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

Oral SERDs for Breast Cancer

A CME/MOC-Accredited Live Webinar

Tuesday, March 31, 2026
5:00 PM – 6:00 PM ET

Faculty

Aditya Bardia, MD, MPH
Erica Mayer, MD, MPH, FASCO

Moderator

Neil Love, MD

RTP Year in Review 2026

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

Erica Mayer, MD, MPH, FASCO
Director of Breast Cancer Clinical Research
Breast Oncology Center
Dana-Farber Cancer Institute
Associate Professor of Medicine
Harvard Medical School
Boston, Massachusetts

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Commercial Support

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Dr Love — Disclosures

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Dr Bardia — Disclosures

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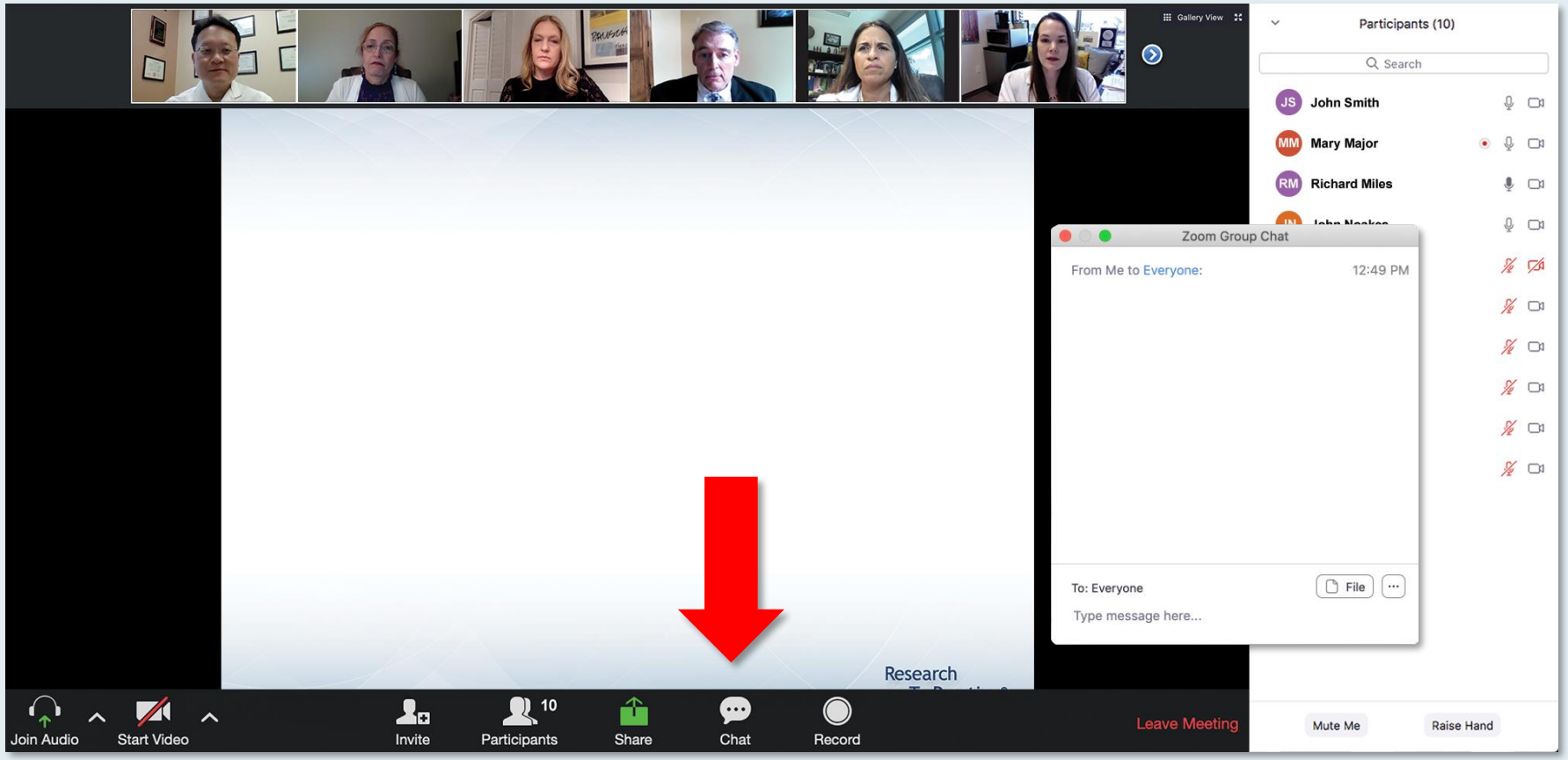
We Encourage Clinicians in Practice to Submit Questions



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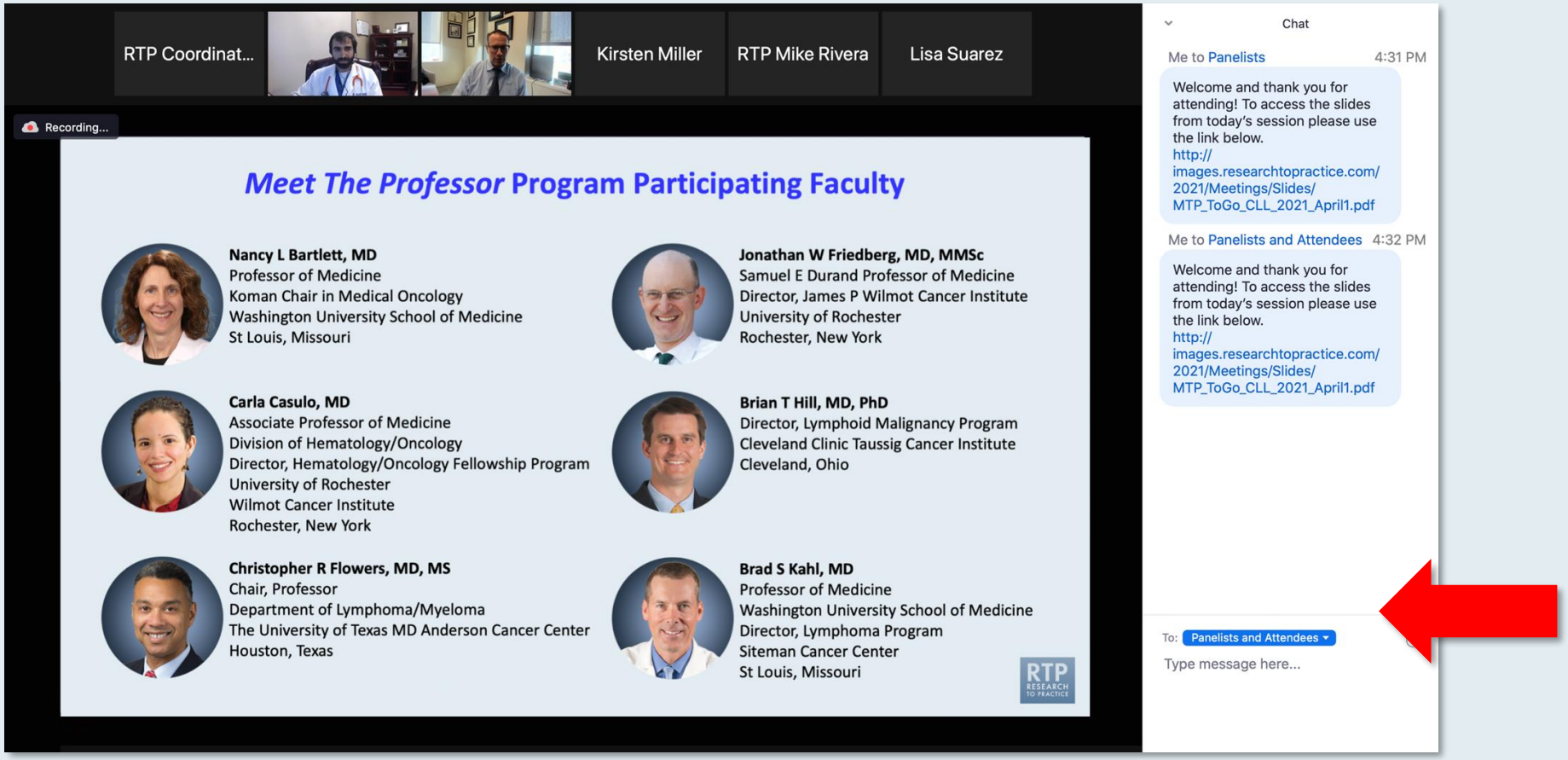

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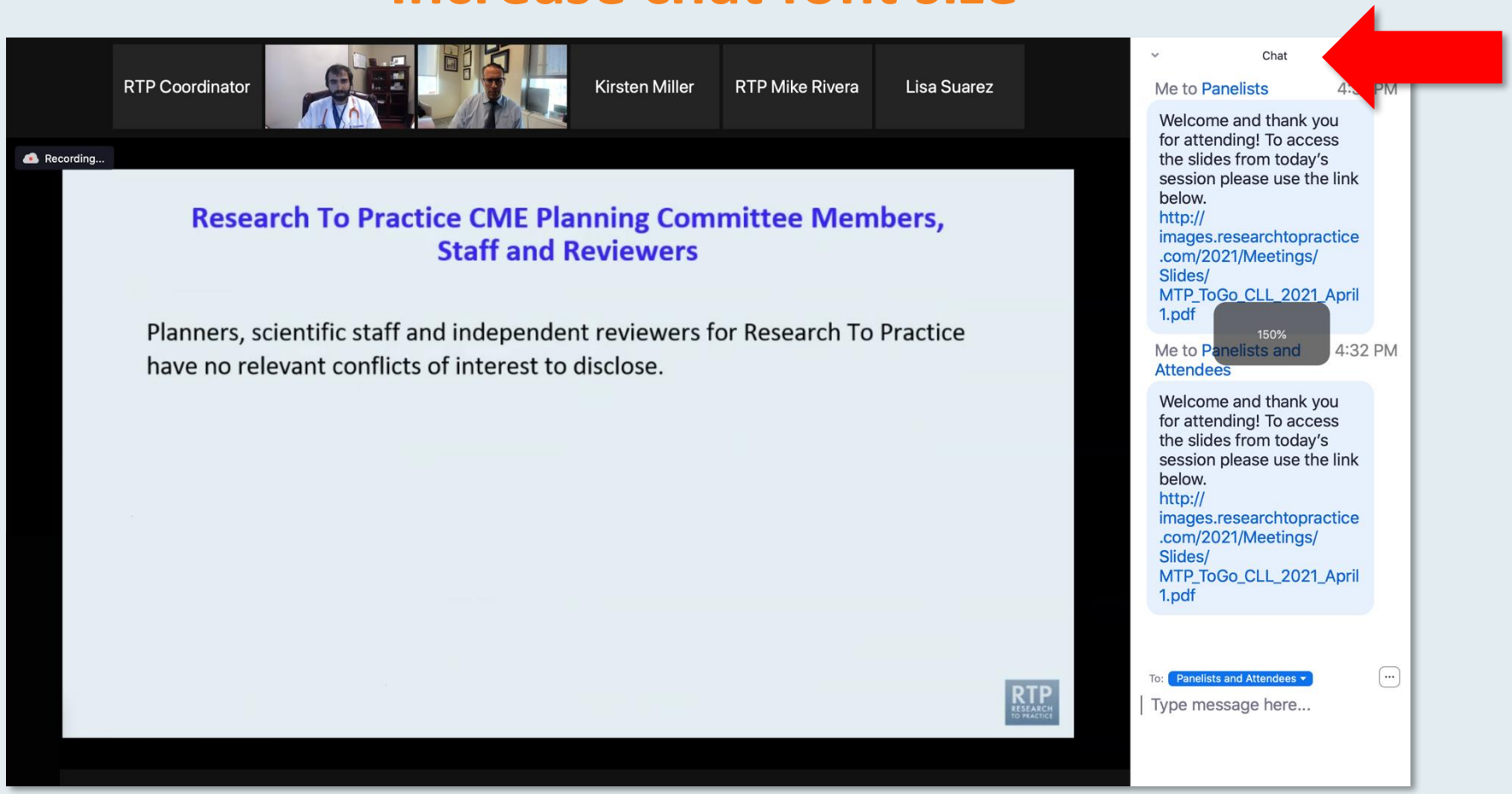

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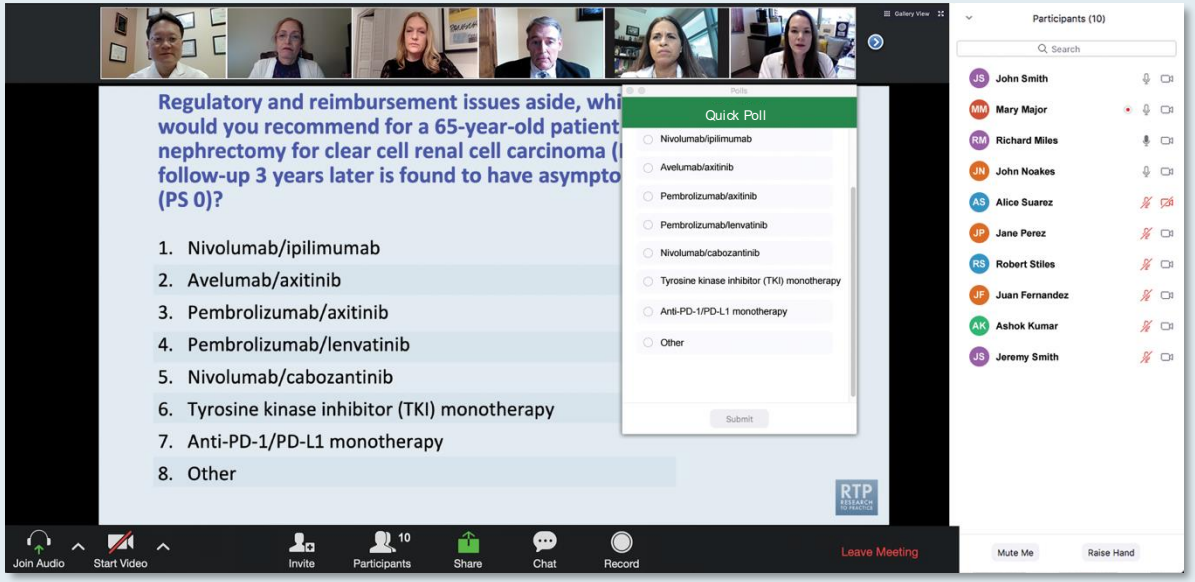

Breast Cancer — 5-Minute Journal Club Issue 2 with Lajos Pusztai, MD, DPhil, FASCO: Current and Future Role of Tumor-Informed Circulating Tumor DNA Assays

LAJOS PUSZTAI, MD, DPHIL, FASCO
YALE CANCER CENTER

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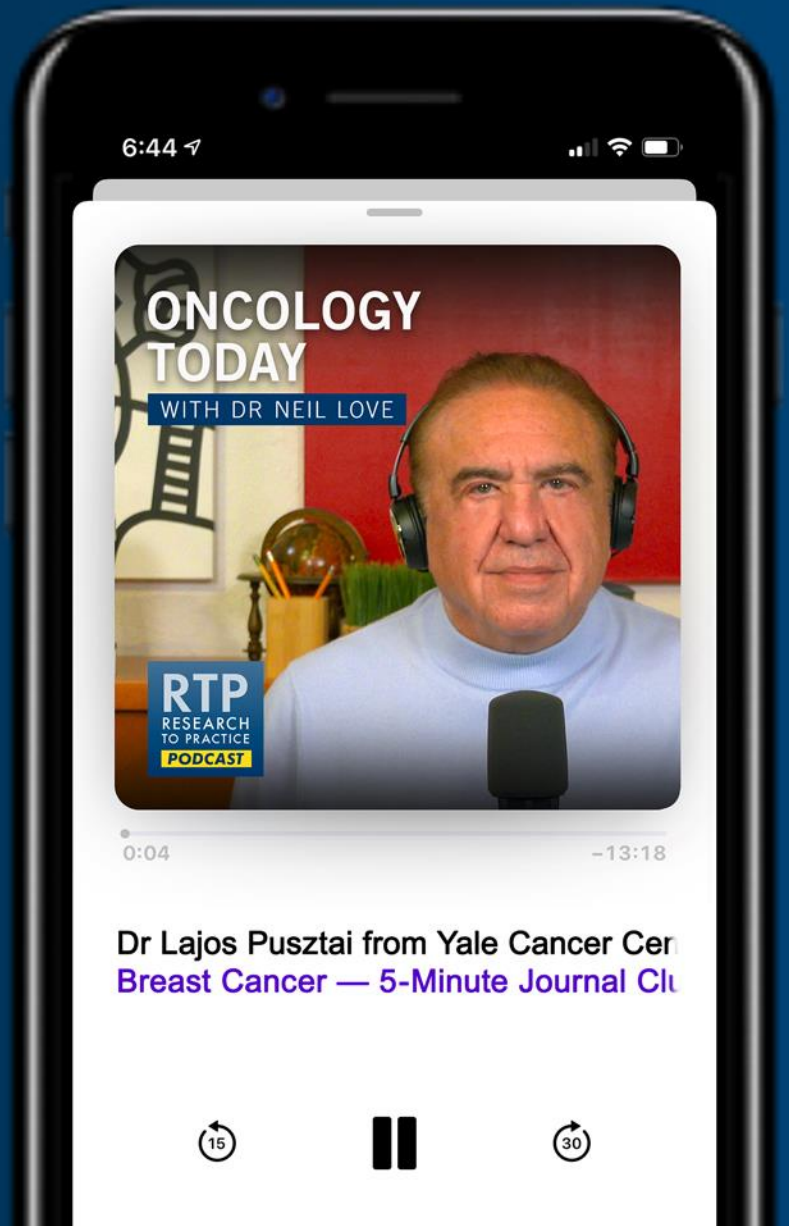

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Developed in Partnership with Florida Cancer Specialists & Research Institute

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

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Keynote Session: Diffuse Large B-Cell Lymphoma and Follicular Lymphoma

Manali Kamdar, MD, MBBS
Krish Patel, MD
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Year in Review:
Oral SERDs for Breast Cancer

INTRODUCTION: How SERDs work

MODULE 1: Second-line treatment for metastatic disease

MODULE 2: First-line therapy for metastatic disease

MODULE 3: Adjuvant therapy

MODULE 4: Toxicity, quality of life

MODULE 5: New Directions

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Thank you for joining us!

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

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

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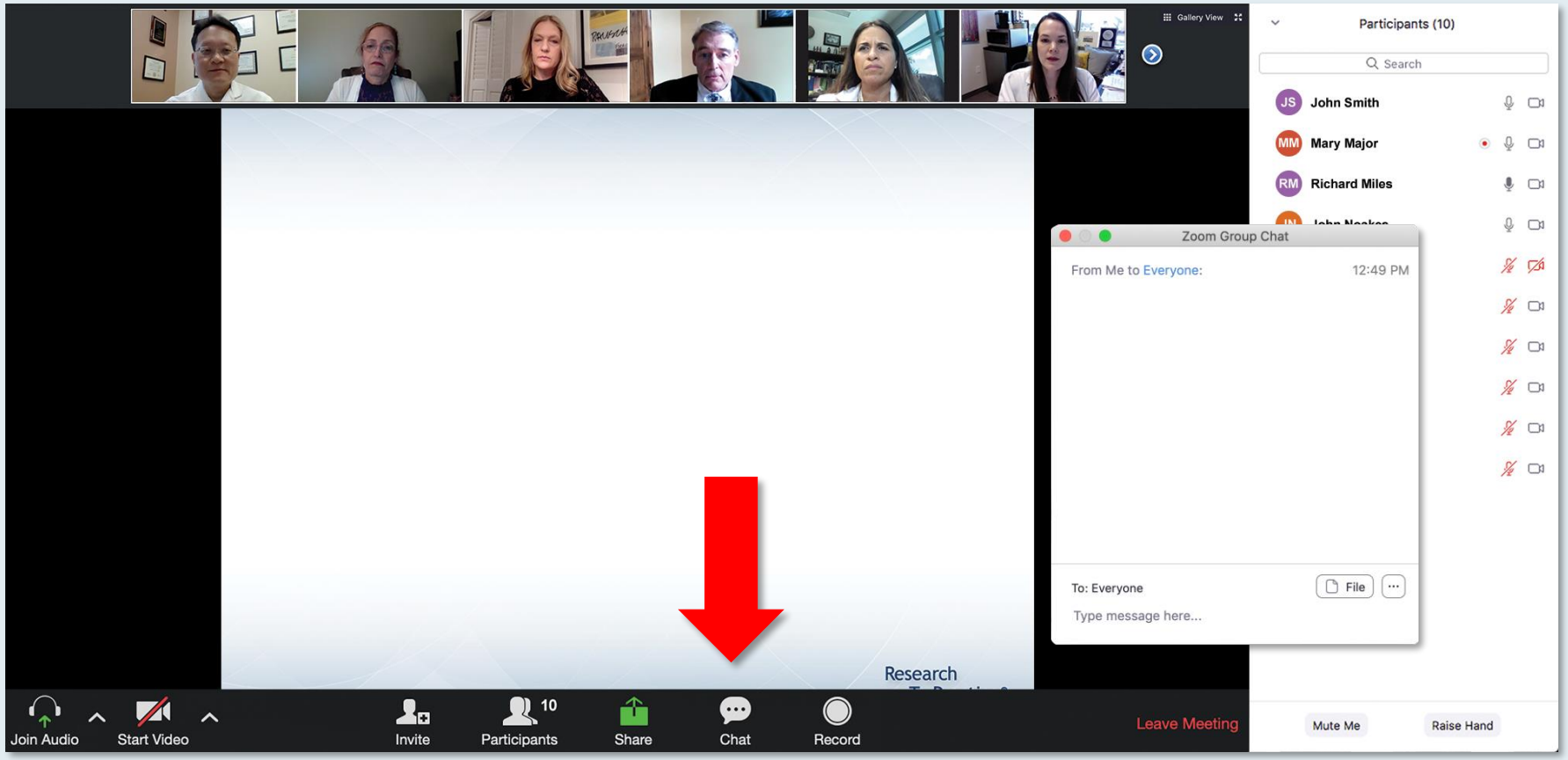

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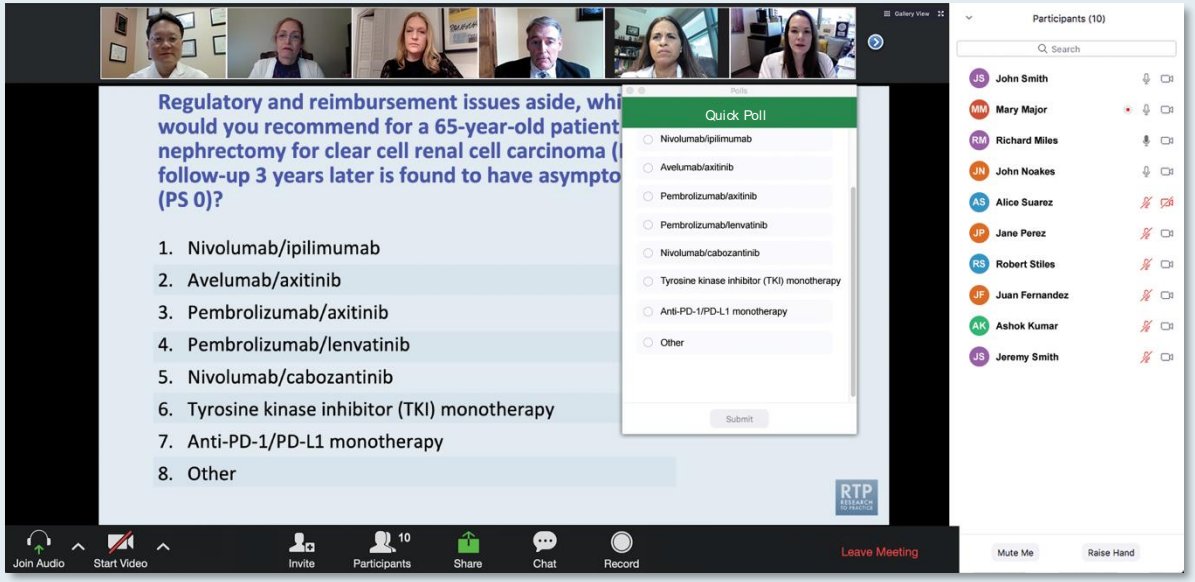

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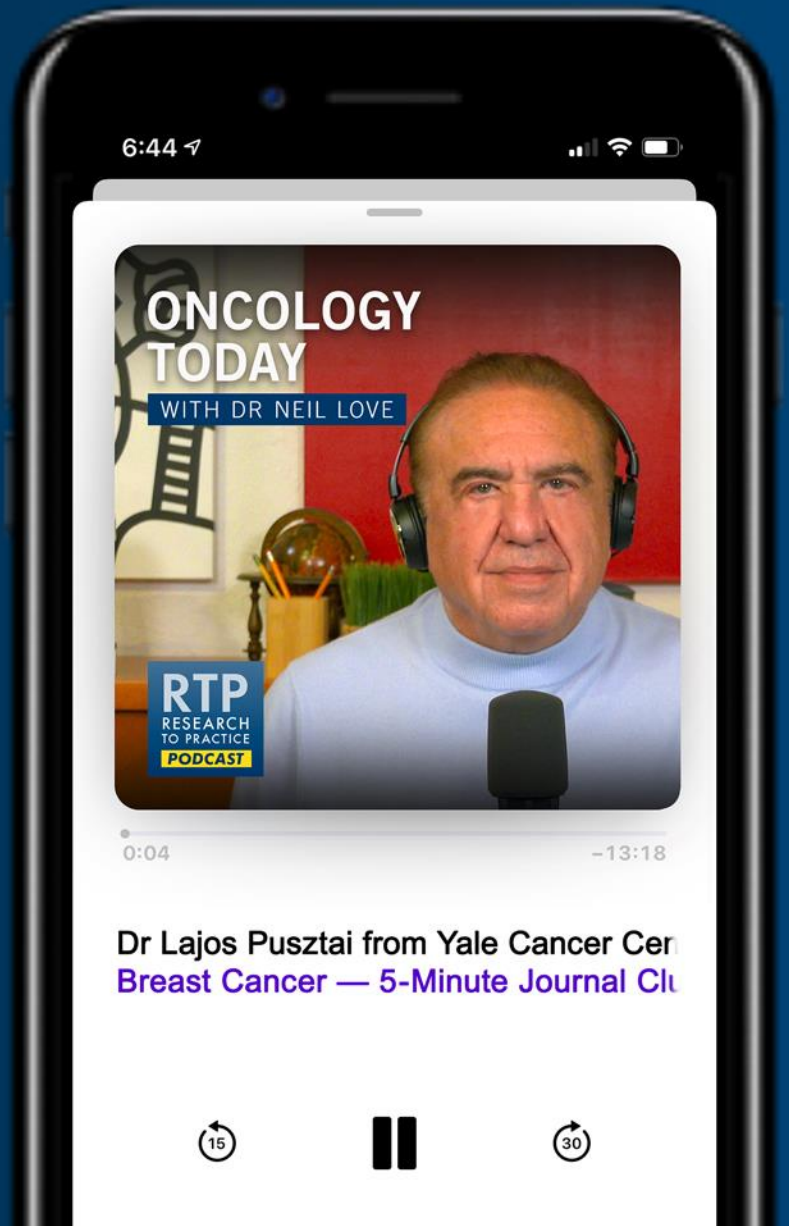

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2026

Future Directions in the Use of Oral SERDs for HR-Positive, HER2-Negative Breast Cancer

Erica L. Mayer MD, MPH

Division of Breast Oncology

Dana-Farber Cancer Institute
Boston, MA

Dana-Farber Cancer Institute | HARVARD MEDICAL SCHOOL

Year in Review: Appropriate Identification of Candidates for and Practical Implementation of Oral Selective Estrogen Receptor Degraders (SERDs) for Progressive HR-Positive, HER2-Negative Metastatic Breast Cancer (mBC)

Aditya Bardia, MD, MPH, FASCO

Director, Breast Oncology Program,
Assistant Chief (Translational Research), Hem-Onc
Director of Translational Research Integration,
UCLA Health Jonsson Comprehensive Cancer Center

@DrAdityaBardia

UCLA David Geffen School of Medicine

RTP Year in Review 2026

Key Datasets

Aditya Bardia, MD, MPH

- Basu GD et al. Characterization of **ESR1** alterations in patients with **breast and gynecologic cancers**. *Breast Cancer Res* 2026;28(1):40.
- Cabel L et al. Kinetics and determinants of **ESR1 mutation detection** in **metastatic breast cancer**. *Ann Oncol* 2026;37(3):329-40.
- Rugo HS et al. **Real-world outcomes** of **elacestrant** in **ER+, HER2-, ESR1-mutant metastatic breast cancer**. *Clin Cancer Res* 2026;32(1):179-87.
- Lloyd M et al. **Clinical and genomic factors** associated with **elacestrant outcomes** in **ESR1-mutant metastatic breast cancer**. *Clin Cancer Res* 2026;32(1):169-78.
- Jhaveri KL et al. **Imlunestrant** with or without abemaciclib in **advanced breast cancer**: **Updated efficacy** results from the **phase III EMBER-3** trial. *Ann Oncol* 2025;[Online ahead of print].
- Manich CS et al. **Imlunestrant (Imlu)** with or without abemaciclib (Abema) in **advanced breast cancer (ABC)**: A **subgroup analysis** in **CDK4/6 inhibitor (CDK4/6i)-pretreated** patients (pts) from **EMBER-3**. ESMO Breast 2025;Abstract 297O.

Key Datasets

Aditya Bardia, MD, MPH (continued)

- Neven P et al. **Imlunestrant** with or without abemaciclib as **first- and second-line therapy** in **advanced breast cancer (ABC)**: A **subgroup analysis** from the **EMBER-3** trial. ESMO Breast 2025;Abstract 306P.
- O'Shaughnessy J et al. **Imlunestrant** with or without abemaciclib in **advanced breast cancer (ABC): Safety analyses** from the **phase III EMBER-3** trial. ASCO 2025;Abstract 1060.

Key Datasets

Erica Mayer, MD, MPH, FASCO

- Bidard FC et al. **Updated results** and an **exploratory analysis** of **ESR1m circulating tumor DNA (ctDNA) dynamics** from **SERENA-6**, a **phase 3** trial of **camizestrant (CAMI)** + CDK4/6 inhibitor (CDK4/6i) for emergent **ESR1 mutations (ESR1m)** during **first-line (1L)** endocrine-based therapy and ahead of disease progression in patients (pts) with **HR+/HER2- advanced breast cancer (ABC)**. San Antonio Breast Cancer Symposium 2025;Abstract RF7-03.
- Mayer E et al. **Giredestrant (GIRE)**, an **oral selective oestrogen receptor (ER) antagonist and degrader**, + everolimus (E) in patients (pts) with **ER-positive, HER2-negative advanced breast cancer (ER+, HER2– aBC) previously treated with a CDK4/6 inhibitor (i): Primary results** of the **phase III evERA BC** trial. ESMO 2025;Abstract LBA16.
- Rugo HS et al. Clinical and biomarker **subgroup analysis** of **evERA Breast Cancer:** A **phase III** trial of **giredestrant** plus everolimus in patients with **estrogen receptor-positive, HER2-negative advanced breast cancer previously treated with a CDK4/6 inhibitor**. San Antonio Breast Cancer Symposium 2025;Abstract GS3-09.

Key Datasets

Erica Mayer, MD, MPH, FASCO (continued)

- Rugo H et al. **Elacestrant** in combination with everolimus or abemaciclib in patients with **ER+/HER2- locally advanced or metastatic breast cancer (mBC): Phase 2** results from **ELEVATE**, an open-label, umbrella study. San Antonio Breast Cancer Symposium 2025;Abstract RF7-01.
- Baird RD et al. **Camizestrant** in combination with three globally approved CDK4/6 inhibitors in women with **ER+, HER2- advanced breast cancer: Results** from **SERENA-1**. *Clin Cancer Res* 2025;31(20):4244-54.
- Bardia A et al. **Giredestrant** vs standard-of-care endocrine therapy as adjuvant treatment for patients with **estrogen receptor-positive, HER2-negative early breast cancer: Results** from the global **phase III lidERA** Breast Cancer trial. San Antonio Breast Cancer Symposium 2025;Abstract GS1-10.
- Vidal M et al. **Elacestrant** in women with **estrogen receptor-positive and HER2-negative early breast cancer: Results** from the preoperative **window-of-opportunity ELIPSE** trial. *Clin Cancer Res* 2025;31(7):1223-32.
- Robertson JFR et al. **Pharmacodynamics** of **camizestrant** treatment in **postmenopausal women with estrogen receptor-positive, human epidermal growth factor receptor 2-negative primary breast cancer: Results** from the randomized, **presurgical SERENA-3** study. *J Clin Oncol* 2026;[Online ahead of print].

Year in Review:
Oral SERDs for Breast Cancer

INTRODUCTION: How SERDs work

MODULE 1: Second-line treatment for metastatic disease

MODULE 2: First-line therapy for metastatic disease

MODULE 3: Adjuvant therapy

MODULE 4: Toxicity, quality of life

MODULE 5: New Directions

RTP Year in Review 2026

Year in Review:
Oral SERDs for Breast Cancer

INTRODUCTION: How SERDs work

- Memorable San Antonio moments: Dose-dense chemotherapy, ATAC, 21-gene RS, BCIRG 006, lidERA Breast Cancer
- Are SERDs the new osimertinib? Is ESR1 the new T790M?
- Impact of SERDs on ER/PR assays
- SERDs in premenopausal women
- Window of opportunity studies: Ki-67, ER/PR
- SERDs in endocrine therapy-naïve settings
- SERDs in endocrine therapy-resistant settings
- Press release: First-line treatment of mBC with giredestrant/CDK inhibitor

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

Part 3 of a 3-Part CME Satellite Symposium Series

Thursday, December 11, 2025

7:00 PM – 9:00 PM CT

Faculty

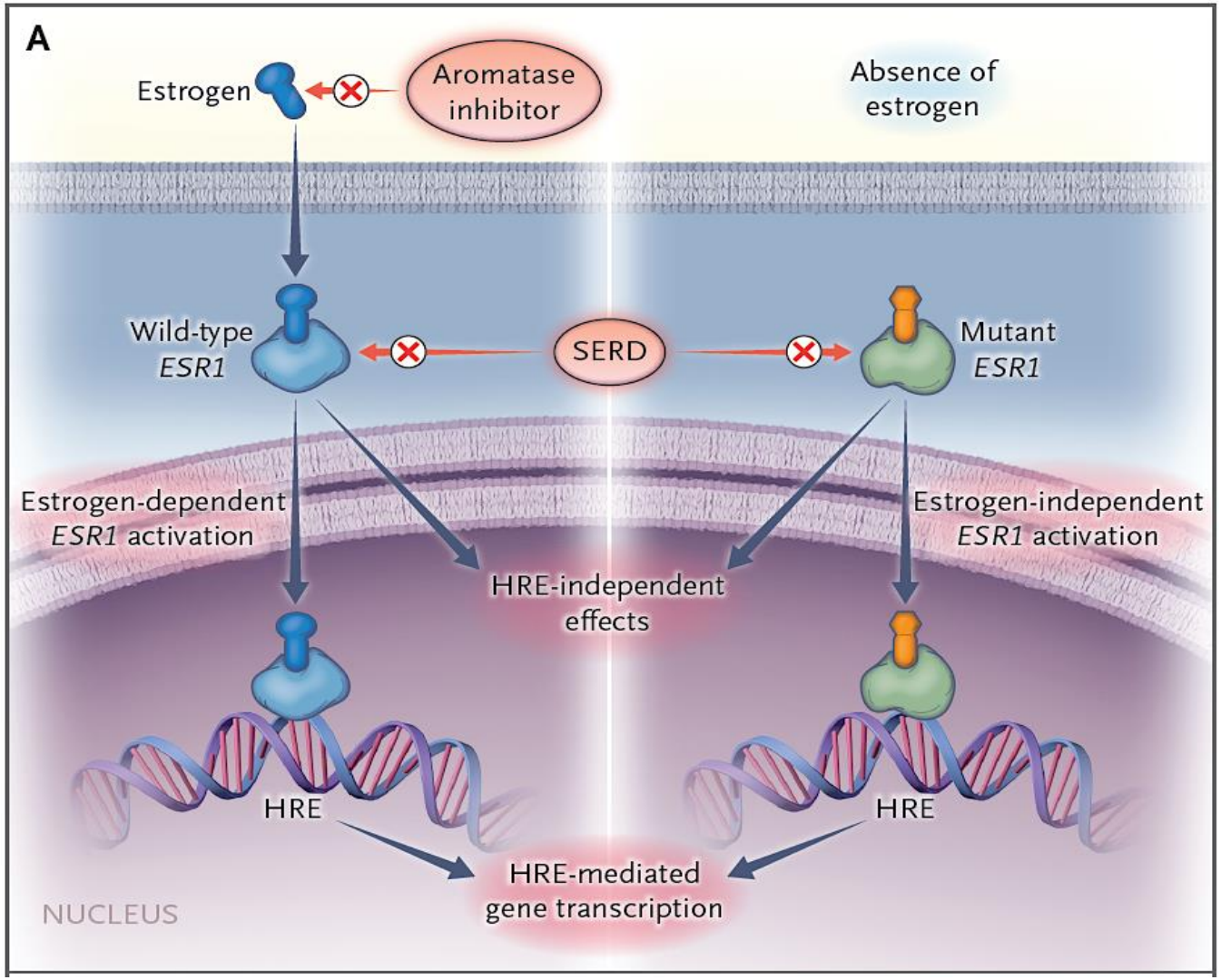
Angela DeMichele, MD, MSCE
Komal Jhaveri, MD, FACP, FASCO
Erica Mayer, MD, MPH, FASCO
Hope S Rugo, MD
Seth Wander, MD, PhD

Moderator

Neil Love, MD

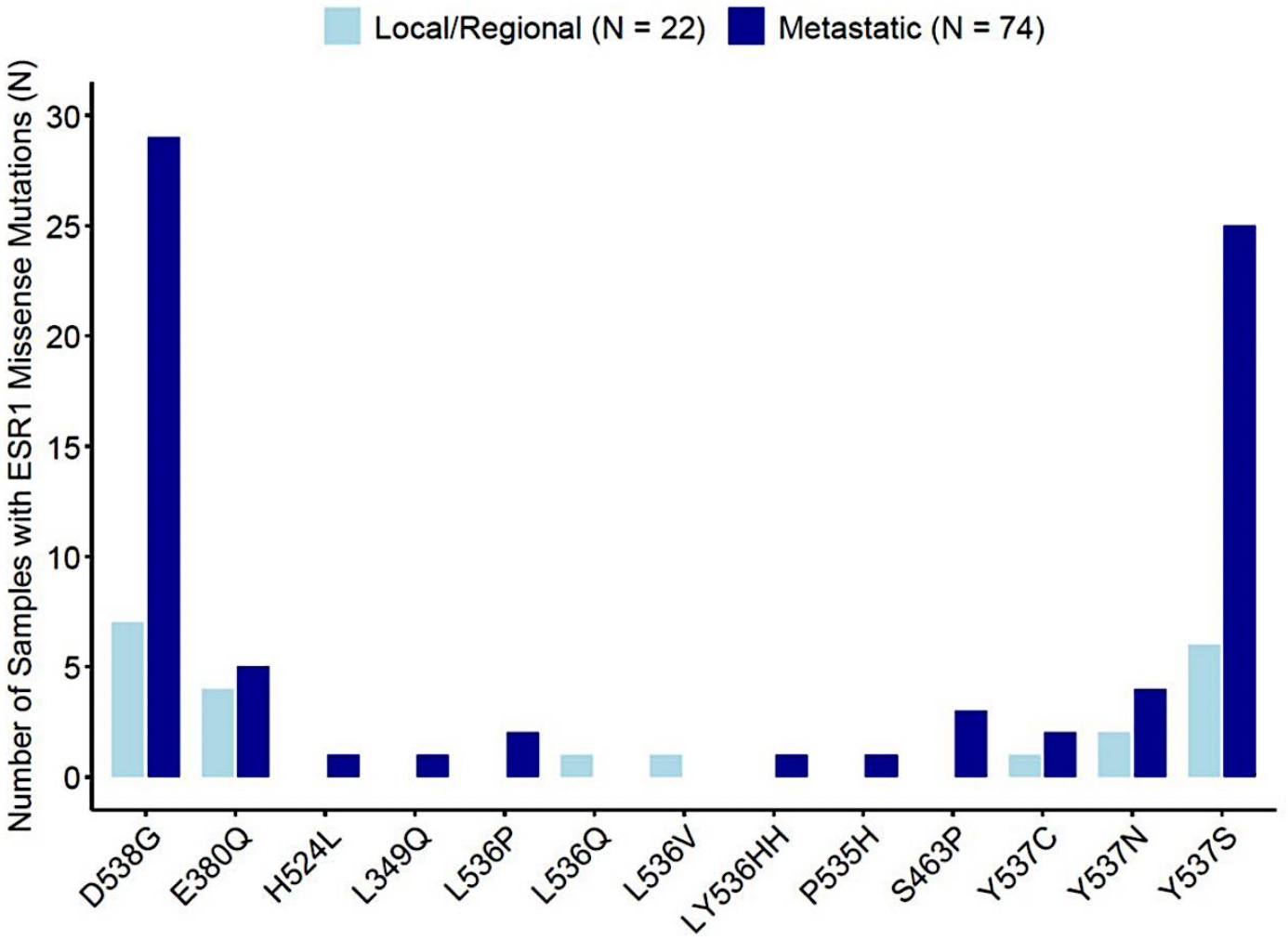
RTP RESEARCH TO PRACTICE

ESR1 (Acquired) Mutations: Resistance to AI



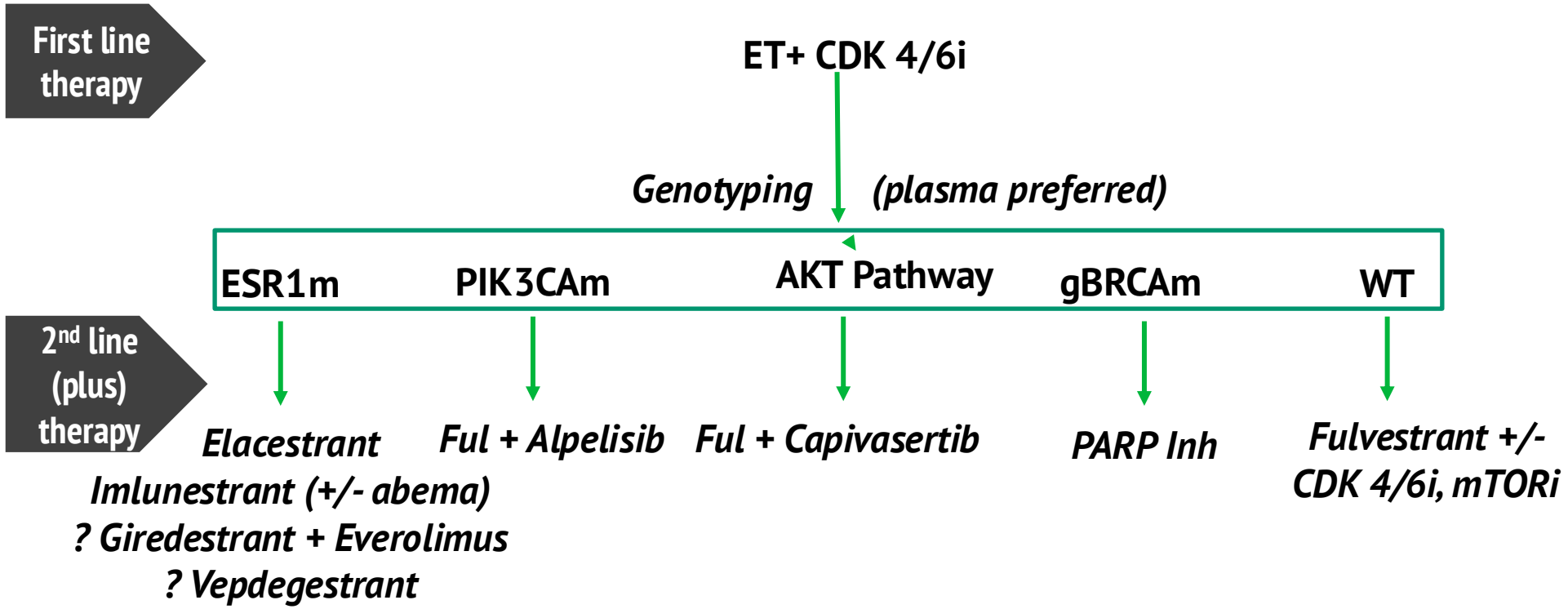
Bardia A, et al. *N Engl J Med*. 2018

ESR1 (Acquired) Mutations: Detection in Metastatic Setting



Basu et al. Breast Cancer Research 2026

Management of HR+/HER2- MBC: Treatment Algorithm



Courtesy of Aditya Bardia, MD, MPH

RESEARCH ARTICLE | OCTOBER 08 2024

A preoperative window-of-opportunity study of oral SERD, imlunestrant, in newly diagnosed ER-positive, HER2-negative early breast cancer: Results from EMBER-2 Study.

Patrick Neven; Nicole Stahl; Maria Vidal; Miguel Martín; Peter A. Kaufman; Nadia Harbeck; Kelly K. Hunt; Stacey Carter; Francois-Clement Bidard; Peter A. Fasching; Philippe Aftimos; Duncan Wheatley; Erika Hamilton; Rebecca Aft; Swati Kulkarni; Peter Schmid; Manali Bhave; Roohi Ismail-Khan; Claudia Karacsonyi; Shawn T. Estrem; Bastien Nguyen; Umut Ozbek; Eunice Yuen; Vanessa Rodrik-Outmezguine; Eva Ciruelos

Clin Cancer Res 2024;30(23):5304-13.

Elacestrant in Women with Estrogen Receptor–Positive and HER2-Negative Early Breast Cancer: Results from the Preoperative Window-of-Opportunity ELIPSE Trial

Maria Vidal[1,2,3,4], Claudette Falato[1,3,5], Tomás Pascual[1,2,3,4], Rodrigo Sanchez-Bayona[1,6], Montserrat Muñoz-Mateu[1,2,3,4], Isaac Cebrecos[2], Xavier Gonzalez-Farré[7], Tomás Cortadellas[8], Mireia Margelí Vila[1,9,10], Miguel A. Luna[9], Christian Siso[11], Kepa Amillano[12], Patricia Galván[3], Milana A. Bergamino[1,2,3,9], Juan M. Ferrero-Cafiero[1], Fernando Salvador[1], Alejandra Espinosa Guerrero[1], Laia Pare[1], Esther Sanfeliu[3,13], Aleix Prat[2,3,4], and Meritxell Bellet[1,11,10,14]

- Preoperative window of opportunity study with elacestrant
- Postmenopausal women (N=22), T1c-T2 N0 ER+ HER2- eBC with Ki67 ≥10%
- Received 4 weeks elacestrant prior to surgery
- Primary endpoint: complete cell cycle arrest (Ki67 ≤2.7%) at day 28

Vidal et al. CCR 2025

Original Reports | Breast Cancer

Pharmacodynamics of Camizestrant Treatment in Postmenopausal Women With Estrogen Receptor–Positive Human Epidermal Growth Factor Receptor 2–Negative Primary Breast Cancer: Results From the Randomized Presurgical SERENA-3 Study

John F.R. Robertson, MD[1]; Teimuraz Gogitidze, MD[2]; Zaza Katashvili, MD[3]; Juan Enrique Bargalló Rocha, MD[4]; Ekaterine Arkania, MD[5]; Iain Moppett, MD[6]; Kwok-Leung Cheung, MD[1]; Gia Nemsadze, MD[7]; Maxine Ajimi, PhD[8]; Teresa Klinowska, PhD[9]; Justin P.O. Lindemann, MBChB, MBA[8]; Alastair Mathewson, PhD[8]; Christopher J. Morrow, PhD[8]; Myria Nikolaou, PhD[8]; Maurizio Scaltriti, MD, PhD[10]; Andy Sykes, PhD[11]; and Giorgi Dzagnidze, MD, PhD[12]

DOI https://doi.org/10.1200/JCO-25-01548

- Preoperative window of opportunity study with camizestrant
- Randomized 132 postmenopausal women with T>1cm to camizestrant dose levels
- Patients received 5-7 days of camizestrant 75 mg, 150 mg, or 300 mg, or 75 mg, 150 mg for 12-15 days
- Primary endpoint: change in ER; Secondary endpoints: change in PR expression, Ki67

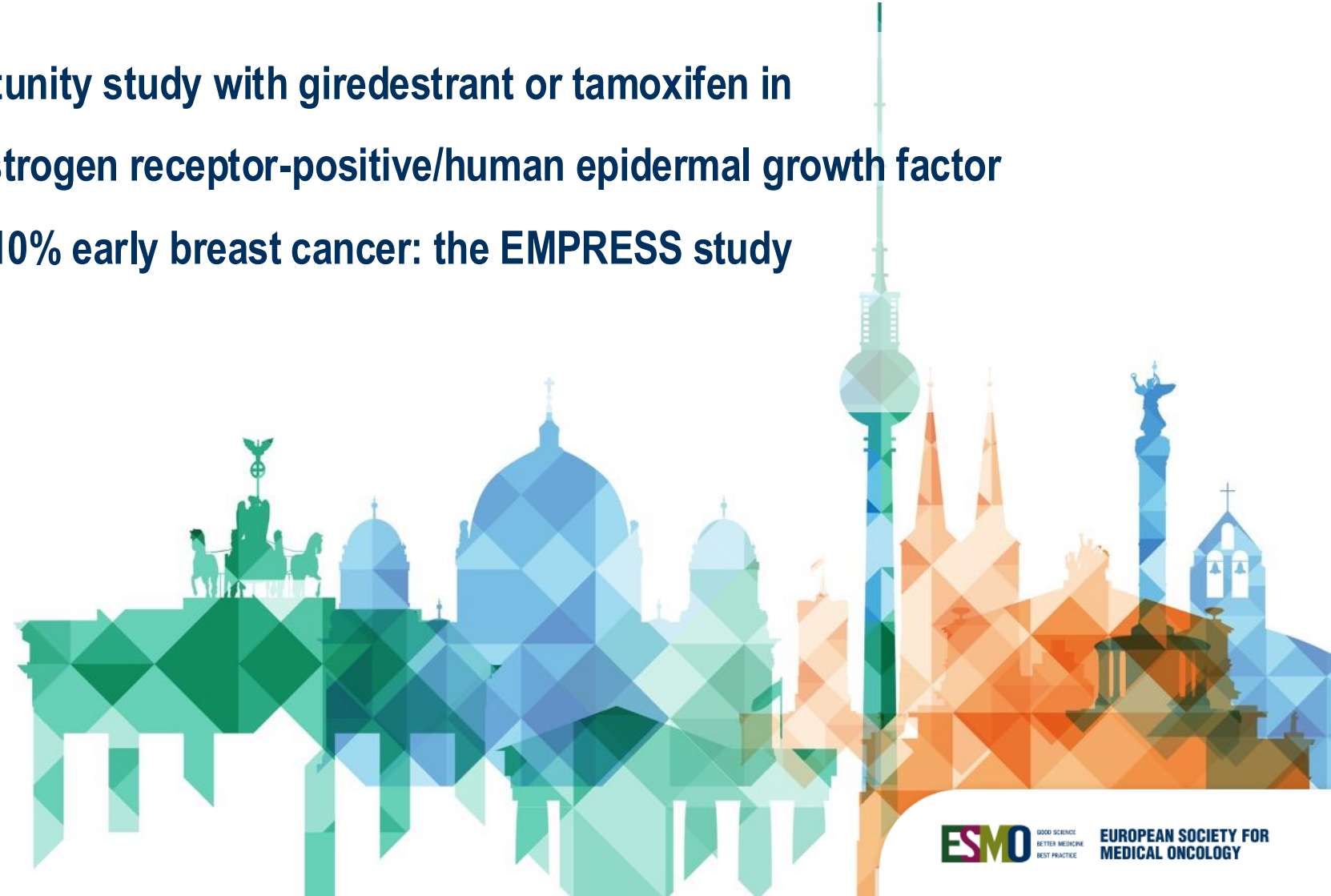
Robertson et al. JCO 2026

BERLIN 2025 ESMO congress

Preoperative window-of-opportunity study with giredestrant or tamoxifen in premenopausal women with estrogen receptor-positive/human epidermal growth factor receptor 2-negative and Ki67≥10% early breast cancer: the EMPRESS study

Antonio Llombart-Cussac, Giuseppe Viale, Manuel Ruiz-Borrego, Vicente Carañana, Elena López-Miranda, María Isabel Blancas, Laia Garrigós, María Gión, Mariana Lopez, Ángel Guerrero, Cristina Saavedra, Juan Miguel Cejalvo, Juan de la Haba, Cinta Albacar, Meritxell Aguiló, José Antonio Guerrero, Pari Skamnioti, Jacques Medioni, José Manuel Pérez-García, Javier Cortés

October, 2025



ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY

Preoperative SERD Window Trials: Discussion

- SOLTI-ELIPSE
  - Short exposure to elacestrant in postmenopausal patients leads to 27% CCCA rate, induces a more endocrine-sensitive, less proliferative tumor phenotype
- SERENA-3
  - Short exposure to camizestrant 75 mg in postmenopausal patients leads to suppression in ER, PR, Ki67
- EMPRESS
  - Short exposure to giredestrant in premenopausal patients leads to substantial decrease in Ki67, ER/PR levels versus tamoxifen, without GNRH agonist

- Question of premenopausal patients: is GNRH agonist needed or can SERD function in presence of high estrogen levels? Is there toxicity in young patients? Await randomized trials.
  - SOLTI-PREMIERE (elacestrant, NCT05982093)
  - Pre-EMBER (imlunestrant, NCT07287098)

- Evidence of molecular response supports exploration in early breast cancer setting

- WOO studies offer ability to evaluate activity, safety, and dosing in curative population, preparing for larger adjuvant trials.

Llombart-Cussac A et al. ESMO 2025

Update on Phase III persevErA Breast Cancer Study in ER-Positive Advanced Breast Cancer

Press Release: March 8, 2026

“ [The manufacturer] announced today results from the Phase III persevERA Breast Cancer study evaluating investigational giredestrant in combination with palbociclib for people with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer.

The study did not meet its primary objective of a statistically significant improvement in progression-free survival in the intent-to-treat population versus letrozole plus palbociclib, but a numerical improvement was observed. The adverse events for the giredestrant combination were manageable and consistent with the known safety profiles of each individual treatment.

The full results from persevERA will be presented at an upcoming medical meeting.”

https://www.gene.com/media/press-releases/15106/2026-03-08/genentech-provides-update-on-phase-iii-p

Year in Review:
Oral SERDs for Breast Cancer

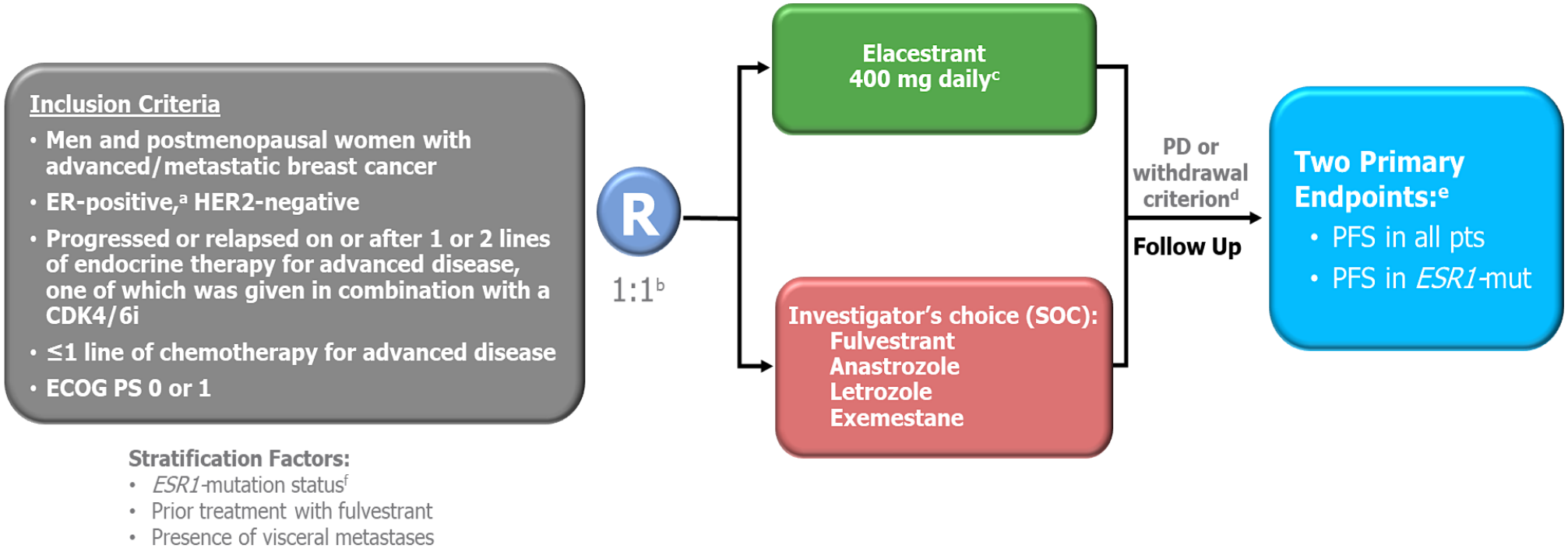
MODULE 1: Second-line treatment for metastatic disease

- Timing of CDK inhibition: Endocrine therapy versus chemotherapy/ADC
- Choice of monotherapy?
- Double-mutant tumors (ESR1, AKT/PI3K/PTEN): EMERALD, evERA
- Use of SERENA-6 strategy?
- Does reduction in ESR1 allele fraction predict benefit? SERENA-6
- EMBER-3: Breaking the 6-month PFS ceiling
- Abemaciclib ramp-up
- Other SERD/CDK4/6 inhibitor combinations
- Indirect comparison of SERD monotherapy to giredestrant/everolimus: evERA

RTP Year in Review 2026

Phase 3 EMERALD: Study Design

A multicenter, international, randomized, open-label, active-controlled phase 3 trial for postmenopausal patients with ER+/HER2- MBC



[a]Documentation of ER+ tumor with ≥ 1% staining by immunohistochemistry; [b]Recruitment from February 2019 to October 2020; [c]Protocol-defined dose reductions permitted; [d]Restaging CT scans every 8 weeks; [e]Blinded Independent Central Review; [f]*ESR1*-mutation status was determined by ctDNA analysis using the Guardant360 assay (Guardant Health, Redwood City, CA).

PFS, progression-free survival; Pts, patients; R, randomized; SOC, standard of care.

Bardia A et al, SABCS 2022: Abstract GS-301.

Initial Phase 3 Trials with Oral SERDs: Differences in prior CDK 4/6i and primary outcomes

	EMERALD[1]	AMEERA-3[4,5]	acelERA[6,7]
Treatment	**Elacestrant**	**Amcenestrant**	**Giredestrant**
Control arm	Fulvestrant / AIs	Fulvestrant / AIs / tamoxifen	Fulvestrant / AIs
Phase (N)	Ph 3 (478)	Ph 3 (367)	Ph 2/3 (303)
Patient population	Men or postmenopausal women	Men or women (any menopausal status)	Men or women (any menopausal status)
***% ESR1*m**	48%	46.4%	39%
Prior CDK4/6i	Required (100%)	Permitted (80%)	Permitted (42%)
Allowed prior fulvestrant	YES	YES	YES
Primary Endpoint	Dual (All and ESR1m)	Single (All)	Single (All)
Data readout	Positive	Negative	Negative

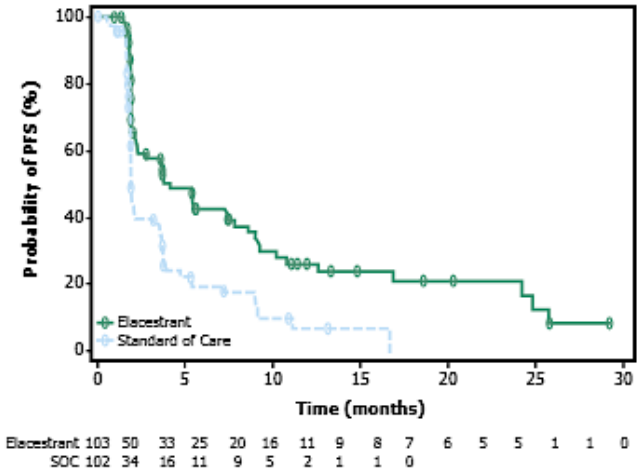
1. Bidard FC et al. *J Clin Oncol*. 2022;40(28):3246-3256. 2. Oliveira M et al. *Lancet Oncol*. 2024;25(11):1424-1439. 3. EMBER-3. NCT04975308. Updated Oct 18, 2024. Accessed Oct 22, 2024. https://clinicaltrials.gov/ct2/show/NCT04975308. 4. Tolaney SM et al. *J Clin Oncol*. 2023;41(24):4014-4024. 5. Sanofi Press Release. https://www.sanofi.com/en/media-room/press-releases/2022/2022-08-17-05-30-00-2499668. August 17, 2022. Accessed Oct 22, 2024. 6. Martin M et al. ASCO 2021. Abstract TPS1100. 7. Jimenez MM et al. *J Clin Oncol*. 2024;42(18):2149-2160.

Courtesy of Aditya Bardia, MD, MPH

EMERALD:
PFS by Duration of CDK 4/6i (*ESR1*m)

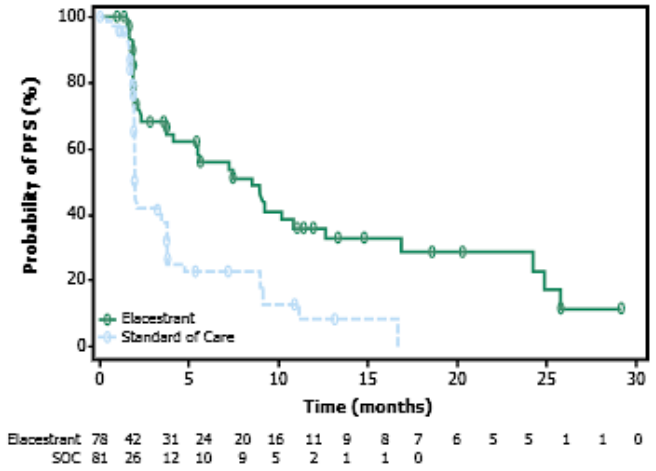
Patients with *ESR1*-mut Tumors: PFS by Duration of CDK4/6i

At least 6 mo CDK4/6i



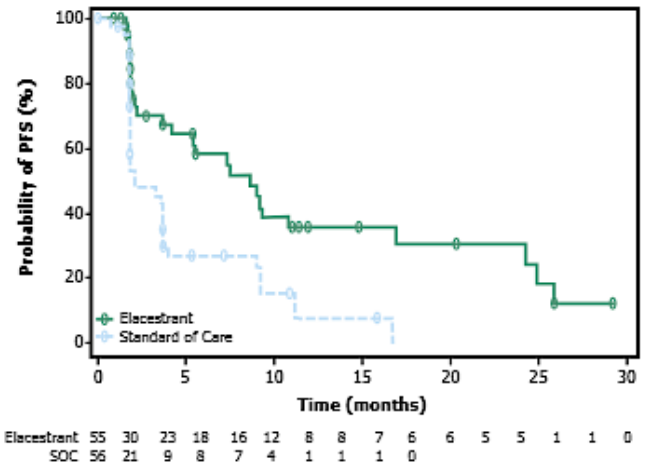
	Elacestrant	SOC Hormonal Therapy
Median PFS, months (95% CI)	**4.14** (2.20 - 7.79)	**1.87** (1.87 - 3.29)
PFS rate at 12 months, % (95% CI)	26.02 (15.12 - 36.92)	6.45 (0.00 - 13.65)
Hazard ratio (95% CI)	**0.517** (0.361 - 0.738)	

At least 12 mo CDK4/6i



	Elacestrant	SOC Hormonal Therapy
Median PFS, months (95% CI)	**8.61** (4.14 - 10.84)	**1.91** (1.87 - 3.68)
PFS rate at 12 months, % (95% CI)	35.81 (21.84 - 49.78)	8.39 (0.00 - 17.66)
Hazard ratio (95% CI)	**0.410** (0.262 - 0.634)	

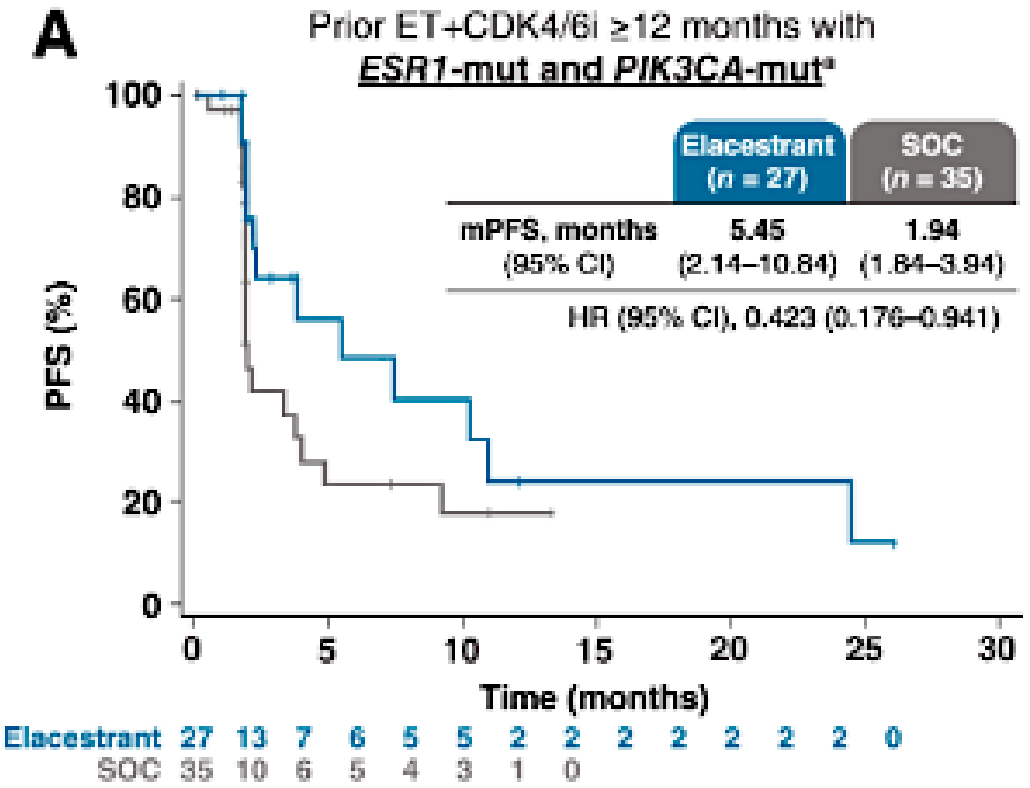
At least 18 mo CDK4/6i

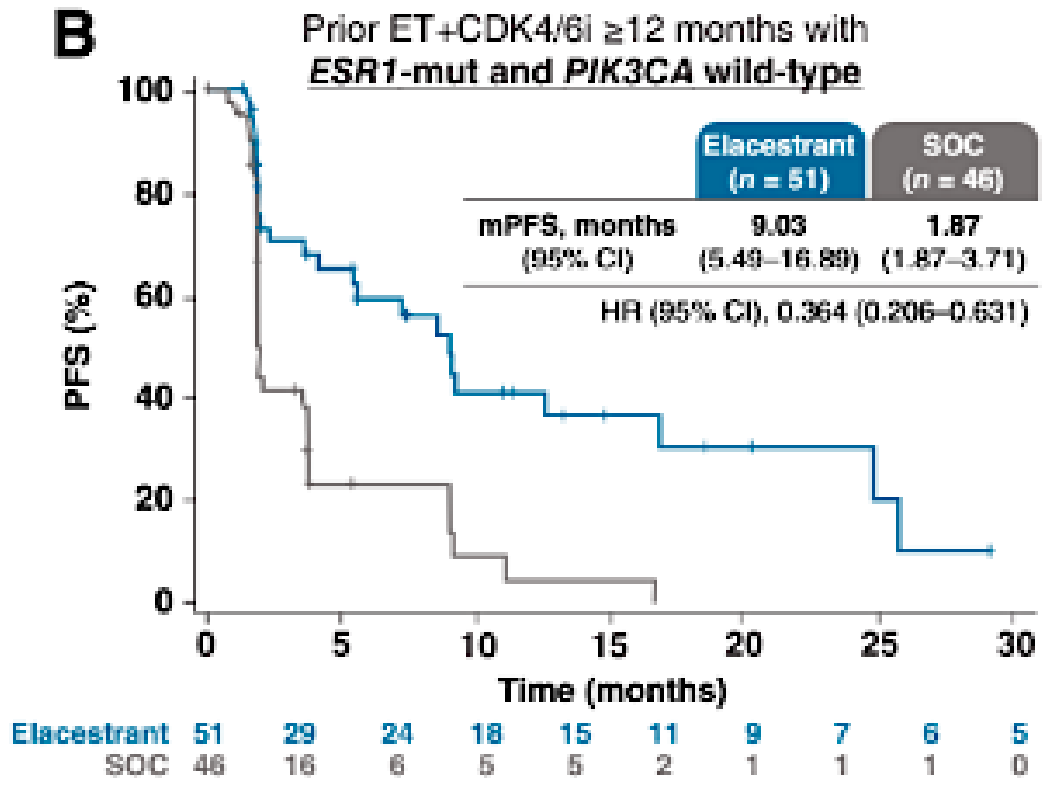


	Elacestrant	SOC Hormonal Therapy
Median PFS, months (95% CI)	**8.61** (5.45 - 16.89)	**2.10** (1.87 - 3.75)
PFS rate at 12 months, % (95% CI)	35.79 (19.54 - 52.05)	7.73 (0.00 - 20.20)
Hazard ratio (95% CI)	**0.466** (0.270 - 0.791)	

Bardia A, et al. Cancer Res. 2024.

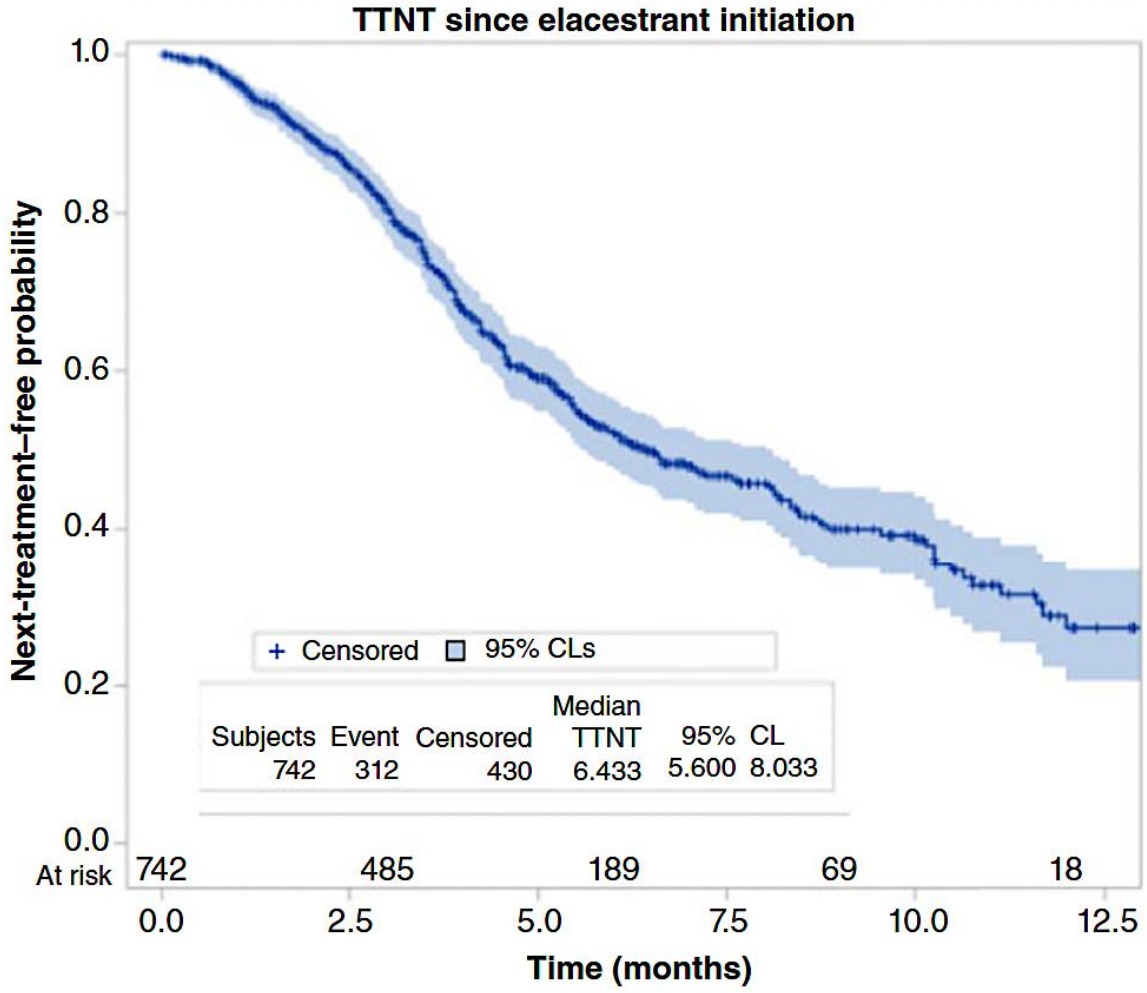
EMERALD: ≥ 12m on prior CDK 4/6i and *mESR1 and mPIK3CA* Group

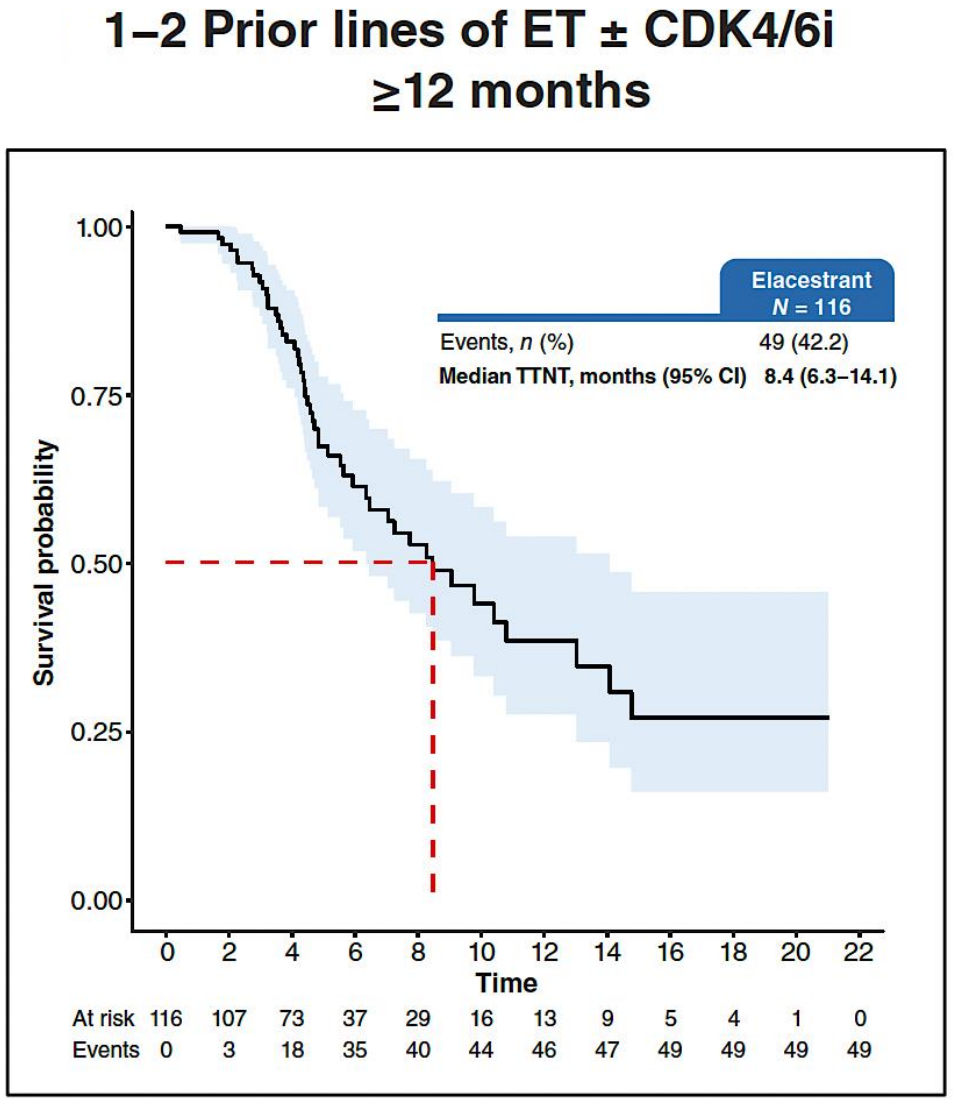




Bardia A, et al. Cancer Res. 2024.

ELACESTRANT:
Real World Setting





Lloyd et al. Clin Cancer Res 2026
Rugo et al. Clin Cancer Res 2026

EMBER-3
Imlunestrant (+/- Abema) vs ET

ER+, HER2- ABC

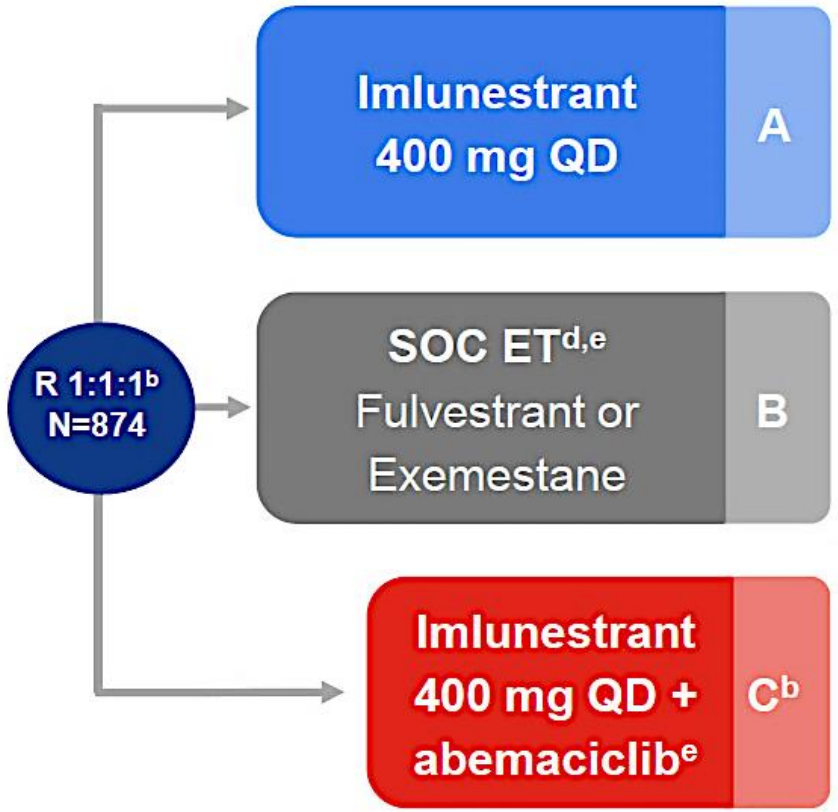
Men and Pre-[a]/Post-menopausal women

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[c]



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[h] patients

Key Secondary Endpoints

- OS, PFS by BICR, and ORR
- Safety

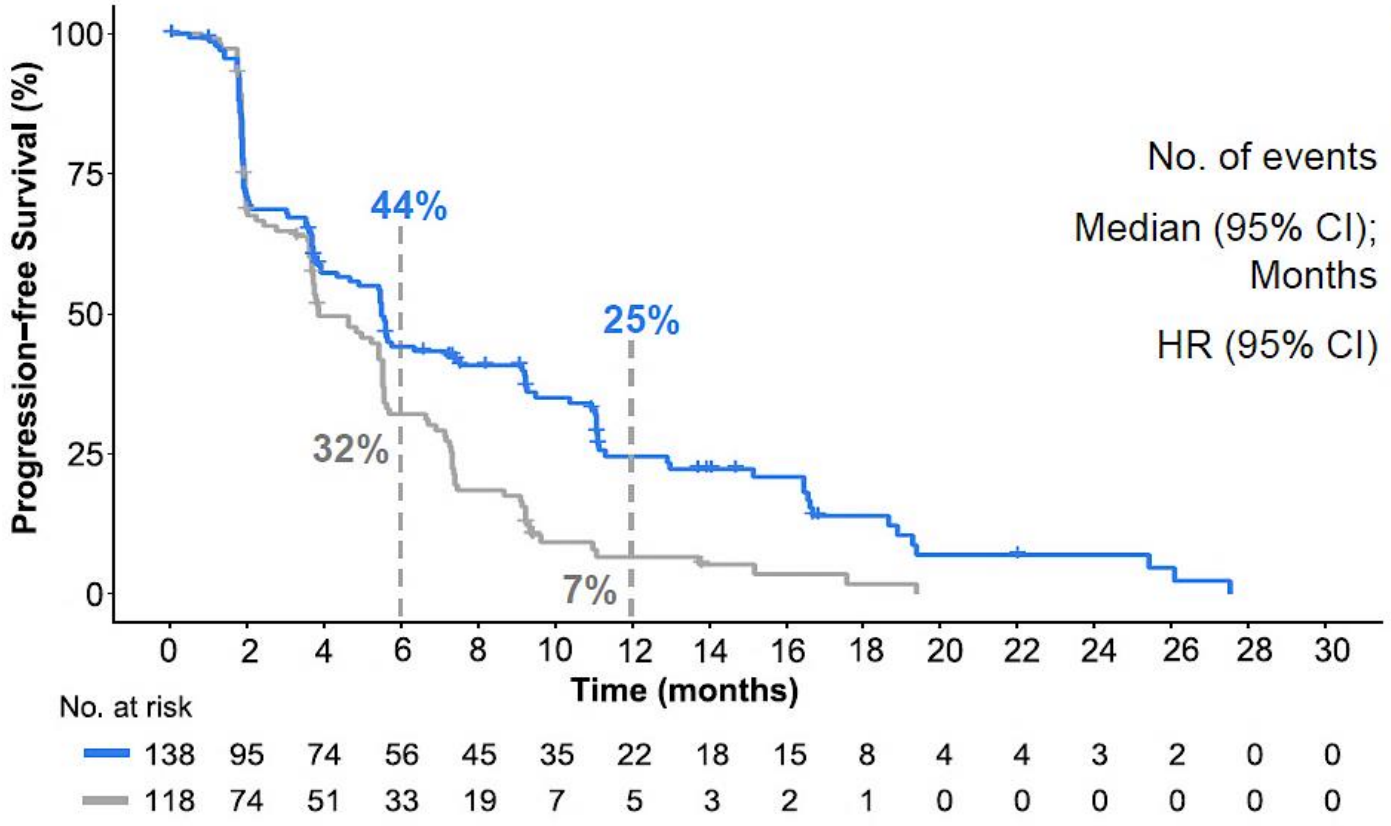
Exploratory Endpoints

- PFS and OS for C vs B in all[h] patients

ABC, advanced breast cancer; AI, aromatase inhibitor; BICR, blinded independent central review; CDK4/6i CDK4/6 inhibitor; ER, estrogen receptor; *ESR1*m, *ESR1* mutation; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; QD, once daily; SOC ET, standard of care endocrine therapy. Patients were enrolled from October 2021 to November 2023 across 195 sites in 22 countries. [a] A GnRH agonist was required in men and premenopausal women; [b] Enrollment into Arm C started with Protocol Amendment A (at which point 122 patients had been randomized across Arms A and B); [c] East Asia vs United States/European Union vs others; [d] Investigator's choice; [e] Labeled dose; [f] Scans every 8 weeks for the first 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.

•Jhaveri KL, et al. NEJM. December 11, 2024. DOI: 10.1056/NEJMoa2410858; Jhaveri KL, et al. NEJM. Presented at 2024 SABCS. December 11-13, 2024. San Antonio, Texas. Abstract GS1-01.

EMBER-3:
PFS in ESR1m (Imlunestrant vs ET)

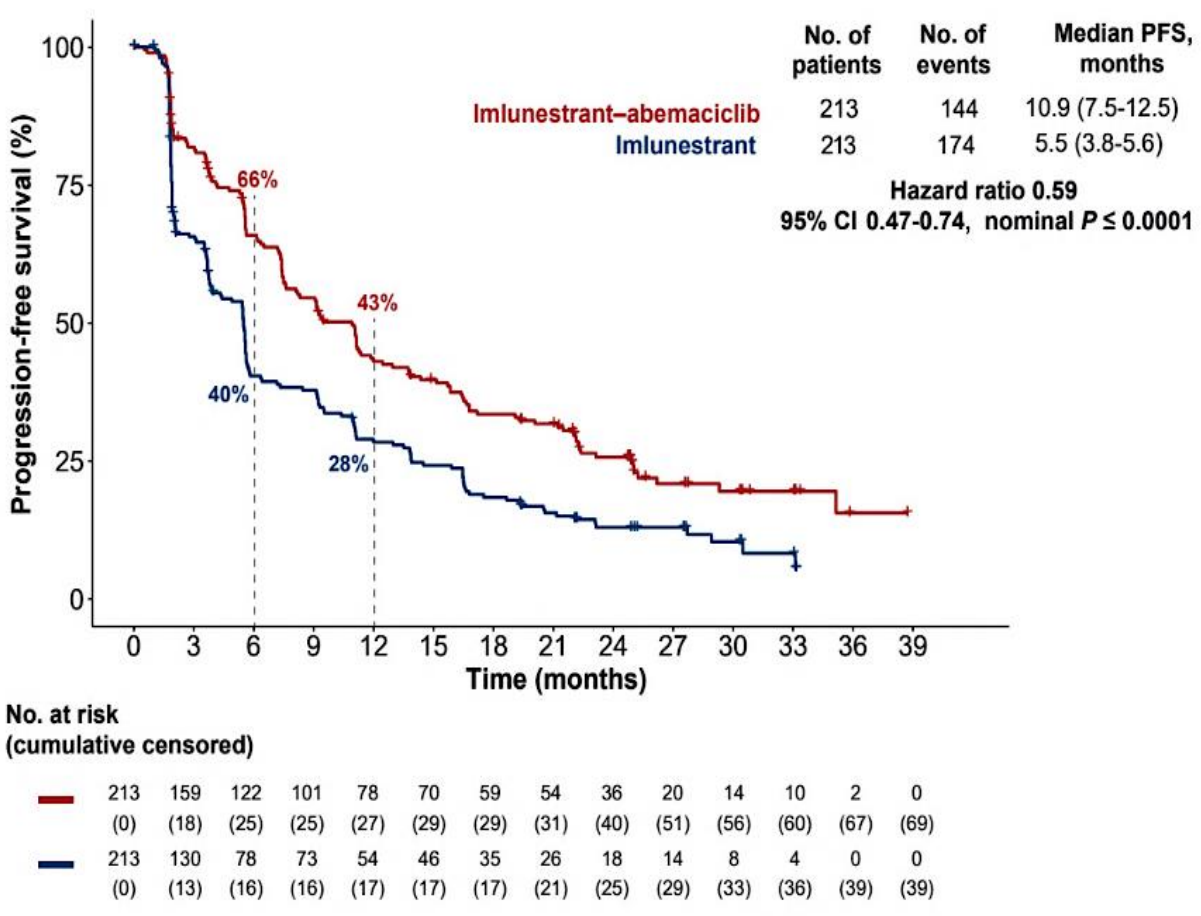


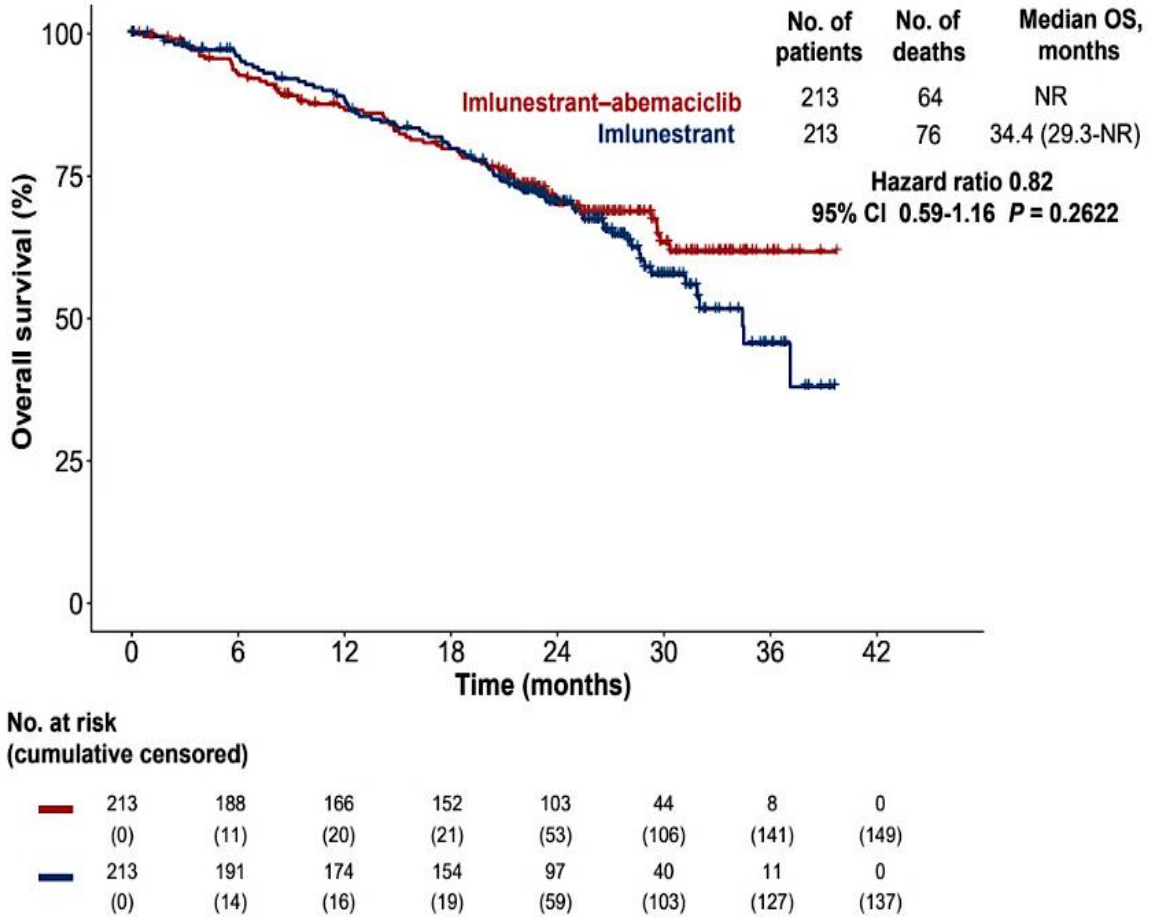
	Imlunestrant n=138	SOC ET n=118
No. of events	109	102
Median (95% CI); Months	**5.5** (3.9-7.4)	**3.8** (3.7-5.5)
HR (95% CI)	**0.62 (0.46-0.82)[a]** *p*-value<0.001	

Imlunestrant led to a 38% reduction in the risk of progression or death in patients with *ESR1*m

Jhaveri KL, et al. NEJM. 2024.

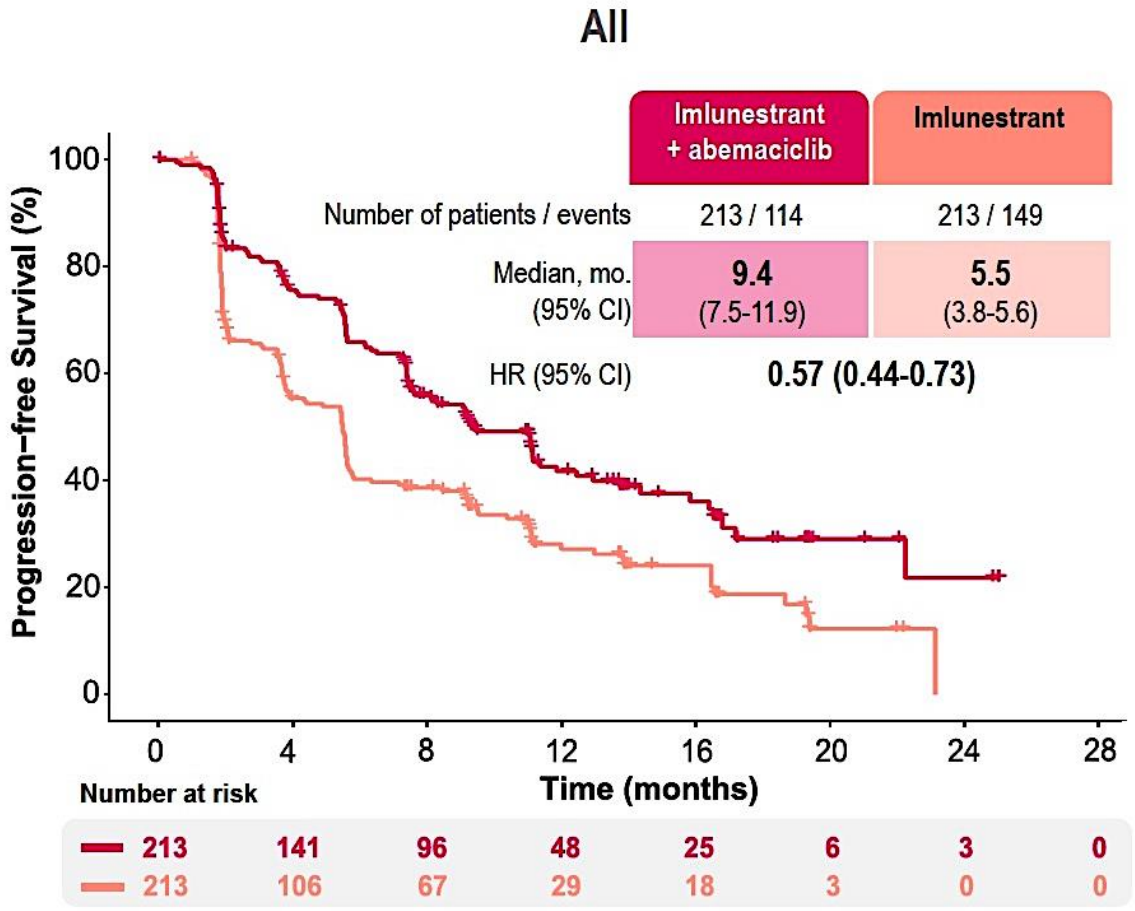
EMBER-3 PFS:
Imlunestrant + Abema vs Imlunestrant

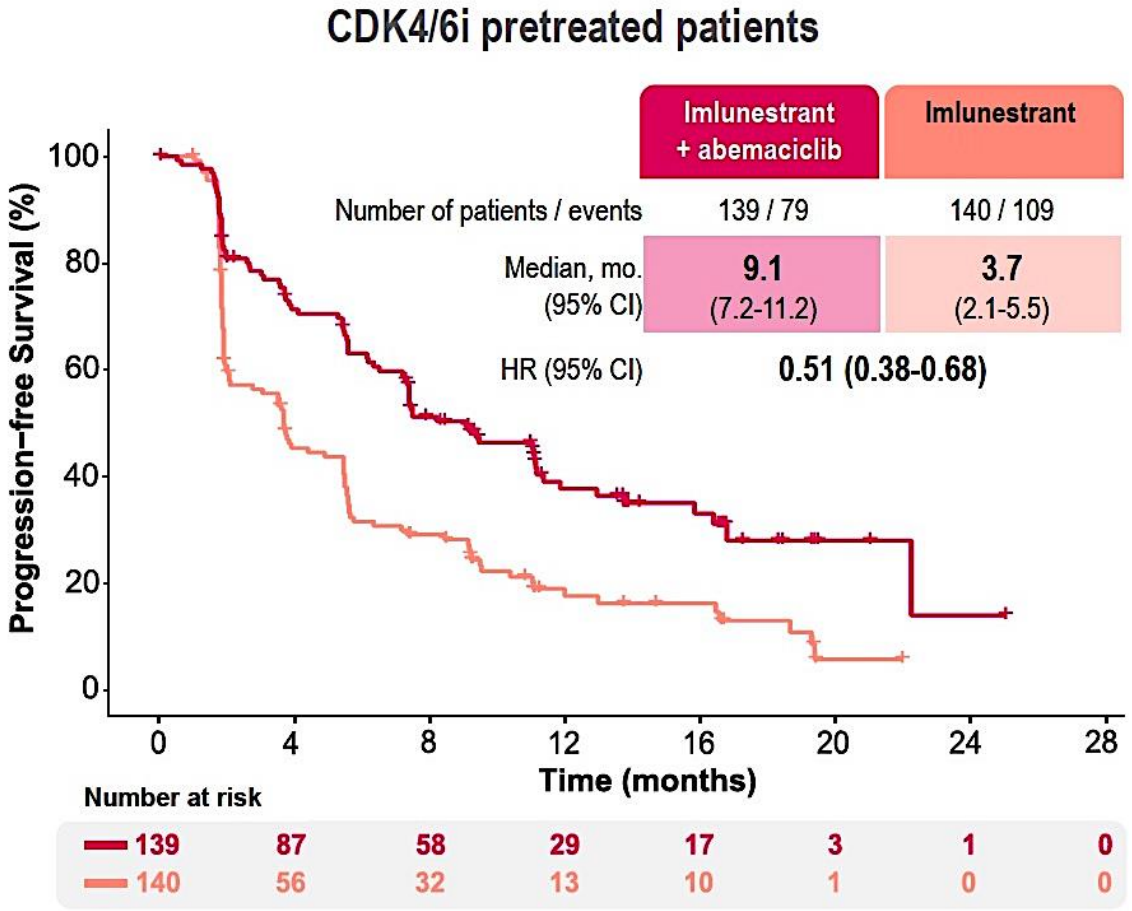




Jhaveri KL, et al. Ann Oncol 2025

EMBER-3: Progression-Free Survival for All Patients and Those with CDK4/6i-Pretreated Disease



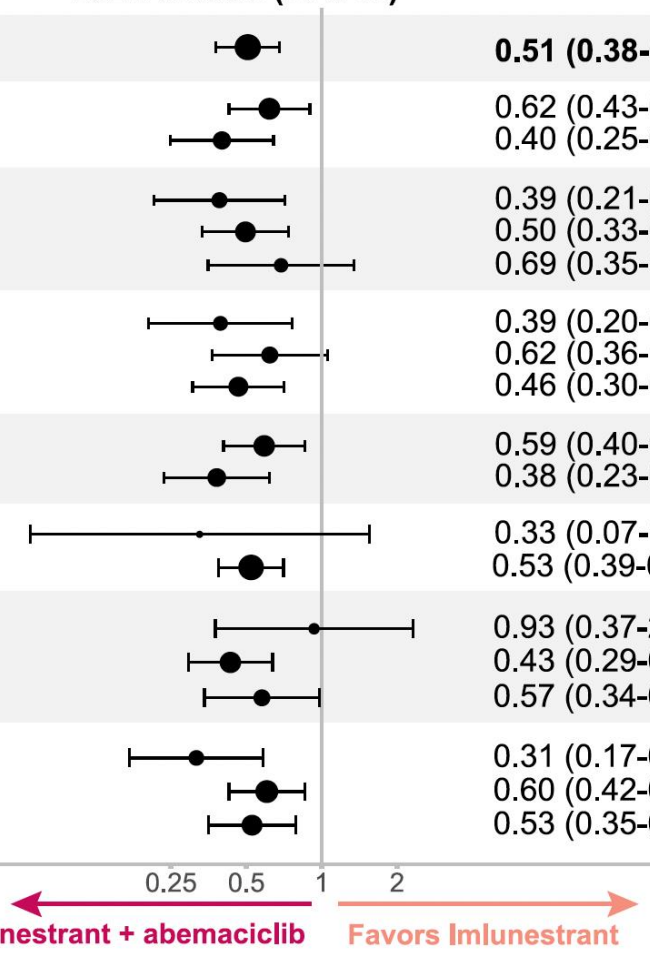


Consistent benefit of imlunestrant + abemaciclib in patients previously treated with a CDK4/6i

Manich CS et al. ESMO Breast 2025;Abstract 297O.

EMBER-3: Benefit Across Subgroups in CDK4/6i-Pretreated Disease

Subgroup		Imlunestrant + abemaciclib No. of Events/Total No.	Imlunestrant No. of Events/Total No.	Hazard Ratio (95% CI)
CDK4/6i pretreated patients		**79/139**	**109/140**	**0.51 (0.38-0.68)**
Age	< 65	47/77	70/92	0.62 (0.43-0.90)
	≥ 65	32/62	39/48	0.40 (0.25-0.64)
Region	East Asia	20/32	29/34	0.39 (0.21-0.71)
	North America/Western Europe	44/77	59/77	0.50 (0.33-0.74)
	Other	15/30	21/29	0.69 (0.35-1.35)
No. of metastatic sites	1	16/47	23/36	0.39 (0.20-0.76)
	2	22/33	36/48	0.62 (0.36-1.06)
	≥ 3	41/59	50/56	0.46 (0.30-0.71)
Liver metastasis	No	51/94	61/86	0.59 (0.40-0.86)
	Yes	28/45	48/54	0.38 (0.23-0.62)
Previous CDK4/6i indication	Adjuvant	2/7	8/11	0.33 (0.07-1.55)
	Advanced	77/132	101/129	0.53 (0.39-0.71)
Choice of previous CDK4/6i[a]	Abemaciclib	9/10	10/13	0.93 (0.37-2.31)
	Palbociclib	44/90	66/86	0.43 (0.29-0.63)
	Ribociclib	25/37	32/39	0.57 (0.34-0.98)
Duration of previous CDK4/6i[b]	< 12 Months	21/40	25/32	0.31 (0.17-0.58)
	≥ 12 Months	56/92	76/97	0.60 (0.42-0.85)
	≥ 18 Months	41/72	61/77	0.53 (0.35-0.78)



[a] Adjuvant or Advanced. [b] Advanced. The total number of patients may not add up due to missing data in certain subgroups.

Manich CS et al. ESMO Breast 2025;Abstract 297O.

Phase 3 Trials with Oral SERDs: Differences in prior CDK 4/6i and primary outcomes

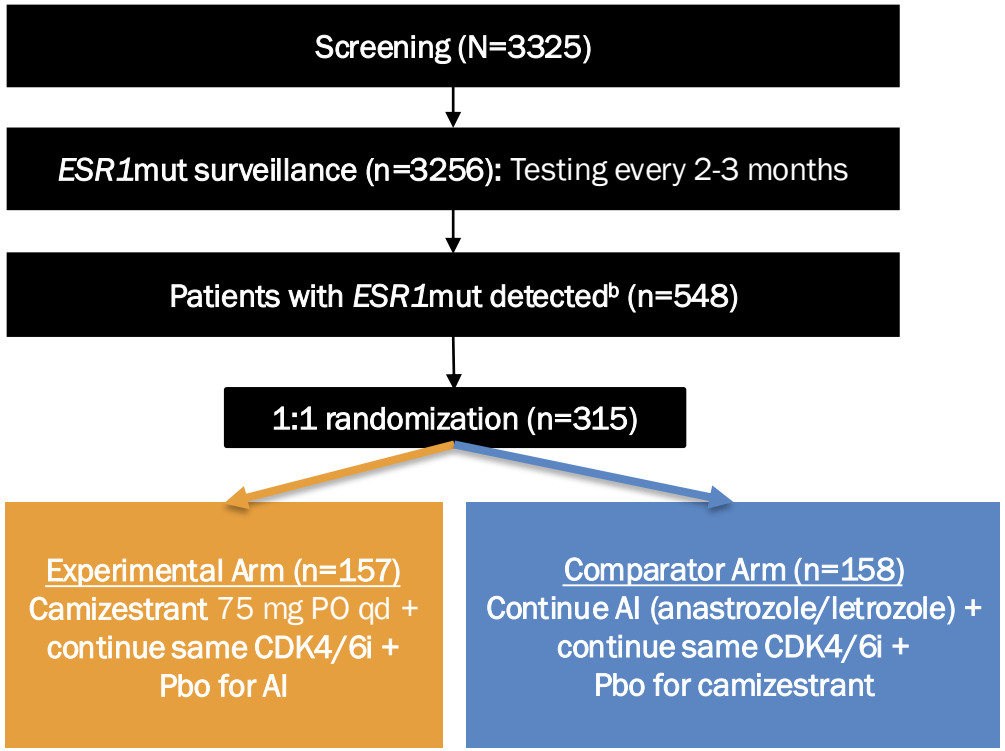
	EMERALD[1]	AMEERA-3[4,5]	acelERA[6,7]	EMBER-3	VERITAC-2
Treatment	**Elacestrant**	**Amcenestrant**	**Giredestrant**	**Imlunestrant (+/- Abema)**	**Vepdegestrant**
Control arm	Fulvestrant / AIs	Fulvestrant / AIs / tamoxifen	Fulvestrant / AIs	Fulvestrant / AIs	Fulvestrant
Sample Size	478	367	303	874	624
***% ESR1*m**	48%	46.4%	39%	29.2%	43.2%
Prior CDK4/6i	Required	Permitted	Permitted	Permitted	Required
Primary Endpoint	Dual (All and ESR1m)	Single (All)	Single (All)	Dual (All and ESR1m)	Dual (All and ESR1m)
Data readout	Positive	Negative	Negative	Positive	Positive
Adverse Effect	Nausea	GI	Bradycardia	Diarrhea	Anemia, Neutropenia

Courtesy of Aditya Bardia, MD, MPH

SERENA-6:
Camizestrant + CDK4/6i vs ET + CDK 4/6i

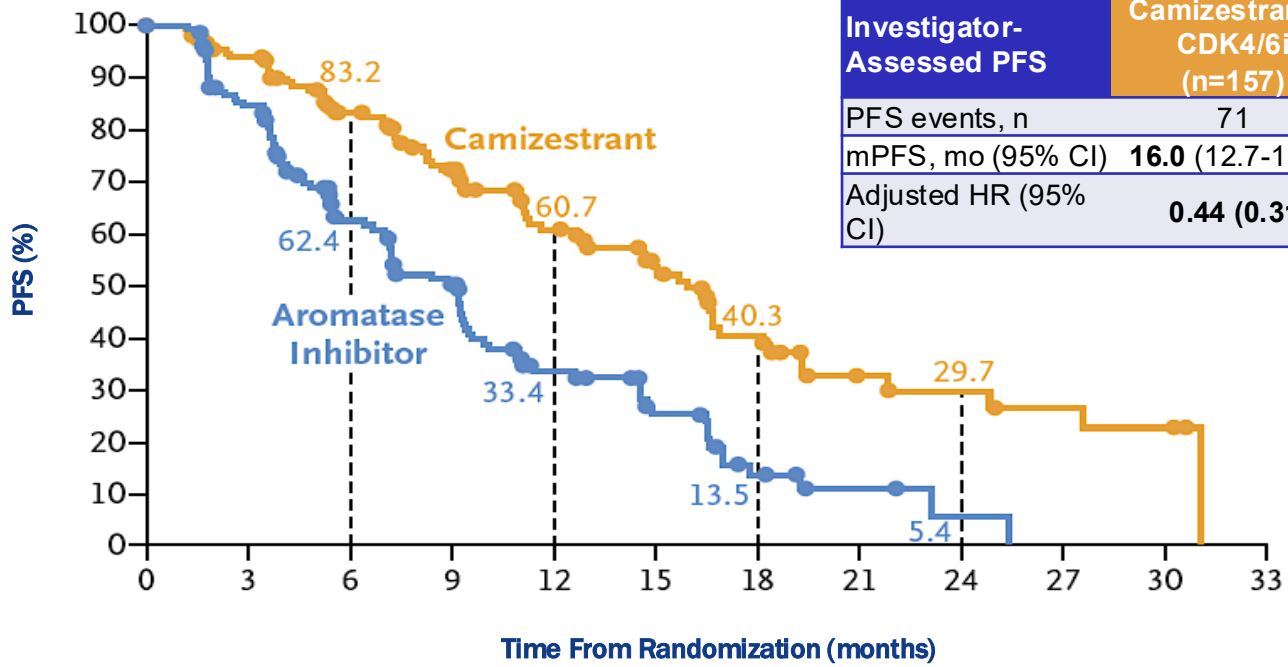
Key Eligibility Criteria

- ER+/HER2– ABC[a]
- On 1L AI + CDK4/6i for ≥6 months
- *ESR1*mut detected in ctDNA with no evidence of disease progression



[a] Pre- or perimenopausal women, and men received an LHRH agonist per clinical guidelines. [b] 51% tested positive on first test, 38% after 2-5 tests, and 11% after >5 tests. [c] Stratification factors.
Turner NC, et al. ASCO 2025. Abstract LBA4.

SERENA-6:
Camizestrant + CDK4/6i Results



Investigator-Assessed PFS	Camizestrant + CDK4/6i (n=157)	AI + CDK4/6i (n=158)
PFS events, n	71	100
mPFS, mo (95% CI)	**16.0** (12.7-18.2)	**9.2** (7.2-9.5)
Adjusted HR (95% CI)	**0.44 (0.31-0.60); *P*<0.00001**	

No. at Risk

Camizestrant	157	138	105	82	55	41	26	11	9	7	6	0
Aromatase inhibitor	158	124	73	55	29	17	7	3	1	0	0	0

- Median follow-up: 12.6 mo
- PFS benefit was consistent across the CDK4/6i and clinically relevant subgroups

PFS2[a]	Camizestrant + CDK4/6i (n=157)	AI + CDK4/6i (n=158)
PFS2 events, n	38	47
12-mo PFS2 rate, %	**85.4**	**74.4**
Adjusted HR (95% CI)	**0.52 (0.33-0.81); *P*=0.0038** [interim analysis threshold *P*=0.0001]	

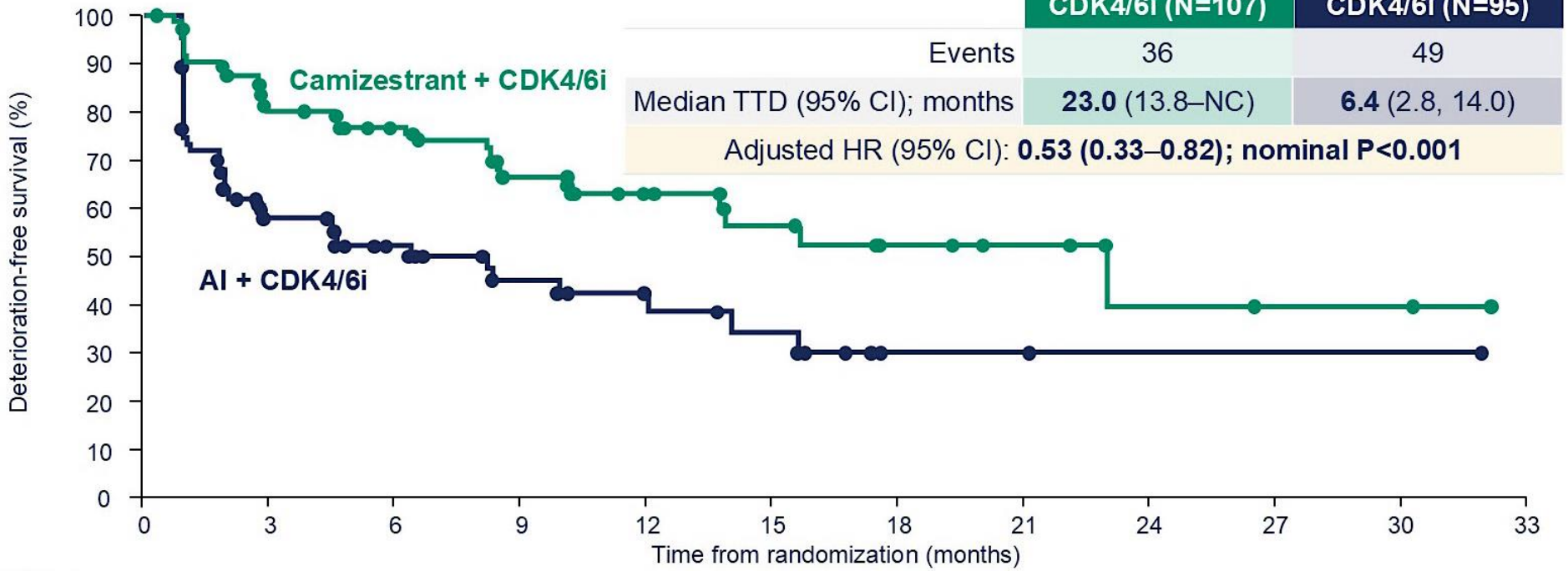
[a] Information fraction: 54%. Final PFS2 analysis will occur at 158 PFS2 events.

Turner NC, et al. ASCO 2025. Abstract LBA4.

SERENA-6:
QOL Results

Time to deterioration in global health status/quality of life

EORTC QLQ-C30



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

Number of patients at risk

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

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

Courtesy of Aditya Bardia, MD, MPH

SAN ANTONIO BREAST CANCER SYMPOSIUM®
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AACR American Association for Cancer Research
DECEMBER 9–12, 2025
HENRY B. GONZALEZ CONVENTION CENTER • SAN ANTONIO, TX

Updated results and an exploratory analysis of *ESR1*m circulating tumor DNA dynamics from SERENA-6, a phase 3 trial of camizestrant + CDK4/6 inhibitor for emergent *ESR1*m during first-line endocrine-based therapy and ahead of disease progression in patients with HR+/HER2– advanced breast cancer

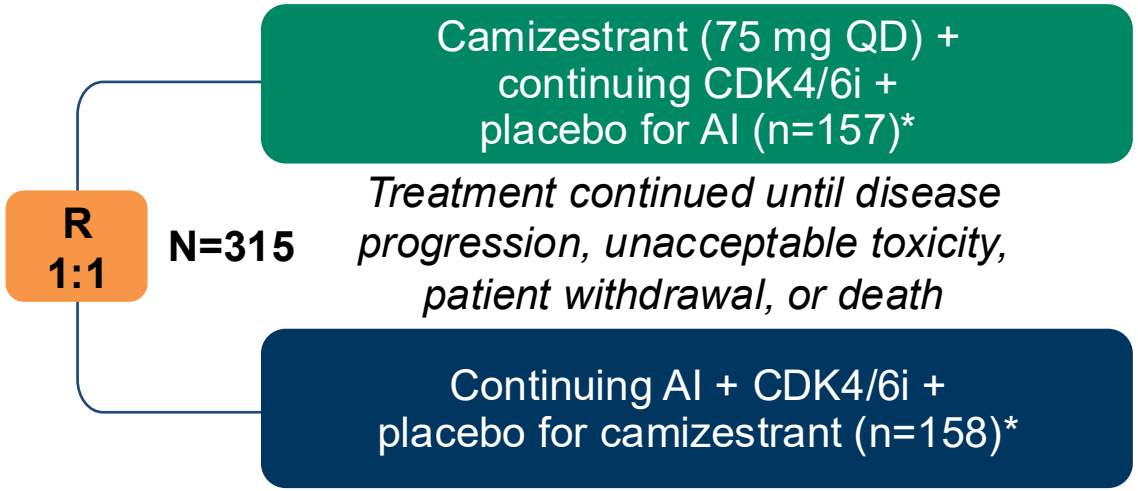
SERENA-6

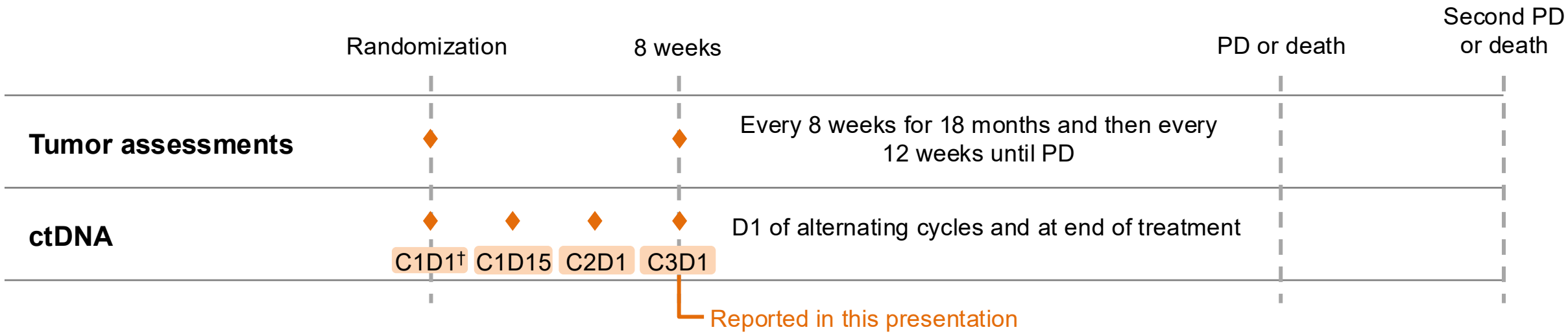
François-Clément Bidard,[1] Erica L. Mayer,[2] Yeon Hee Park,[3] Wolfgang Janni,[4] Cynthia Ma,[5] Massimo Cristofanilli,[6] Giampaolo Bianchini,[7] Kevin Kalinsky,[8] Hiroji Iwata,[9] Stephen Chia,[10] Adam Brufsky,[11] Peter Fasching,[12] Zbigniew Nowecki,[13] Javier Pascual,[14] Einav Gal-Yam,[15] Wei-Pang Chung,[16] Seock-Ah Im,[17] Alberto Zambelli,[18] Florence Dalenc,[19] Mafalda Oliveira,[20] Steven Fox,[21] Manuel Selvi Miralles,[21] Christopher Morrow,[22] Cynthia Huang Bartlett,[23] and Nicholas C Turner[24]

[1]Institut Curie, Paris, France; [2]Dana-Farber Cancer Institute, Boston, MA, USA; [3]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [4]Universitätsklinikum Ulm, Ulm, Germany; [5]Washington University School of Medicine, Saint Louis, MO, USA; [6]Weill-Cornell Medicine/ New York-Presbyterian Hospital, New York, NY, USA; [7]IRCCS Ospedale San Raffaele, Milan, Italy; [8]Winship Cancer Institute, Atlanta, GA, USA; [9]Nagoya City University, Nagoya, Japan; [10]BC Cancer Agency, Vancouver, BC, Canada; [11]UMPC Magee-Womens Hospital, Pittsburgh, PA, USA; [12]University Hospital Erlangen, Comprehensive Cancer Center Erlangen-EMN, Erlangen, Germany; [13]Narodowy Instytut Onkologii im. Marii Skłodowskiej-Curie, Warsaw, Poland; [14]Medical Oncology Department, Hospital Universitario Virgen de la Victoria. IBIMA. Málaga, Spain; [15]Sheba Medical Center, Tel-Hashomer, Israel; [16]National Cheng-Kung University Hospital, Tainan, Taiwan; [17]Cancer Research Institute, Seoul National University College of Medicine, Seoul, Republic of Korea; [18]IRCCS Istituto Clinico Humanitas, Milan, Italy; [19]Institut Claudius Regaud, IUCT-Oncopole, Toulouse, France; [20]Medical Oncology Department, Vall d'Hebron University Hospital, Barcelona, Spain; [21]Late Development, Oncology R&D, AstraZeneca, Cambridge, UK; [22]Research and Early Development, Oncology R&D, AstraZeneca, Cambridge, UK; [23]Late Development, Oncology R&D, AstraZeneca, Gaithersburg, MD, USA; [24]Royal Marsden Hospital, London, UK

SERENA-6 Study design

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





D, Day; C, Cycle; ER+, estrogen receptor-positive; IHC, immunohistochemical; PD, progressive disease; QD, once daily; R, randomized.
*Pre- or perimenopausal women and men received a luteinizing hormone-releasing hormone agonist per clinical guidelines. †Prior to receiving study treatments.
ctDNA from patient blood samples were tested for *ESR1*m using Guardant360CDx (Guardant Health).

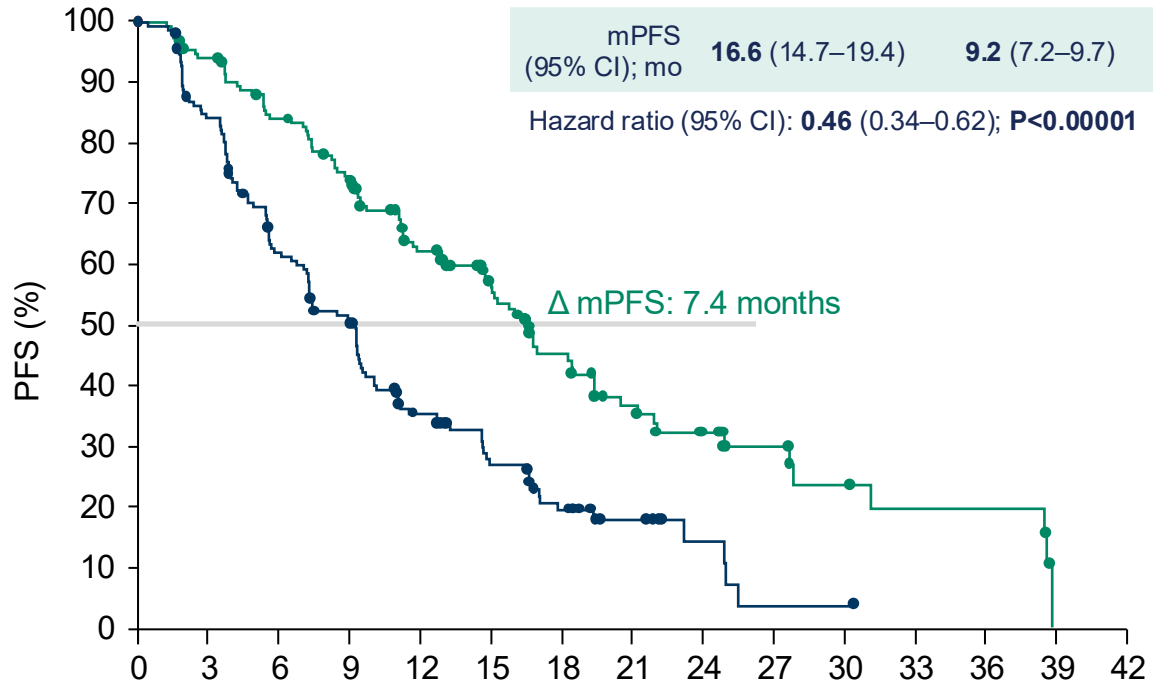
Bidard FC et al. SABCS 2025

Switching to camizestrant + CDK4/6i prolongs time to progression and time to first subsequent therapy

Updated PFS*

	CAMI + CDK4/6i	AI + CDK4/6i
Events	90/157	115/158
mPFS (95% CI); mo	**16.6** (14.7–19.4)	**9.2** (7.2–9.7)

Hazard ratio (95% CI): **0.46** (0.34–0.62); **P<0.00001**



Patients at risk

CAMI + CDK4/6i	157	143	125	109	82	62	39	26	18	11	7	5	5	0
AI + CDK4/6i	158	127	90	72	42	28	17	9	4	1	1	0	0	0

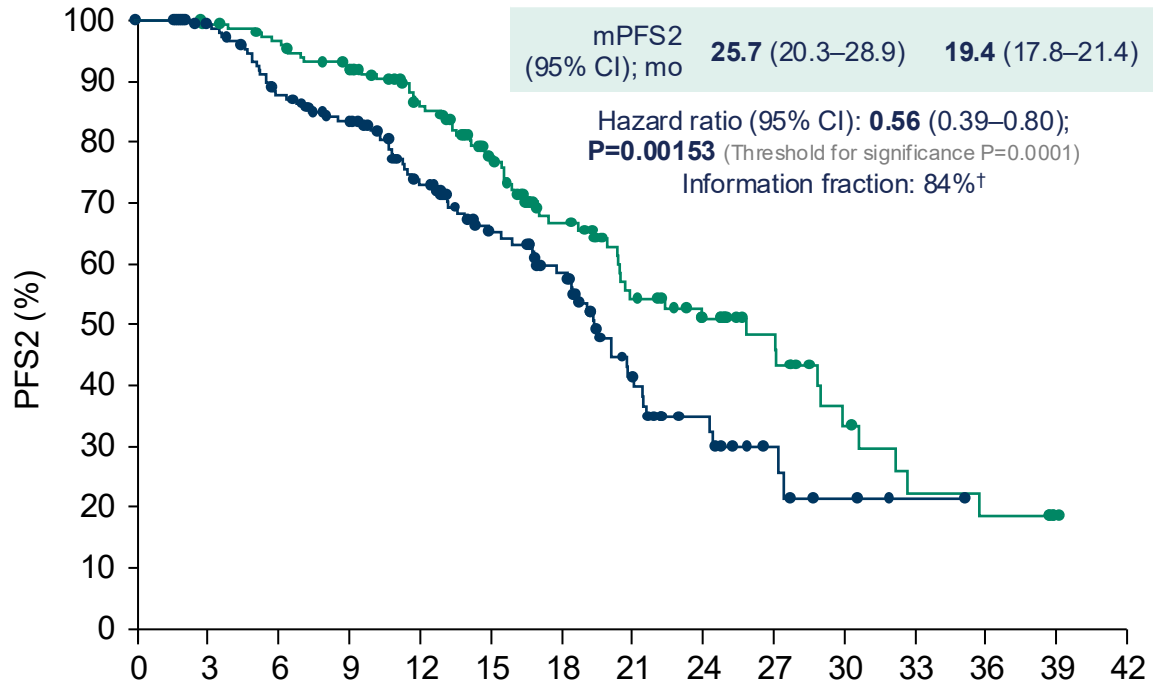
Switching to camizestrant + CDK4/6i treatment led to a clinically meaningful improvement in PFS compared with continuing AI + CDK4/6i

- The **time to first subsequent therapy** (defined as the time from randomization to receiving a first subsequent therapy, or death) also favored the camizestrant + CDK4/6i arm compared with the AI + CDK4/6i arm; **hazard ratio (95% CI): 0.47 (0.35–0.62)**
- The magnitude of benefit in time to first subsequent therapy was **consistent with PFS**

CAMI, camizestrant; mo, months; CI, confidence interval; DCO2, data cutoff 2; mPFS, median PFS; TFST, time to first subsequent therapy; RECIST, Response Evaluation Criteria in Solid Tumors.
*Second pre-specified data cut **DCO2: June 30, 2025.** At DCO2, 58 patients in the camizestrant + CDK4/6i arm and 23 patients in the AI + CDK4/6i arm were still receiving study treatments.
There were 88/157 TFST events in the camizestrant + CDK4/6i arm and 117/158 in the AI + CDK4/6i arm. PFS was defined per RECIST v1.1. The PFS and TFST hazard ratio and 95% CI are estimated using a Cox proportional hazards model stratified by disease site, *ESR1*m status detectable at first versus subsequent ctDNA tests, and time from initiation of AI + CDK4/6i to randomization.

Switching to camizestrant + CDK4/6i prolongs time to second progression and time to second subsequent therapy

Updated PFS2*



Patients at risk

CAMI + CDK4/6i	157	149	143	134	113	86	56	38	28	17	10	6	5	0
AI + CDK4/6i	158	149	127	114	85	62	49	25	14	7	3	1	0	0

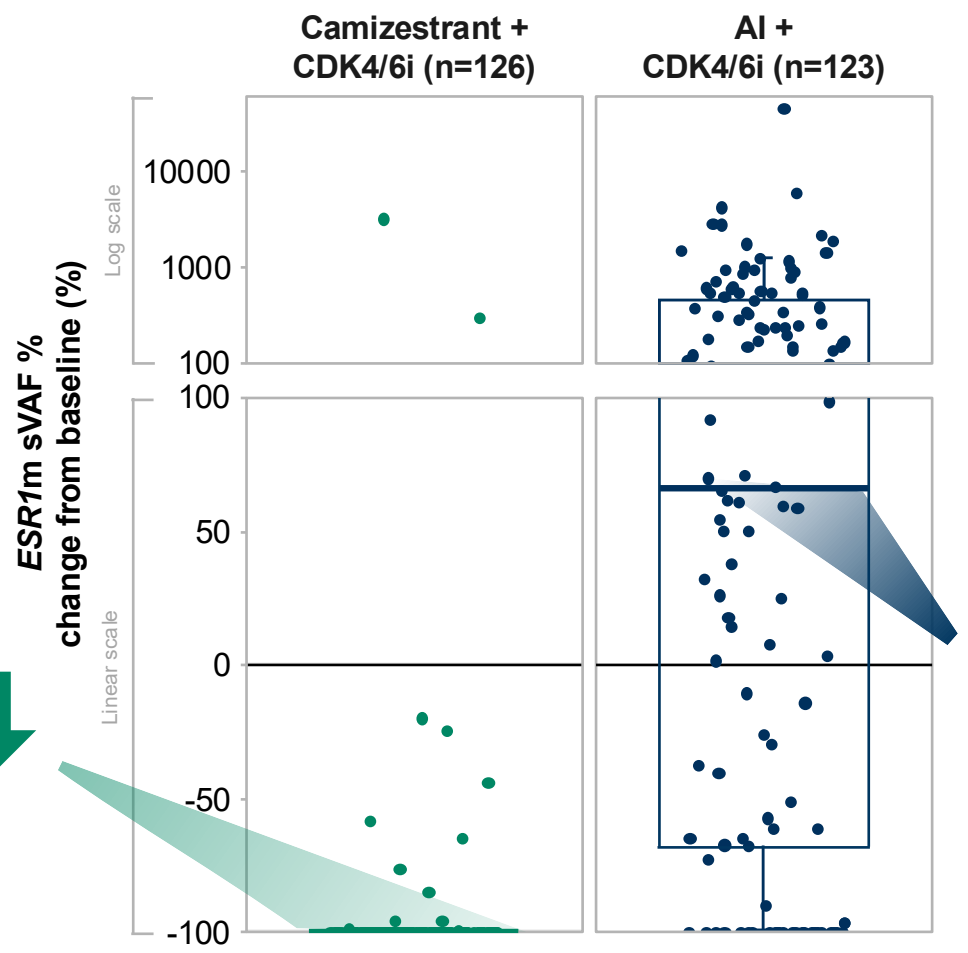
(m)PFS2, (median) PFS2; TSST, time to second subsequent therapy.
*Second pre-specified data cut **DCO2: June 30, 2025.** †Information fraction: the number of PFS2 events at this interim analysis divided by the number of PFS2 events expected at final analysis, multiplied by 100.
There were 60/157 TSST events in the camizestrant + CDK4/6i arm and 77/158 in the AI + CDK4/6i arm. The PFS2 and TSST hazard ratio and 95% CI are estimated using a stratified Cox proportional hazards model stratified by *ESR1*m detectable at first versus subsequent ctDNA tests and time from initiation of AI + CDK4/6i to randomization.

Switching to camizestrant + CDK4/6i treatment led to a clinically meaningful prolongation in PFS2 compared with continuing AI + CDK4/6i, demonstrating that the PFS gain is maintained in the subsequent line of therapy

- The **time to second subsequent therapy** (defined as the time from randomization to receiving a second subsequent therapy, or death) also favored the camizestrant + CDK4/6i arm compared with the AI + CDK4/6i arm; **hazard ratio (95% CI): 0.57 (0.40–0.81)**
- The magnitude of benefit in time to second subsequent therapy was **consistent with PFS2**

Camizestrant + CDK4/6i profoundly reduces *ESR1*m ctDNA vs AI + CDK4/6i

*ESR1*m allele frequency was **profoundly reduced** in the camizestrant + CDK4/6i arm vs the AI + CDK4/6i arm (Wilcoxon nominal P<0.00001)



In the AI + CDK4/6i arm, *ESR1*m allele frequency increased >500% from baseline in **24.4%** of patients vs **0.8%** of patients in the camizestrant + CDK4/6i arm

Median change from baseline at C3D1 (8 weeks):

−100% (IQR: −100 to −100)

Median change from baseline at C3D1 (8 weeks):

+66.7% (IQR: −67.9 to +465.0)

Baseline VAF were balanced across arms.
IQR, interquartile range; (s)VAF, (summed) variant allele fraction.
Second pre-specified data cut **DCO2: June 30, 2025.**

Bidard FC et al. SABCS 2025

SERENA-6 Discussion

- Updated results from SERENA-6, with greater maturity, continue to support that changing to camizestrant at time of emergence of *ESR1* mutation significantly prolongs PFS, favorably prolongs PFS2, and prolongs time to second therapy.

- Reduced *ESR1m* levels with exposure to oral SERD support pharmacodynamic activity of camizestrant and molecular benefit.

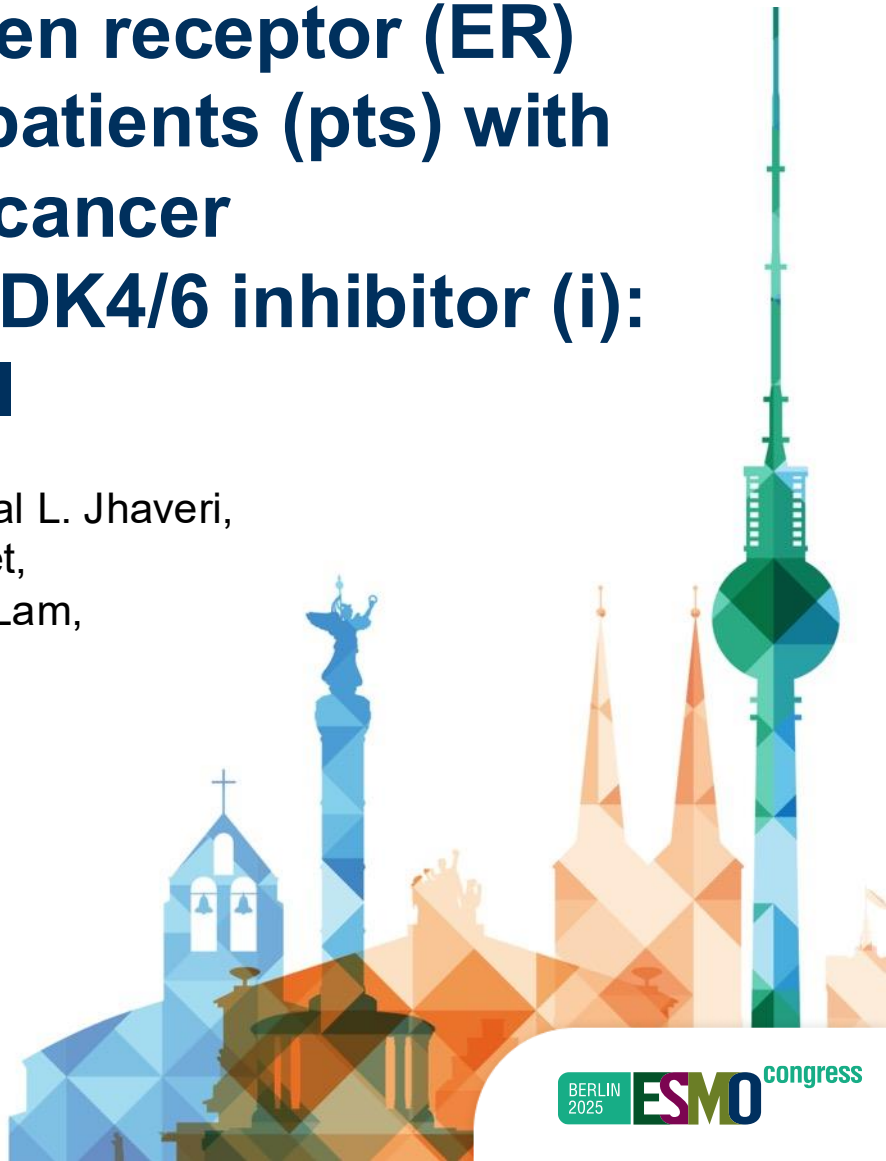
- Await mature PFS2 and OS data, as well as possible drug approval, to understand if SERENA-6 approach will become a new standard of care.

Giredestrant (GIRE), an oral selective oestrogen receptor (ER) antagonist and degrader, + everolimus (E) in patients (pts) with ER-positive, HER2-negative advanced breast cancer (ER+, HER2– aBC) previously treated with a CDK4/6 inhibitor (i): Primary results of the Phase III evERA BC trial

Erica L. Mayer, Sara M. Tolaney, Miguel Martin, Gregory A. Vidal, Luca Moscetti, Komal L. Jhaveri, Adam Brufsky, William J. Gradishar, Andreas Schneeweiss, Naoki Niikura, Anne Favret, Margarita Alfie, Keun Seok Lee, Sarah Khan, Merilin B. Feldman, Bann-mo Day, Lisa Lam, Walter C. Darbonne, Pablo Perez-Moreno, Hope S. Rugo

Presenting author: Erica L. Mayer, MD, MPH

Dana-Farber Cancer Institute, Boston, MA, USA



BERLIN 2025 ESMO congress

Giredestrant + Everolimus vs ET + Everolimus: EVERA Study Design

Study design

A global, randomised, 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

Enrolment period: August 2022 to October 2024

N = 373*

R 1:1

Giredestrant (30 mg) + everolimus (10 mg)†

SOC ET‡ + everolimus (10 mg)†
‡Exemestane/fulvestrant/tamoxifen

Until PD or unacceptable toxicity

† Dexamethasone mouthwash prophylaxis and treatment was strongly recommended per SWISH trial protocol[1]

* Trial was enriched to 55% of patients with *ESR1*m at baseline (centrally tested via circulating tumour DNA)

Stratification factors

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

Coprimary endpoints (RECIST v1.1)

- INV-PFS in patients whose tumours had *ESR1*m
- INV-PFS in the ITT population

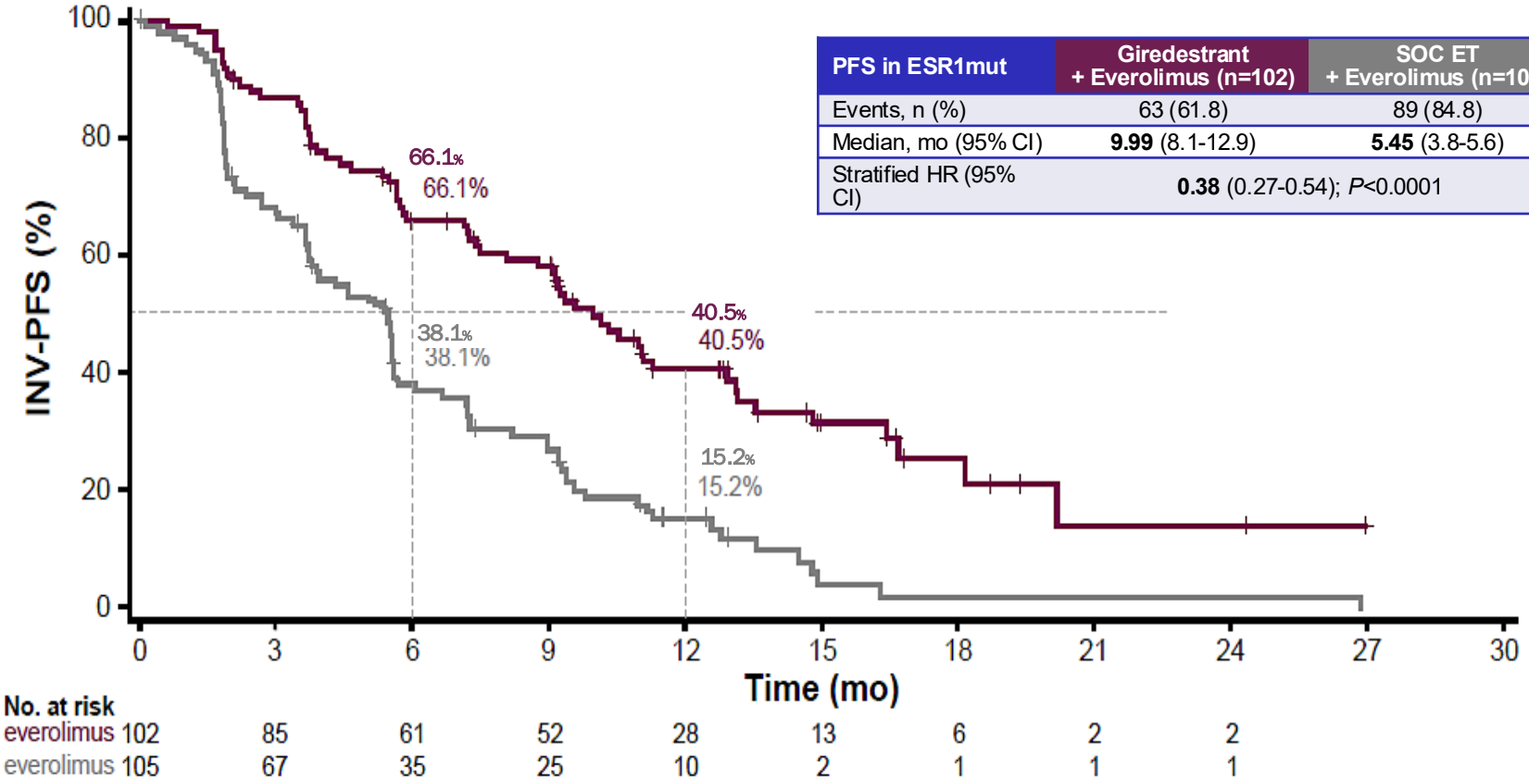
Key secondary endpoints

- OS
- INV-assessed ORR, DoR

Presented by: Erica L. Mayer, MD, MPH.

ClinicalTrials.gov number, NCT05306340. Adapted from Mayer EL, *et al.* SABCS 2022 (poster OT2-01-07) with permission.
1–3L, first to third line; aBC, advanced breast cancer; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; DoR, duration of response; ER+, oestrogen receptor-positive; *ESR1*m, *ESR1* mutation; ET, endocrine therapy; HER2–, HER2-negative; INV, investigator-assessed; ITT, intention to treat; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; R, randomisation; RECIST, Response Evaluation Criteria in Solid Tumours; SOC ET, standard of care endocrine therapy.
1. Rugo HS, *et al. Lancet Oncology* 2017; **18**:654–662.

Giredestrant + Everolimus vs ET + Everolimus: PFS in ESR1 mutant setting (EVERA)



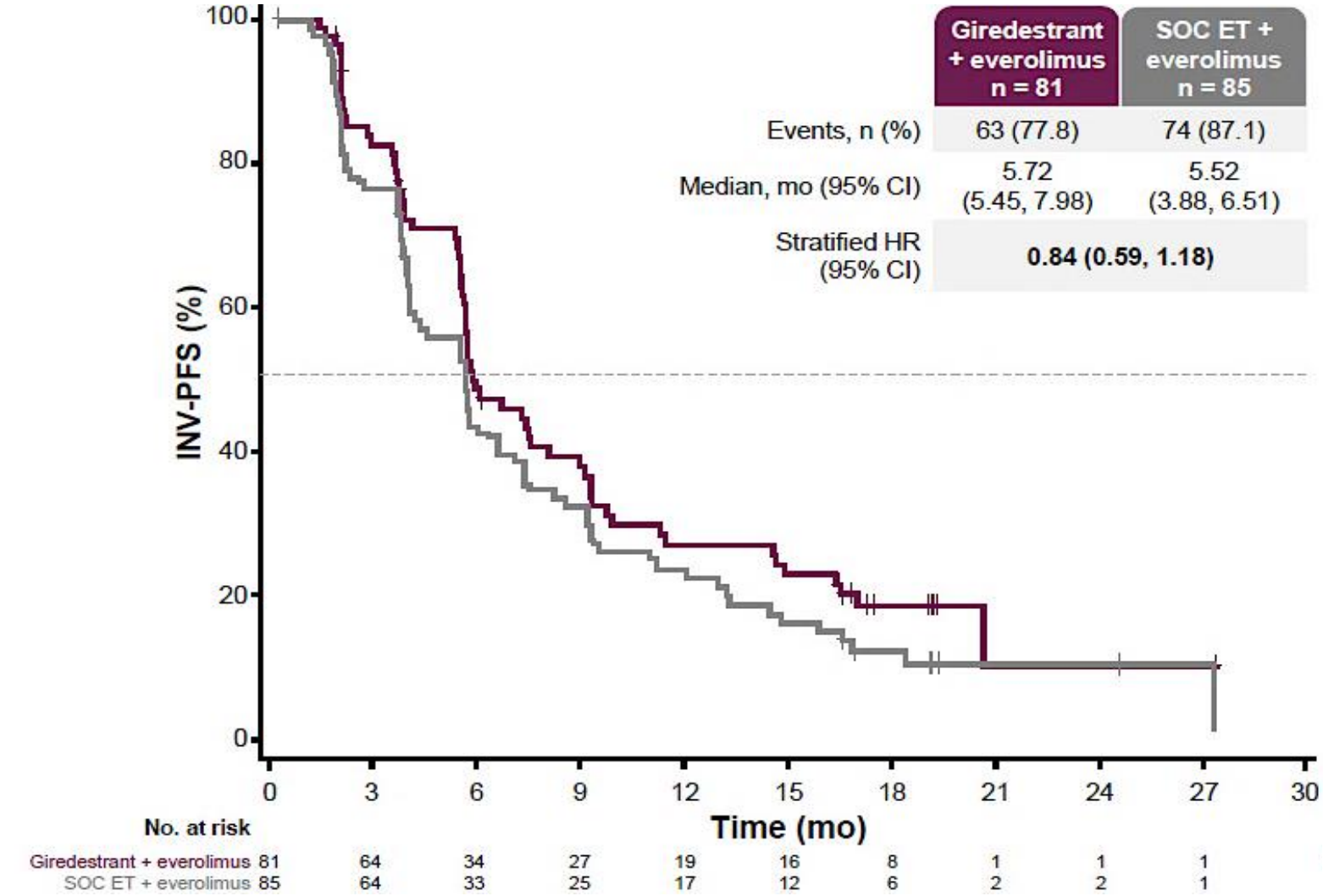
PFS in ESR1mut	Giredestrant + Everolimus (n=102)	SOC ET + Everolimus (n=105)
Events, n (%)	63 (61.8)	89 (84.8)
Median, mo (95% CI)	**9.99** (8.1-12.9)	**5.45** (3.8-5.6)
Stratified HR (95% CI)	**0.38** (0.27-0.54); *P*<0.0001	

INV-PFS in *ESR1*mut Population

- PFS benefit was consistent across key subgroups and regardless of SOC ET

Mayer E, et al. ESMO 2025. Abstract LBA16.

Giredestrant + Everolimus vs ET + Everolimus: PFS in non-ESR1 mutant setting (EVERA)



INV-PFS in Non-*ESR1*mut Population

Mayer E, et al. ESMO 2025. Abstract LBA16.

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AACR American Association for Cancer Research
DECEMBER 9–12, 2025
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Clinical and biomarker subgroup analysis of evERA Breast Cancer: A Phase III trial of giredestrant plus everolimus in patients with estrogen receptor-positive, HER2-negative advanced breast cancer previously treated with a CDK4/6 inhibitor

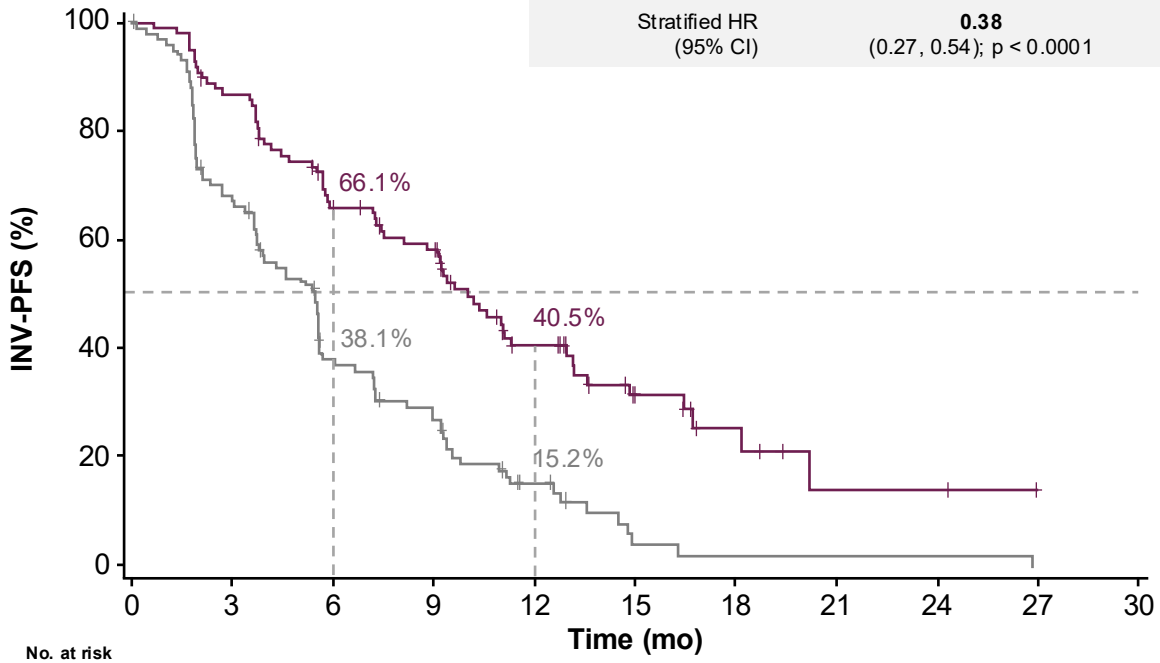
Hope S. Rugo, Sara M. Tolaney, Komal L. Jhaveri, Miguel Martin, Gregory A. Vidal, Luca Moscetti, Adam Brufsky, William J. Gradishar, Andreas Schneeweiss, Naoki Niikura, Anne Favret, Margarita Alfie, Keun Seok Lee, Sarah Khan, Merilin B. Feldman, Bann-mo Day, Lisa H. Lam, Walter C. Darbonne, Tharu M. Fernando, Pablo Perez-Moreno, Erica L. Mayer

Presenting author: Hope S. Rugo, MD
City of Hope Comprehensive Cancer Center, Duarte, CA, USA

Co-primary endpoints – INV-PFS in the *ESR1*m and ITT populations

*ESR1*m

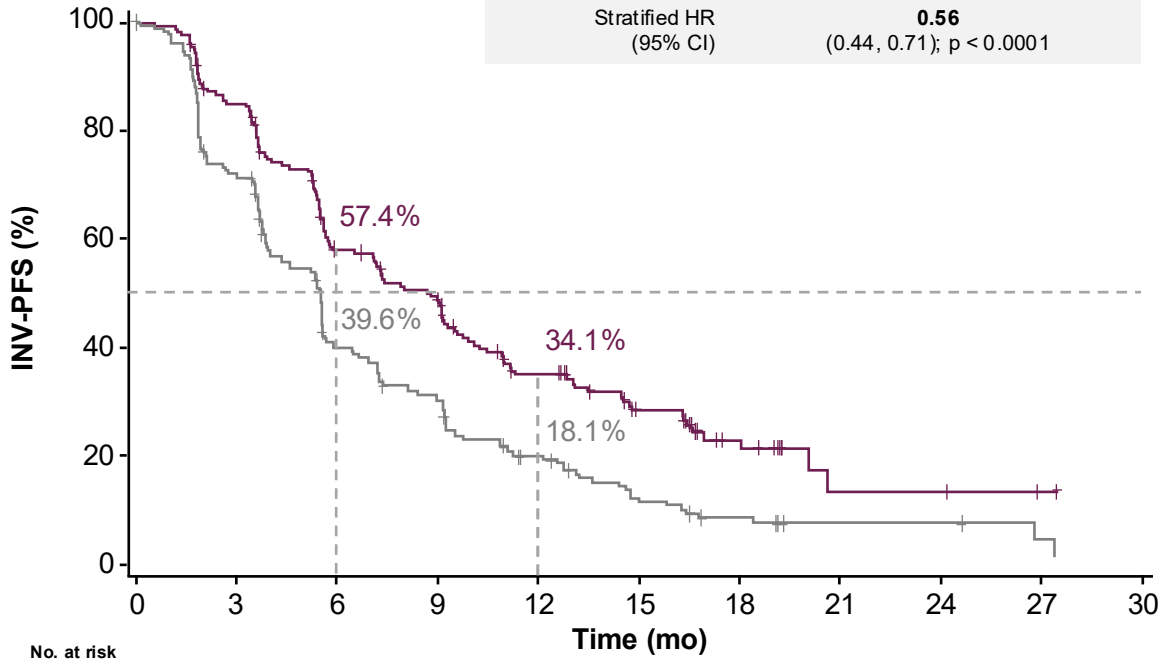
	Giredestrant + everolimus n = 102	SOC ET + everolimus n = 105
Events, n (%)	63 (61.8)	89 (84.8)
Median, mo (95% CI)	**9.99** (8.08, 12.94)	**5.45** (3.75, 5.62)
Stratified HR (95% CI)	**0.38** (0.27, 0.54); p < 0.0001	



No. at risk									
Giredestrant + everolimus	102	85	61	52	28	13	6	2	2
SOC ET + everolimus	105	67	35	25	10	2	1	1	1

ITT

	Giredestrant + everolimus n = 183	SOC ET + everolimus n = 190
Events, n (%)	126 (68.9)	163 (85.8)
Median, mo (95% CI)	**8.77** (6.60, 9.59)	**5.49** (4.01, 5.59)
Stratified HR (95% CI)	**0.56** (0.44, 0.71); p < 0.0001	



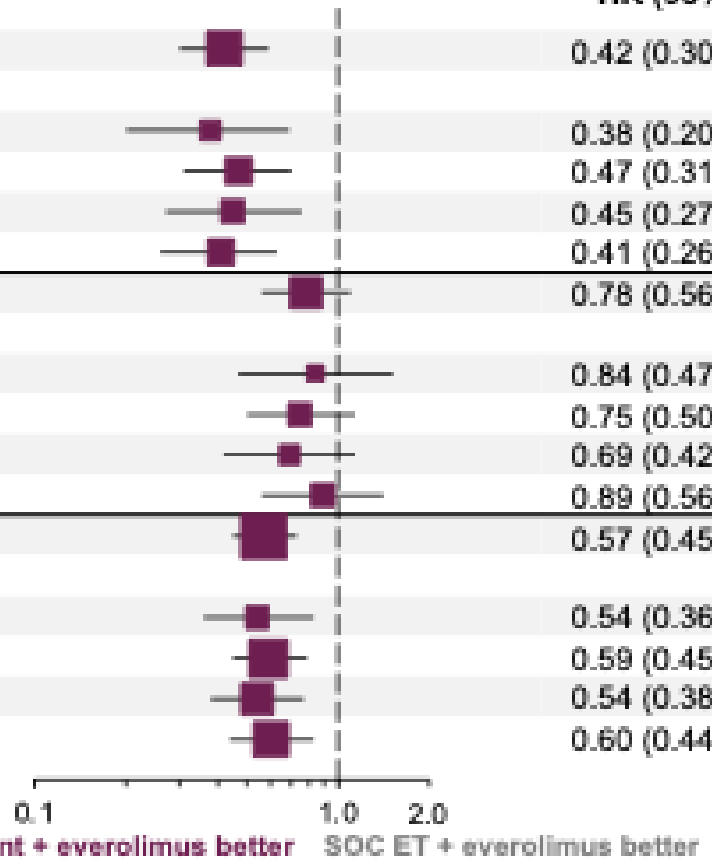
No. at risk										
Giredestrant + everolimus	183	149	95	70	47	29	14	3	3	1
SOC ET + everolimus	190	131	68	50	27	14	7	3	3	1

Data cutoff: July 16, 2025. Median follow-up in the ITT population was 18.4 mo in the giredestrant + everolimus arm and 18.7 mo in the SOC ET + everolimus arm. Adapted from Mayer EL, *et al*. ESMO 2025 (oral LBA16) with permission. CI, confidence interval; *ESR1*m, *ESR1* mutation; HR, hazard ratio; INV-PFS, investigator-assessed progression-free survival; ITT, intention-to-treat; mo, months; SOC ET, standard-of-care endocrine therapy.

Presented by: Hope S. Rugo, MD.

INV-PFS by *PIK3CA/AKT1/PTEN* alteration status

	Total, n	Patients, n: Giredestrant + everolimus	Patients, n: SOC ET + everolimus	HR (95% CI)
All patients with *ESR1*m[1]	207	102	105	0.42 (0.30, 0.59)
Genomic alteration				
*PIK3CA*m detected	64	35	29	0.38 (0.20, 0.69)
*PIK3CA*m not detected	143	67	76	0.47 (0.31, 0.70)
PIK3CA/AKT1/PTEN alteration detected	89	47	42	0.45 (0.27, 0.76)
PIK3CA/AKT1/PTEN alteration not detected	118	55	63	0.41 (0.26, 0.63)
All patients with *ESR1*m not detected	166	81	85	0.78 (0.56, 1.10)
Genomic alteration				
*PIK3CA*m detected	51	29	22	0.84 (0.47, 1.52)
*PIK3CA*m not detected	115	52	63	0.75 (0.50, 1.14)
PIK3CA/AKT1/PTEN alteration detected	73	35	38	0.69 (0.42, 1.14)
PIK3CA/AKT1/PTEN alteration not detected	93	46	47	0.89 (0.56, 1.41)
All ITT patients[1]	373	183	190	0.57 (0.45, 0.73)
Genomic alteration				
*PIK3CA*m detected	115	64	51	0.54 (0.36, 0.83)
*PIK3CA*m not detected	258	119	139	0.59 (0.45, 0.79)
PIK3CA/AKT1/PTEN alteration detected	162	82	80	0.54 (0.38, 0.77)
PIK3CA/AKT1/PTEN alteration not detected	211	101	110	0.60 (0.44, 0.83)



Data cutoff: July 16, 2025. HR estimates are unstratified. *AKT1*, AKT serine/threonine kinase 1; CI, confidence interval; *ESR1*m, *ESR1* mutation; HR, hazard ratio; INV-PFS, investigator-assessed progression-free survival; ITT, intention-to-treat; *PIK3CA*, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; *PIK3CA*m, *PIK3CA* mutation; *PTEN*, phosphatase and tensin homolog; SOC ET, standard-of-care endocrine therapy.

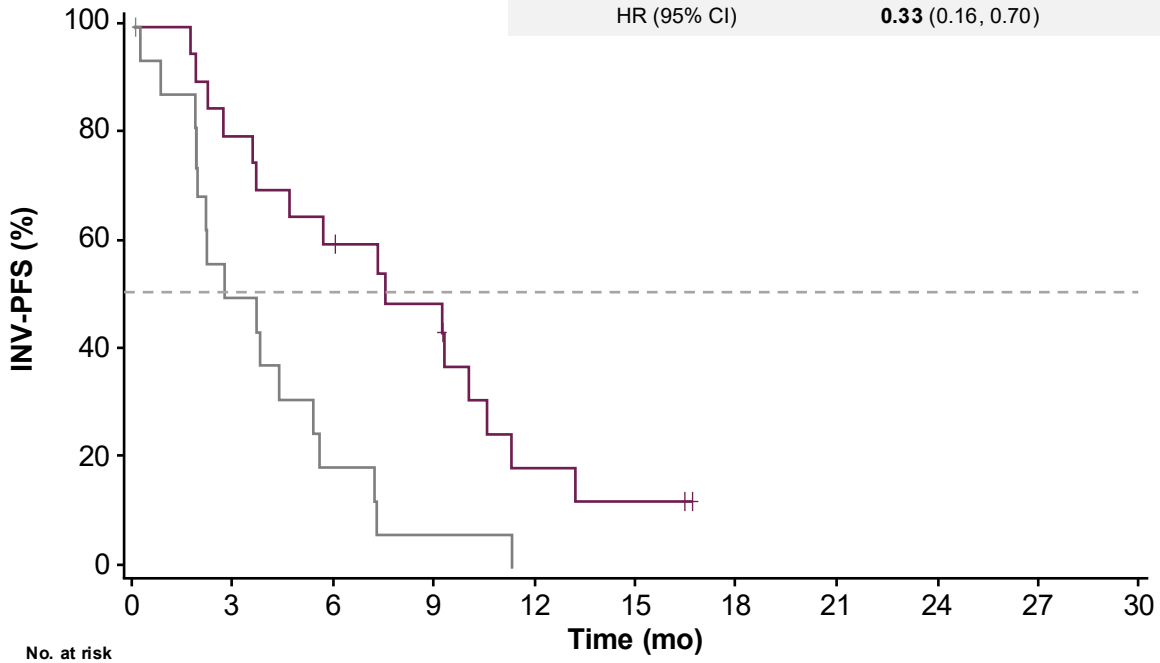
1. Mayer EL, *et al.* ESMO 2025 (oral LBA16).

Presented by: Hope S. Rugo, MD.

INV-PFS by duration of prior CDK4/6i (*ESR1*m population)

< 12 mo*

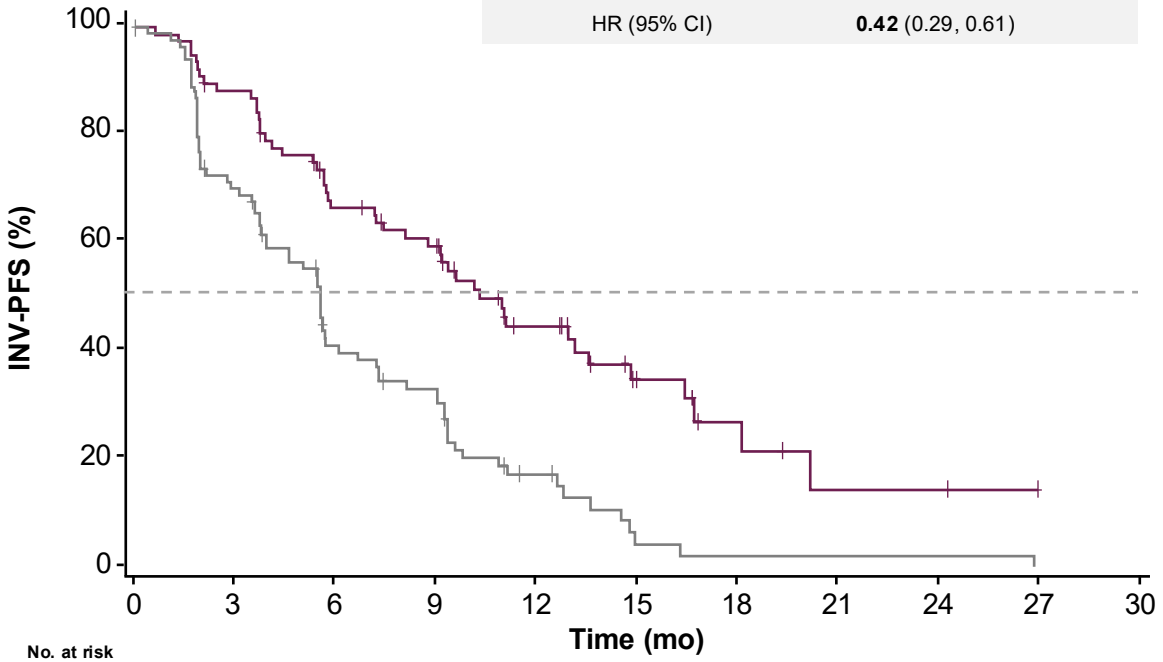
	Giredestrant + everolimus n = 20	SOC ET + everolimus n = 18
Events, n (%)	16 (80.0)	16 (88.9)
Median, mo (95% CI)	**7.49** (3.65, 10.55)	**3.17** (1.87, 5.36)
HR (95% CI)	**0.33** (0.16, 0.70)	



No. at risk						
Giredestrant + everolimus	20	16	11	9	3	2
SOC ET + everolimus	18	8	3	1		

≥ 12 mo*

	Giredestrant + everolimus n = 80	SOC ET + everolimus n = 86
Events, n (%)	47 (58.8)	73 (84.9)
Median, mo (95% CI)	**10.32** (8.08, 14.82)	**5.55** (3.91, 6.67)
HR (95% CI)	**0.42** (0.29, 0.61)	



No. at risk									
Giredestrant + everolimus	80	67	48	41	23	10	5	2	2
SOC ET + everolimus	86	58	31	23	9	2	1	1	1

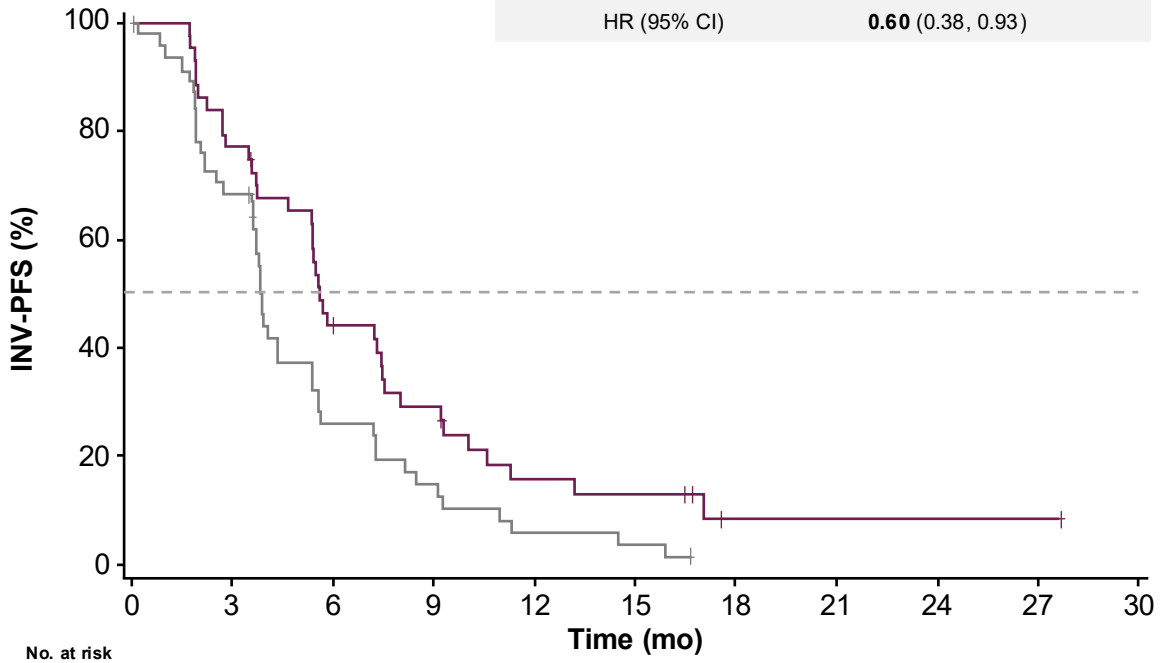
Data cutoff: July 16, 2025. HR estimates are unstratified. * Most recent line of CDK4/6i for mBC. CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; CI, confidence interval; *ESR1*m, *ESR1* mutation; HR, hazard ratio; INV-PFS, investigator-assessed progression-free survival; mBC, metastatic breast cancer; mo, months; SOC ET, standard-of-care endocrine therapy.

Presented by: Hope S. Rugo, MD.

INV-PFS by duration of prior CDK4/6i (ITT population)

< 12 mo*

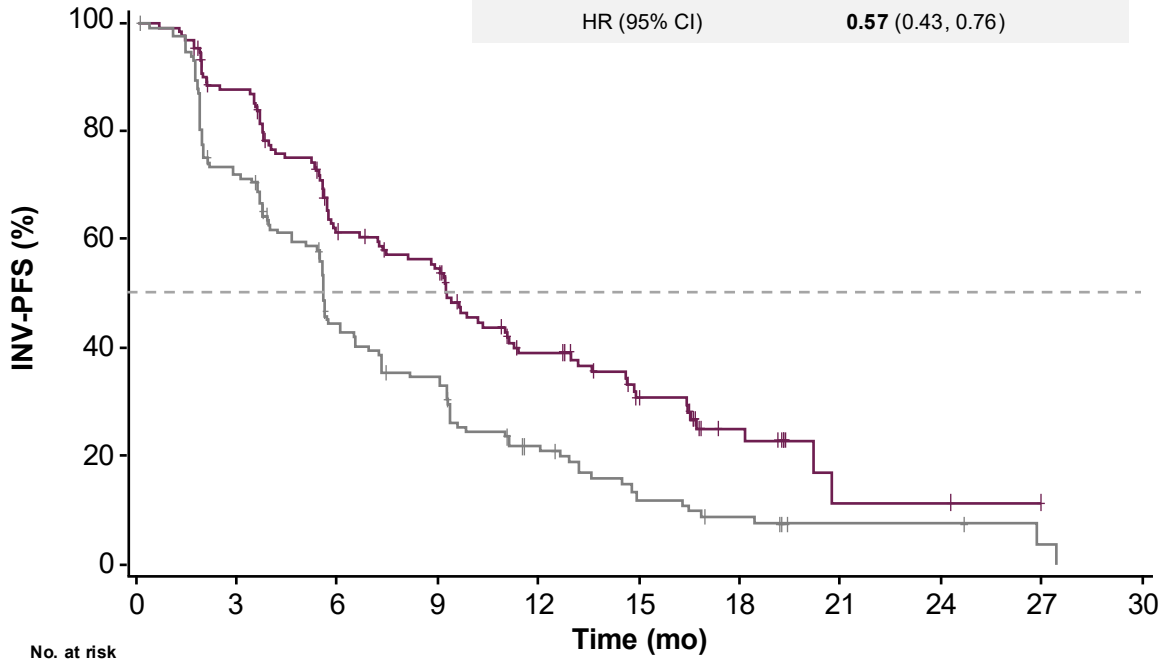
	Giredestrant + everolimus n = 44	SOC ET + everolimus n = 50
Events, n (%)	37 (84.1)	45 (90.0)
Median, mo (95% CI)	**5.55** (5.32, 7.43)	**3.81** (3.61, 5.36)
HR (95% CI)	**0.60** (0.38, 0.93)	



No. at risk											
Giredestrant + everolimus	44	34	18	12	6	5	1	1	1	1	
SOC ET + everolimus	50	33	12	7	3	2					

≥ 12 mo*

	Giredestrant + everolimus n = 136	SOC ET + everolimus n = 135
Events, n (%)	88 (64.7)	115 (85.2)
Median, mo (95% CI)	**9.23** (7.33, 11.24)	**5.55** (5.36, 6.51)
HR (95% CI)	**0.57** (0.43, 0.76)	



No. at risk											
Giredestrant + everolimus	136	113	75	65	39	23	12	2	2		
SOC ET + everolimus	135	95	54	41	22	12	7	3	3	1	

Data cutoff: July 16, 2025. HR estimates are unstratified. * Most recent line of CDK4/6i for mBC. CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; CI, confidence interval; HR, hazard ratio; INV-PFS, investigator-assessed progression-free survival; ITT, intention-to-treat; mBC, metastatic breast cancer; mo, months; SOC ET, standard-of-care endocrine therapy.

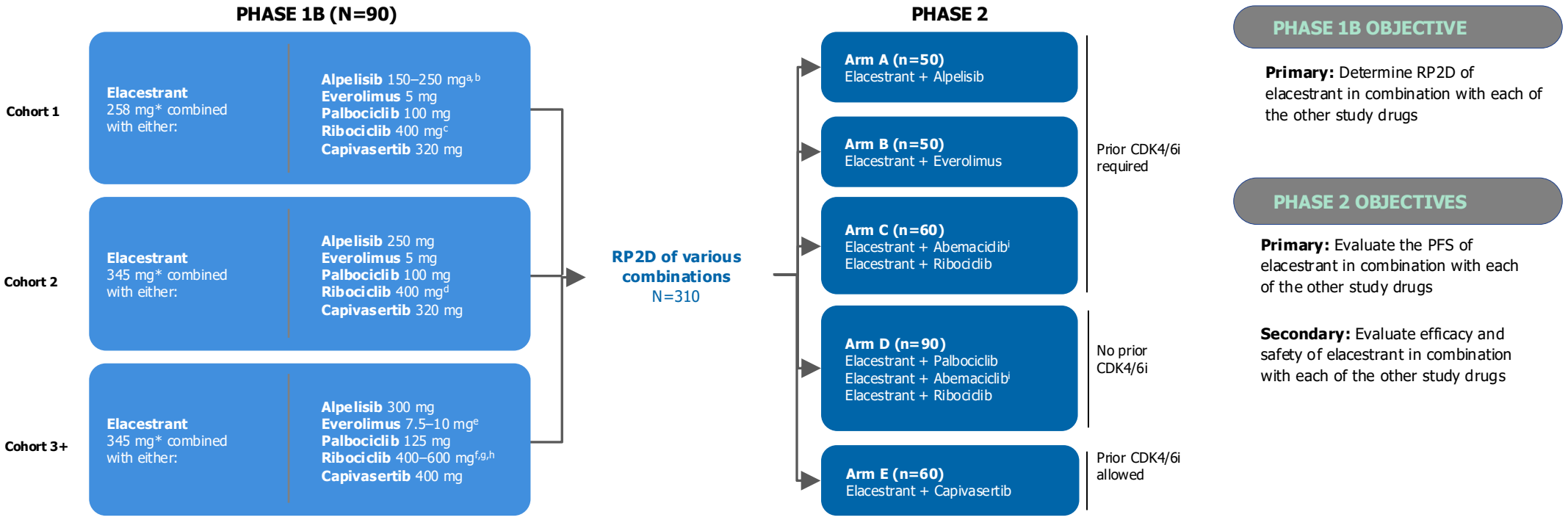
Presented by: Hope S. Rugo, MD.

evERA Discussion

- In the evERA trial, the combination of giredestrant and everolimus prolongs PFS in both ITT and *ESR1m* populations.
- First trial to compare an oral SERD combination to a standard-of-care combination, rather than a monotherapy arm.
- Benefit was observed in prespecified subgroups, including *PIK3CA* mutated (co-mutations *ESR1* and *PIK3CA*) and regardless of duration of prior CDK4/6 inhibitor therapy. Benefit not pronounced in *ESR1m* not detected population.
- Await potential regulatory approval.

How about Elacestrant based combos? (ELEVATE)

ELEVATE Study Design



PHASE 1B OBJECTIVE

Primary: Determine RP2D of elacestrant in combination with each of the other study drugs

PHASE 2 OBJECTIVES

Primary: Evaluate the PFS of elacestrant in combination with each of the other study drugs

Secondary: Evaluate efficacy and safety of elacestrant in combination with each of the other study drugs

Elacestrant 86 mg is equivalent to 100 mg elacestrant hydrochloride; elacestrant 172 mg is equivalent to 200 mg elacestrant hydrochloride; elacestrant 258 mg is equivalent to 300 mg elacestrant hydrochloride; and elacestrant 345 mg is equivalent to 400 mg elacestrant hydrochloride; [a]Elacestrant 258 mg + alpelisib 200 mg (cohort -1); [b]Elacestrant 258 mg* + alpelisib 150 mg (cohort -2); [c]Elacestrant 86 mg* + ribociclib (cohort 1); [d]Elacestrant 172 mg* + ribociclib (cohort 2); [e]Elacestrant 345 mg* + everolimus 7.5 mg (cohort 4); [f]Elacestrant 258 mg* + ribociclib 400 mg (cohort 3); [g]Elacestrant 172 mg* + ribociclib 600 mg (cohort 4); [h]Elacestrant 345 mg + ribociclib 400 mg (cohort 5); [i]The RP2D for the combination of elacestrant and abemaciclib was determined in the ongoing ELECTRA trial (NCT05386108). +, additional Cohorts; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; PFS, progression-free survival; RP2D, recommended phase 2 dose.

NCT05563220

Chan N, et al ASCO 2025: Abstract #1079

Combination of oral SERD with other targeted therapies

SAN ANTONIO BREAST CANCER SYMPOSIUM®
UT Health San Antonio Mays Cancer Center
AACR American Association for Cancer Research
DECEMBER 9–12, 2025
HENRY B. GONZALEZ CONVENTION CENTER • SAN ANTONIO, TX

Elacestrant in combination with everolimus or abemaciclib in patients with ER+/HER2- locally advanced or metastatic breast cancer: phase 2 results from ELEVATE, an open-label umbrella trial

Hope S. Rugo,[1] Sara M. Tolaney,[2] Nancy Chan,[3] Giuliano Borges,[4] Rinat Yerushalmi,[5] Marina N. Sharifi,[6] Wassim McHayleh,[7] Thaddeus Beck,[8] Neelima Vidula,[9] Erika Hamilton,[10] Kristine J. Rinn,[11] Joyce O'Shaughnessy,[12] Giuseppe Curigliano,[13] Javier Cortés,[14] Paula Muñoz Romero,[15] Giulia Tonini,[15] Alessandro Paoli,[15] Li Cheng,[16] Jennifer A. Crozier,[16] Tomer Wasserman,[16] Virginia Kaklamani[17]

1. City of Hope Cancer Center, Duarte, CA, USA; 2. Dana-Farber Cancer Institute, Boston, MA, USA; 3. NYU Langone Health, New York, NY, USA; 4. Catarina Pesquisa Clínica, Santa Catarina, Brazil; 5. Rabin Medical Center, Petah Tikva, Israel; 6. University of Wisconsin, Madison, WI, USA; 7. AdventHealth Cancer Institute, Orlando, FL, USA; 8. Highlands Oncology, Springdale, AR, USA; 9. Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; 10. Sarah Cannon Research Institute, Nashville, TN, USA; 11. Cancer Care Northwest, Spokane, WA, USA; 12. Baylor University Medical Center, Texas Oncology, US Oncology, Dallas, TX, USA; 13. Istituto Europeo di Oncologia, IRCCS, and University of Milano, Milano, Italy; 14. International Breast Cancer Center (IBCC), Quironsalud Group, Barcelona, Spain; 15. Menarini Group, Florence, Italy; 16. Menarini Group, New York, NY, USA; 17. University of Texas Health Sciences Center San Antonio, San Antonio, TX, USA

ELEVATE Trial Design

KEY ELIGIBILITY

- Women (pre-, peri-, or postmenopausal) or men
- ER+, HER2- a/mBC
- 1-2 lines of prior ET +/- CDK4/6i
- Prior fulvestrant allowed
- Primary endocrine resistance allowed
- No prior chemotherapy in the a/mBC setting
- ≥1 measurable lesion as per RECIST v1.1 or a mainly lytic bone lesion

ELEVATE PHASE 1b (n=90)

Elacestrant 86-345 mg* combined with either:

Alpelisib 150-250 mg[a,b,c]
Everolimus 5-10 mg[d,e,f,g]
Palbociclib 100-125 mg[h,i,j]
Ribociclib 400-600 mg[k,l,m,n,o]
Capivasertib 320-400 mg[p,q,r]

ELECTRA PHASE 1b (n=27)

Elacestrant 258-345 mg* combined with **Abemaciclib** 100-150 mg[s,t,i]

RP2D

ELEVATE PHASE 2

- **Elacestrant 345 mg + Everolimus 7.5 mg (n=50)**
- **Elacestrant 345 mg + Abemaciclib 150 mg (n=60)**
- **Elacestrant 345 mg + Ribociclib 400 mg** (n=30)
- **Elacestrant 345 mg + Capivasertib 320 mg** (n=60)

Elacestrant and everolimus dose are administered QD.
Abemaciclib is administered BID.

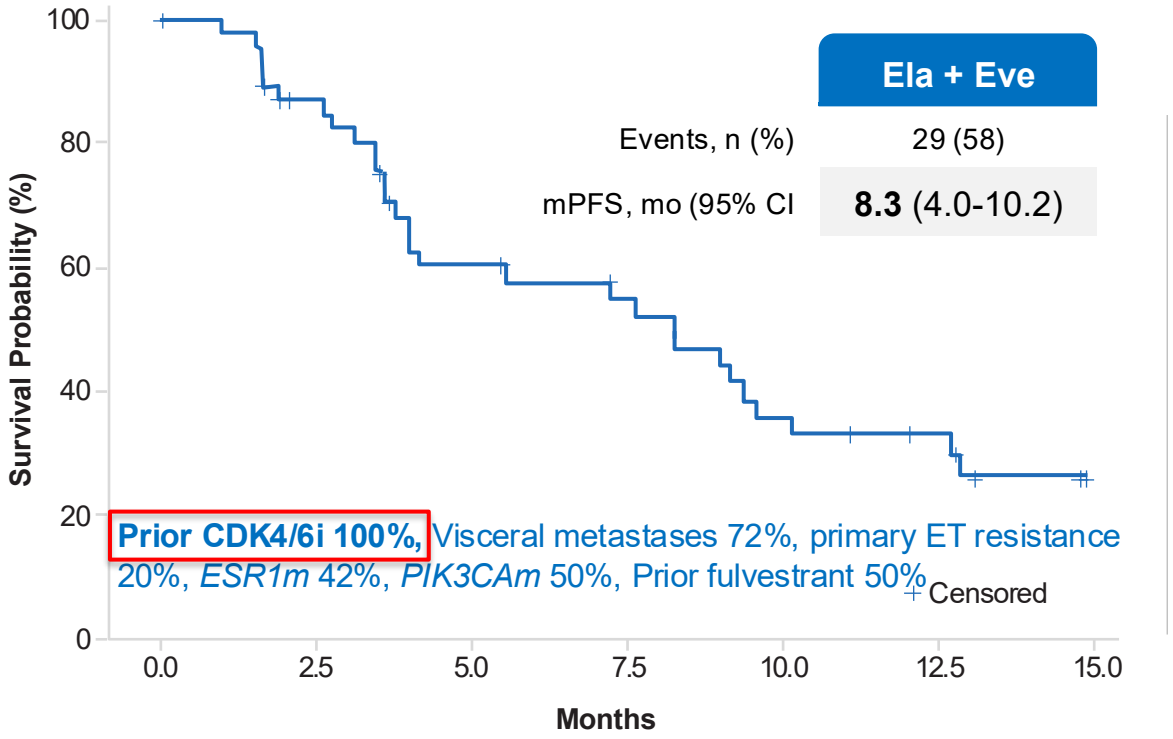
Phase 2 Objectives

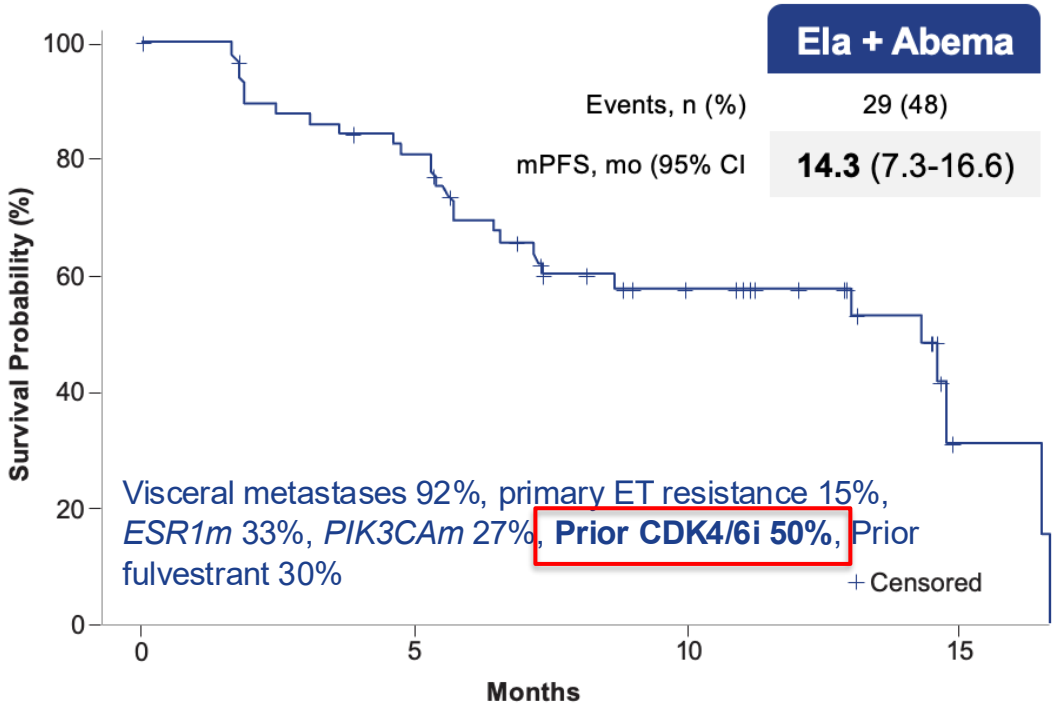
Primary: PFS (RECIST v1.1)
Secondary: ORR, DoR, CBR, PFS, OS, and safety

Elacestrant 86 mg is equivalent to 100 mg elacestrant hydrochloride; elacestrant 172 mg is equivalent to 200 mg elacestrant hydrochloride; elacestrant 258 mg is equivalent to 300 mg elacestrant hydrochloride; elacestrant 345 mg is equivalent to 400 mg elacestrant hydrochloride. [a]Elacestrant 258 mg + alpelisib 250 mg (cohort 1); [b]Elacestrant 258 mg* + alpelisib 200 mg (cohort -1); [c]Elacestrant 258 mg* + alpelisib 150 mg (cohort -2); [d]Elacestrant 258 mg* + everolimus 5 mg (cohort 1); [e]Elacestrant 345 mg* + everolimus 5 mg (cohort 2); [f]Elacestrant 345 mg* + everolimus 10 mg (cohort 3); [g]Elacestrant 345 mg* + everolimus 7.5 mg (cohort 4); [h]Elacestrant 258 mg* + palbociclib 100 mg (cohort 1); [i]Elacestrant 345 mg* + palbociclib 100 mg (cohort 2); [j]Elacestrant 345 mg* + palbociclib 125 mg (cohort 3); [k]Elacestrant 86 mg* + ribociclib 400 mg (cohort 1); [l]Elacestrant 172 mg* + ribociclib 400 mg (cohort 2); [m]Elacestrant 258 mg* + ribociclib 400 mg (cohort 3); [n]Elacestrant 172 mg* + ribociclib 600 mg (cohort 4); [o]Elacestrant 345 mg* + ribociclib 400 mg (cohort 5); [p]Elacestrant 258 mg* + capivasertib 320 mg (cohort 1); [q]Elacestrant 345 mg* + capivasertib 320 mg (cohort 2); [r]Elacestrant 345 mg* + capivasertib 400 mg (cohort 3); [s]Elacestrant 258 mg* + abemaciclib 100 mg (cohort 1); [t]Elacestrant 345 mg* + abemaciclib 100 mg (cohort 2); [i]Elacestrant 345 mg* + abemaciclib 150 mg (cohort 3). a/mBC, advanced or metastatic breast cancer; CBR, clinical benefit rate; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; DoR, duration of response; ER, estrogen receptor; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; n, number; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; RP2D, recommended phase 2 dose; v, version.*

References: 1. Open-Label Umbrella Trial to Evaluate Safety and Efficacy of Elacestrant in Various Combination in Patients With Metastatic Breast Cancer (ELEVATE). ClinicalTrials.gov. May 20, 2024. Accessed August 26, 2024. https://clinicaltrials.gov/trial/NCT05563220. 2. A Phase 1b/2, Open-Label Umbrella Trial to Evaluate Safety and Efficacy of Elacestrant in Various Combinations in Patients with Metastatic Breast Cancer (ELEVATE). STML-ELA-0222. Updated December 22, 2023.

ELEVATE: PFS elacestrant + everolimus or elacestrant + abemaciclib





Ela + Eve showed 82.9% DCR, 19.5% ORR, 8.54 mo mDOR

Ela + Abema showed 91.2% DCR, 24.6% ORR, 14.75 mo mDOR

Elacestrant + everolimus or elacestrant + abemaciclib combinations showed a consistent PFS benefit across all subgroups

Data cut-off: Sept 15, 2025. CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; CI, confidence interval; Ela, elacestrant; *ESR1m*, estrogen receptor 1 mutation; ET, endocrine therapy; Eve, everolimus; mo, months; mPFS, median progression-free survival; n, number; NR, not reached; *PIK3CAm*, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha mutation; PFS, progression-free survival; wt, wild-type. DCR Disease Control Rate, ORR Overall Response Rate, mDOR Median Duration of Response

Rugo HS et al. SABCS 2025

ELEVATE Discussion

- Elacestrant combinations are active and tolerable.
  - Ribociclib combination already reported (PFS 7.8 mo, Rugo et al, ASCO 2025); capivasertib cohort ongoing.
  - In contrast to other oral SERD combination trials (EMBER-3, evERA, SERENA-6), lack of randomization limits interpretation.
  - Cannot compare to PFS in other trials due to difference in degree of patient pre-treatment.

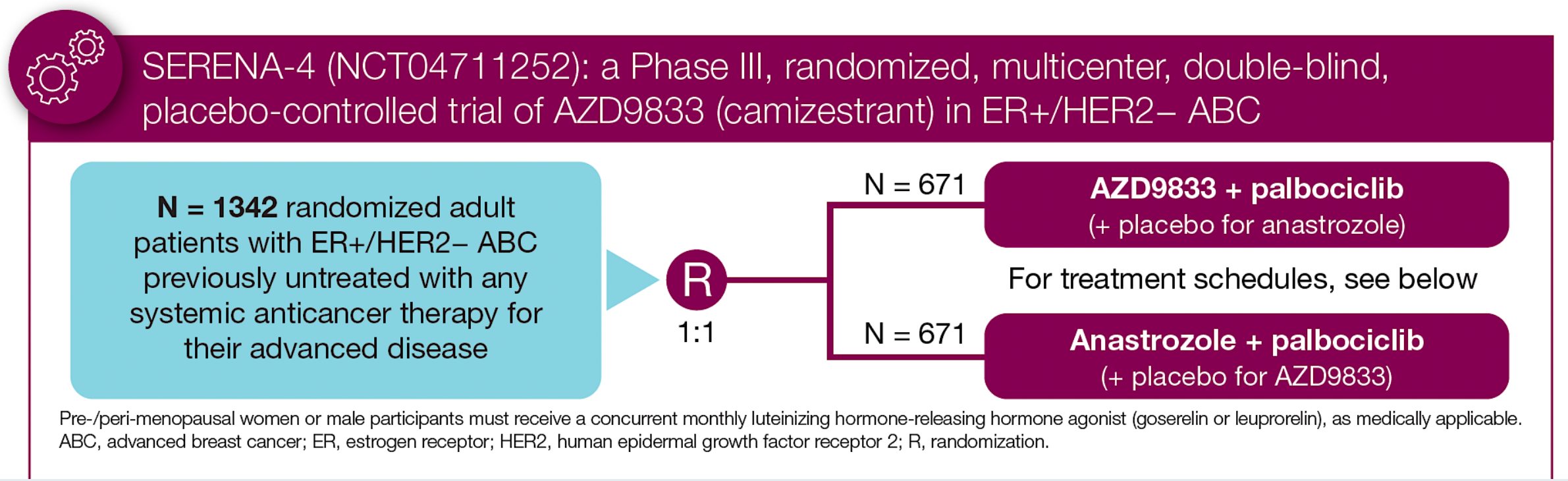
- Oral SERD combinations are the way forward, as PFS consistently >6 months with little additional toxicity from the endocrine agent.

Year in Review:
Oral SERDs for Breast Cancer

MODULE 2: First-line therapy for metastatic disease

- Existing data: EMBER-3?

Phase III SERENA-4 Study Design



Pre-/peri-menopausal women or male participants must receive a concurrent monthly luteinizing hormone-releasing hormone agonist (goserelin or leuprorelin), as medically applicable.
ABC, advanced breast cancer; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; R, randomization.

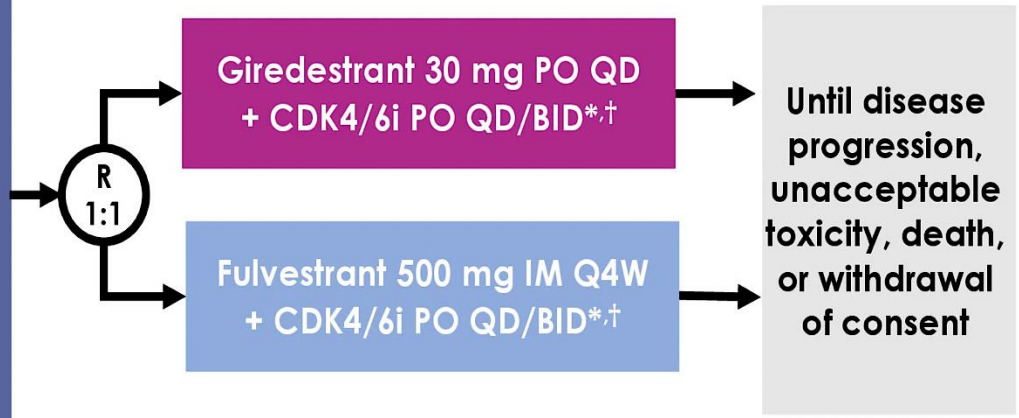
Im S-A et al. ASCO 2021;Abstract TPS1101.

Phase III pionERA Breast Cancer Study Design

Pts with ET-resistant, ER+, HER2– LA/mBC

- Relapse on prior standard adj ET on treatment after ≥12 months or off treatment within 12 months of completion (prior neo/adj CDK4/6i allowed)
- Documented *ESR1* mutation status by ctDNA
- No prior systemic treatment for LA/mBC
- Post- or pre-/perimenopausal women, men

N = ~1050 (planned)



Stratification factors

- Disease site (visceral vs. non-visceral)
- *ESR1* mutation status (*ESR1*mut vs. *ESR1*nmd)
- Choice of CDK4/6i
- Prior adj CDK4/6i (yes vs. no)

Co-primary endpoints

- Investigator-assessed PFS in the *ESR1*mut population and in the full analysis set (per RECIST v1.1)

Secondary endpoints

- PFS (*ESR1*nmd population)
- OS‡
- Investigator-assessed confirmed ORR‡, DoR‡, and CBR‡ (per RECIST v1.1)
- Time to chemotherapy‡
- PROs‡ (time to confirmed deterioration in pain, physical and role functioning, GHS/QoL)
- Safety

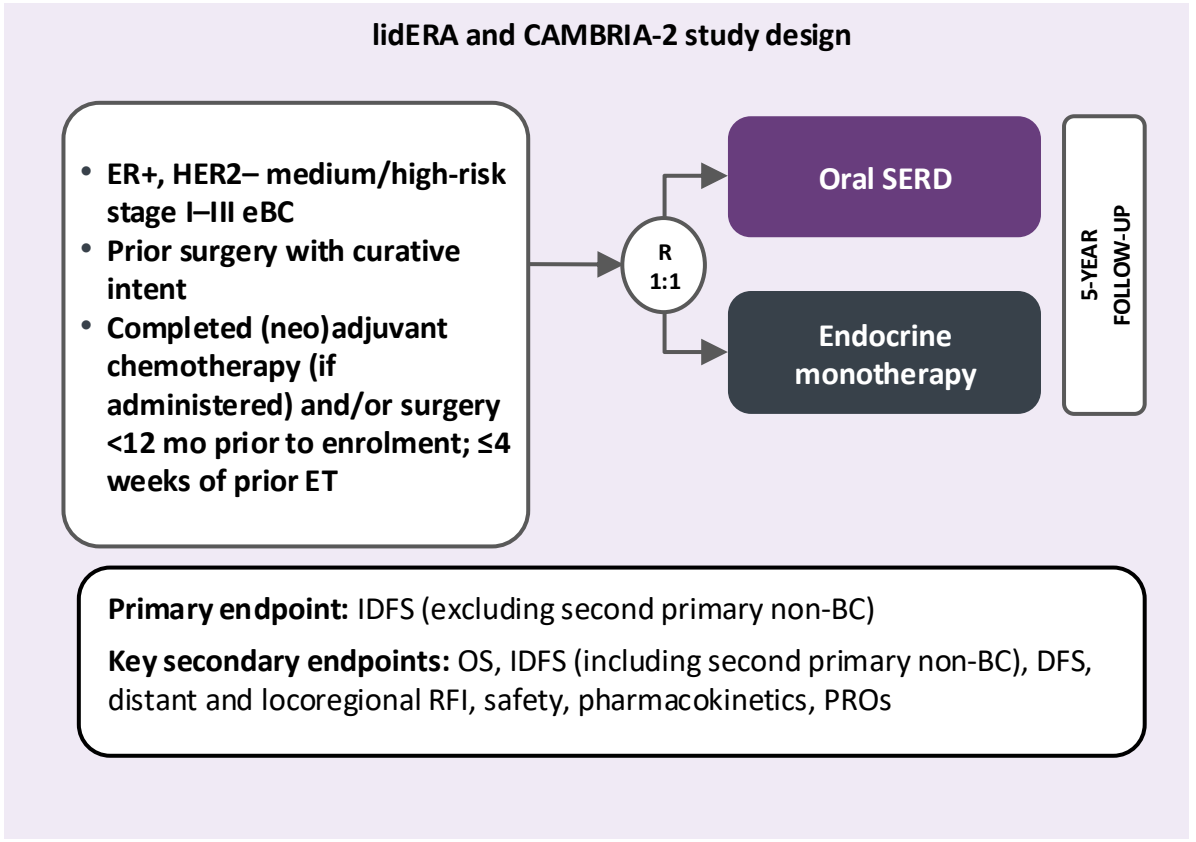
Kalinsky K et al. ASCO 2024;Abstract TPS1130.

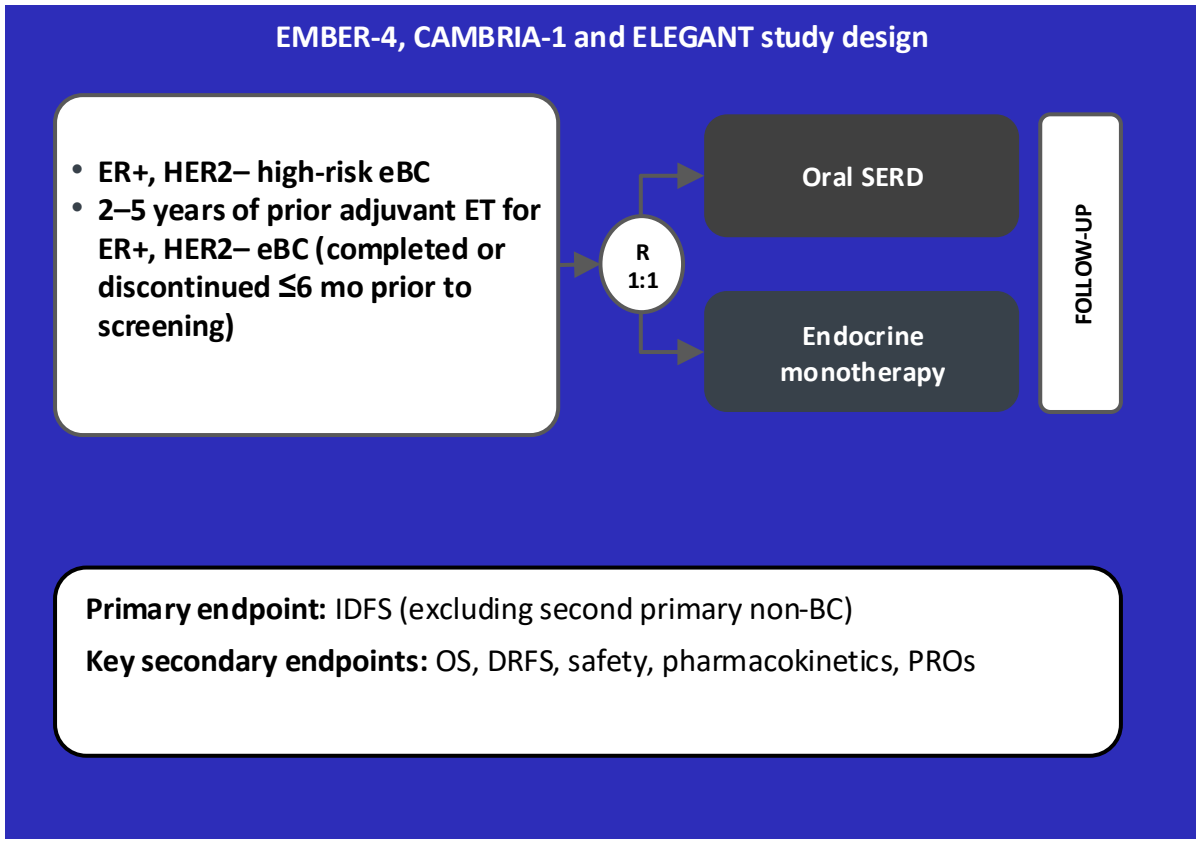
Year in Review:
Oral SERDs for Breast Cancer

MODULE 3: Adjuvant therapy

- Calculating absolute benefits of treatment and benefit versus risk
- Dr Carey's discussion (Lisa A Carey, MD, ScM, FASCO)
- How much benefit was from more drug received than from antitumor effect?
- Premenopausal versus postmenopausal
- Emerging algorithms: SERD/CDK4/6 inhibitor combinations
- Switching therapy for patients experiencing aromatase inhibitor side effects
- Tolerability of tamoxifen versus giredestrant

Adjuvant Studies: Upfront Vs Switch Strategy

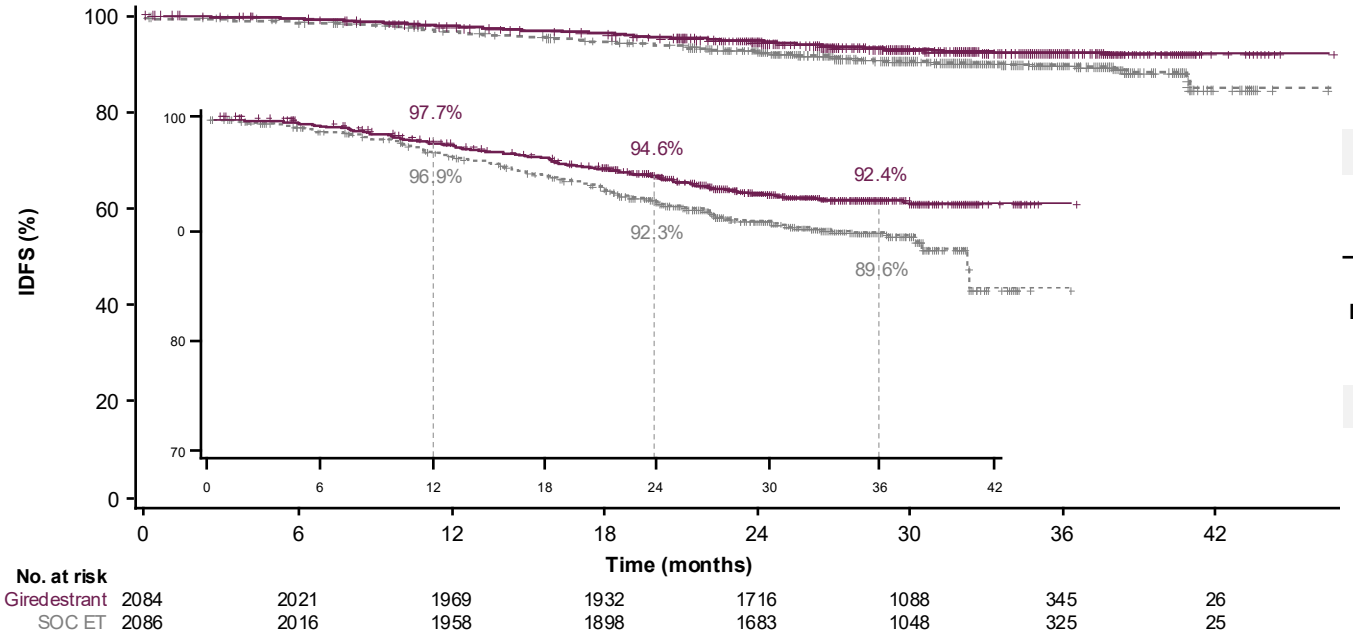




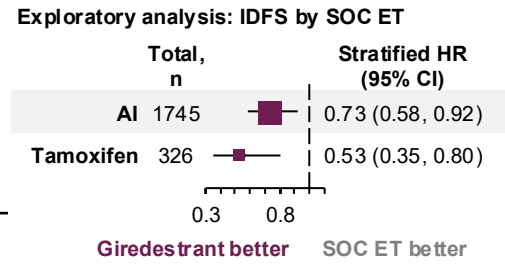
Courtesy of Aditya Bardia, MD, MPH

Giredestrant vs ET in Early Breast Cancer: iDFS (Lidera)

Primary endpoint: IDFS



	Giredestrant n = 2084	SOC ET n = 2086
Events, n (%)	140 (6.7)	196 (9.4)
Stratified HR (95% CI)	**0.70** (0.57, 0.87); **p = 0.0014***	

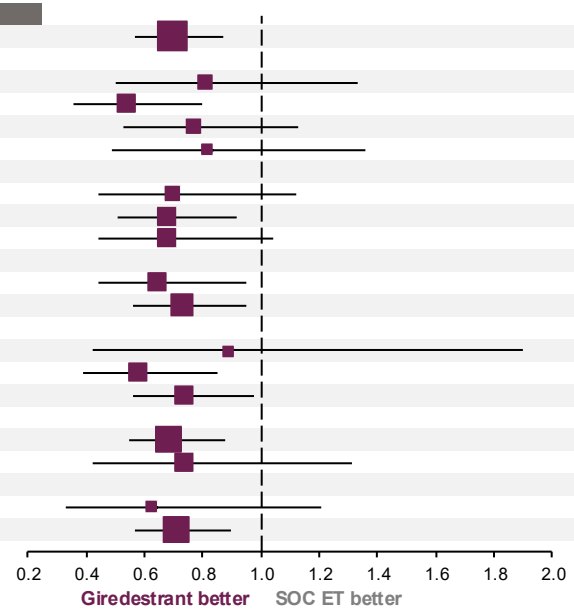


Statistically significant and clinically meaningful improvement in IDFS:
Giredestrant reduced the risk of invasive disease recurrence or death by 30% compared with SOC ET

Giredestrant vs ET in Early Breast Cancer: iDFS (Lidera)

IDFS in key subgroups

	Total, n	Patients, n: Giredestrant	Patients, n: SOC ET	HR (95% CI)
All patients	4170	2084	2086	0.70 (0.57, 0.87)
Age group, years				
≤ 45	906	472	434	0.81 (0.50, 1.33)
> 45 to ≤ 55	1355	660	695	0.54 (0.36, 0.80)
> 55 to ≤ 65	1118	567	551	0.77 (0.53, 1.13)
> 65	791	385	406	0.82 (0.49, 1.36)
Region				
Asia–Pacific	1088	544	544	0.70 (0.44, 1.12)
Latin America/Africa/Eastern Europe	1317	680	637	0.68 (0.51, 0.92)
USA/Canada/Western Europe	1765	860	905	0.68 (0.44, 1.04)
Menopausal status				
Pre-menopausal	1680	841	839	0.65 (0.44, 0.95)
Post-menopausal	2490	1243	1247	0.73 (0.56, 0.95)
AJCC stage at surgery*				
I	537	254	283	0.89 (0.42, 1.90)
II	1963	1013	950	0.58 (0.39, 0.85)
III	1643	799	844	0.74 (0.56, 0.98)
Risk				
High	2895	1448	1447	0.69 (0.55, 0.88)
Medium	1275	636	639	0.74 (0.42, 1.31)
Previous chemotherapy				
No	787	392	395	0.63 (0.33, 1.21)
Yes	3383	1692	1691	0.71 (0.57, 0.90)



IDFS benefit was consistent across key prespecified subgroups

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Giredestrant vs standard-of-care endocrine therapy as adjuvant treatment for patients with estrogen receptor-positive, HER2-negative early breast cancer: Results from the global Phase III lidERA Breast Cancer trial

Presenting author: Aditya L. Bardia, MD
University of California, Los Angeles, Los Angeles, CA, USA

Aditya L. Bardia,* Peter Schmid,* Miguel Martín, Sara A. Hurvitz, Kyung Hae Jung, Mothaffar F. Rimawi, Shigehira Saji, Gustavo Werutsky, Nadia Harbeck, Sherene Loi, Akiko Ogiya, Manuel Ruiz-Borrego, Ahmet Alacacıoğlu, Jiong Wu, Chenglin Ye, Mario Liste-Hermoso, Nimali P. Withana, Tanja Badovinac Crnjevic, Mona D. Shah, Pablo Pérez-Moreno, Charles E. Geyer, Jr.*

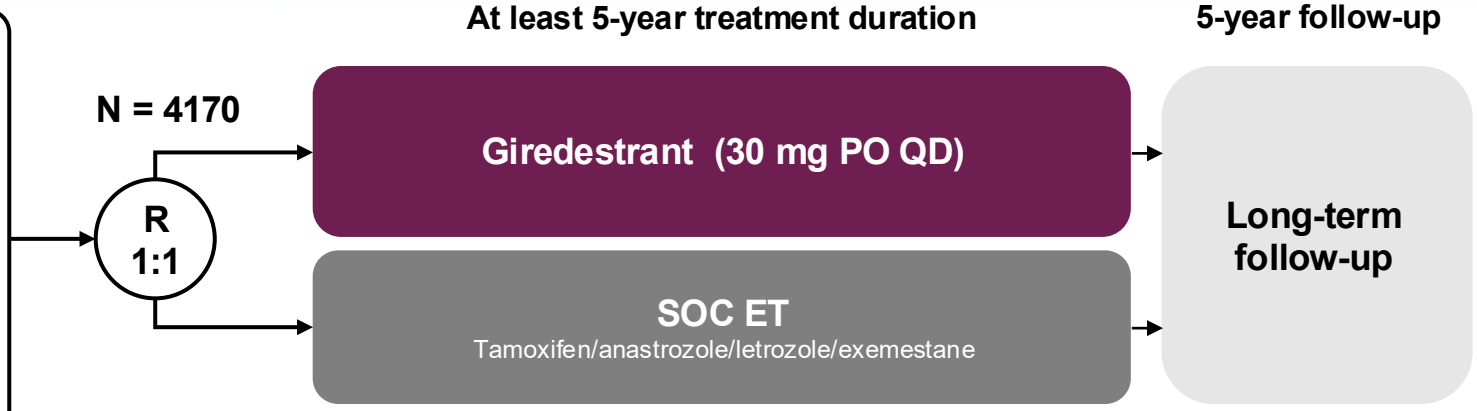
* Equal contributions

lidERA Breast Cancer study design

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

Key eligibility criteria

- Participants with ER+, HER2-negative early breast cancer
- Stage I–III disease (anatomical)
  - 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†
- Breast cancer surgery within 12 months
- (Neo)adjuvant chemotherapy if indicated



Stratification factors

- Risk: Medium-‡ vs high-risk§ Stage I–III breast cancer
- 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-breast cancer)

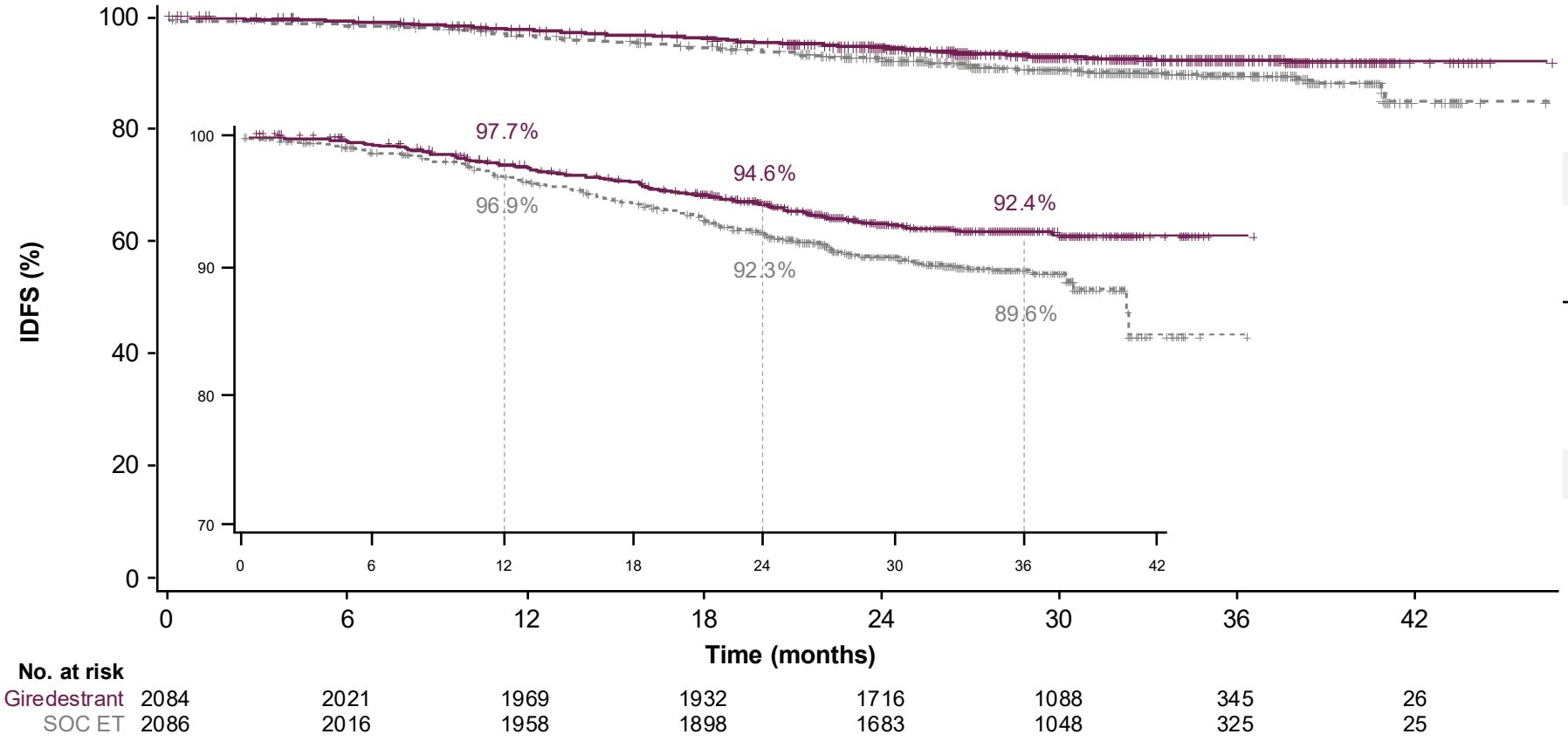
Key secondary endpoints

- 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

Giredestrant is currently also being investigated in combination with abemaciclib in the adjuvant setting (lidERA Breast Cancer substudy 1)

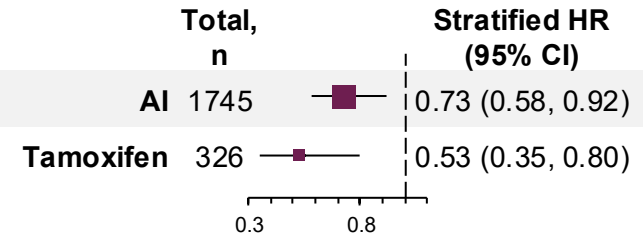
Enrollment: August 2021 to September 2023. Up to 12 weeks of ET ± CDK4/6i were allowed. ER+ was defined as ≥ 1% positive cells by immunohistochemistry. * OncotypeDx ≥ 26 or high-risk Mammaprint.
† Pre-menopausal patients on aromatase inhibitors or giredestrant had to receive ovarian function suppression with an approved luteinizing hormone-releasing hormone agonist. ‡ 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]).
CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; DFS, disease-free survival; DRFI, distant recurrence-free interval; ER+, estrogen receptor-positive; ET, endocrine therapy; IDFS, invasive disease-free survival; LRRFI, locoregional recurrence-free interval; OS, overall survival; PO, orally; QD, once daily; R, randomization; RoW, rest of the world; SOC, standard-of-care.
ClinicalTrials.gov number, NCT04961996. Adapted from Geyer CE, *et al*. ASCO 2023 (TPS616), with permission.
Presented by: Aditya L. Bardia, MD.

Primary endpoint: IDFS



	Giredestrant n = 2084	SOC ET n = 2086
Events, n (%)	140 (6.7)	196 (9.4)
Stratified HR (95% CI)	**0.70** (0.57, 0.87); **p = 0.0014***	

Exploratory analysis: IDFS by SOC ET



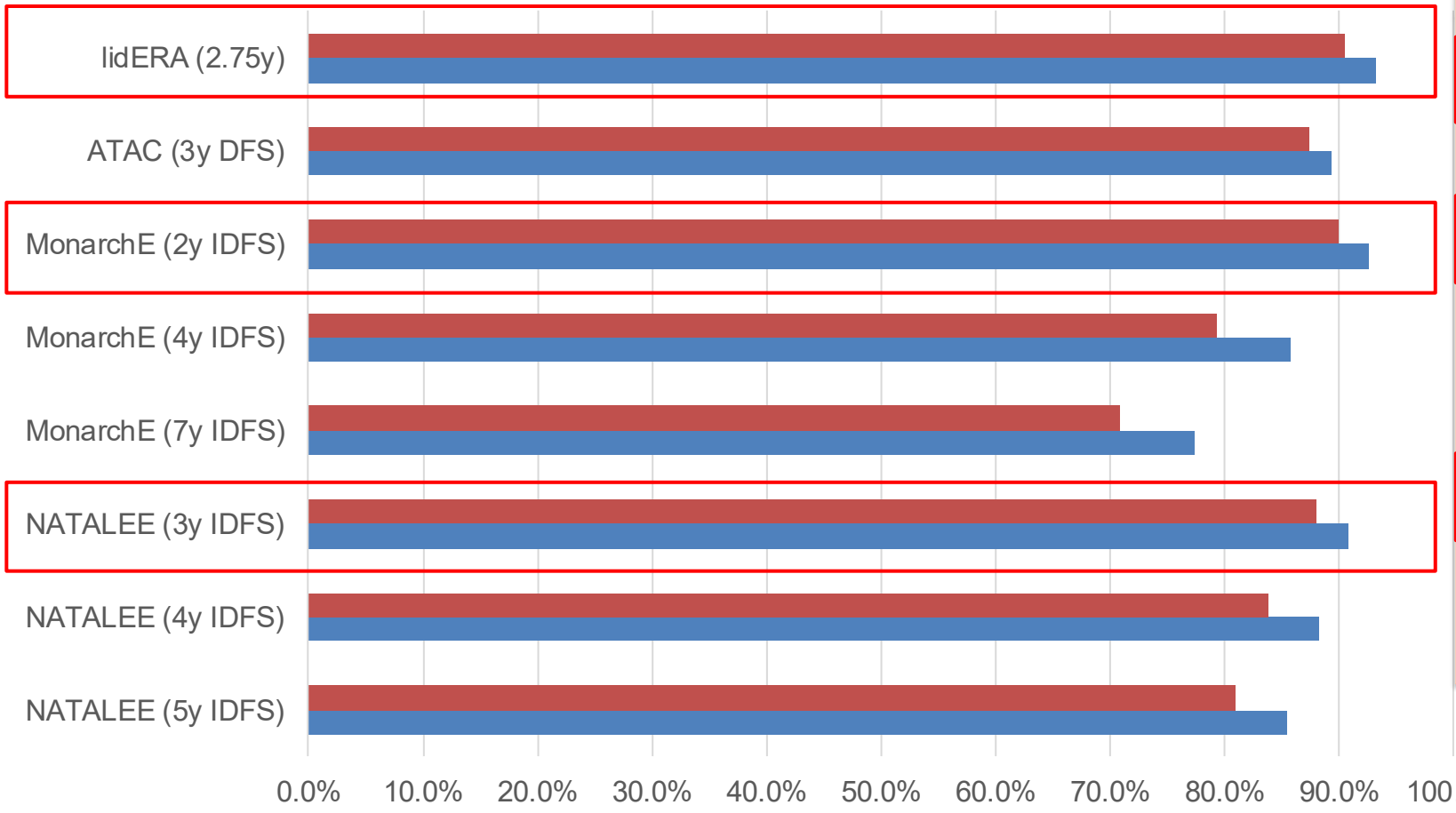
Median follow-up: 32.3 months

Statistically significant and clinically meaningful improvement in IDFS:
Giredestrant reduced the risk of invasive disease recurrence or death by 30% compared with SOC ET

Data cutoff: August 8, 2025. Median follow-up, 32.4 months in the giredestrant arm and 32.3 months in the SOC ET arm; maximum follow-up, 46.6 months and 46.3 months, respectively. * Log-rank (2-sided). p-value boundary for IDFS interim analysis was 0.0217 (2-sided). AI, aromatase inhibitor; CI, confidence interval; ET, endocrine therapy; HR, hazard ratio; IDFS, invasive disease-free survival; SOC, standard-of-care.

Presented by: Aditya L. Bardia, MD.

lidERA in Context of Other Adjuvant Advances



	absolute △	HR
lidERA (2.75y)	2.8%	0.70
ATAC (3y)	2.0%	0.83
MonarchE (2y)	2.8%	0.75
MonarchE (4y)	6.4%	0.66
MonarchE (7y)	6.5%	0.73
NATALEE (3y)	2.7%	0.75
NATALEE (4y)	4.4%	0.72
NATALEE (5y)	4.5%	0.72

Highly similar HR and absolute iDFS benefit for adjuvant CDK4/6i trials and lidERA at same timepoint: Are these agents interchangeable?

B… ncol 2025; Crown J, ESMO2025

Adjuvant Trial Inclusion Criteria by Stage

Anatomic Stage (AJCC 8)	TNM Stage	LidERA BC	NATALEE	MonarchE
IA	*T1 N0 M0*	Tumor larger than 1 cm and at least one high risk feature: Grade 3, or Ki67 ≥20%, or Oncotype DX ≥ 26 or High-Risk MammaPrint	X	X
IB	*T0 N1mi M0*	✓	X	N1 with one high risk feature
	T1 N1mi M0	✓	X	N1 with one high risk feature
IIA	*T0 N1 M0*	✓	✓	N1 with one high risk feature
	T1 N1 M0	✓	✓	N1 with one high risk feature
	T2 N0 M0	One high risk feature: Grade 3, or Ki67 ≥20%, or Oncotype DX ≥ 26 or High-Risk MammaPrint	Grade 3 or high risk Grade 2: Ki67 >20% or high genomic risk	X
IIB	*T2 N1 M0*	✓	✓	✓
	T3 N0 M0	One high risk feature: Grade 3, or Ki67 ≥20%, or Oncotype DX ≥ 26 or High-Risk MammaPrint	✓	X
IIIA	*T0 N2 M0*	✓	✓	✓
	T1 N2 M0	✓	✓	✓
	T2 N2 M0	✓	✓	✓
	T3 N1 M0	✓	✓	✓
	T3 N2 M0	✓	✓	✓
IIIB	*T4 N0 M0*	✓	✓	X
	T4 N1 M0	✓	✓	✓
	T4 N2 M0	✓	✓	✓
IIIC	*Any T N3 M0*	✓	✓	✓

Courtesy of Erica Mayer, MD, MPH, FASCO

lidERA Discussion

- Early readout – will benefits persist over time? Early events vs late events? Time-dependent effects on luminal B vs luminal A disease?
- Few events in Stage I or medium-risk subgroups at early readout, need more maturity
- No concurrent or sequential CDK4/6i used in the trial; unclear if combined SERD and CDK4/6i treatment would be additive or not.
- Heterogenous treatment in premenopausal patients, comprising 40% of population.
- Likely low percentage *ESR1m* positive tumors; how to explain activity of SERD over AI monotherapy in absence of mutation? Are there any biomarkers to predict benefit?
- Financial costs should giredestrant be approved

Courtesy of Erica Mayer, MD, MPH, FASCO

Selection of Adjuvant Systemic Therapy for HR+ HER2- eBC

Stage	CDK4/6i yes/no	Oral SERD yes/no
I (higher risk)	N	Select cases
IIA	Consider	Consider
IIB	Y	After CDK?
III	Y	After CDK?

* If contraindication for CDK4/6i or deciding not to give, then more strongly consider giredestrant

Await results of CAMBRIA1/2, EMBER-4, ELEGANT

Courtesy of Erica Mayer, MD, MPH, FASCO

Year in Review:
Oral SERDs for Breast Cancer

MODULE 4: Toxicity, quality of life

- What do you say to patients who are starting treatment?
- GI toxicity: Elacestrant versus imlunestrant
- Bradycardia
- Ophthalmic issues

Elacestrant: Adverse Affects

AEs Occurring in ≥ 10% of Patients in Any Arm

AE, by Preferred Term	ELA (n = 237), No. (%)		SoC, No. (%)					
			Total (n = 229)		FUL (n = 161)		AI (n = 68)	
	All Grades	Grade 3/4	All Grades	Grade 3/4	All Grades	Grade 3/4	All Grades	Grade 3/4
Nausea	83 (35.0)	6 (2.5)	43 (18.8)	2 (0.9)	26 (16.1)		17 (25.0)	2 (2.9)
Fatigue	45 (19.0)	2 (0.8)	43 (18.8)	2 (0.9)	35 (21.7)	1 (0.6)	8 (11.8)	1 (1.5)
Vomiting	45 (19.0)	2 (0.8)	19 (8.3)		12 (7.5)		7 (10.3)	
Decreased appetite	35 (14.8)	2 (0.8)	21 (9.2)	1 (0.4)	12 (7.5)		9 (13.2)	1 (1.5)
Arthralgia	34 (14.3)	2 (0.8)	37 (16.2)		28 (17.4)		9 (13.2)	
Diarrhea	33 (13.9)	--	23 (10.0)	2 (0.9)	14 (8.7)	1 (0.6)	9 (13.2)	1 (1.5)
Back pain	33 (13.9)	6 (2.5)	22 (9.6)	1 (0.4)	16 (9.9)	1 (0.6)	6 (8.8)	
AST increased	31 (13.1)	4 (1.7)	28 (12.2)	2 (0.9)	20 (12.4)	2 (1.2)	8 (11.8)	
Headache	29 (12.2)	4 (1.7)	26 (11.4)		18 (11.2)		8 (11.8)	
Constipation	29 (12.2)		15 (6.6)		10 (6.2)		5 (7.4)	
Hot flush	27 (11.4)		19 (8.3)		15 (9.3)		4 (5.9)	
Dyspepsia	24 (10.1)		6 (2.6)		4 (2.5)		2 (2.9)	
ALT increased	22 (9.3)	5 (2.1)	23 (10.0)	1 (0.4)	17 (10.6)		6 (8.8)	1 (1.5)

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Bidard FC, et al. J Clin Oncol. 2022

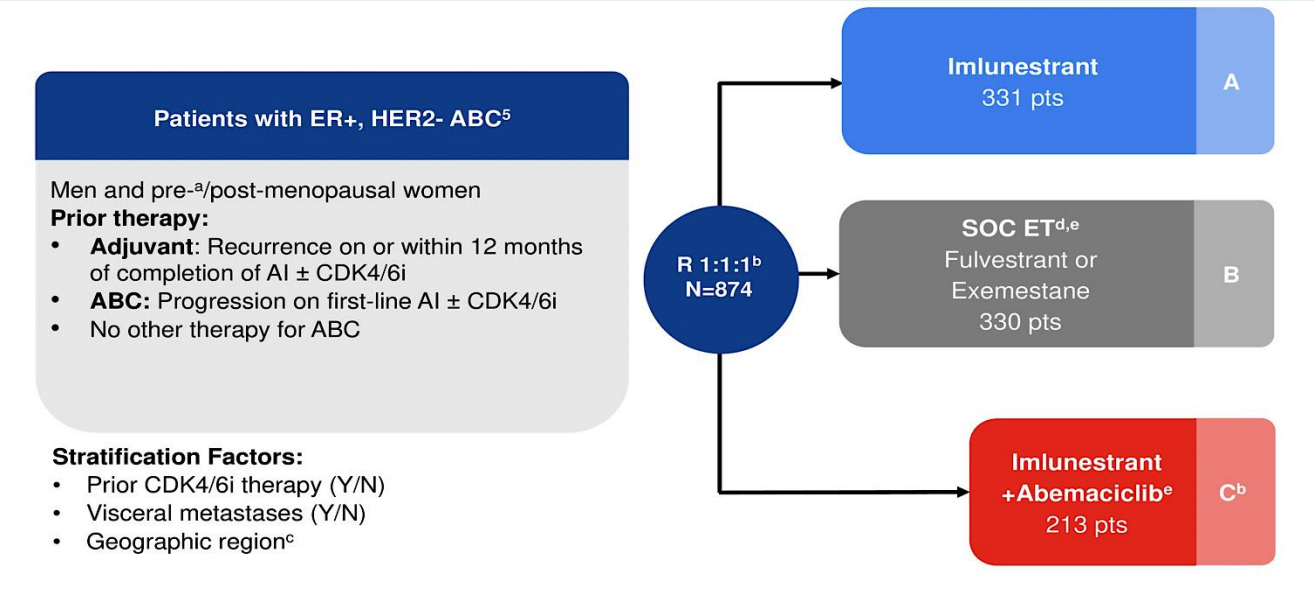
EMBER-3
Safety and Tolerability

TEAEs in ≥ 10% of Patients, %	Imlunestrant n=327		SOC ET n=324	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Patients with ≥ 1 TEAE	83	17	84	21
Fatigue[a]	23	<1	13	1
Diarrhea	21	<1	12	0
Nausea	17	<1	13	0
Arthralgia	14	1	14	<1
AST increased	13	1	13	1
Back pain	11	1	7	<1
ALT increased	10	<1	10	1
Anemia[a]	10	2	13	3
Constipation	10	0	6	<1
Patients with ≥ 1 SAE, %		10		12
Dose reductions due to AE, %		2		0
Discontinuations due to AE, %		4		1
Deaths due to AE on study, %		2		1

TEAEs in ≥ 20% of Patients, %	Imlunestrant + abemaciclib n=208	
	Any Grade	Grade ≥3
Patients with ≥ 1 TEAE	98	49
Diarrhea	86	8
Nausea	49	2
Neutropenia[a]	48	20
Anemia[a]	44	8
Fatigue[a]	39	5
Vomiting	31	1
Leukopenia[a]	26	4
Hypercreatinemia[a]	22	1
Abdominal pain[a]	20	2
Decreased appetite	20	1
Patients with ≥ 1 SAE, %		17
Dose reductions due to AE, %[d]		39
Discontinuations due to AE, %		6
Deaths due to AE on study, %		1

Jhaveri KL, et al. NEJM. 2024.

Phase III EMBER-3: Safety Analyses



- Safety population: all patients who received **at least one dose of any study drug**
- TEAEs were assessed for severity per **CTCAE v5.0** at baseline and at every visit throughout the study
- Labs were assessed at **baseline, at every cycle,** and approximately **30 days after discontinuation of study therapy**

Dose Adjustment	Imlunestrant Dose
1	200 mg QD

Dose Adjustment	Abemaciclib Dose
1	100 mg BID
2	50 mg BID

Patients receiving **imlunestrant+abemaciclib** could discontinue either drug and continue the other per investigator's decision

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

Phase III EMBER-3 Safety Analysis: Diarrhea

Diarrhea		Imlu N=327	SOC ET N=324	Imlu+Abema N=208
% pts	Any grade	21	12	86
	G1 AE	18	9	50
	G2 AE	3	3	28
	G≥3 AE	<1	0	8
	Pts with >1 occurrences of AE	5	1	34
	Pts with >1 occurrences of G≥3 AE	0	0	<1
	Dose interruption/reduction/discontinuation	<1/0/0	0/0/0	19[a]/18[b]/<1[c,d]
	Antidiarrheal medication[e]	10	7	68
Median days	Time to onset (Q1-Q3)	30 (15–129)	52 (17–132)	5 (2–17)
	Duration of G2 AE (range)	3 (1–28)	5 (1–55)	13 (1–87)
	Duration of G≥3 AE (range)	8 (8–8)	–	9 (1–47)

- In both **imlunestrant** arms, the majority of events were G1 and occurred in the first month
- Diarrhea in the **imlunestrant+abemaciclib** arm was comparable to that observed previously with abemaciclib[6] and was well managed with dose adjustments and antidiarrheals

[a] 14 (6.7%) pts had only abemaciclib interrupted and 3 (1.4%) pts had only imlunestrant interrupted; [b] 29 (14%) pts had only abemaciclib reduced; [c] Pts who discontinued both drugs; [d] One (0.5%) more pt discontinued only abemaciclib. [e] Proportion of total safety population treated.

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

Phase III EMBER-3 Safety Analysis: Treatment-Emergent Adverse Events (TEAEs) of Interest

TEAE, Consolidated terms, %	Imlu+Abema N=208	
	Any Grade	G≥3
Neutropenia[a]	48	20
Infection[b]	31	4
ILD[c]	2	0
VTE[d]	3	<1

[a]Includes both neutropenia and neutrophil count decreased; [b]Includes all infections and infestations system organ class; [c]Includes Interstitial lung disease, pneumonitis, pulmonary fibrosis, and pulmonary toxicity; [d]Includes central venous catheterization, deep vein thrombosis, pelvic venous thrombosis, peripheral vein thrombosis, portal vein thrombosis, pulmonary embolism, and superficial vein thrombosis.

TEAE, %	Imlu N=327		SOC ET N=324		Imlu+Abema N=208	
	Any Grade	G≥3	Any Grade	G≥3	Any Grade	G≥3
Bradycardia[a]	2	0	0	0	1	0
Photopsia	0	0	0	0	0	0
Dyslipidemia[b]	7	<1	9	0	8	0
Pts receiving lipid-modifying agents[c]	6		4		2	

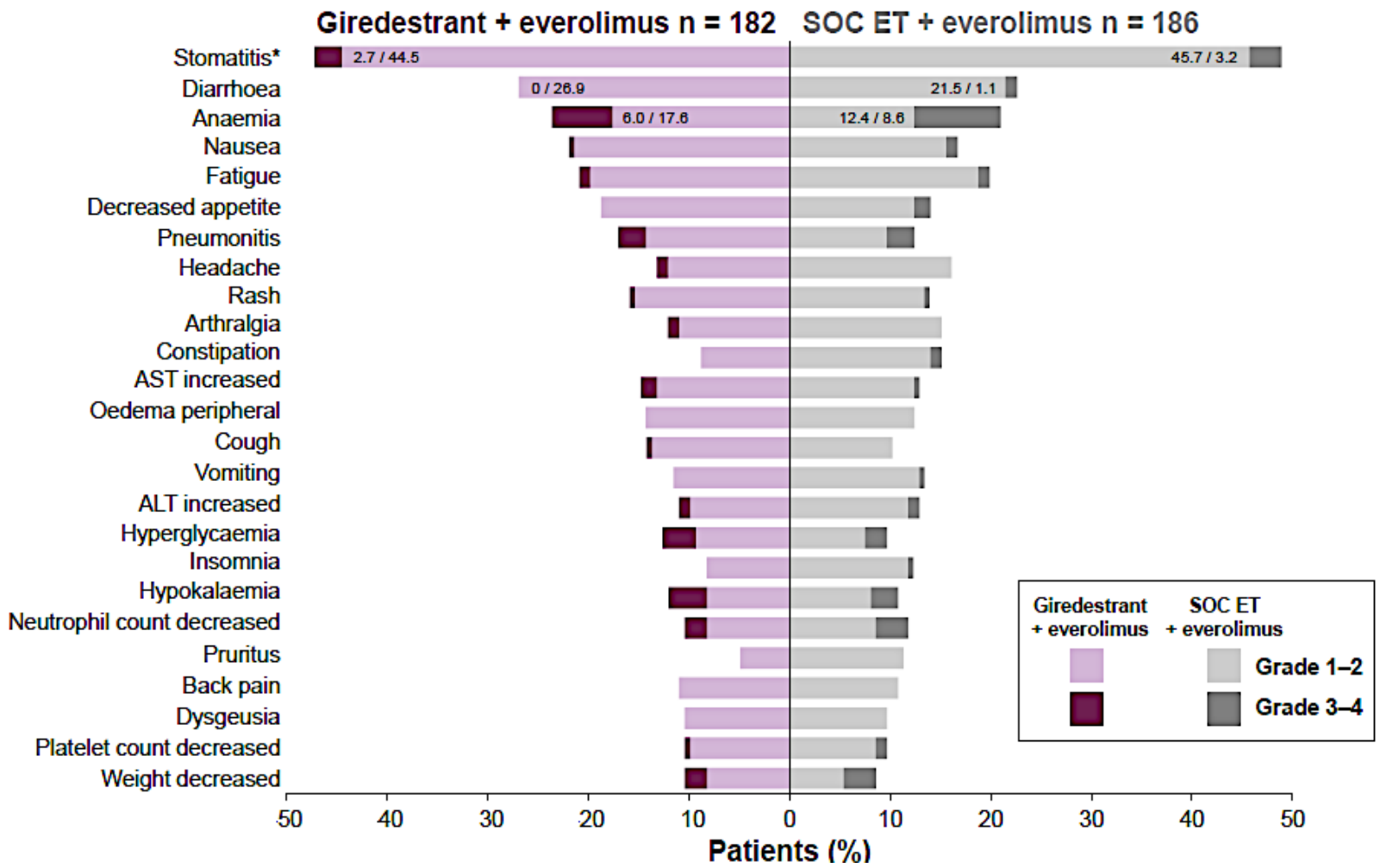
[a] Includes bradycardia and sinus bradycardia; [b] Includes dyslipidaemia, hypercholesterolaemia, hyperlipidaemia, hypertriglyceridaemia, and low-density lipoprotein increased; [c] Patients who started lipid-modifying agents while on study treatment.

- Incidence of VTE, ILD, dyslipidemia, bradycardia, and photopsia were relatively low or not observed in both **imlunestrant arms**
- The use of lipid-modifying agents was generally similar between the **imlunestrant** and **SOC ET** arms

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

Giredestrant + Everolimus vs ET + Everolimus: Treatment Related Adverse Events (EVERA)

TEAEs in ≥10% of Patients

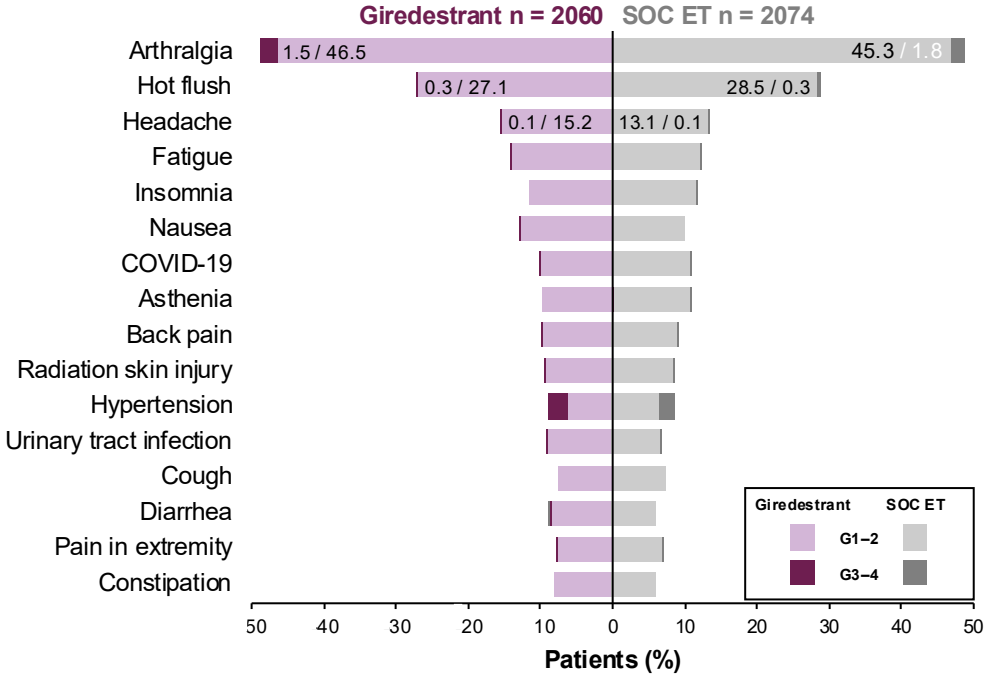


Mayer E, et al. ESMO 2025. Abstract LBA16.

Giredestrant vs ET in Early Breast Cancer: Adverse Events (Lidera)

AE overview *(safety-evaluable population)*

Common TEAEs (≥ 7.5% of patients in either arm at any grade)



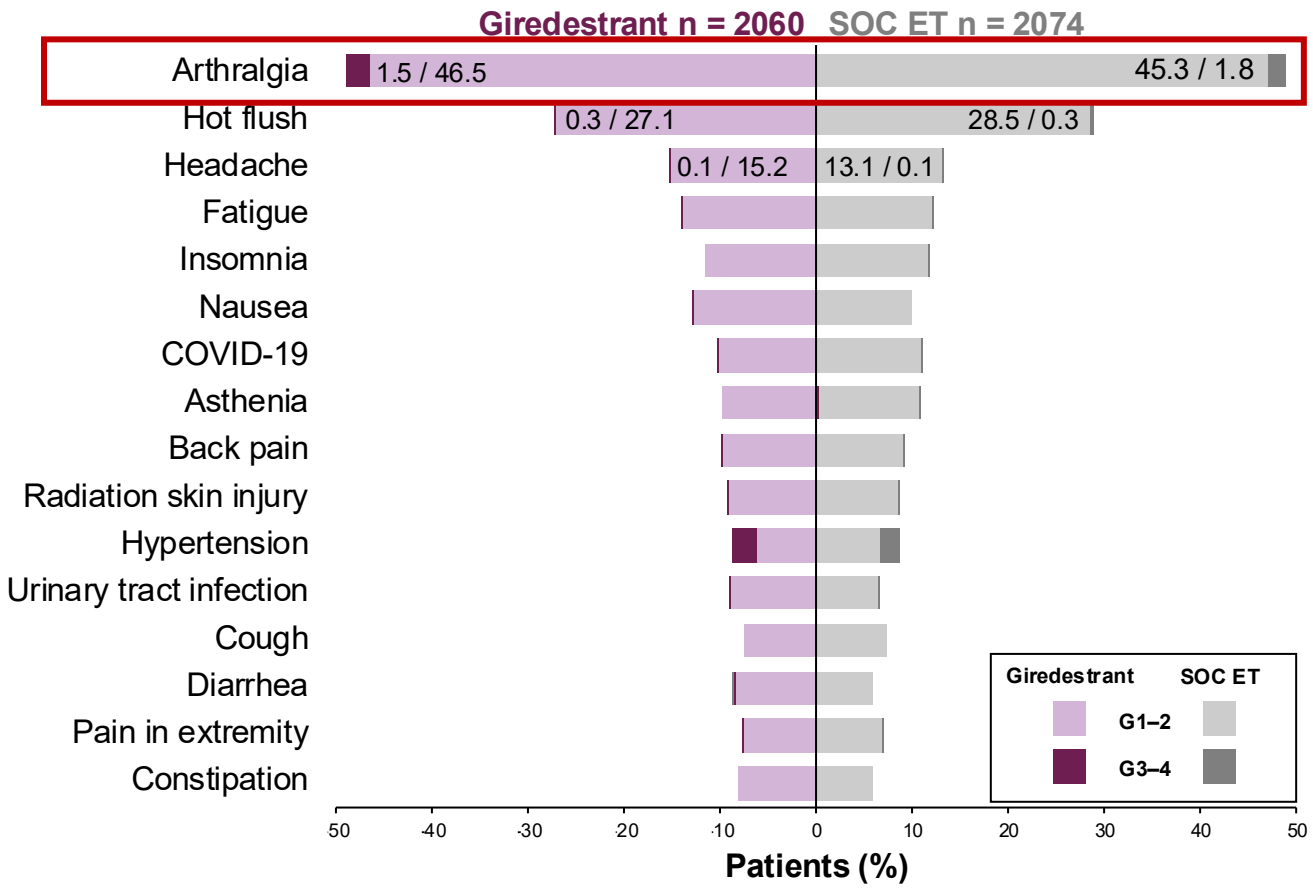
Selected AEs

	Giredestrant n = 2060	SOC ET n = 2074
Patients, n (%) with treatment discontinuations due to AEs		
Musculoskeletal disorders	38 (1.8)	92 (4.4)
• Arthralgias (PT)	32 (1.6)	76 (3.7)
Vasomotor disorders	2 (< 0.1)	18 (0.9)
• Hot flush (PT)	1 (< 0.1)	16 (0.8)

	Giredestrant n = 2060			SOC ET n = 2074		
Patients, n (%) with selected AEs by medical concept*						
	G1	**G2**	**G3–4**	**G1**	**G2**	**G3–4**
Bradycardia†	217 (10.5)	15 (0.7)	0	64 (3.1)	2 (< 0.1)	0
Venous thromboembolic events	4 (0.2)	12 (0.6)	2 (< 0.1)‡	3 (0.1)	7 (0.3)	7 (0.3)

lidERA AE Overview

Common TEAEs (≥ 7.5% of patients in either arm at any grade)



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	Giredestrant n = 2060			SOC ET n = 2074		
Patients, n (%) with selected AEs by medical concept*						
	G1	**G2**	**G3–4**	**G1**	**G2**	**G3–4**
Bradycardia†	217 (10.5)	15 (0.7)	0	64 (3.1)	2 (< 0.1)	0
Venous thromboembolic events	4 (0.2)	12 (0.6)	2 (< 0.1)‡	3 (0.1)	7 (0.3)	7 (0.3)

Data cutoff: August 8, 2025. * Assessed as medical concepts using grouped terms; all other AEs by medical concept were comparable between arms, including four patients per arm (0.2%) who experienced photopsia. † G2 events occurred in 17 patients; 13 resolved, four patients discontinued treatment and the events resolved. ‡ G3 only. AE, adverse event; ET, endocrine therapy; G, grade; PT, preferred term; SOC, standard-of-care; TEAE, treatment-emergent adverse event.

Year in Review:
Oral SERDs for Breast Cancer

MODULE 5: New directions

- Can new trial endpoints accelerate progress?
- PROTACs?

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

EGFR-Mutant Non-Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Tuesday, April 7, 2026
5:00 PM – 6:00 PM ET

Faculty

Suresh S Ramalingam, MD
Helena Yu, MD

Moderator

Neil Love, MD

RTP Year in Review 2026

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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.

RTP Year in Review 2026