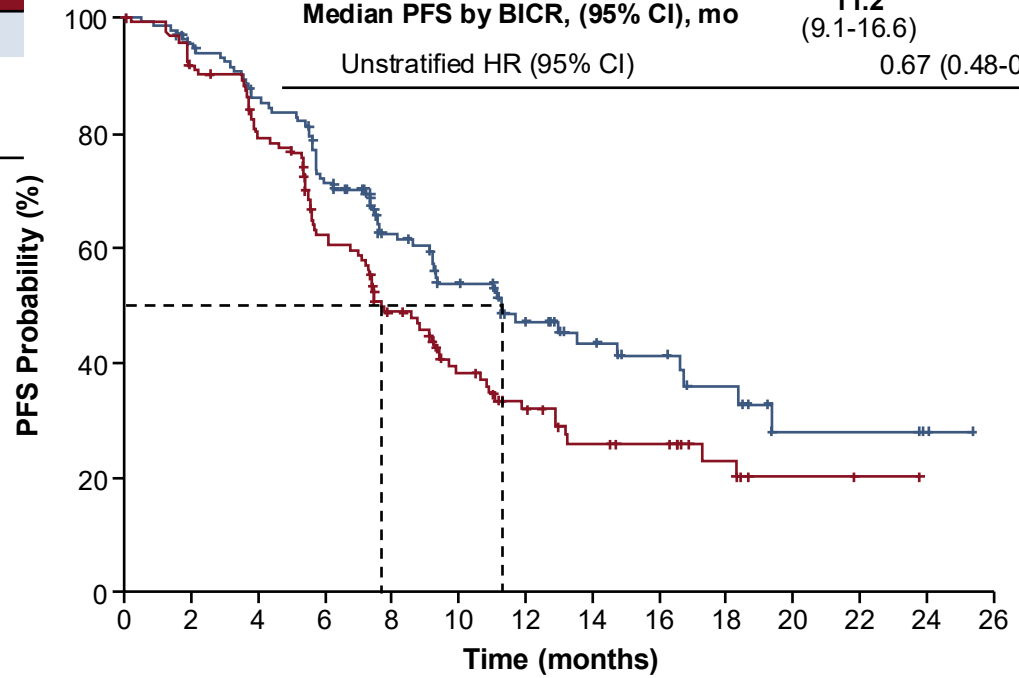
PFS by HER2 Subgroups

	HER2 IHC 0	
	SG + Pembro (n = 84)	Chemo + Pembro (n = 82)
Events	42	54
Median PFS by BICR, (95% CI), mo	**16.6** (9.1-21.2)	**9.0** (7.2-10.8)
Unstratified HR (95% CI)	0.69 (0.46-1.04)	



No. at risk														
HER2 IHC 0, SG + pembro	84	76	64	54	42	32	26	20	17	11	6	1	0	0
HER2 IHC 0, Chemo + pembro	82	70	58	50	37	25	17	13	7	5	4	3	1	0

	HER2 Low	
	SG + Pembro (n = 133)	Chemo + Pembro (n = 136)
Events	65	83
Median PFS by BICR, (95% CI), mo	**11.2** (9.1-16.6)	**7.7** (7.0-9.4)
Unstratified HR (95% CI)	0.67 (0.48-0.92)	



No. at risk														
HER2 Low, SG + pembro	133	122	106	84	60	46	32	22	17	11	5	5	2	0
HER2 Low, Chemo + pembro	136	118	98	71	50	33	23	16	14	8	3	1	0	0

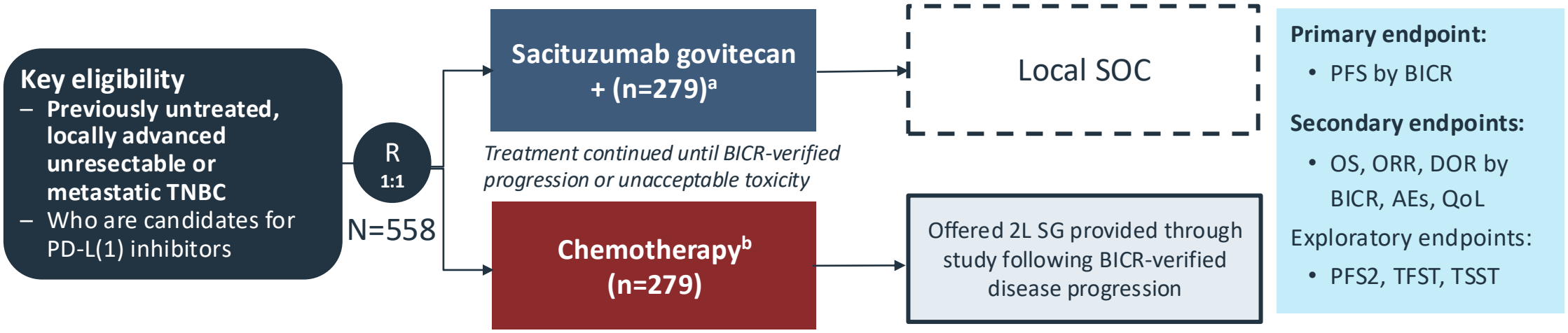
PFS curves showed benefit with SG + pembro compared to chemo + pembro, regardless of HER2 expression status

BICR, blinded independent central review; **chemo**, chemotherapy; **HER2**, human epidermal growth factor receptor 2; **HR**, hazard ratio; **IHC**, immunohistochemistry; **KM**, Kaplan-Meier; **mo**, months; **pembro**, pembrolizumab; **PFS**, progression-free survival; **SG**, sacituzumab govitecan.

PRESENTED BY: Sara M Tolaney, MD, MPH, FASCO

Abstract 1013

ASCENT-03: PFS2 and subsequent therapies of patients with previously untreated metastatic TNBC treated with SG vs chemo



- Data cut-off: April 2, 2025
- At data cut-off, median follow-up (range): 13.2 months (<0.1–29.2)
- PFS2: Time from randomization to first documented progression on next-line therapy per investigator assessment, or death due to any cause, whichever occurred first

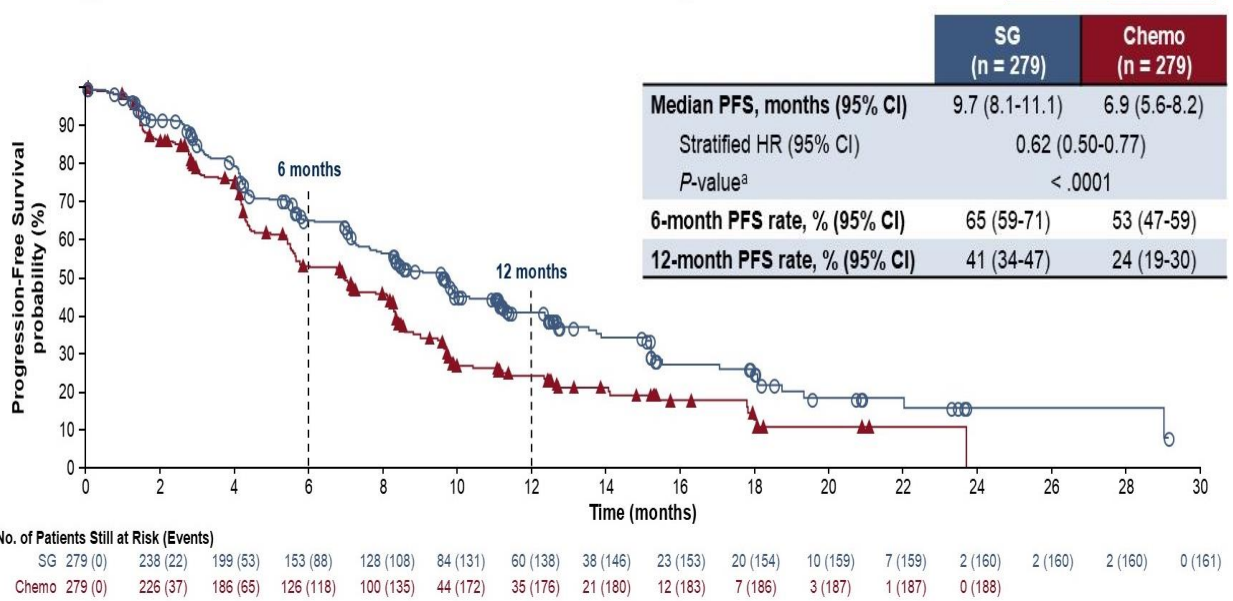
Participant Disposition, n (%)	SG (n = 279)	Chemo (n = 279)
Remaining on study treatment	75 (27)	39 (14)
Discontinued treatment[a]	204 (73)	240 (86)
Progressive disease[b]	161 (79)	195 (81)

[a]10mg/kg IV, Days 1, 8 of 21-day cycles. [b]Paclitaxel or nab-paclitaxel or gemcitabine + carboplatin.

Hurvitz S, et al. ASCO 2026; Abstract 1001

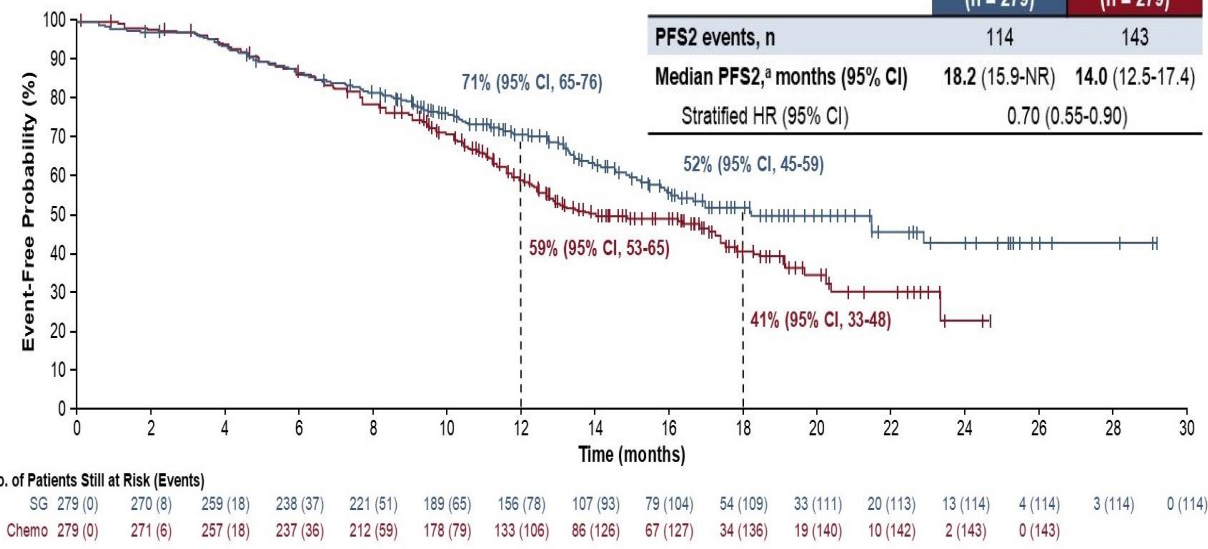
ASCENT-03: Efficacy, PFS and PFS2

PFS by BICR



	SG (n = 279)	Chemo (n = 279)
Median PFS, months (95% CI)	9.7 (8.1-11.1)	6.9 (5.6-8.2)
Stratified HR (95% CI)	0.62 (0.50-0.77)	
P-value[a]	< .0001	
6-month PFS rate, % (95% CI)	65 (59-71)	53 (47-59)
12-month PFS rate, % (95% CI)	41 (34-47)	24 (19-30)

PFS2

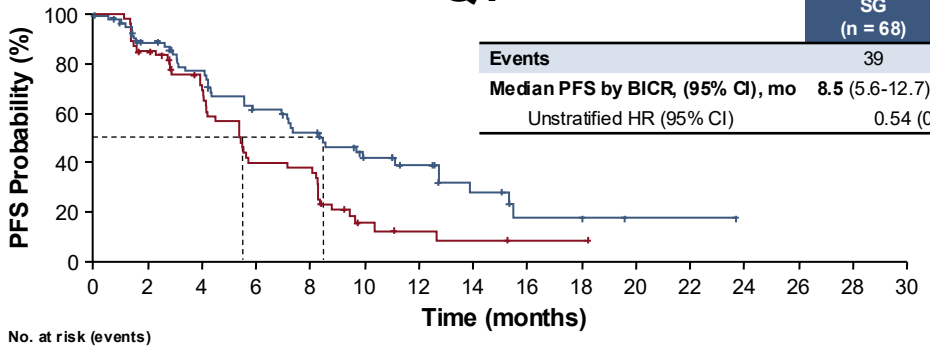


	SG (n = 279)	Chemo (n = 279)
PFS2 events, n	114	143
Median PFS2,[a] months (95% CI)	**18.2** (15.9-NR)	**14.0** (12.5-17.4)
Stratified HR (95% CI)	0.70 (0.55-0.90)	

Hurvitz S, et al. ASCO 2026; Abstract 1001

PFS by Trop-2 H-Score Quartiles[a]

Q1



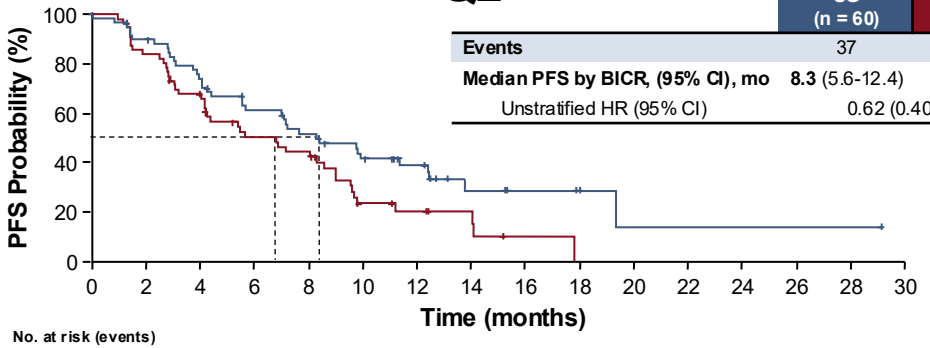
	SG (n = 68)	Chemo (n = 55)
Events	39	43
Median PFS by BICR, (95% CI), mo	**8.5** (5.6-12.7)	**5.5** (4.2-8.1)
Unstratified HR (95% CI)	0.54 (0.35-0.84)	

No. at risk (events)

SG 68 (0) 55 (7) 45 (14) 34 (23) 28 (28) 17 (33) 13 (34) 7 (37) 3 (39) 3 (39) 1 (39) 1 (39) 0 (39)

Chemo 55 (0) 46 (8) 34 (15) 19 (30) 18 (31) 5 (41) 3 (42) 2 (43) 1 (43) 1 (43) 0 (43)

Q2



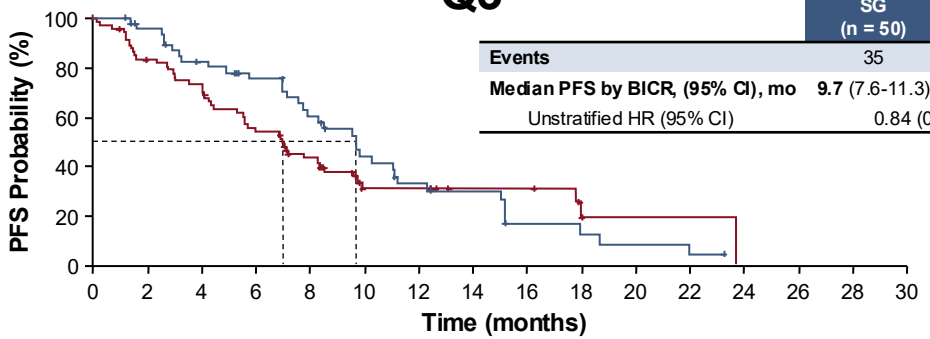
	SG (n = 60)	Chemo (n = 62)
Events	37	43
Median PFS by BICR, (95% CI), mo	**8.3** (5.6-12.4)	**6.8** (4.2-9.0)
Unstratified HR (95% CI)	0.62 (0.40-0.97)	

No. at risk (events)

SG 60 (0) 52 (6) 42 (15) 33 (22) 27 (27) 20 (32) 15 (33) 6 (36) 4 (36) 3 (36) 1 (37) 1 (37) 1 (37) 1 (37) 1 (37) 0 (37)

Chemo 62 (0) 47 (9) 37 (18) 25 (27) 22 (30) 9 (39) 6 (40) 4 (40) 1 (42) 0 (43)

Q3



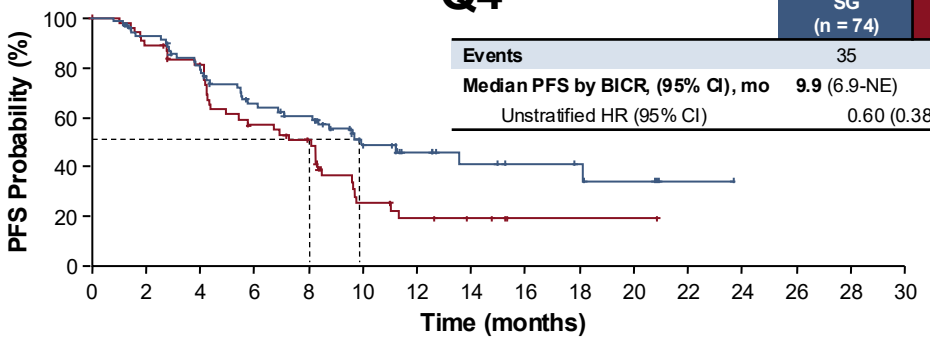
	SG (n = 50)	Chemo (n = 74)
Events	35	48
Median PFS by BICR, (95% CI), mo	**9.7** (7.6-11.3)	**7.0** (5.3-8.5)
Unstratified HR (95% CI)	0.84 (0.54-1.31)	

No. at risk (events)

SG 50 (0) 44 (2) 36 (8) 31 (11) 24 (17) 16 (23) 11 (27) 9 (28) 4 (32) 4 (32) 2 (34) 2 (34) 0 (35)

Chemo 74 (0) 58 (12) 51 (19) 38 (31) 25 (39) 12 (45) 12 (45) 7 (45) 7 (45) 3 (47) 1 (47) 1 (47) 0 (48)

Q4



	SG (n = 74)	Chemo (n = 56)
Events	35	37
Median PFS by BICR, (95% CI), mo	**9.9** (6.9-NE)	**8.1** (4.4-8.5)
Unstratified HR (95% CI)	0.60 (0.38-0.95)	

No. at risk (events)

SG 74 (0) 64 (5) 54 (13) 41 (23) 36 (26) 21 (32) 13 (33) 9 (34) 7 (34) 6 (34) 4 (35) 1 (35) 0 (35)

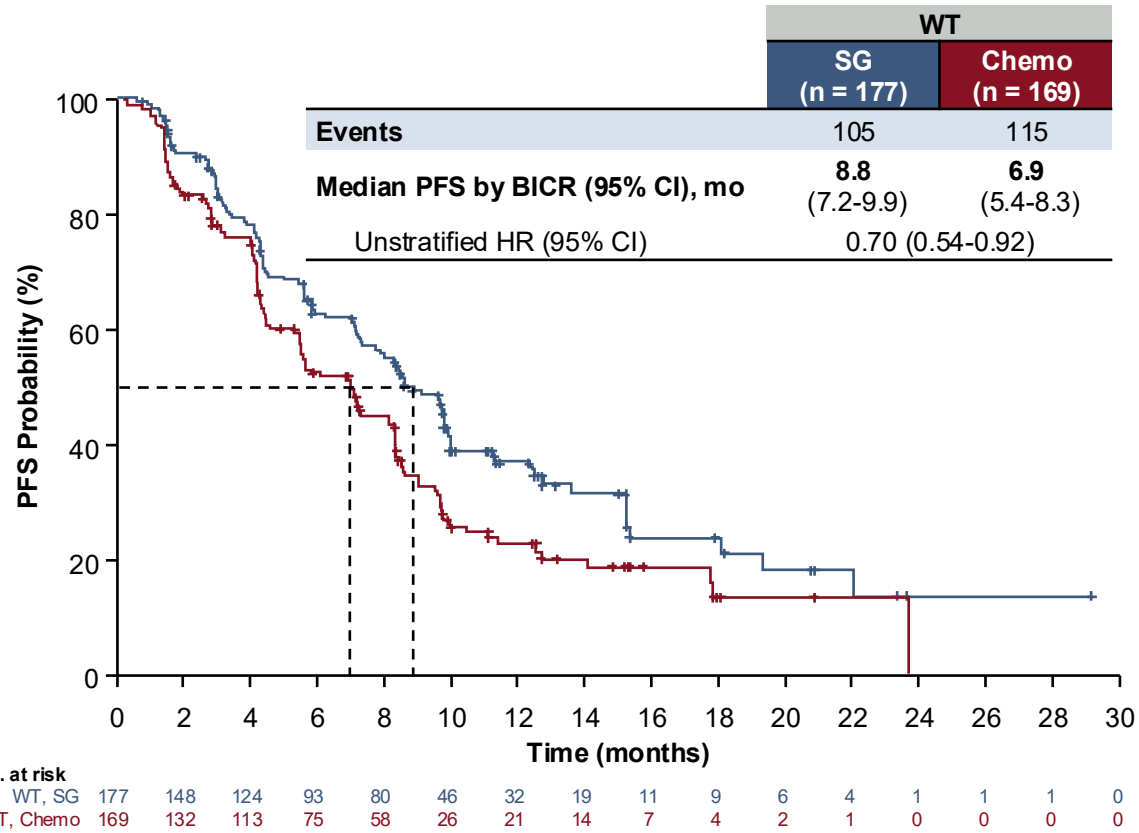
Chemo 56 (0) 48 (6) 40 (10) 27 (22) 22 (25) 9 (35) 6 (37) 4 (37) 1 (37) 1 (37) 1 (37) 0 (37)

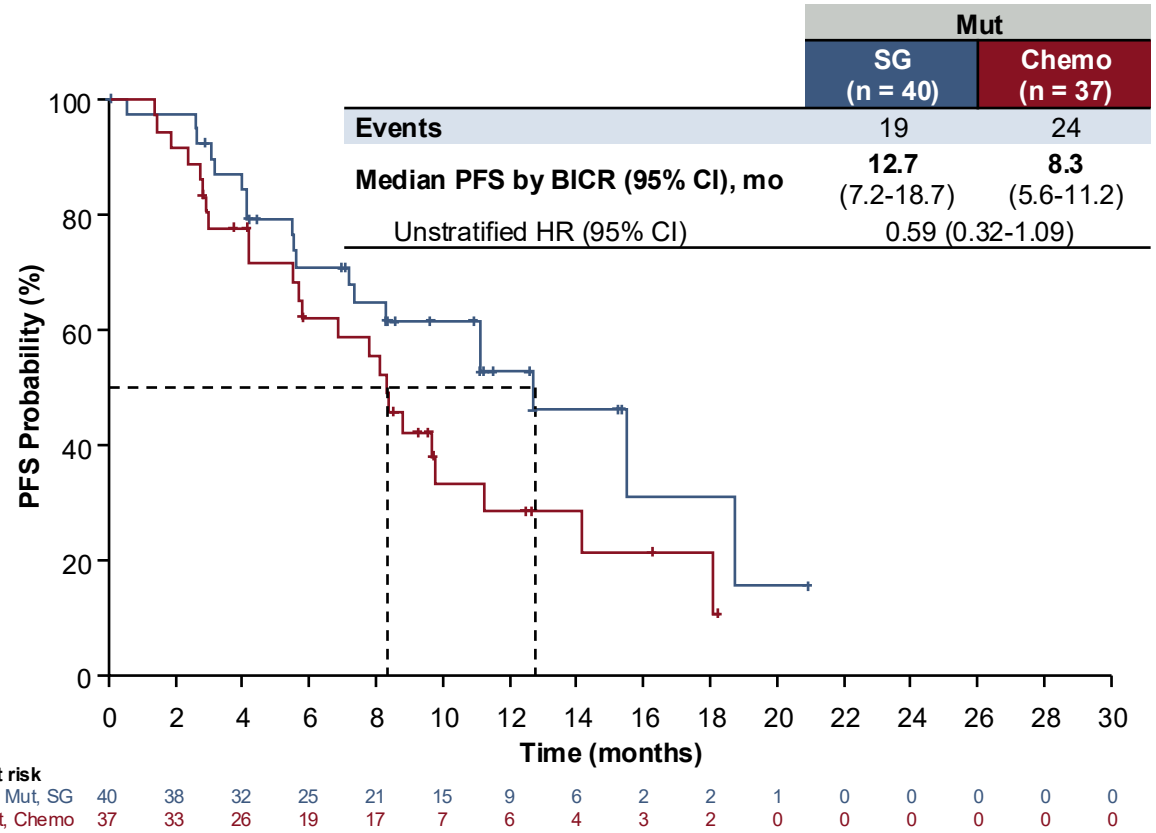
PFS curves separated early in all Trop-2 quartiles

[a]Trop-2 H-score quartiles: Q1, 0-184; Q2, 185-239; Q3, 240-283; Q4, 284-300.

BICR, blinded independent central review; **chemo**, chemotherapy; **HR**, hazard ratio; **mo**, months; **NE**, not estimable; **PFS**, progression-free survival; **Q**, quartile; **SG**, sacituzumab govitecan.

PFS by tBRCA Subgroups

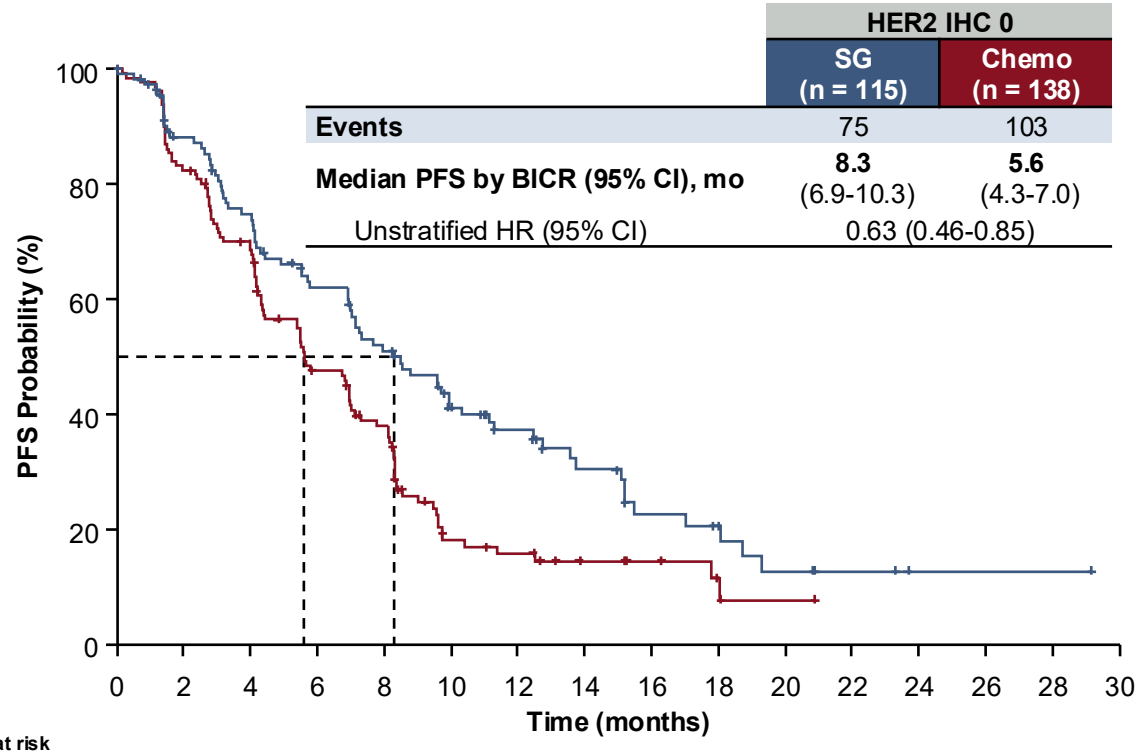


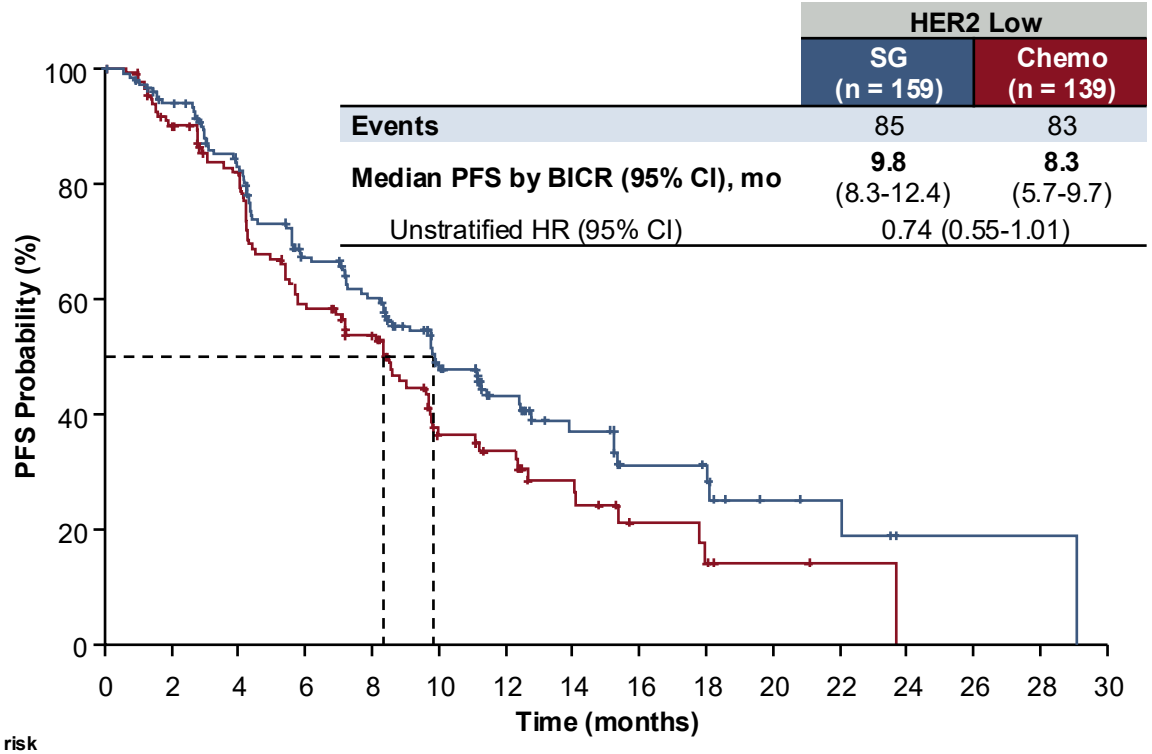


The SG and chemotherapy PFS curves separated early within the tBRCA WT and tBRCA mut subgroups and show PFS improvement with SG vs chemo regardless of tBRCA status

BICR, blinded independent central review; **chemo**, chemotherapy; **HR**, hazard ratio; **mo**, months; **mPFS**, median progression-free survival; **mut**, mutant; **PFS**, progression-free survival; **SG**, sacituzumab govitecan; **tBRCA**, tumor BRCA; **WT**, wild-type.

PFS by HER2 Subgroups





PFS curves separated early and remained separated during the study period, showing PFS benefit with SG over chemo across HER2 subgroups

BAS, biomarker analysis set; **BICR**, blinded independent central review; **chemo**, chemotherapy; **HR**, hazard ratio; **mo**, months; **mPFS**, median progression-free survival; **mut**, mutant; **PFS**, progression-free survival; **SG**, sacituzumab govitecan; **tBRCA**, tumor BRCA; **WT**, wild-type.

TROPION-Breast02: 1L Dato-DXd vs chemo in locally recurrent inoperable or metastatic TNBC for whom immunotherapy was not an option

Key inclusion criteria:

- Patients with histologically or cytologically documented locally recurrent inoperable or metastatic TNBC
- No prior chemotherapy or targeted systemic therapy in the locally recurrent inoperable or metastatic setting
- Immunotherapy not an option
- ECOG PS 0 or 1
- No minimum disease-free interval (DFI)

1:1

Dato-DXd
6 mg/kg IV Day 1 Q3W
(n=323)

Investigator's choice of chemotherapy (ICC)
Paclitaxel, nab-paclitaxel, capecitabine, eribulin mesylate/eribulin, carboplatin
(n=321)

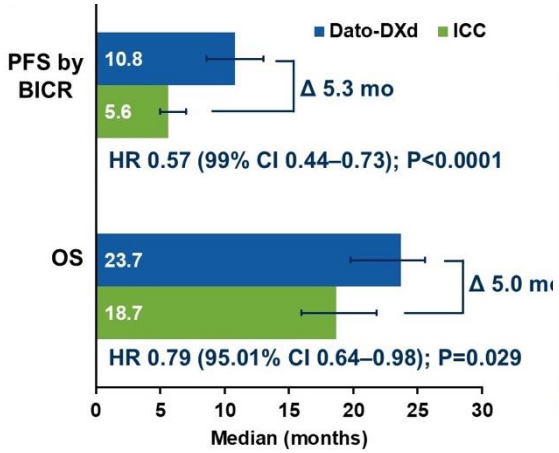
Endpoints

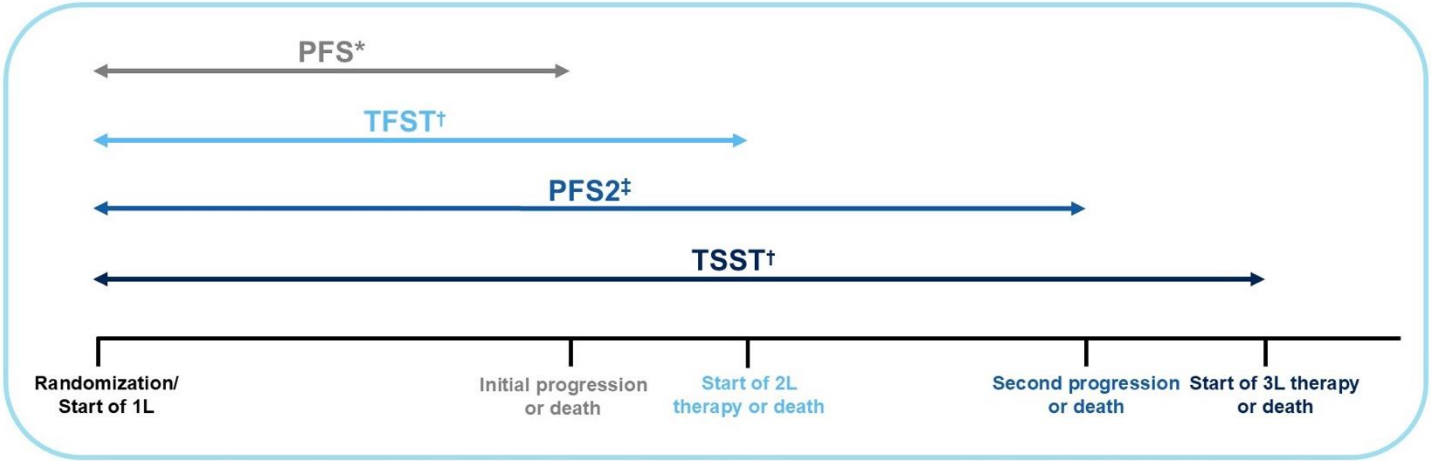
- **Dual primary:** PFS by BICR per RECIST v1.1, and OS
- **Secondary included:** PFS (investigator-assessed), ORR, DoR, DCR at 12 weeks, safety, PROs, TFST, PFS2, and TSST

Randomization stratified by:

- Geographic region (US/Canada/Europe vs other geographic regions)
- PD-L1 status (high [CPS ≥10] vs low [CPS <10])
- DFI history (*de novo* vs prior DFI 0–12 months vs prior DFI >12 months)

Treatment continued until investigator-assessed RECIST v1.1 progressive disease, unacceptable toxicity, or another discontinuation criterion was met; following progression or discontinuation of study treatment, patients could receive subsequent therapies, including approved ADCs or chemotherapy, at the investigator's discretion.





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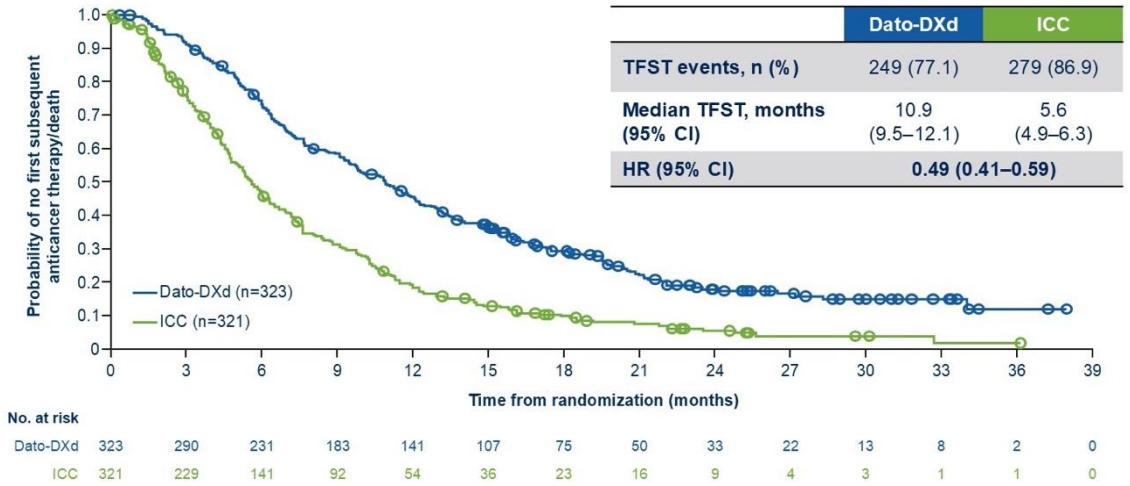
TROPION-Breast02: TFST, PFS2, and TSST

TFST

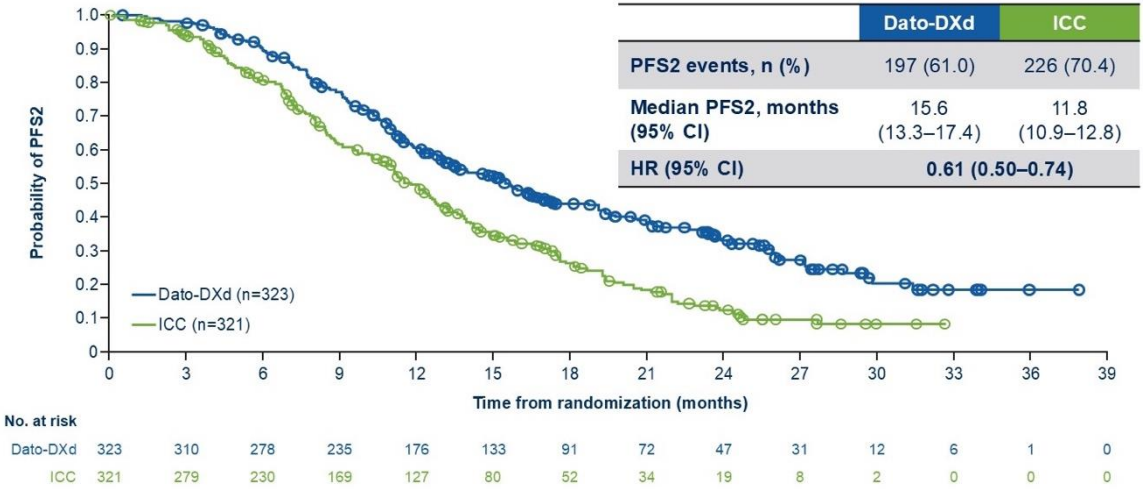


	Dato-DXd	ICC
TFST events, n (%)	249 (77.1)	279 (86.9)
Median TFST, months (95% CI)	10.9 (9.5–12.1)	5.6 (4.9–6.3)
HR (95% CI)	0.49 (0.41–0.59)	

No. at risk

Dato-DXd	323	290	231	183	141	107	75	50	33	22	13	8	2	0
ICC	321	229	141	92	54	36	23	16	9	4	3	1	1	0

PFS2

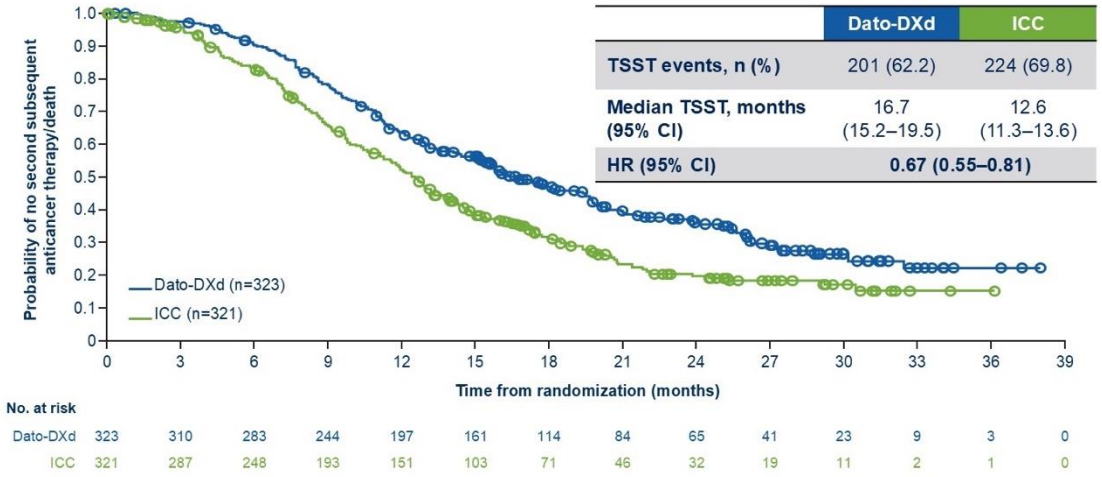


	Dato-DXd	ICC
PFS2 events, n (%)	197 (61.0)	226 (70.4)
Median PFS2, months (95% CI)	15.6 (13.3–17.4)	11.8 (10.9–12.8)
HR (95% CI)	0.61 (0.50–0.74)	

No. at risk

Dato-DXd	323	310	278	235	176	133	91	72	47	31	12	6	1	0
ICC	321	279	230	169	127	80	52	34	19	8	2	0	0	0

TSST

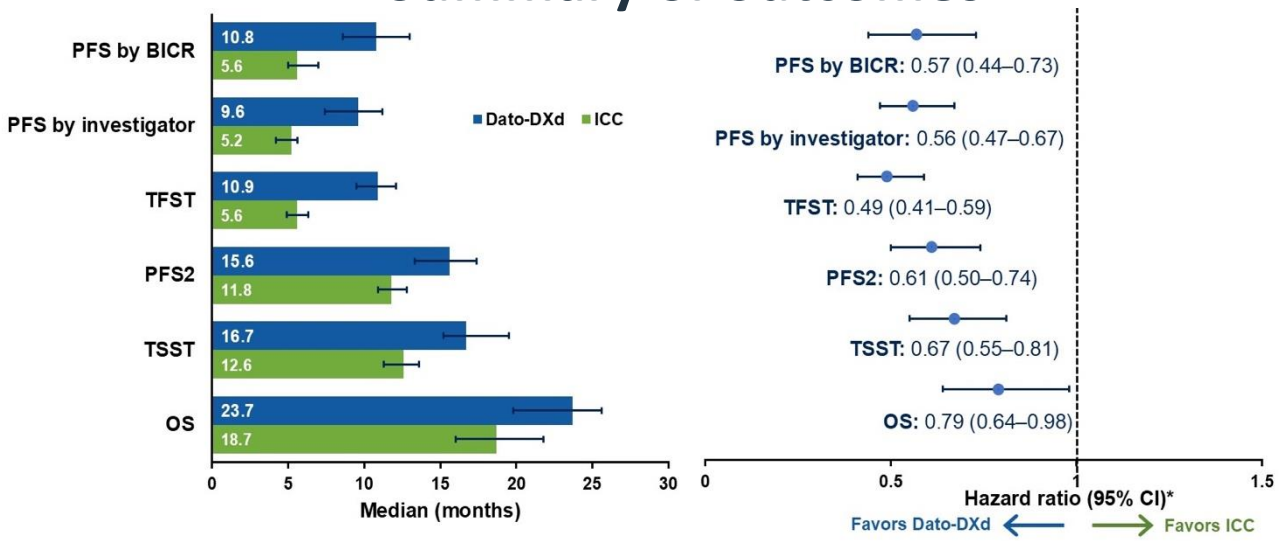


	Dato-DXd	ICC
TSST events, n (%)	201 (62.2)	224 (69.8)
Median TSST, months (95% CI)	16.7 (15.2–19.5)	12.6 (11.3–13.6)
HR (95% CI)	0.67 (0.55–0.81)	

No. at risk

Dato-DXd	323	310	283	244	197	161	114	84	65	41	23	9	3	0
ICC	321	287	248	193	151	103	71	46	32	19	11	2	1	0

Summary of outcomes



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TROPION-Breast02: Subsequent ADC therapy

Subsequent therapy (in any treatment line), n (%)	Patients off study treatment at data cutoff	
	Dato-DXd n=278	ICC n=313
Any subsequent therapy*	210 (76)	232 (74)
Any ADC†	44 (21)	95 (41)
Sacituzumab govitecan	33 (16)	76 (33)
Sacituzumab tirumotecan	0	1 (<1)
Trastuzumab deruxtecan	16 (8)	34 (15)

Cescon D, et al. ASCO 2026; Abstract 1002

Dr O'Shaughnessy Case Presentation #2

- 44 yo woman presented with T3N2M0 TNBC. Germline - no PV
- She received KN-522 regimen with clinical CR and at mastectomy had 2+ axillary LNs and no residual disease in her breast
- She underwent PMRT and adjuvant pembrolizumab and 6 mos of capecitabine therapy
- 1 year later she presented with mediastinal LNs and no other disease on PET CT
- Transbronchial biopsy showed PDL1- TNBC
- She was treated with datopotamab and had CR on repeat PET after 4 cycles
- She developed grade 2 stomatitis in spite of steroid mouth rinse treated with dose reduction
- After 6 cycles she received proton radiation to mediastinal LNs and then resumed reduced-dose datopotamab – monitoring blood ctDNA

PANKU-Breast02 Study Design

A multicenter, randomized, open-label, phase III study conducted at 81 study centers across China.

Key eligibility criteria:

- Unresectable locally advanced or metastatic TNBC
- Progressed after 1–2 prior lines of systemic therapy for advanced disease—including prior taxanes
- Measurable lesion per RECIST v1.1
- ECOG PS 0-1

Treatment until
Disease progression per RECIST v1.1 or intolerable toxicity

R 1:1
N=406

Iza-bren
2.5 mg/kg D1D8 Q3W

Chemotherapy
- Eribulin, D1D8 Q3W
- Capecitabine, BID, Q3W
- Gemcitabine, D1D8 Q3W
- Vinorelbine, D1D8 Q3W

Stratified by
- Previous lines of chemotherapy (1 line vs 2 lines)
- Prior anti-PD(L)-1 (yes vs no)
- HER2 expression (IHC 0 vs IHC 1+/2+ ISH-)

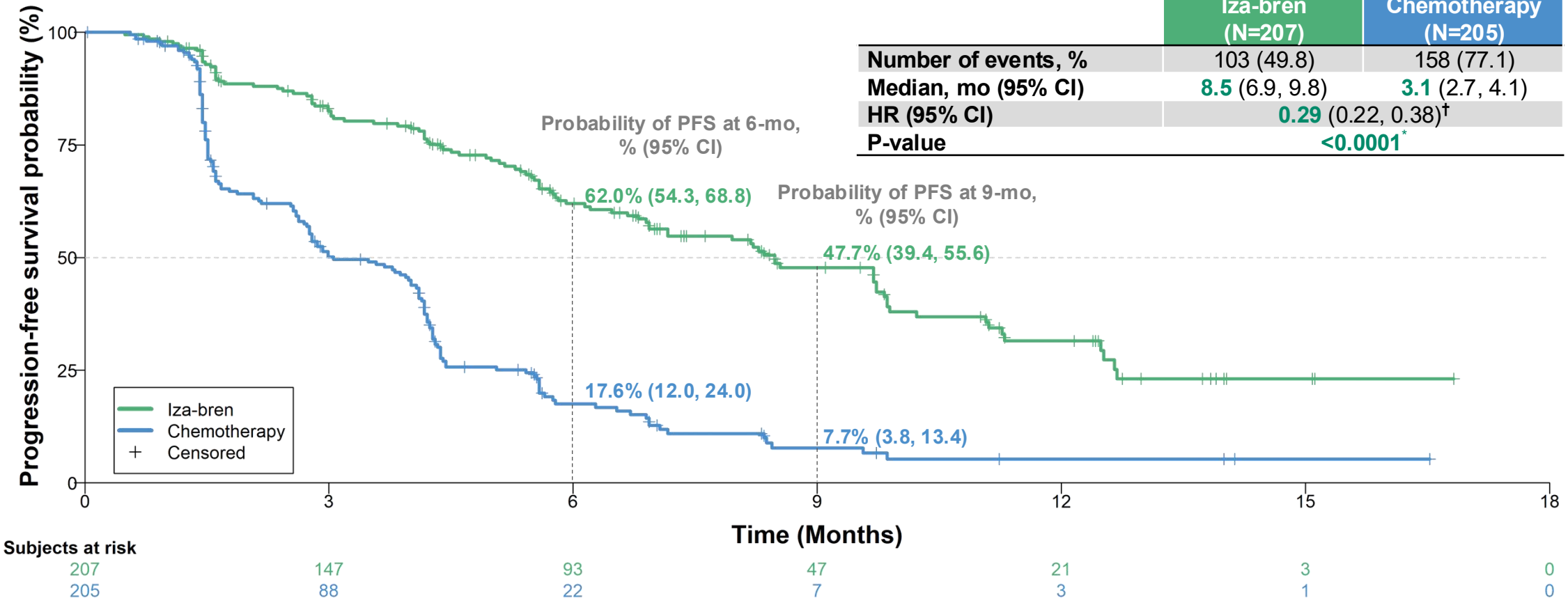
Dual primary endpoints
PFS (BICR) & OS
H_{PFS} α=0.025 → H_{OS} α=0

Secondary endpoints
ORR (BICR)
PFS (INV)
DCR, DoR, Safety, PK, Immunogenicity

Note: The planned enrollment was 406 subjects. Iza-bren was dosed with 10% compensation per protocol; eribulin 1.4 mg/m^2 on days 1 and 8 Q3W; capecitabine 1000-1250 mg/m^2, BID from days 1 to 14 Q3W; gemcitabine 1000 mg/m^2 on days 1 and 8 Q3W; vinorelbine 25 mg/m^2 on days 1 and 8 Q3W.

ECOG PS, Eastern Cooperative Oncology Group performance status; **Q3W**, every 3 weeks; **D**, day; **BICR**, blinded independent central review; **INV**, investigator assessed; **PFS**, progression-free survival; **OS**, overall survival; **ORR**, objective response rate (confirmed); **PK**, pharmacokinetics; **DCR**, disease control rate; **DoR**, duration of response.

PFS (BICR): Dual Primary Endpoint



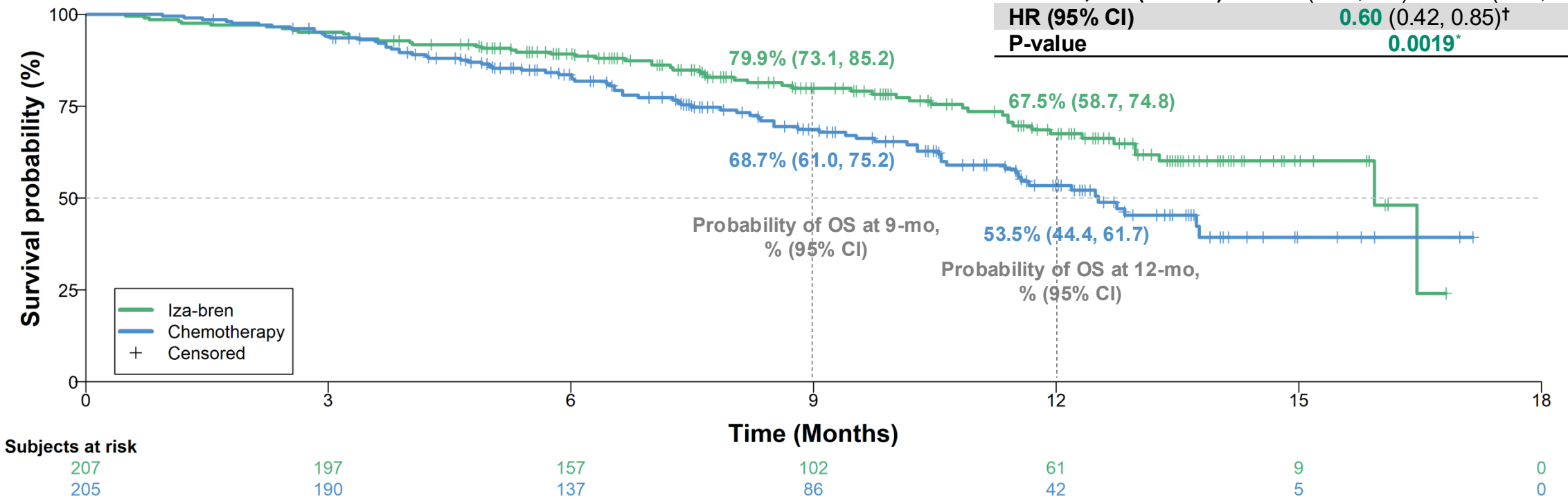
	Iza-bren (N=207)	Chemotherapy (N=205)
Number of events, %	103 (49.8)	158 (77.1)
Median, mo (95% CI)	**8.5** (6.9, 9.8)	**3.1** (2.7, 4.1)
HR (95% CI)	**0.29** (0.22, 0.38)†	
P-value	**<0.0001***	

Iza-bren showed statistically significant and clinically meaningful improvement in PFS vs chemotherapy (median Δ 5.4 mo).

PFS (BICR) was evaluated in the mITT population. The median duration of follow-up for PFS was 8.5 months.
Similar results were observed for PFS (BICR) in the ITT population, with 103 events in the iza-bren arm and 158 events in the chemotherapy arm. The hazard ratio (95% CI) was 0.29 (0.22,0.38).
†Based on a stratified Cox regression model. *One-sided, based on a stratified log-rank test.

OS: Dual Primary Endpoint

	Iza-bren (N=207)	Chemotherapy (N=205)
Number of events, %	56 (27.1)	77 (37.6)
Median, mo (95% CI)	**15.9** (13.3, NR)	**12.5** (11.4, NR)
HR (95% CI)	**0.60** (0.42, 0.85)†	
P-value	**0.0019***	



Subjects at risk

207	197	157	102	61	9	0
205	190	137	86	42	5	0

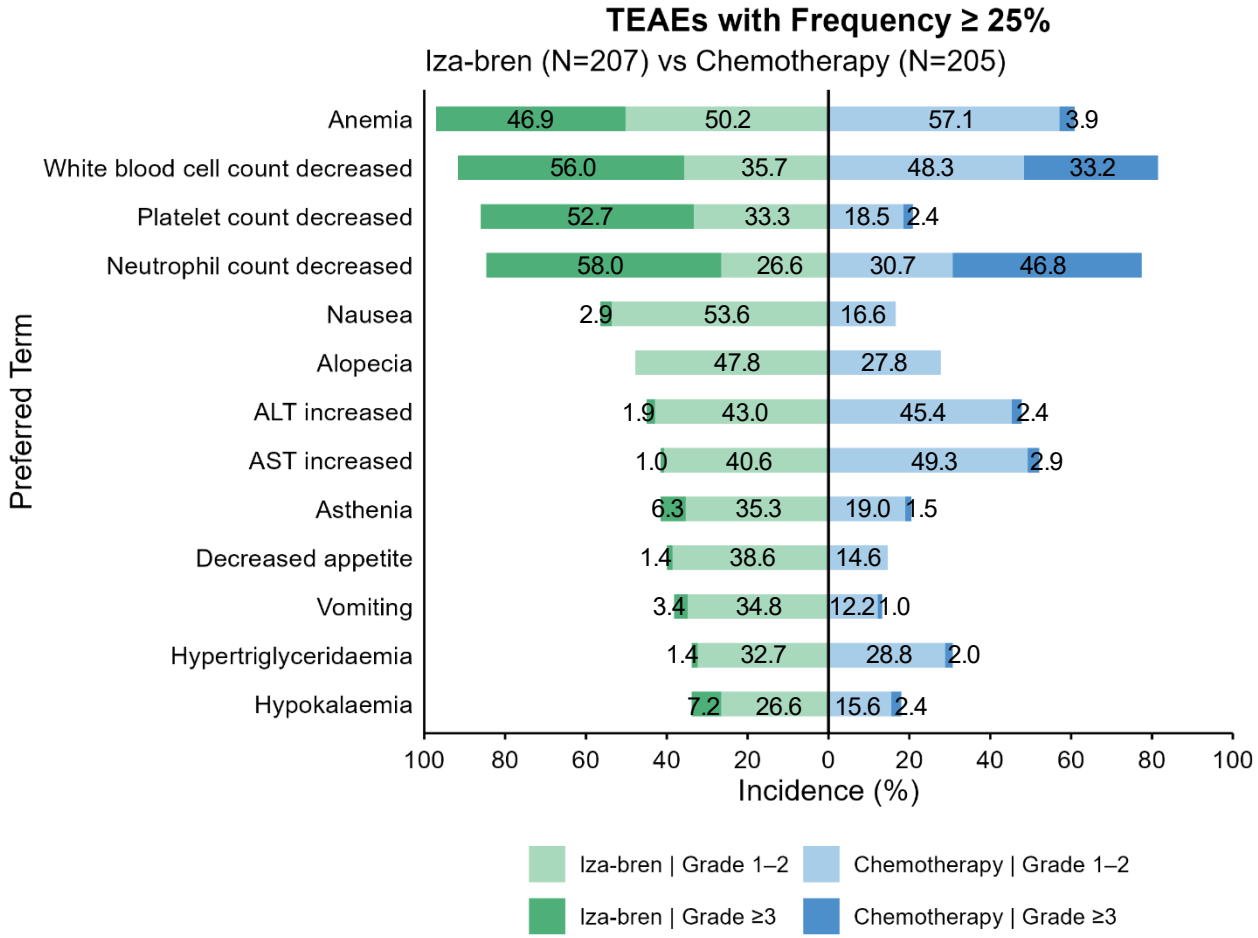
Iza-bren showed statistically significant and clinically meaningful improvement in OS vs chemotherapy (median Δ 3.4 mo) at pre-specified interim analysis.

OS was evaluated in the mITT population, with a median follow-up duration of 11.0 months. The pre-specified interim analysis was planned upon the observation of 255 BICR-confirmed PFS events, with approximately 175 OS events (70% information fraction) expected at the same time. At the analysis, the actual information fraction was 53.2%. **A P-value of 0.0021 was required for interim analysis superiority.**

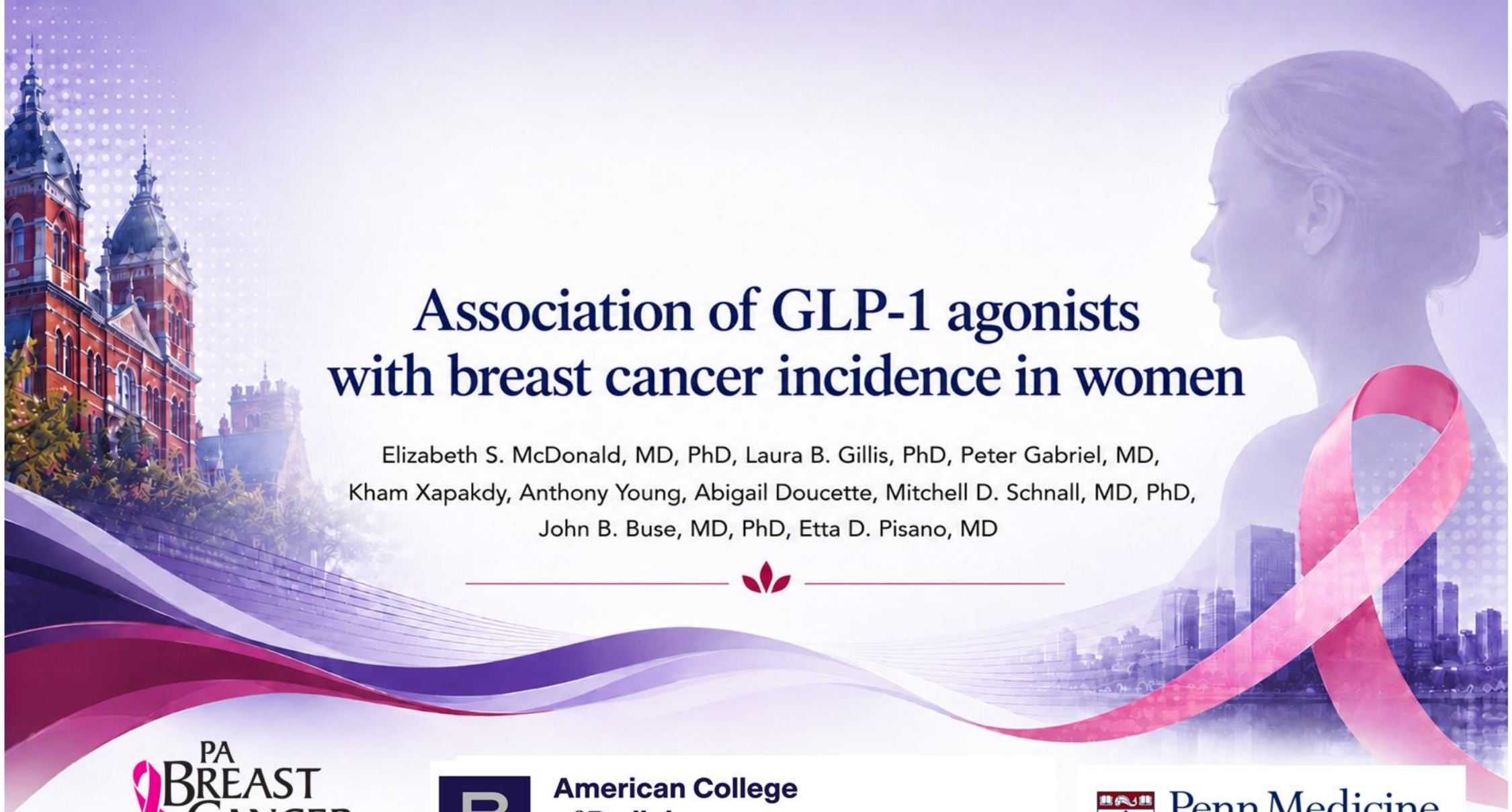
Similar results were observed for OS in the ITT population, with 56 events in the iza-bren arm and 77 events in the chemotherapy arm. The hazard ratio (95% CI) was 0.60 (0.42, 0.85).

†Based on a stratified Cox regression model. *One-sided, based on a stratified log-rank test.

TEAEs in >25% of Patients



- The most frequent Grade ≥3 TEAEs in the iza-bren arm were hematologic and were effectively managed by standard supportive care.
- In the iza-bren arm, median time to resolution of Grade 3 or 4 neutropenia was 4 days. Most patients had only 1 episode. G-CSF was not mandatory in this study.
- Febrile neutropenia occurred in 5.3% (n=11) of patients in the iza-bren arm vs. 0.5% in the control arm. Grade ≥ 3 infection rates were 6.8% in the iza-bren arm vs. 5.4% in the control arm.
- Per investigator's assessment, all-grade ILD were reported in 3 (1.4%) patients in the iza-bren arm, including 1 case of Grade 1 and 2 cases of Grade 2.
- Per independent ILD adjudication committee, only 1 (0.5%) case of Grade 2 ILD occurred in the iza-bren arm.
- No new safety signals were observed.



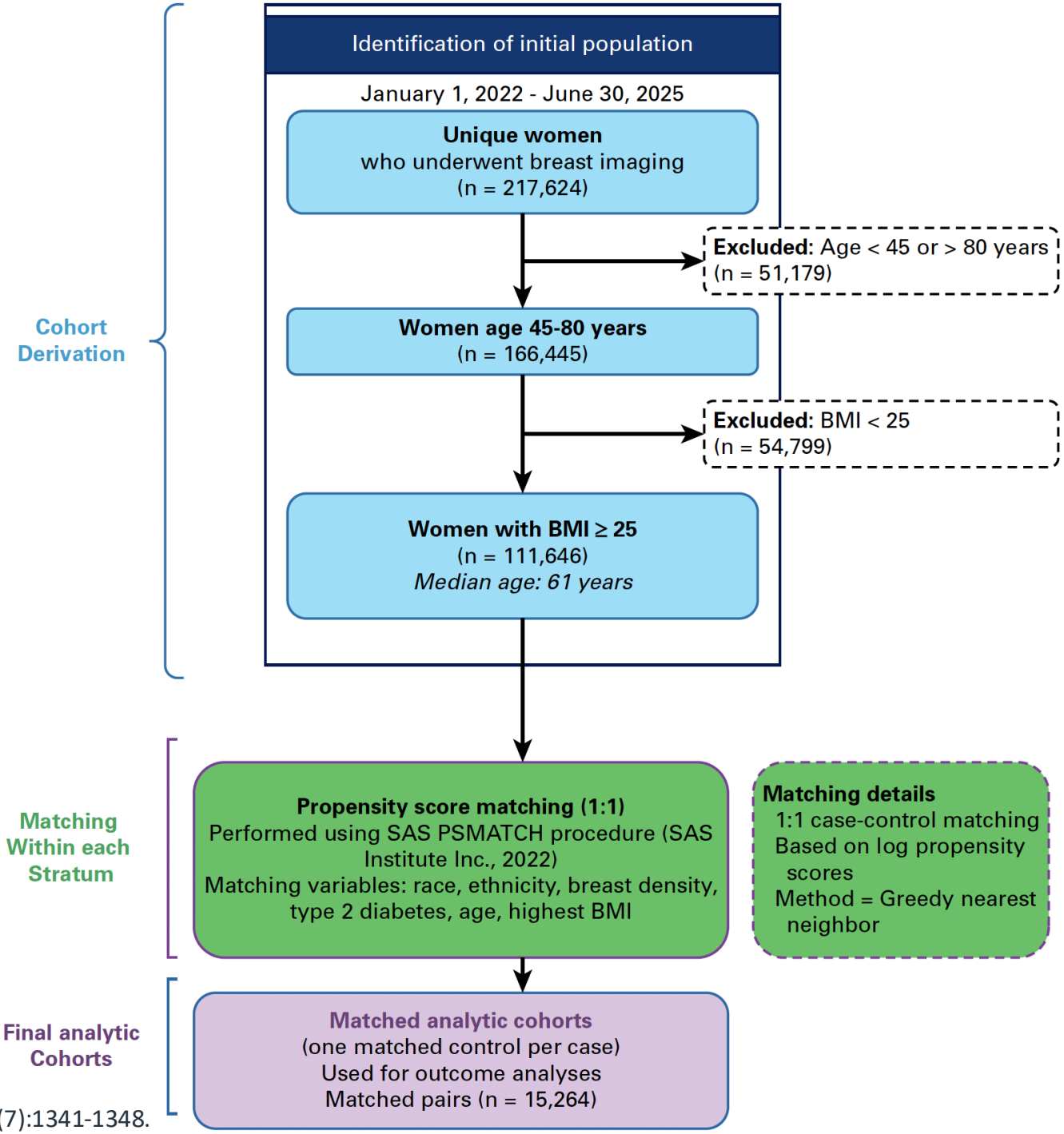
Association of GLP-1 agonists with breast cancer incidence in women

Elizabeth S. McDonald, MD, PhD, Laura B. Gillis, PhD, Peter Gabriel, MD,
Kham Xapakdy, Anthony Young, Abigail Doucette, Mitchell D. Schnall, MD, PhD,
John B. Buse, MD, PhD, Etta D. Pisano, MD

PA Breast Cancer Coalition

American College of Radiology™
Center for Research and Innovation

Penn Medicine
Abramson Cancer Center



McDonald E et al. JCO Oncol Pract. 2026 Jul;22(7):1341-1348.

Absolute Risk Reduction (ARR) in Breast Cancer Within Matched Dataset (N = 30,528)

Purpose: To quantify the absolute reduction in the risk of breast cancer associated with prior GLP-1 receptor agonist exposure.

Measure	Estimate	95% Wald CI
No GLP-1 Risk	2.31%	(2.07%, 2.55%)
With GLP-1 Risk	1.62%	(1.42%, 1.82%)
Absolute Risk Reduction (ARR)	**0.69%**	**(0.38%, 1.01%)**

Women with prior GLP-1 receptor agonist exposure had an absolute reduction of 0.69% in the risk of breast cancer compared with women without exposure.

Conclusion: GLP-1 receptor agonist exposure is associated with an absolute reduction in breast cancer risk in this matched cohort.

McDonald E et al. ASCO 2026; Abstract 10506

KEY TAKEAWAYS TNBC. ASCO 2026

SG +/- pembro is more effective in prolonging PFS1 and PFS2 as 1L vs 2L Rx

Dato-DXd prolongs PFS1 and PFS2 and OS (no X-over to 2L Dato-DXd)

SG +/- pembro is more effective than chemotherapy +/- pembro regardless of TROP2 and HER2 expression and tBRCA status

Iza-Bren has impressive activity vs SOC chemotherapy in unselected, pretreated mTNBC with myelosuppression as main toxicity – has moved in 1L mTNBC trial

Preop pembrolizumab with chemotherapy improves OS in TNBC

GLP1 RAs may decrease breast cancer incidence (and recurrence)

Dr O’Shaughnessy Case Presentation #3

- 61 yo woman presented with a 6cm N+ grade 3 IDC
- PET CT showed axillary and subpectoral LNs and no metastases
- ER 20% PR- HER2 0 with Ki-67 80%
- Blueprint showed basal breast cancer
- She was treated with preop KN-522 with excellent clinical response
- Mastectomy showed pCR in breast and LNs
- She received PMRT and adjuvant pembrolizumab
- Repeat ER IHC at reference lab on biopsy showed 1-10% ER+
- She was not treated with adjuvant endocrine therapy and remains NED

Join Us In Person or Virtually

Integrating New Advances into Community Oncology Practice

A Multitumor Symposium Hosted in Conjunction with the American Oncology Network

Saturday, August 22, 2026

JW Marriott Nashville | Nashville, Tennessee

Chronic Lymphocytic Leukemia
9:05 AM – 9:55 AM CT

Gastroesophageal Cancers
9:55 AM – 10:45 AM CT

Gynecologic Cancers
11:00 AM – 11:50 AM CT

Diffuse Large B-Cell Lymphoma
12:40 PM – 1:30 PM CT

Lung Cancer
1:30 PM – 2:20 PM CT

Moderator
Stephen “Fred” Divers, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!

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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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Questions?

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