Addressing Current Knowledge and Practice Gaps in the Community — Optimizing the Use of Oral Selective Estrogen Receptor Degraders for Metastatic Breast Cancer — Part 1

A CME/MOC-Accredited Live Webinar

Tuesday, July 29, 2025

5:00 PM – 6:00 PM ET

Faculty

Komal Jhaveri, MD, FACP

Virginia Kaklamani, MD, DSc

Moderator

Neil Love, MD

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Faculty

Komal Jhaveri, MD, FACP
Patricia and James Cayne Chair for Junior Faculty
Associate Attending Physician
Breast Medicine Service and Early Drug Development Service
Section Head, Endocrine Therapy Research Program
Clinical Director, Early Drug Development Service
Department of Medicine
Memorial Sloan Kettering Cancer Center
Associate Professor of Medicine
Weill Cornell College of Medicine
New York, New York

Virginia Kaklamani, MD, DSc
Professor of Medicine
Ruth McLean Bowman Bowers Chair in Breast Cancer
Research and Treatment
AB Alexander Distinguished Chair in Oncology
Leader, Breast Oncology Program
UT Health San Antonio MD Anderson Cancer Center
San Antonio, Texas

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

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This activity is supported by an educational grant from Lilly.

Dr Love — Disclosures

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Speakers Bureaus	AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Gilead Sciences Inc

This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

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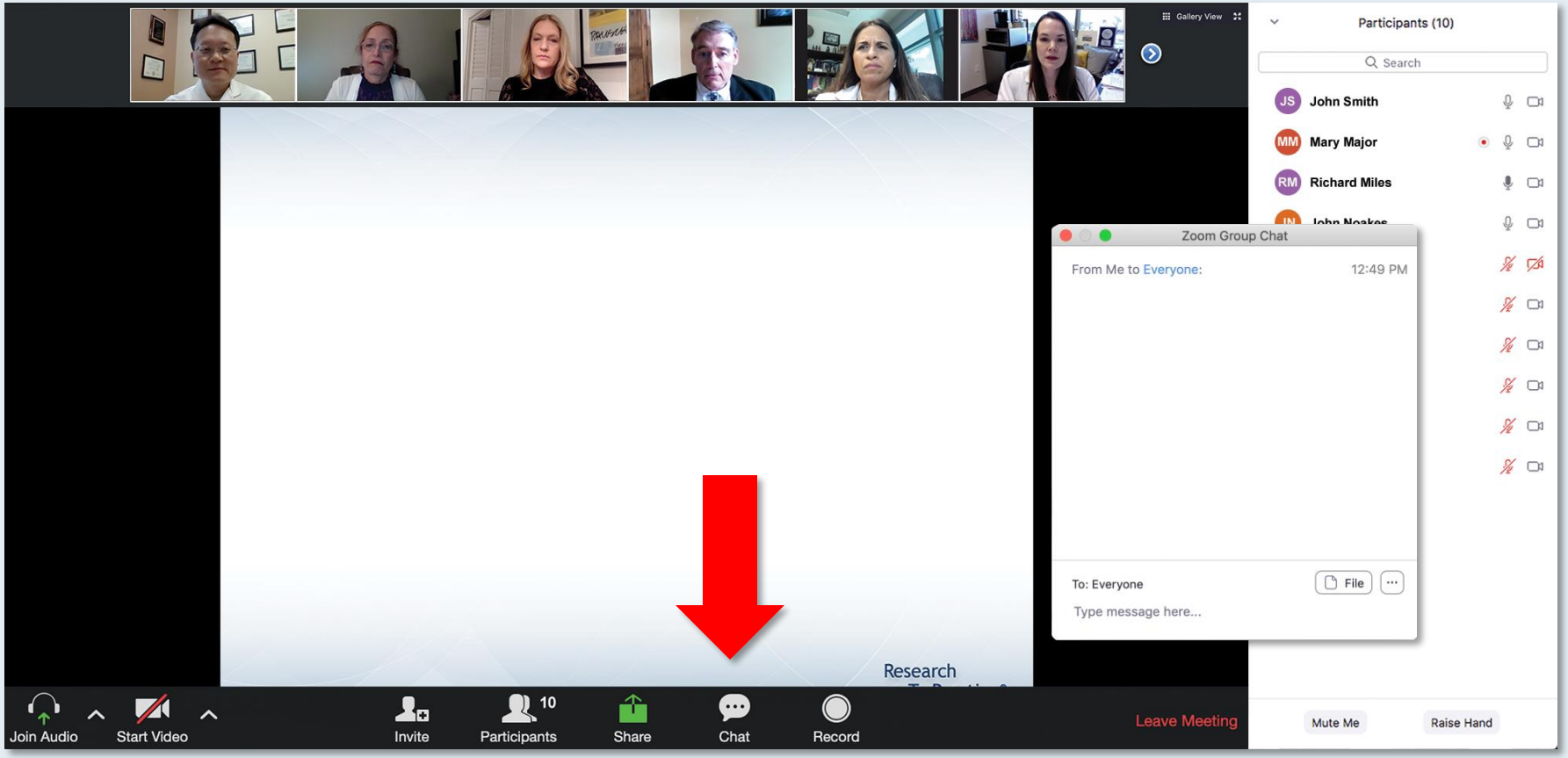

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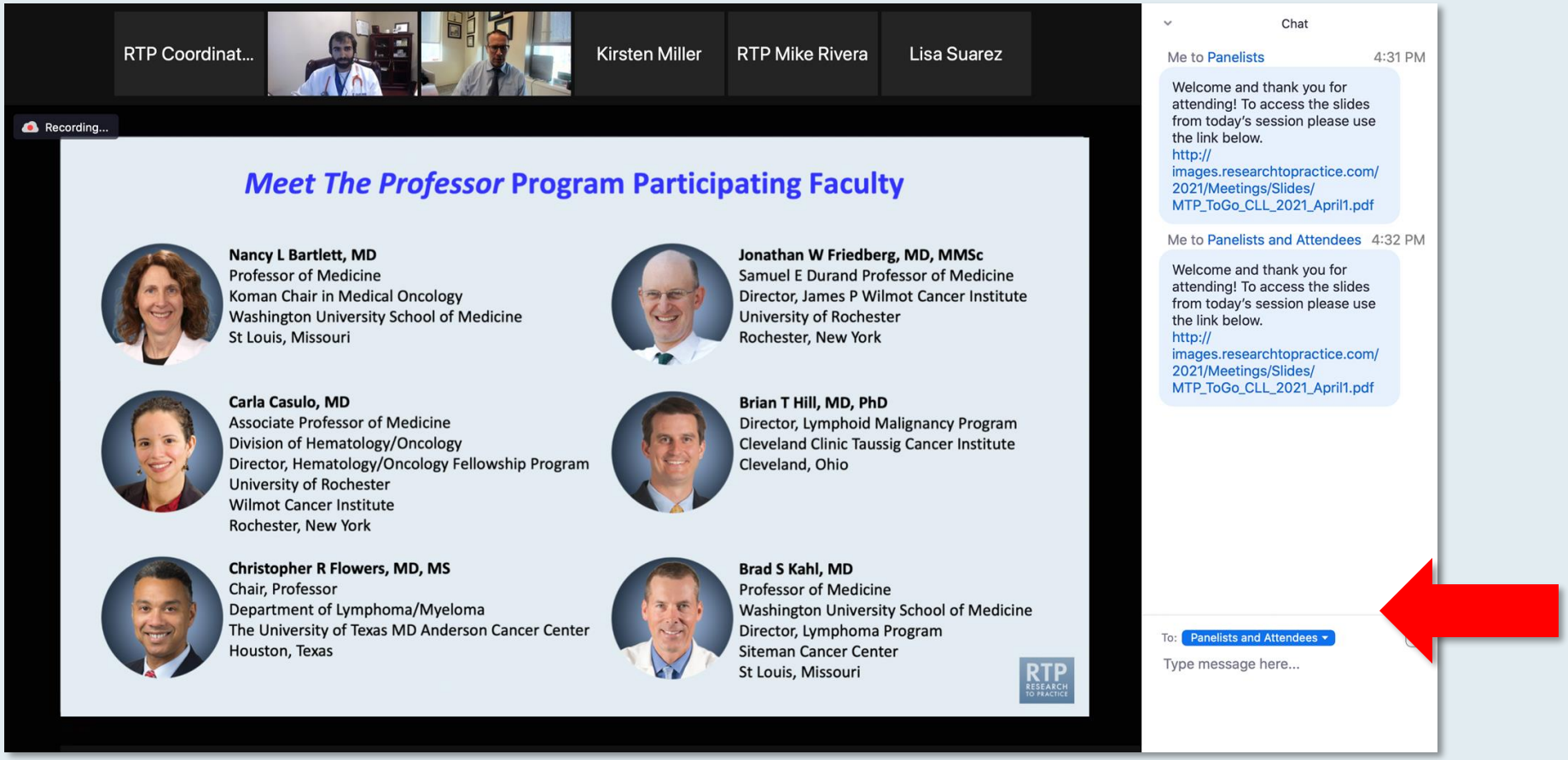
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



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

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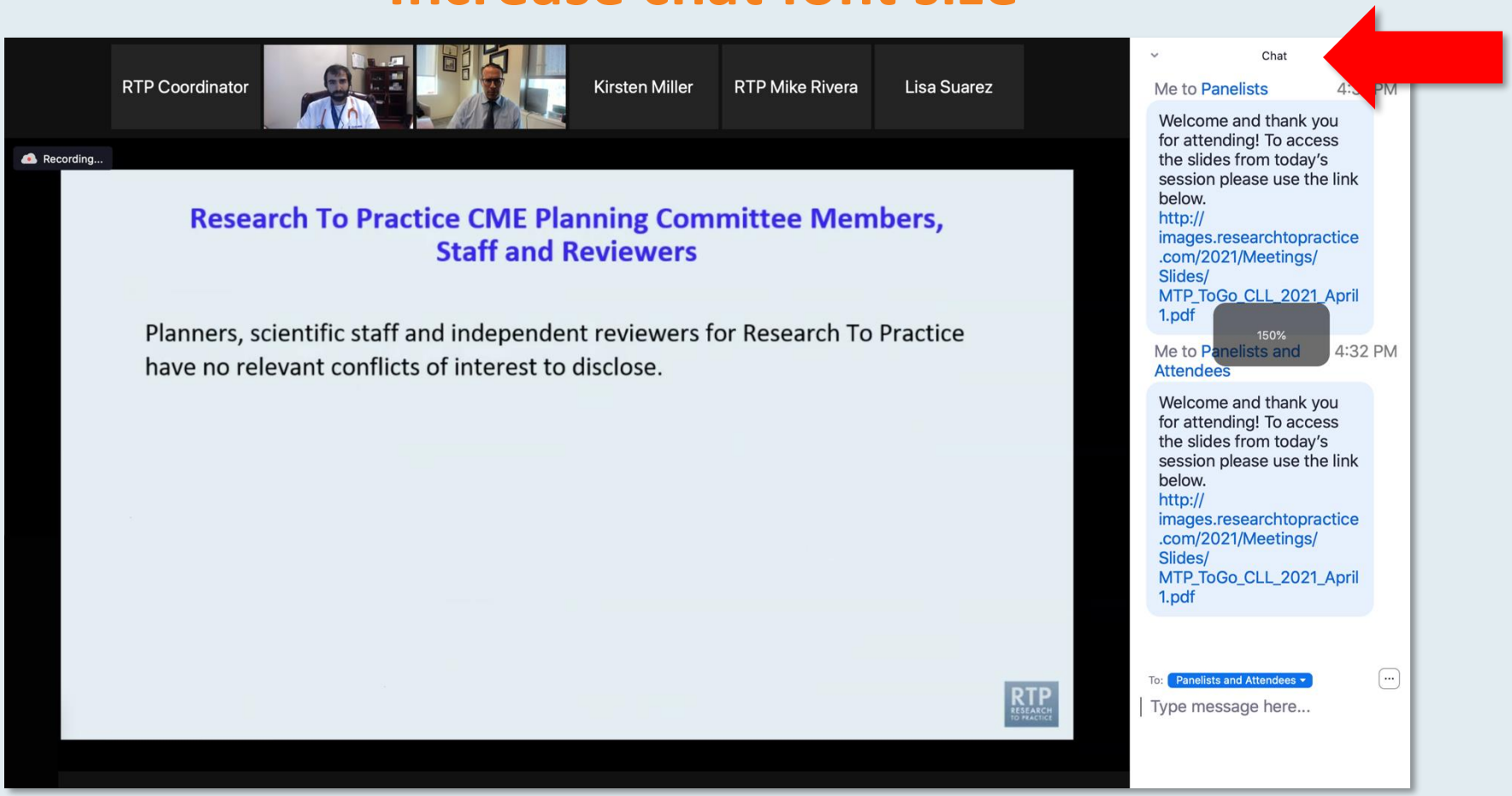
Increase chat font size



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

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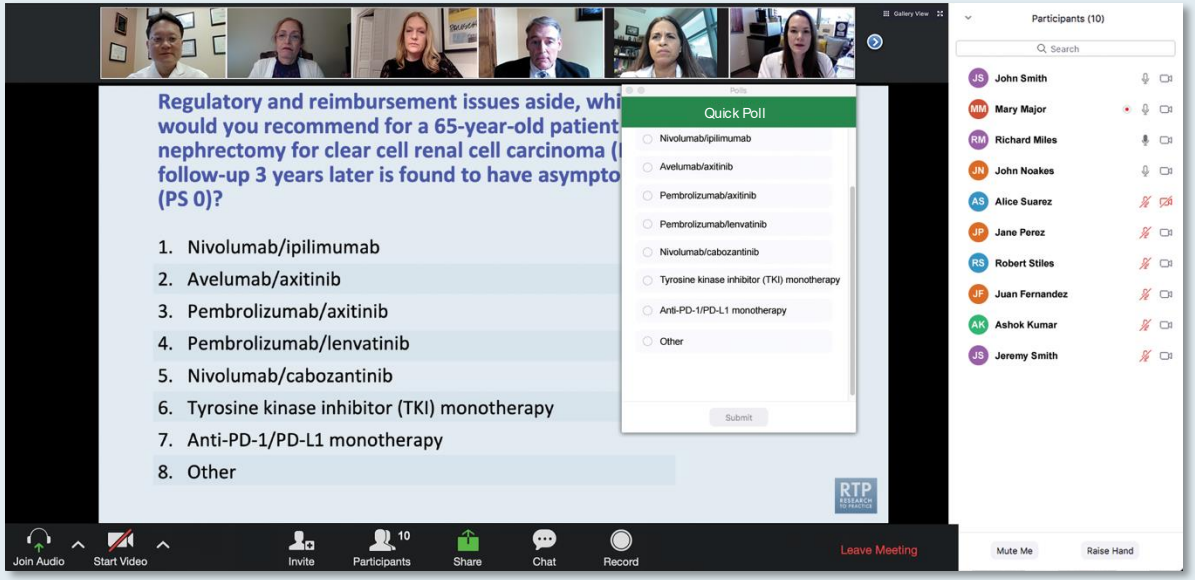

Endocrine-Resistant HR-Positive Metastatic Breast Cancer — An Interview with Dr Hope S Rugo on Optimal Management

DR HOPE S RUGO
CITY OF HOPE COMPREHENSIVE CANCER CENTER

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Practical Perspectives: Experts Review
Actual Cases of Patients with Biliary Tract Cancers

A CME/MOC-Accredited Live Webinar

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

Faculty

Haley Ellis, MD
James J Harding, MD

Moderator

Neil Love, MD

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RESEARCH TO PRACTICE

Cancer Q&A: Addressing Common Questions Posed by Patients with Relapsed/Refractory Multiple Myeloma

A CME/MOC-Accredited Webinar Developed in Partnership with Cancer*Care*®

Thursday, August 7, 2025
5:00 PM – 6:00 PM ET

Faculty

Natalie S Callander, MD
Sagar Lonial, MD, FACP

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

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

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5:00 PM – 6:00 PM ET

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Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

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

A CME/MOC-Accredited Live Webinar

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

Faculty

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

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

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

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

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

Faculty

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

Moderator

Joseph Mikhael, MD, MEd

RTP RESEARCH TO PRACTICE

Consensus or Controversy? Clinical Investigators Provide Perspectives on the Current and Future Care of Patients with Follicular Lymphoma

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

Friday, September 5, 2025

11:47 AM – 12:47 PM CT

Faculty

Jennifer Crombie, MD

Laurie H Sehn, MD, MPH

Moderator

Jeremy S Abramson, MD, MMSc

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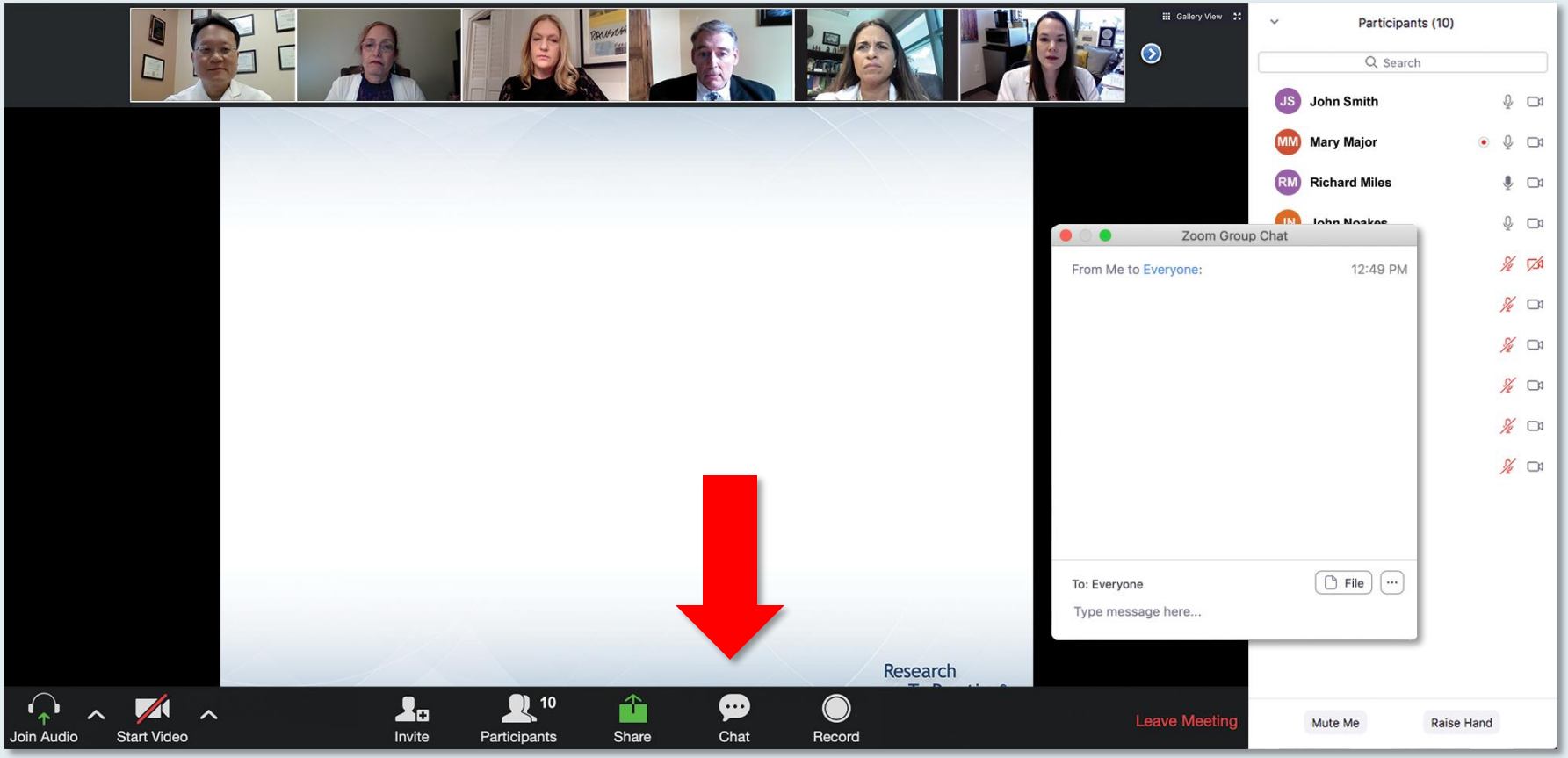

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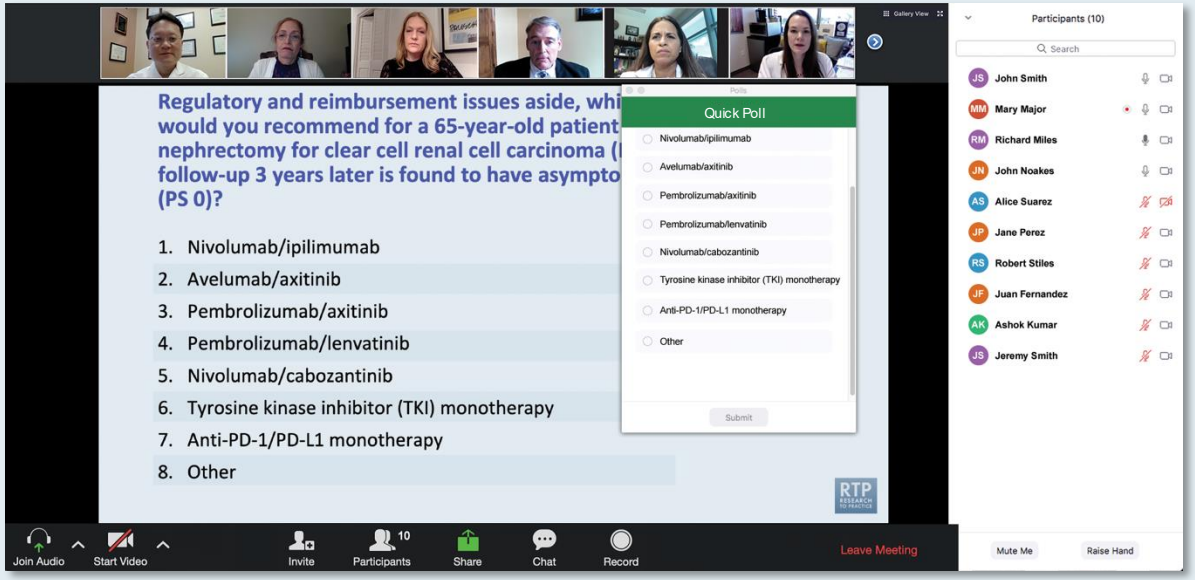

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RTP RESEARCH TO PRACTICE

Striving for Consensus: Clinical Investigators Review the Current and Future Role of Oral Selective Estrogen Receptor Degraders in the Care of Patients with ER-Positive Metastatic Breast Cancer

A Clinical Investigator Think Tank and Enduring Audio/Video/Podcast Activity

Thursday, September 18, 2025

12:00 PM – 3:00 PM ET

Faculty

Francois-Clement Bidard, MD, PhD

Hope S Rugo, MD

Rebecca Shatsky, MD

Seth Wander, MD, PhD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

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

A CME/MOC-Accredited Live Webinar

Wednesday, October 29, 2025

5:00 PM – 6:00 PM ET

Faculty

Rinath M Jeselsohn, MD

Joyce O'Shaughnessy, MD

Moderator

Neil Love, MD

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Agenda

Introduction: ER-Positive Metastatic Breast Cancer — Bringing Research Data into Practice

Module 1: Key Issues from the General Medical Oncologists (GMO) Survey

Module 2: Faculty Cases and GMO Questions

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Survey of 50 General Medical Oncologists: Breast Cancer

Survey Dates: 7/22/25 to 7/25/25

Agenda

Introduction: ER-Positive Metastatic Breast Cancer — Bringing Research Data into Practice

Module 1: Key Issues from GMO Survey

Module 2: Faculty Cases and GMO Questions

nature reviews clinical oncology

https://doi.org/10.1038/s41571-024-00935-6

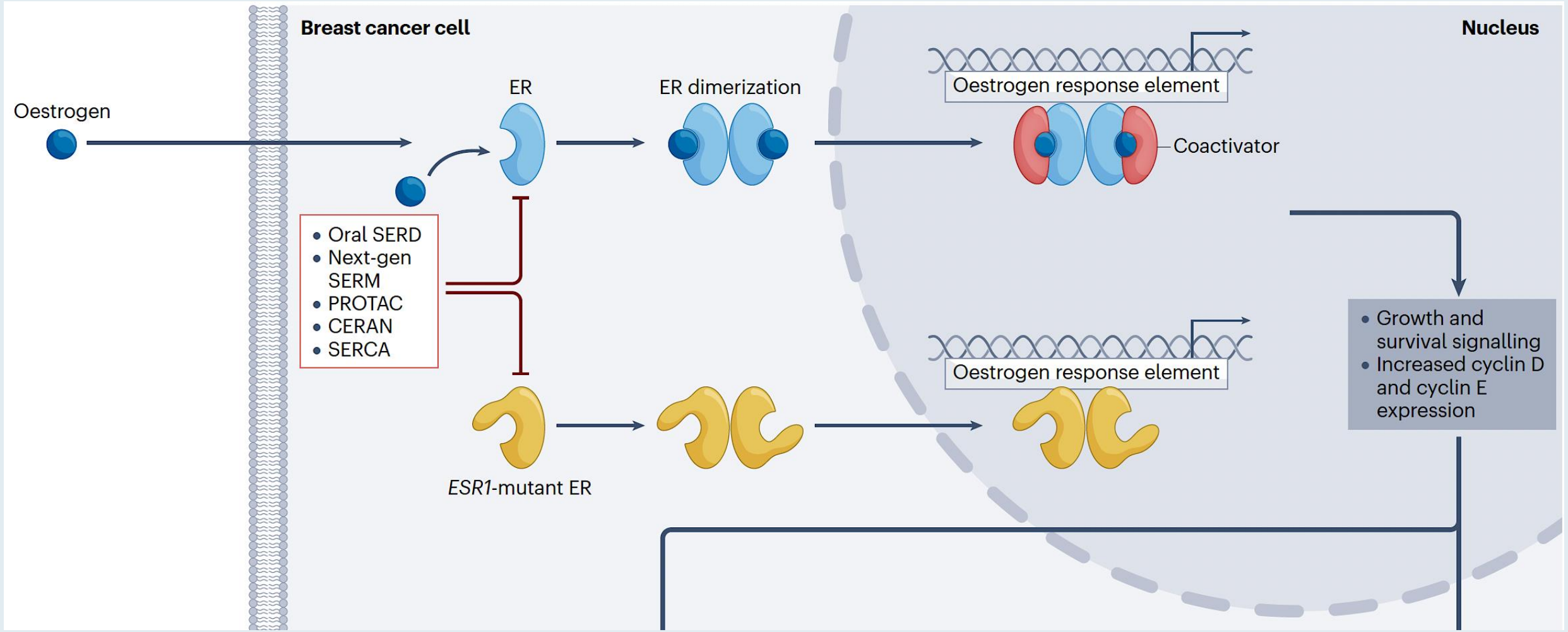
Review article

Precision therapeutics and emerging strategies for HR-positive metastatic breast cancer

Maxwell R. Lloyd[1], Komal Jhaveri[2], Kevin Kalinsky[3], Aditya Bardia[4] & Seth A. Wander[5]

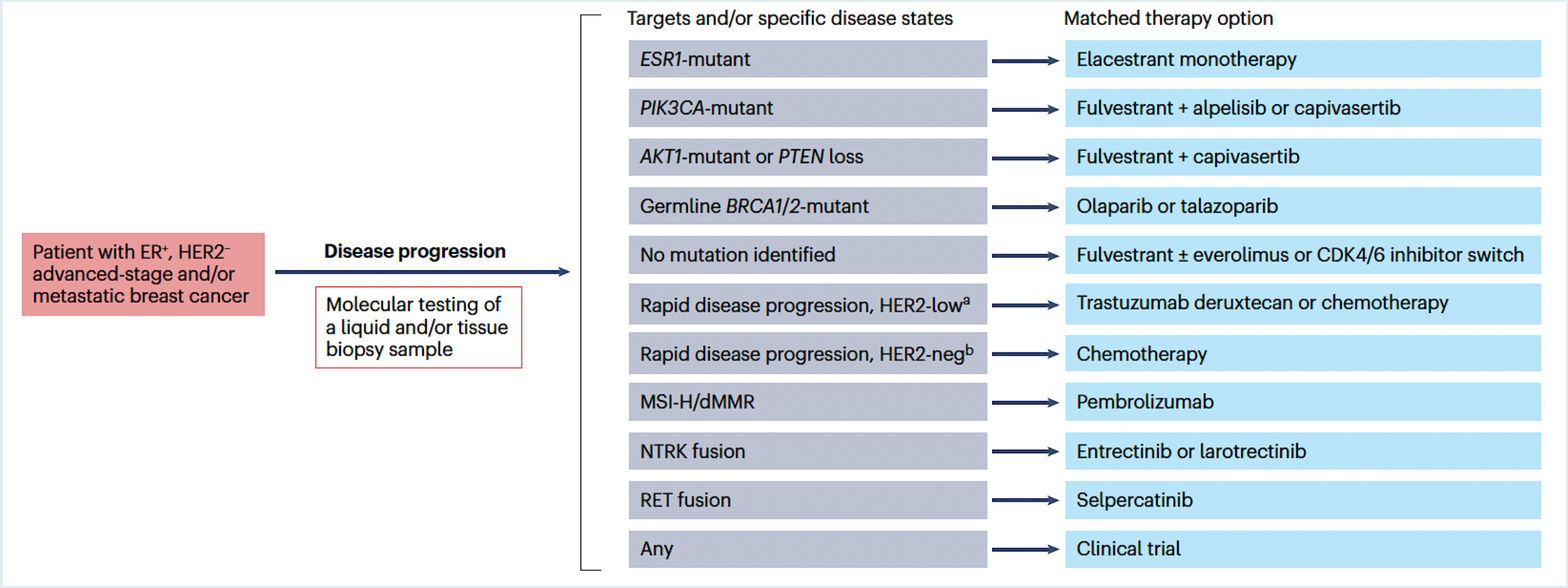
2024;21(10):743-61.

Overview of Biological Signaling in HR-Positive Breast Cancer



Lloyd MR et al. *Nat Rev Clin Oncol* 2024;21(10):743-61.

Targeted Selection of Second-Line or Later-Line Therapies for Patients with Metastatic ER-Positive Breast Cancer



Lloyd MR et al. *Nat Rev Clin Oncol* 2024;21(10):743-61.

Clinically Meaningful Improvement in Both Progession-Free Survival (PFS) Primary Endpoints in the PIK3CA Wild-Type Cohort of the Phase III VIKTORIA-1 Trial

Press Release: July 28, 2025

"[The manufacturer] today announced positive topline results from the *PIK3CA* wild-type cohort of the Phase 3 VIKTORIA-1 clinical trial evaluating gedatolisib plus fulvestrant with and without palbociclib versus fulvestrant in adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, *PIK3CA* wild-type, locally advanced or metastatic breast cancer, following progression on, or after, treatment with a CDK4/6 inhibitor and an aromatase inhibitor.

In the trial, the gedatolisib triplet demonstrated a statistically significant and clinically meaningful improvement in PFS among patients, reducing the risk of disease progression or death by 76% compared to fulvestrant (based on a hazard ratio [HR] of 0.24, 95% confidence interval [CI] 0.17-0.35; $p < 0.0001$). The mPFS, as assessed by blinded independent central review ('BICR'), was 9.3 months with the gedatolisib triplet versus 2.0 months with fulvestrant, an incremental improvement of 7.3 months.

The gedatolisib doublet also demonstrated a statistically significant and clinically meaningful improvement in PFS among patients, reducing the risk of disease progression or death by 67% compared to fulvestrant (HR of 0.33, 95% CI 0.24-0.48; $p < 0.0001$). The mPFS, as assessed by BICR, was 7.4 months with the gedatolisib doublet versus 2.0 months with fulvestrant, an incremental improvement of 5.4 months."

https://finance.yahoo.com/news/celcuity-announces-clinically-meaningful-improvement-110000421.html

Agenda

Introduction: ER-Positive Metastatic Breast Cancer — Bringing Research Data into Practice

Module 1: Key Issues from GMO Survey

Module 2: Faculty Cases and GMO Questions

Eleven Key Agents/Regimens for ER-Positive Breast Cancer

Agent	FDA status	Pivotal trial
Elacestrant	Approved (1/27/23)	EMERALD
Camizestrant	Investigational	SERENA-6
Imlunestrant	Investigational	EMBER-3
Alpelisib	Approved (5/24/2019)	SOLAR-1
Capivasertib	Approved (11/16/2023)	CAPItello-291
Inavolisib	Approved (10/10/2024)	INAVO120
Trastuzumab deruxtecan	Approved: HER2 low (8/5/2022)	DESTINY-Breast04
	Approved: HER2 ultralow/low (1/27/2025)	DESTINY-Breast06
Datopotamab deruxtecan	Approved (1/17/2025)	TROPION-Breast01
Sacituzumab govitecan	Approved: HR-positive, HER2-negative (2/3/2023)	TROPiCS-02
PATINA regimen (palbociclib + trastuzumab ± pertuzumab + endocrine therapy)	Investigational	PATINA
Vepdegestrant	Investigational	VERITAC-2

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Clinical Trials in ER-Positive Metastatic Breast Cancer

Clinical trial	Very familiar with	Very interested in learning about
EMERALD	32%	62%
SERENA-6	28%	72%
EMBER-3	14%	68%
SOLAR-1	30%	42%
CAPItello-291	28%	60%
INAVO120	16%	70%
DESTINY-Breast04	40%	58%
DESTINY-Breast06	32%	64%
TROPION-Breast01	12%	62%
TROPiCS-02	20%	54%
PATINA	18%	68%
VERITAC-2	8%	70%

Survey of 50 General Medical Oncologists July 2025

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Educational Topics

Educational topics	Well informed about	Very interested in learning about
Incidence and clinical implications of ESR1 mutations in ER-positive metastatic breast cancer (mBC)	30%	78%
Best practices for detection of and monitoring for ESR1 mutations in patients with mBC	30%	66%
Comparison of available and investigational oral SERDs	12%	80%
Efficacy of available and investigational oral SERDs in patients with ER-positive, HER2-negative, ESR1-mutated mBC	16%	72%
Available trial data with oral SERDs-based combinations for patients with and without ESR1 mutations	12%	74%
Adverse effects of oral SERDs and strategies for prevention and management	16%	76%

Survey of 50 General Medical Oncologists July 2025

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For approximately how many patients with breast cancer have you prescribed the following agents?

Agent	Median	Mean
Elacestrant	5	7
Alpelisib	2	6
Capivasertib	2	5
Inavolisib	0	2
Trastuzumab deruxtecan (for HER2-low or ultralow disease only)	5	9
Datopotamab deruxtecan	0	2
Sacituzumab govitecan	5	8
Palbociclib + anti-HER2 therapy + ET	1	4

ET = endocrine therapy

Survey of 50 General Medical Oncologists July 2025

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Key Issues in Metastatic ER-Positive Breast Cancer

New Endocrine Agents

- Elacestrant, imlunestrant, camizestrant, vepdegestrant, alpelisib, inavolisib, capivasertib

New Antibody-Drug Conjugates (ADCs)

- Sacituzumab govitecan, datopotamab deruxtecan, trastuzumab deruxtecan

Endocrine Treatment for HER2-Positive Disease

- Palbociclib

Clinical Decision-Making in ER-Positive, HER2-Low/IHC 0 Metastatic Disease

First-line treatment:

- Selective estrogen receptor degrader (SERD) and CDK inhibitor? (Imlunestrant and abemaciclib)
- Inavolisib/palbociclib/fulvestrant?
- Monitor for ESR1 and treat? Camizestrant?

Second-line treatment:

- Endocrine versus ADC? (Time on CDK inhibitor?)
  - Choice of agent: elacestrant, imlunestrant, camizestrant, vepdegestrant, alpelisib, capivasertib or repeat CDK inhibitor?
  - SERD and repeat CDK inhibitor (imlunestrant, abemaciclib)

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Key Endocrine and SERD Questions in 2025 for ER-Positive, HER2-Low or HER2-Negative Disease

4 mutation subsets: ESR+/- or PIK3CA+/- (like ER/HER2)

- Mechanism of action of SERDs
- Endocrine treatment versus chemotherapy/ADC
- Optimal SERD choice
- PROTACs, SERMs, others?
- Treating “molecular progression”
- Eligibility for up-front inavolisib/palbociclib/fulvestrant (de novo? HbA1c?)
- Role of CDKi after CDKi? (abemaciclib)
- Role of CDKi with SERD (abemaciclib/imlunestrant)
- SERD after AKTi and reverse?
- CDKi (palbociclib) after first-line T-DXd (ESR1+, HER2+)?

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Key Endocrine/SERD Questions 2025

Mechanism of action of SERDs

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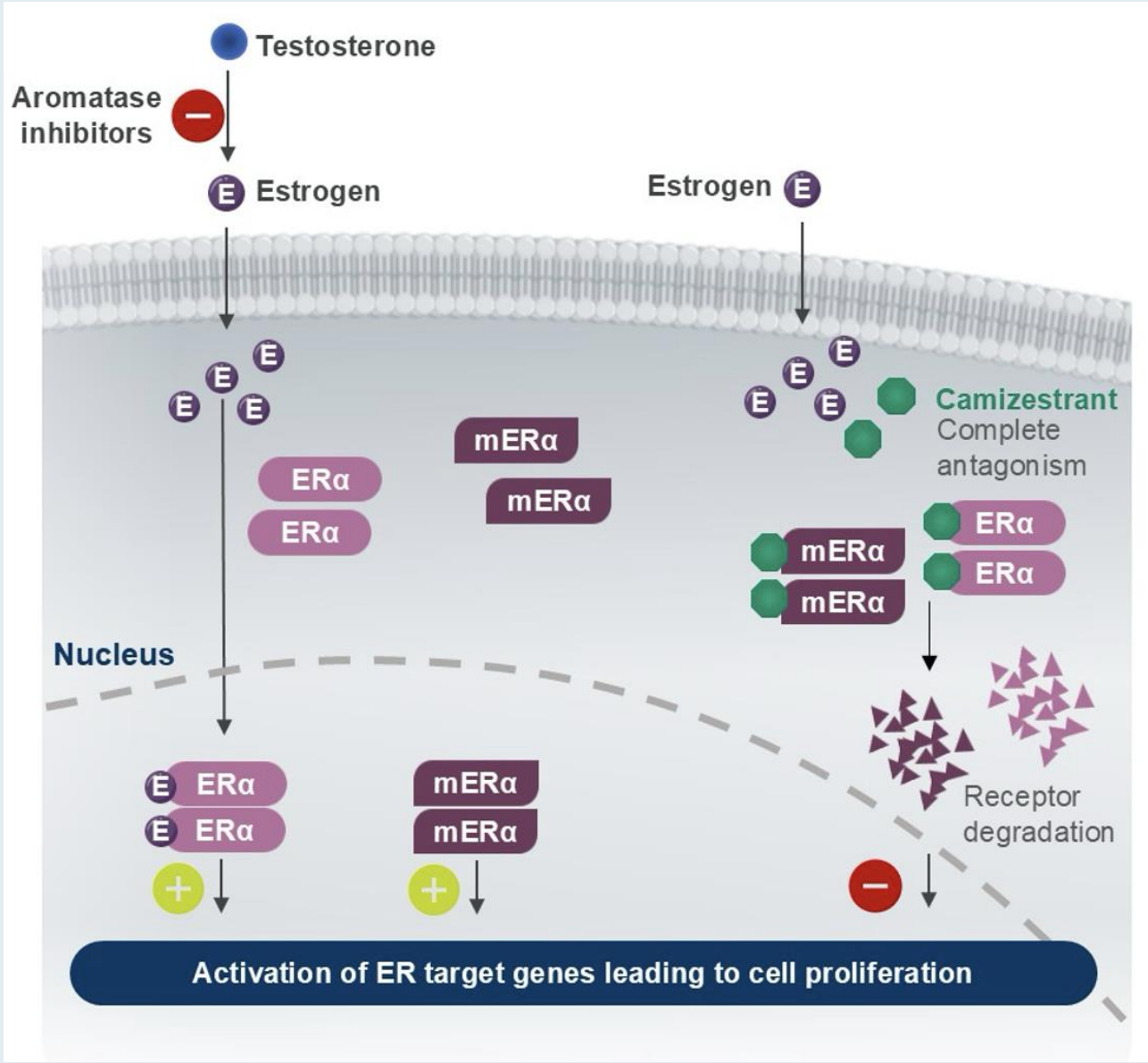
RESEARCH
TO PRACTICE

Mechanism of Action of Oral SERDs



Bidard F-C et al. *N Engl J Med* June 1, 2025;[Online ahead of print]. Turner N et al. ASCO 2025;Abstract LBA4.

Key Endocrine/SERD Questions 2025

Endocrine treatment versus chemotherapy/ADC

CLINICAL CANCER RESEARCH | CLINICAL TRIALS: TARGETED THERAPY

Elacestrant in ER^{+}, HER2^{-} Metastatic Breast Cancer with *ESR1*-Mutated Tumors: Subgroup Analyses from the Phase III EMERALD Trial by Prior Duration of Endocrine Therapy plus CDK4/6 Inhibitor and in Clinical Subgroups

Aditya Bardia[1], Javier Cortés[2], François-Clément Bidard[3], Patrick Neven[4], José Garcia-Sáenz[5], Phillipe Aftimos[6], Joyce O'Shaughnessy[7], Janice Lu[8], Giulia Tonini[9], Simona Scartoni[9], Alessandro Paoli[9], Monica Binaschi[9], Tomer Wasserman[9], and Virginia Kaklamani[10]

2024 August 1;[Online ahead of print].

Elacestrant After ≥12 Months of Endocrine Therapy and CDK4/6 Inhibition

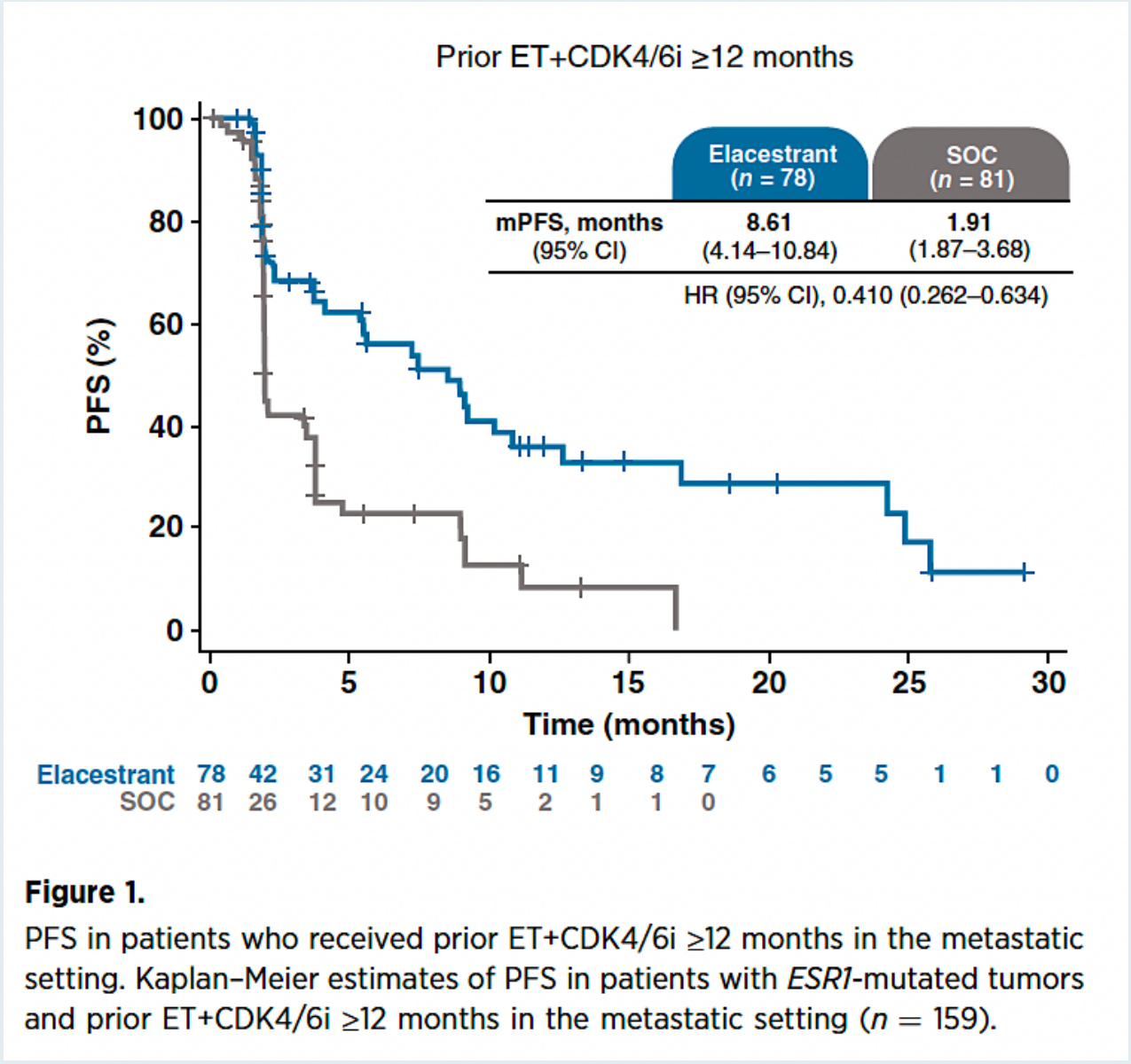


Figure 1.

PFS in patients who received prior ET+CDK4/6i ≥12 months in the metastatic setting. Kaplan–Meier estimates of PFS in patients with *ESR1*-mutated tumors and prior ET+CDK4/6i ≥12 months in the metastatic setting ($n = 159$).

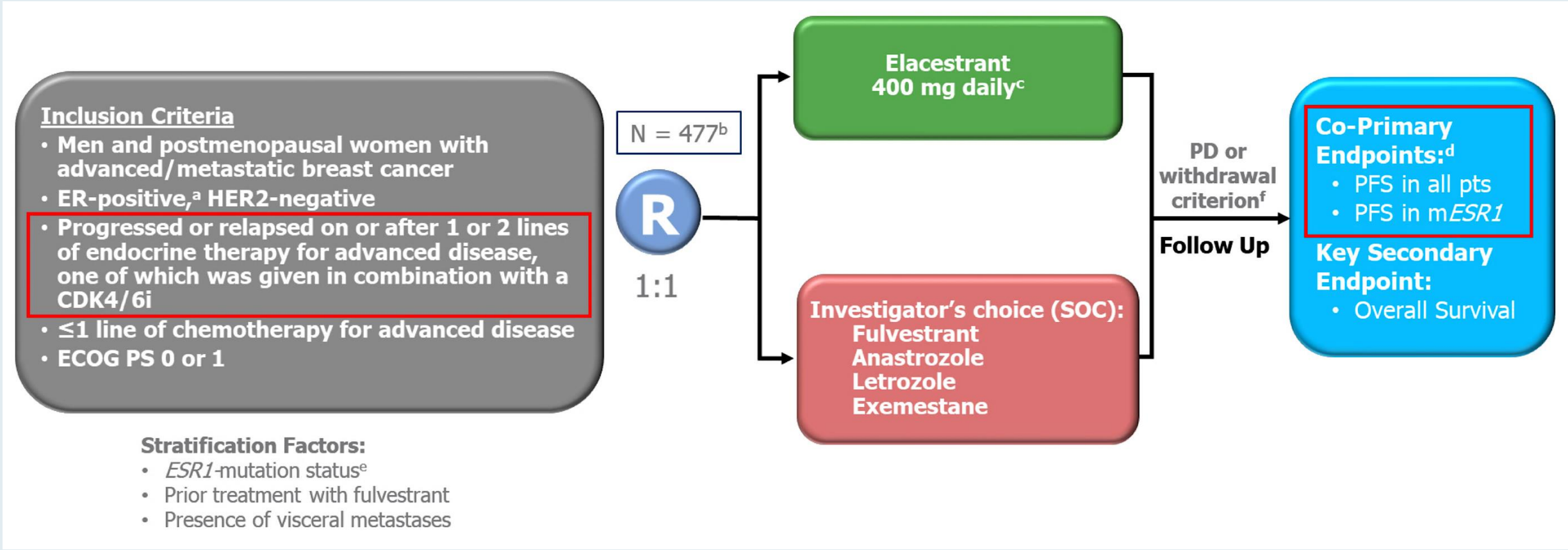
Bardia A et al. *Clin Cancer Res* 2024 August 1;[Online ahead of print].

mPFS = median progression-free survival

Key Endocrine/SERD Questions 2025

Optimal SERD choice

EMERALD Study Design

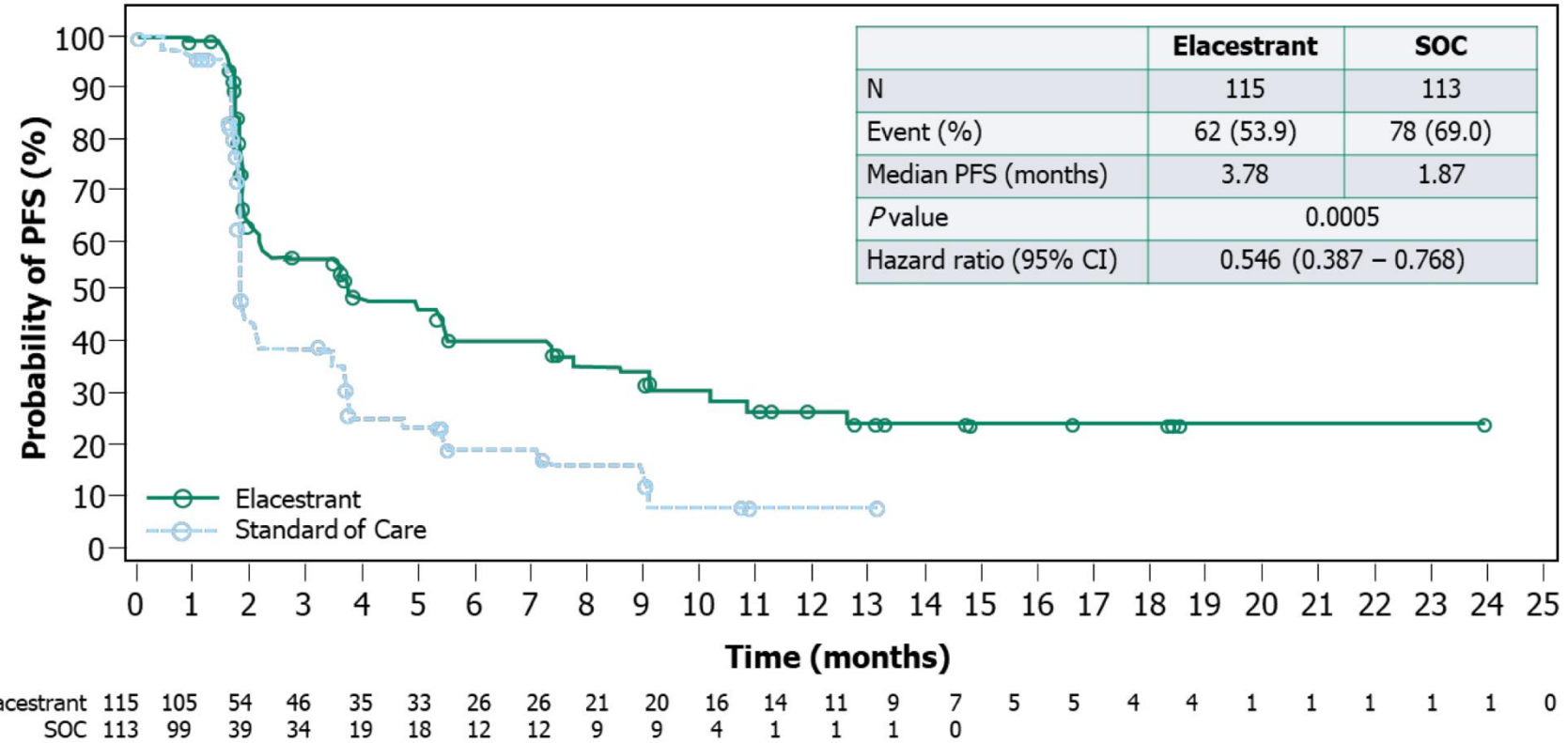


SOC = standard of care; PD = disease progression

Bardia A et al. SABCS 2021;Abstract GS2-02.

EMERALD: PFS for Patients with ESR1 Mutations (mESR1)

Patients With Tumors Harboring *mESR1*



	Elacestrant	SOC
N	115	113
Event (%)	62 (53.9)	78 (69.0)
Median PFS (months)	3.78	1.87
P value	0.0005	
Hazard ratio (95% CI)	0.546 (0.387 – 0.768)	

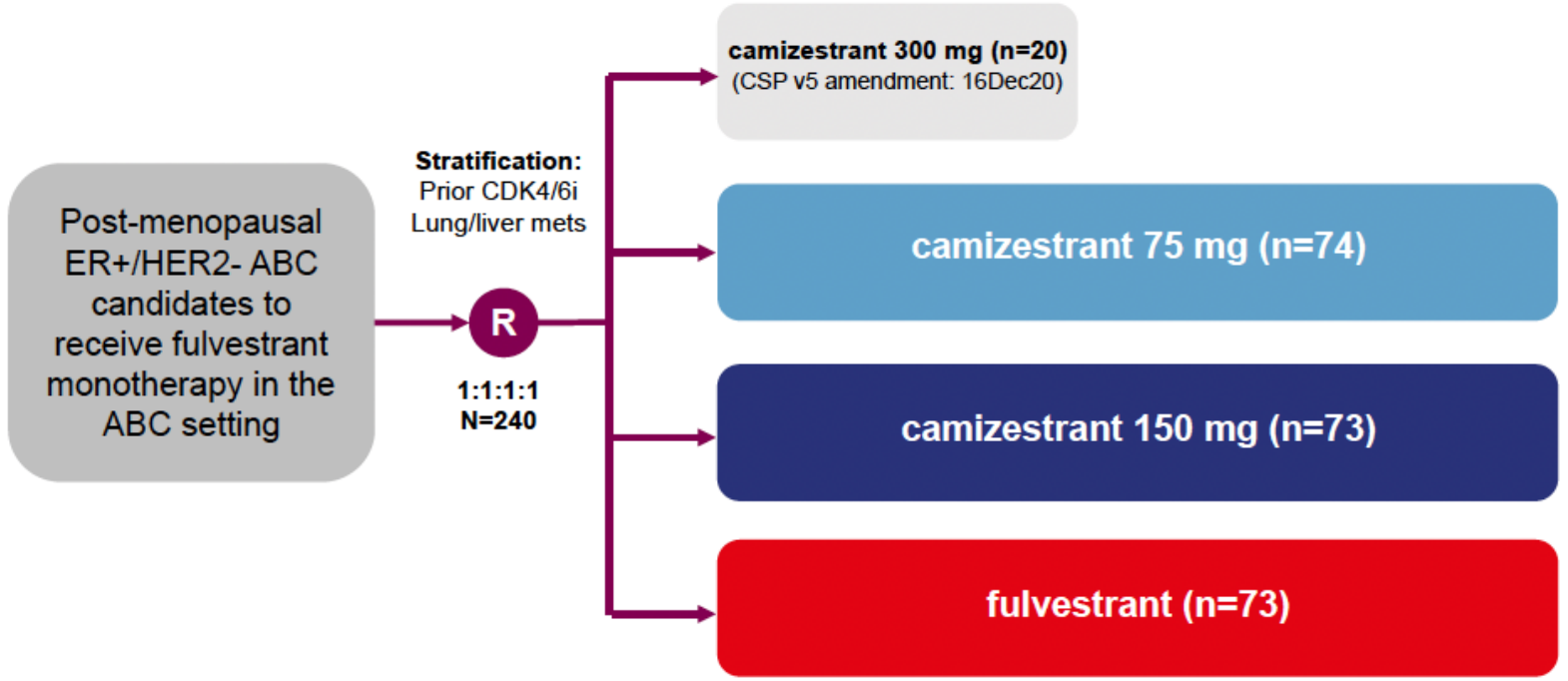
Elacestrant is associated with a 45% reduction in the risk of progression or death in patients harboring *mESR1*

Bardia A et al. SABCS 2021;Abstract GS2-02.

SERENA-2 Study Design

Key inclusion/exclusion criteria:

- Recurrence or progression on at least one line of ET
- No prior fulvestrant or oral SERD in ABC
- No more than one line of ET in ABC setting
- No more than one line CT in ABC setting
- Measurable and non-measurable disease

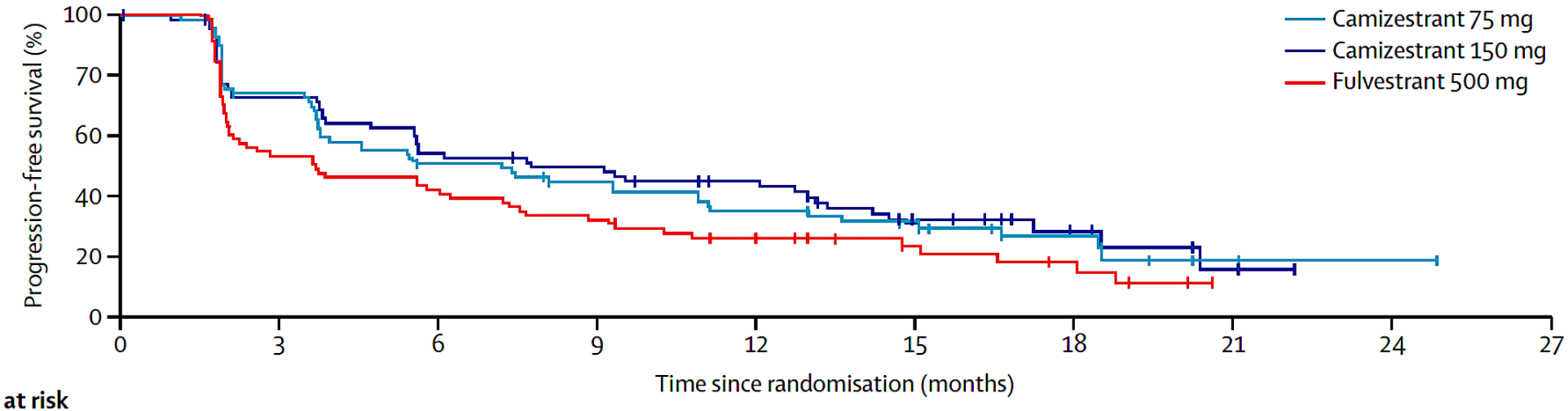


- **Primary endpoint:** PFS (investigator assessment*)
- **Secondary endpoints:** CBR24, ORR, OS, safety
- **Translational endpoints:** serial ctDNA analysis including *ESR1*m, serial CTCs analysis

Oliveira M et al. *Lancet Oncol* 2024;25(11):1424-39; San Antonio Breast Cancer Symposium 2022;Abstract GS3-02.

SERENA-2: PFS Outcomes

	Camizestrant 75 mg (n=74)	Camizestrant 150 mg (n=73)	Fulvestrant 500 mg (n=73)
Patients with events (%)	50 (68%)	48 (66%)	57 (78%)
Median progression-free survival (90% CI), months	7·2 (3·7–10·9)	7·7 (5·5–12·9)	3·7 (2·0–6·0)
HR (90% CI)*	0·59 (0·42–0·82)	0·64 (0·46–0·89)	..
Stratified log-rank p value*	0·017	0·0090	..
6-month progression-free survival rate (90% CI)	50·3% (40·0–59·7)	53·6% (43·3–62·9)	40·0% (30·4–49·4)
12-month progression-free survival rate (90% CI)	34·3% (24·9–44·0)	44·5% (34·4–54·1)	25·3% (17·1–34·2)
Median follow-up (IQR), months	16·6 (12·9–19·4)	16·3 (12·9–18·3)	14·7 (12·7–20·1)



Number at risk (number censored)										
Camizestrant 75 mg	74 (0)	50 (6)	33 (7)	27 (9)	21 (9)	14 (13)	7 (19)	2 (22)	1 (23)	0 (24)
Camizestrant 150 mg	73 (0)	50 (4)	37 (4)	32 (6)	25 (10)	13 (15)	6 (21)	2 (23)	0 (25)	..
Fulvestrant 500 mg	73 (0)	37 (3)	28 (3)	22 (3)	14 (7)	8 (12)	5 (13)	0 (16)	..	..

Oliveira M et al. *Lancet Oncol* 2024;25(11):1424-39.

Imlunestrant, an Oral Selective Estrogen Receptor Degrader, as Monotherapy and in Combination With Targeted Therapy in Estrogen Receptor–Positive, Human Epidermal Growth Factor Receptor 2–Negative Advanced Breast Cancer: Phase Ia/Ib EMBER Study

J Clin Oncol 2024;[Online ahead of print].

Authors: Komal L. Jhaveri, MD, FACP, Elgene Lim, MD, Rinath Jeselsohn, MD, Cynthia X. Ma, MD, Erika P. Hamilton, MD, Cynthia Osborne, MD, Manali Bhave, MD, Peter A. Kaufman, MD, J. Thaddeus Beck, MD, Luis Manso Sanchez, MD, Ritesh Parajuli, MD, Hwei-Chung Wang, MD, Jessica J. Tao, MD, Seock-Ah Im, MD, Kathleen Harnden, MD, Kan Yonemori, MD, Ajay Dhakal, MD, Patrick Neven, MD, Philippe Aftimos, MD, Jean Yves-Pierga, MD, Yen-Shen Lu, MD, Timothy Larson, MD, Yolanda Jerez, MD, Kostandinos Sideras, MD, Joohyuk Sohn, MD, Sung-Bae Kim, MD, Cristina Saura, MD, Aditya Bardia, MD, Sarah L. Sammons, MD, Francesca Bacchion, MS, Yujia Li, PhD, Eunice Yuen, PhD, Shawn T. Estrem, PhD, Vanessa Rodrik-Outmezguine, PhD, Bastien Nguyen, PhD, Roohi Ismail-Khan, MD, Lillian Smyth, MD, and Muralidhar Beeram, MD SHOW FEWER | AUTHORS

Phase Ia/Ib EMBER: Tumor Responses

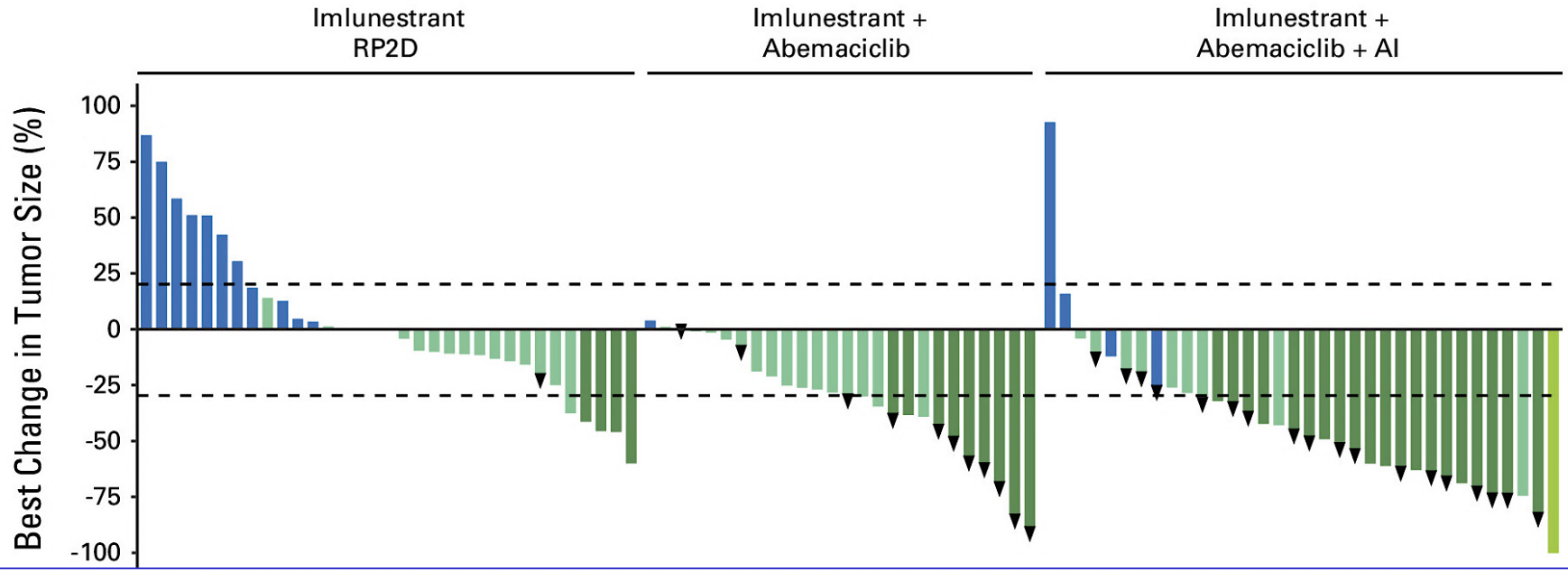


TABLE 3. Efficacy in Patients With ER+/HER2− ABC Who Received Imlunestrant Monotherapy at the RP2D or in Combination With Abemaciclib With or Without AI

	Monotherapy	Combination Therapy	
Parameter	Imlunestrant RP2D (n = 51)	Imlunestrant + Abemaciclib (n = 42)	Imlunestrant + Abemaciclib + AI (n = 43)
ORR, n/N (%)[a]	4/34 (11.8)	9/28 (32.1)	21/34 (61.8)
CBR, No. (%)	28 (54.9)	30 (71.4)	34 (79.1)
Treatment duration, months, median (range)	6.5 (0.3-25.9)	13.9 (0.2-26.3)	14.0 (1.8-23.0)
TTR, months, median (range)	3.6 (1.6-5.4)	5.5 (1.6-10.9)	3.7 (1.7-8.5)
PFS, months, median (95% CI)	7.2 (3.7 to 8.3)	19.2 (13.8 to NA)	NA (18.9 to NA)
ESR1 mutation	7.1 (3.7 to 8.2)	NE	NE
ESR1 mutation not detected	5.6 (1.8 to 8.4)	NE	NE
12-month PFS, % (95% CI)	22.2 (11.3 to 35.3)	74.2 (56.2 to 85.7)	80.7 (65.1 to 89.9)

RP2D = recommended Phase II dose; AI = aromatase inhibitor; ORR = overall response rate; CBR = clinical benefit rate; TTR = time to response

Jhaveri KL et al. *J Clin Oncol* 2024;[Online ahead of print].

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SAN ANTONIO BREAST CANCER SYMPOSIUM®

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DECEMBER 10–13, 2024

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Imlunestrant, an Oral Selective Estrogen Receptor Degrader (SERD), as Monotherapy and Combined with Abemaciclib, for Patients with ER+, HER2- Advanced Breast Cancer (ABC), Pretreated with Endocrine Therapy (ET): Results of the Phase 3 EMBER-3 trial

Abstract GS1-01

Komal L. Jhaveri,[1] Patrick Neven,[2] Monica Lis Casalnuovo,[3] Sung-Bae Kim,[4] Eriko Tokunaga,[5] Philippe Aftimos,[6] Cristina Saura,[7] Joyce O'Shaughnessy,[8] Nadia Harbeck,[9] Lisa A. Carey,[10] Giuseppe Curigliano,[11] Antonio Llombart-Cussac,[12] Elgene Lim,[13] María de la Luz García Tinoco,[14] Joohyuk Sohn,[15] André Mattar,[16] Qingyuan Zhang,[17] Chiun-Sheng Huang,[18] Chih-Chiang Hung,[19] Jorge Luis Martinez Rodriguez,[20] Manuel Ruiz Borrego,[21] Rikiya Nakamura,[22] Kamnesh R. Pradhan,[23] Christoph Cramer von Laue,[23] Emily Barrett,[23] Shanshan Cao,[23] Xuejing Aimee Wang,[23] Lillian M. Smyth,[23] François-Clément Bidard[24]

Imlunestrant with or without Abemaciclib in Advanced Breast Cancer

Authors: Komal L. Jhaveri, M.D., Patrick Neven, M.D., Monica Lis Casalnuovo, M.D., Sung-Bae Kim, M.D., Eriko Tokunaga, M.D., Philippe Aftimos, M.D., Cristina Saura, M.D., Joyce O'Shaughnessy, M.D., Nadia Harbeck, M.D., Lisa A. Carey, M.D., Giuseppe Curigliano, M.D., Antonio Llombart-Cussac, M.D., Elgene Lim, M.D., María de la Luz García Tinoco, M.D., Joohyuk Sohn, M.D., André Mattar, M.D., Ph.D., Qingyuan Zhang, M.D., Chiun-Sheng Huang, M.D., Chih-Chiang Hung, M.D., Jorge Luis Martinez Rodriguez, M.D., Manuel Ruíz Borrego, M.D., Rikiya Nakamura, M.D., Kamnesh R. Pradhan, M.D., Christoph Cramer von Laue, Ph.D., Emily Barrett, M.Sc., Shanshan Cao, Ph.D., Xuejing Aimee Wang, Ph.D., Lillian M. Smyth, M.D., and François-Clément Bidard, M.D., for the EMBER-3 Study Group* -22

Author Info & Affiliations

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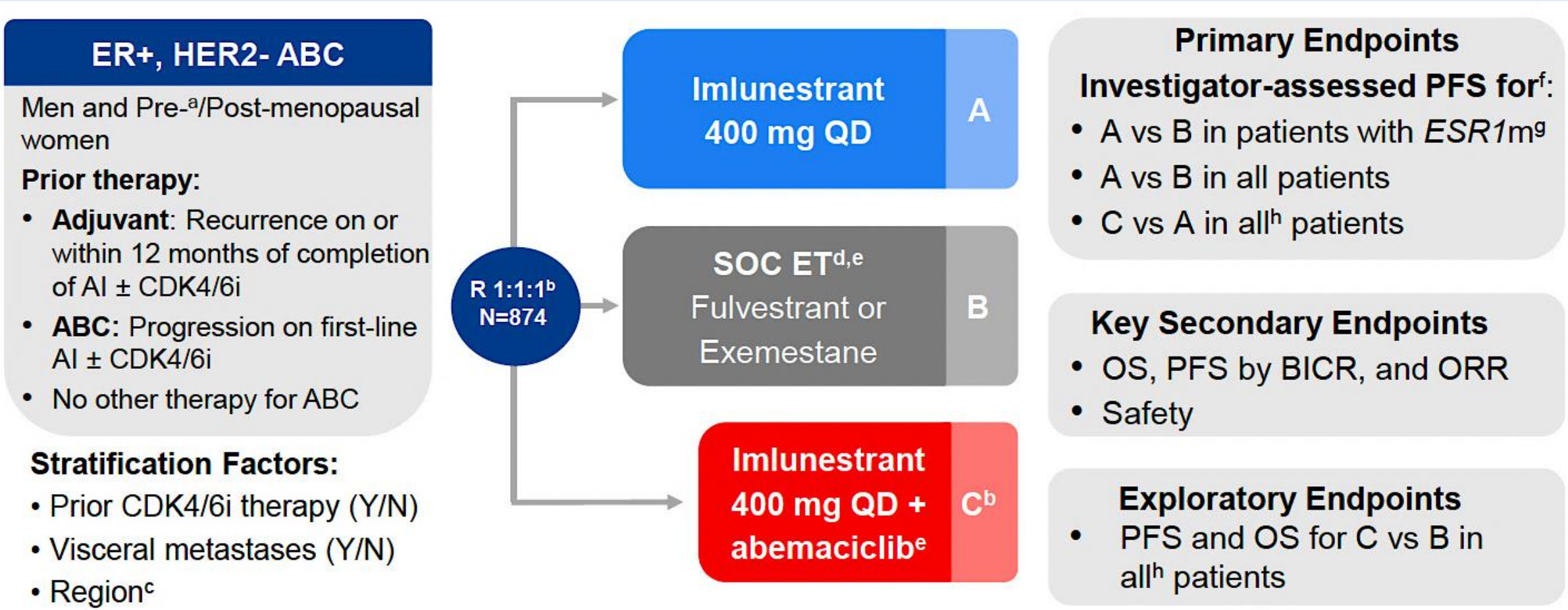
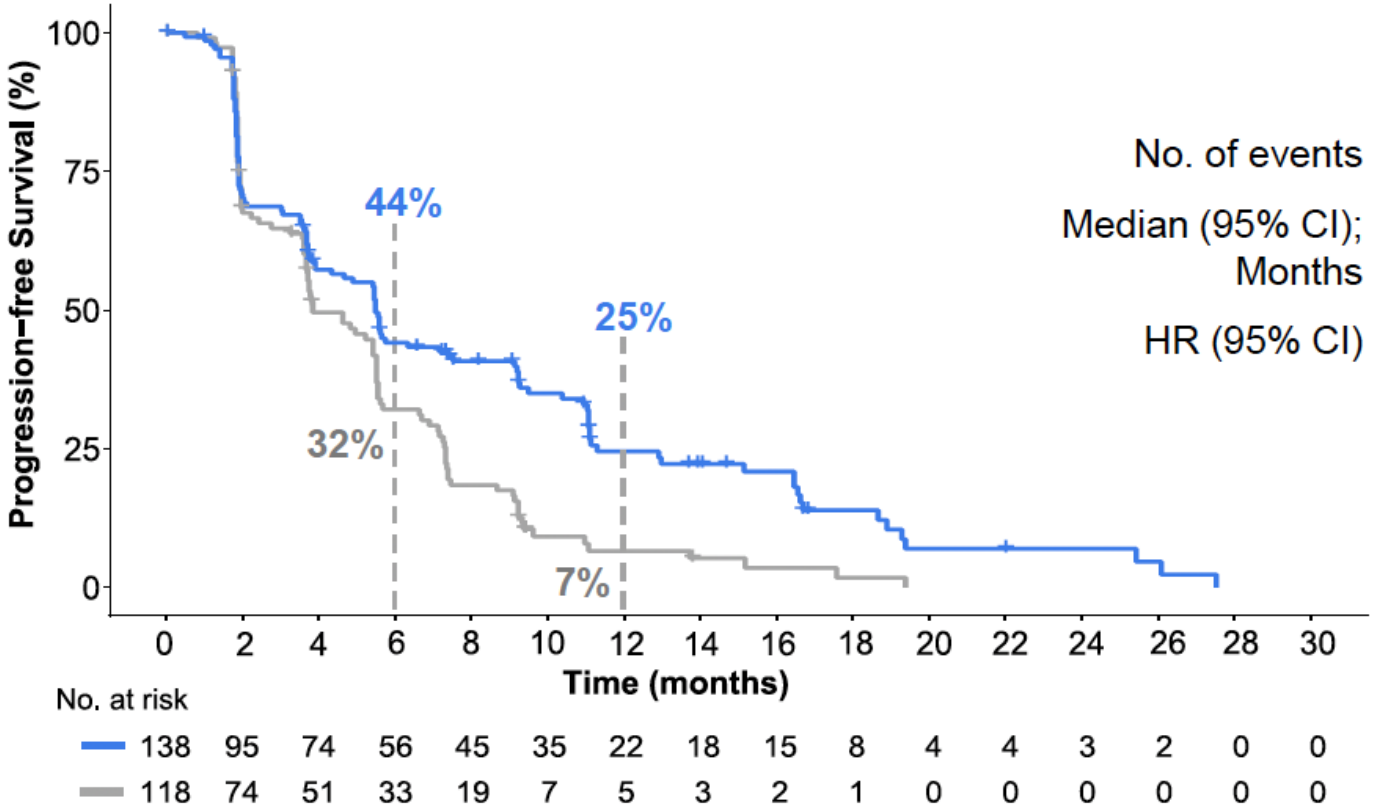
EMBER-3 Study Design



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. San Antonio Breast Cancer Symposium 2024;Abstract GS1-01.

EMBER-3: PFS with Imlunestrant Monotherapy for Patients with ESR1 Mutations



	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

CI, confidence interval; *ESR1*m, *ESR1* mutation; HR, hazard ratio; RMST, restricted mean survival time; SOC ET, standard of care endocrine therapy. The median follow-up was 16.7 months in the imlunestrant arm and 13.8 months in the SOC ET arm.
[a] Due to evidence of non-proportional hazards, a sensitivity analysis of PFS using RMST was conducted. Estimated RSMT at 19.4 months was 7.9 months (95% CI 6.8-9.1) in the imlunestrant arm vs 5.4 months (95% CI 4.6-6.2) in the SOC ET arm [difference 2.6 months (1.2.-3.9)].

Jhaveri KL et al. San Antonio Breast Cancer Symposium 2024;Abstract GS1-01.

Key Endocrine/SERD Questions 2025

PROTACs, SERMs, others?

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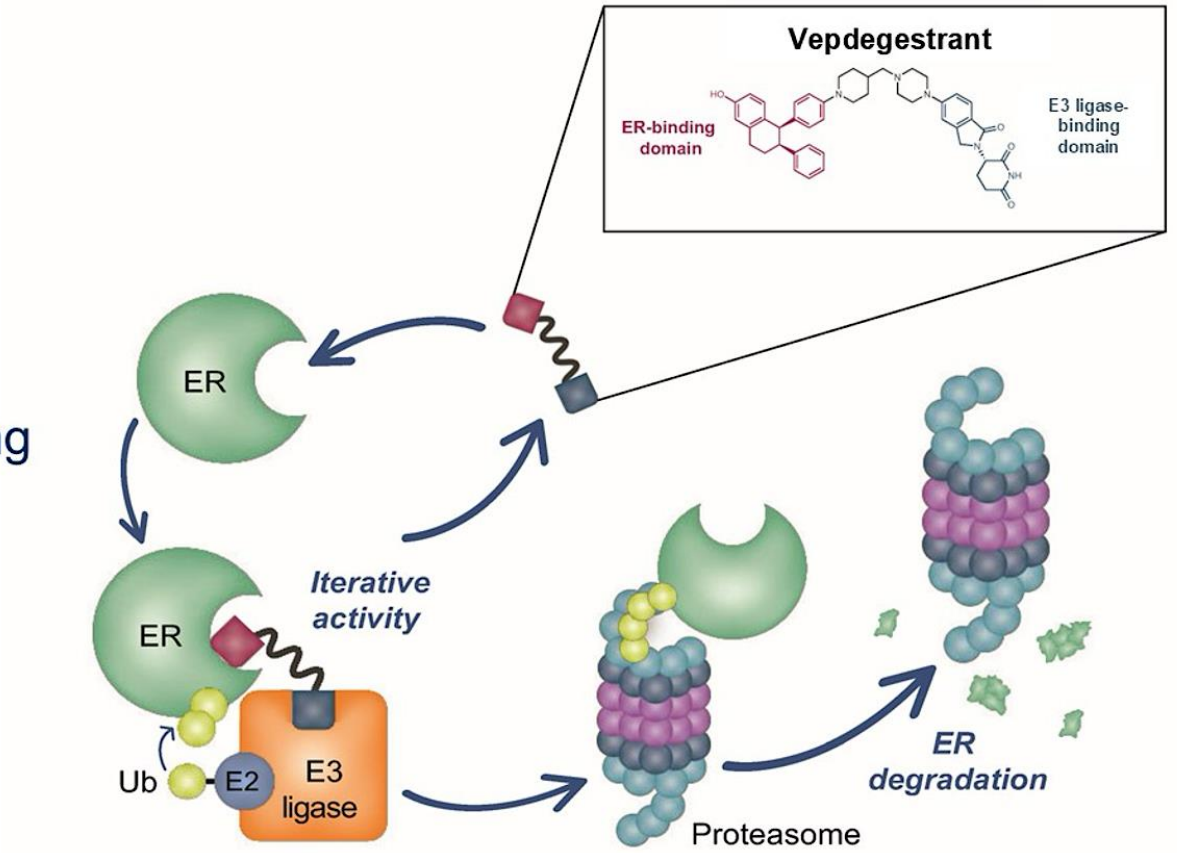
Background and Vepdegestrant Mechanism of Action

- There is no established consensus for treatment of ER+/HER2- advanced breast cancer after progression on first-line ET[1]
- Fulvestrant, a SERD that is administered IM due to poor solubility,[2] has limited PFS benefit following disease progression on a CDK4/6i + ET[3,4]
- Vepdegestrant is a selective, oral PROTAC ER degrader that targets WT and mutant ER[5,6]
- In a first-in-human, phase 1/2 study (NCT04072952), vepdegestrant was well tolerated and demonstrated encouraging clinical activity in heavily pretreated patients with ER+/HER2- advanced breast cancer[7]

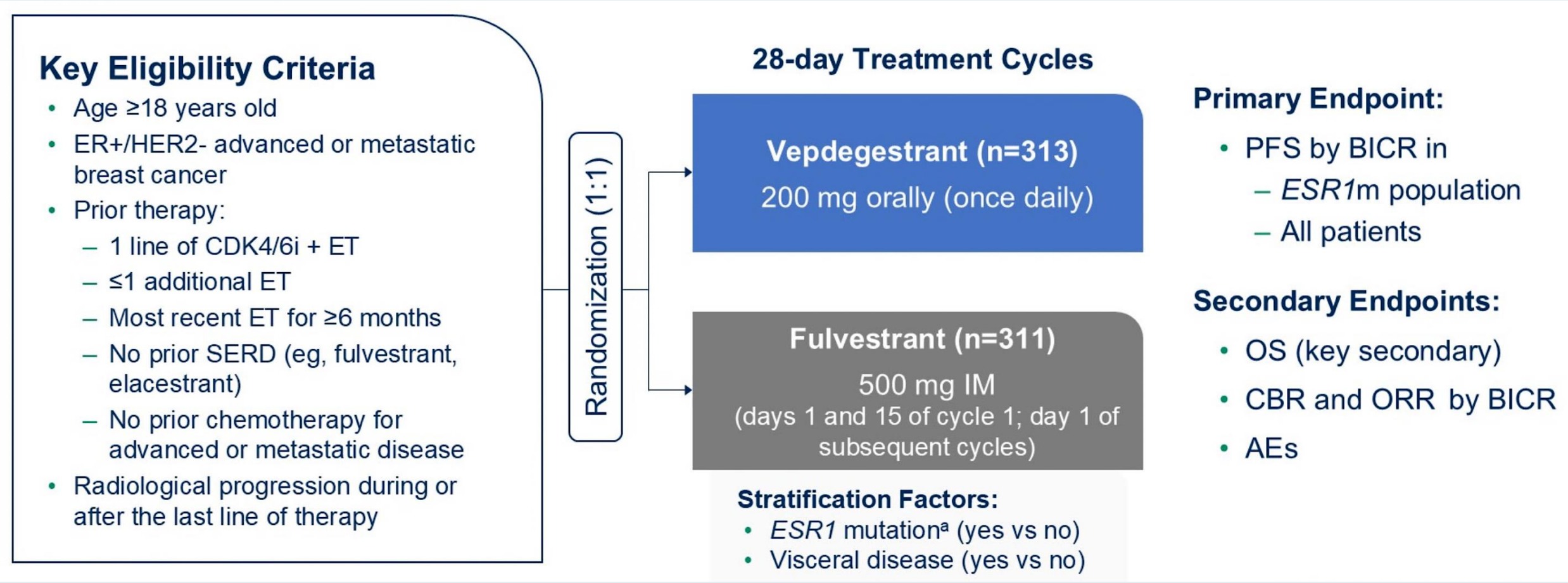


Vepdegestrant has a unique MOA that directly harnesses the ubiquitin-proteasome system to degrade ER[8]

IM = intramuscularly; WT = wild type

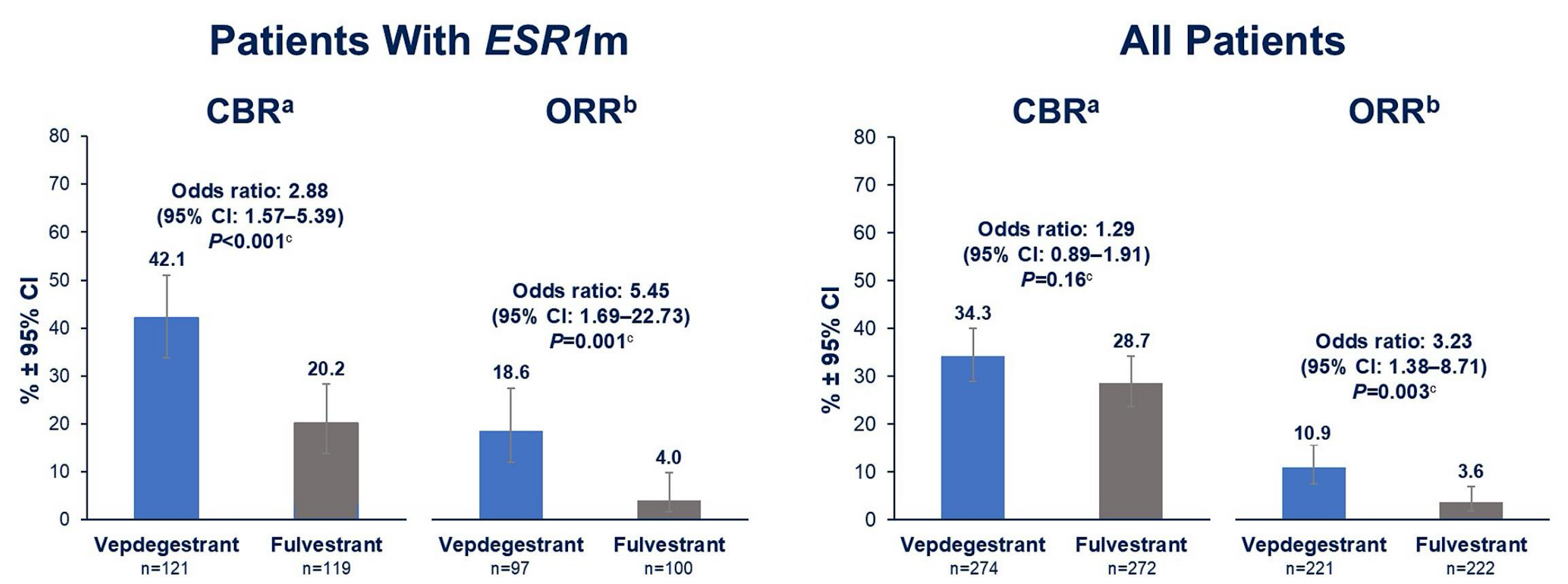
Hamilton E et al. ASCO 2025;Abstract LBA1000.

VERITAC-2 Study Design



Hamilton E et al. ASCO 2025;Abstract LBA1000.

VERITAC-2: Response Data



Hamilton E et al. ASCO 2025;Abstract LBA1000.

Key Endocrine/SERD Questions 2025

Treating “molecular progression”

ORIGINAL ARTICLE

First-Line Camizestrant for Emerging *ESR1*-Mutated Advanced Breast Cancer

F.-C. Bidard,[1] E.L. Mayer,[2] Y.H. Park,[3] W. Janni,[4] C. Ma,[5] M. Cristofanilli,[6] G. Bianchini,[7] K. Kalinsky,[8] H. Iwata,[9] S. Chia,[10] P.A. Fasching,[11] A. Brufsky,[12] Z. Nowecki,[13] J. Pascual,[14] L. Moreau,[15] S.-C. Chen,[16] N. Karadurmus,[17] E.N. Gal-Yam,[18] K.H. Jung,[19] S. Pernas,[20] S. McClain,[21] W. He,[22] T. Klinowska,[23] C. Huang-Bartlett,[21] and N.C. Turner,[24] for the SERENA-6 Study Group*

N Engl J Med June 1, 2025;[Online ahead of print].

Camizestrant + CDK4/6 inhibitor for the treatment of emergent *ESR1* mutations during first-line endocrine-based therapy and ahead of disease progression in patients with HR+/HER2– advanced breast cancer: Phase 3, double-blind ctDNA-guided SERENA-6 trial

Nicholas Turner*
Royal Marsden Hospital, London, UK

Additional authors:
Erica Mayer, Yeon Hee Park, Wolfgang Janni, Cynthia Ma, Massimo Cristofanilli, Giampaolo Bianchini, Kevin Kalinsky, Hiroji Iwata, Stephen Chia, Peter A. Fasching, Adam Brufsky, Zbigniew Nowecki, Javier Pascual, Lionel Moreau, Shin-Cheh Chen, Sasha McClain, Steven Fox, Cynthia Huang Bartlett, François-Clément Bidard*

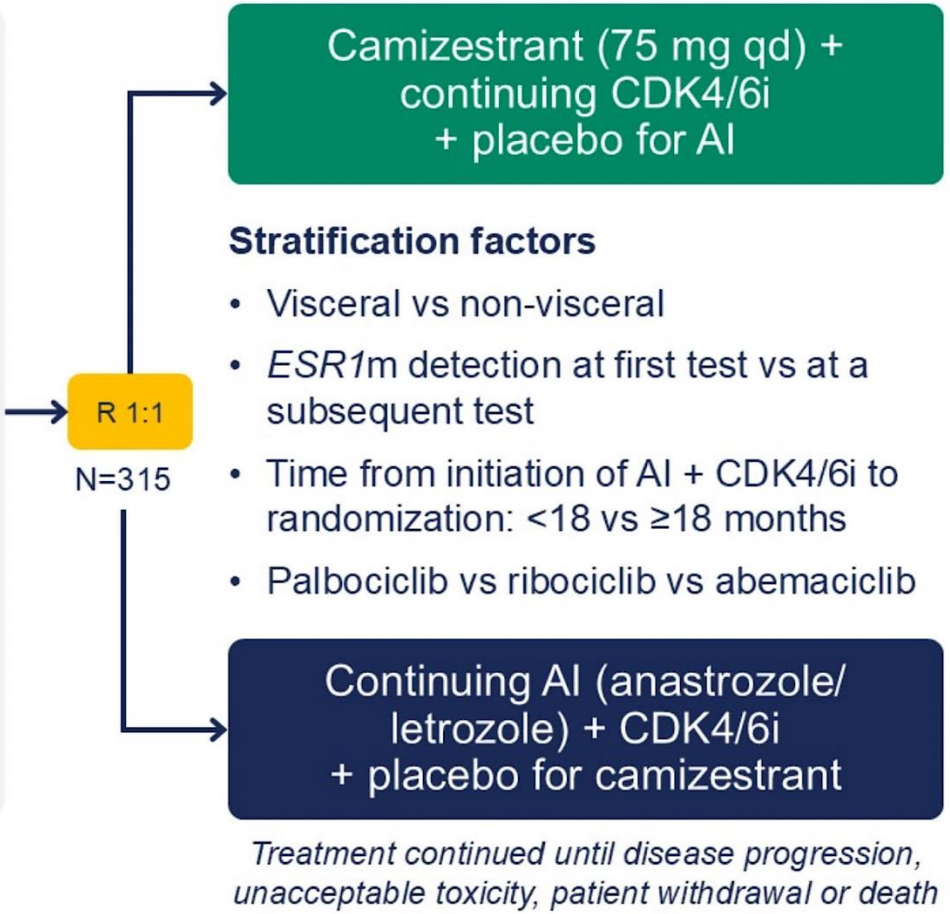
*Contributed equally

ASCO 2025;Abstract LBA4.

RTP RESEARCH TO PRACTICE

SERENA-6 Study Design

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



Primary endpoint

PFS by investigator assessment (RECIST v1.1)

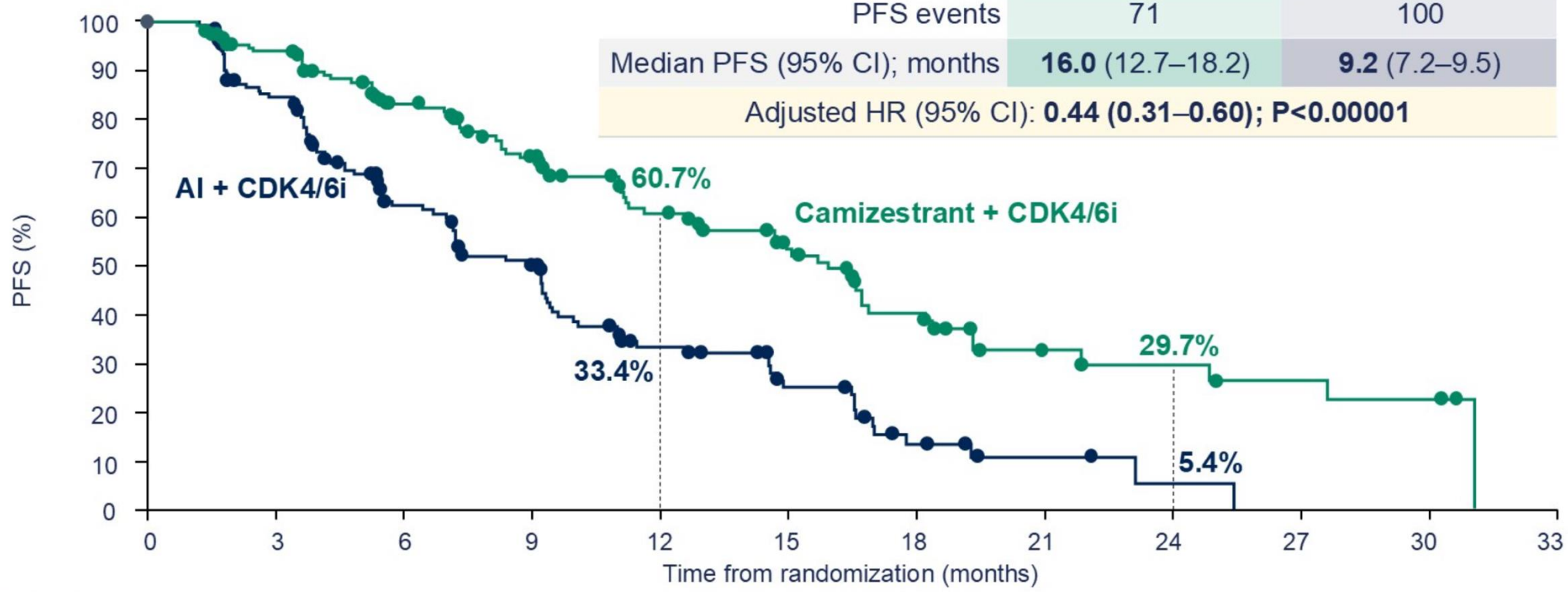
Secondary endpoints

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

Bidard F-C et al. *N Engl J Med* June 1, 2025;[Online ahead of print]. Turner N et al. ASCO 2025;Abstract LBA4.

SERENA-6: PFS Outcomes

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



Number of patients at risk

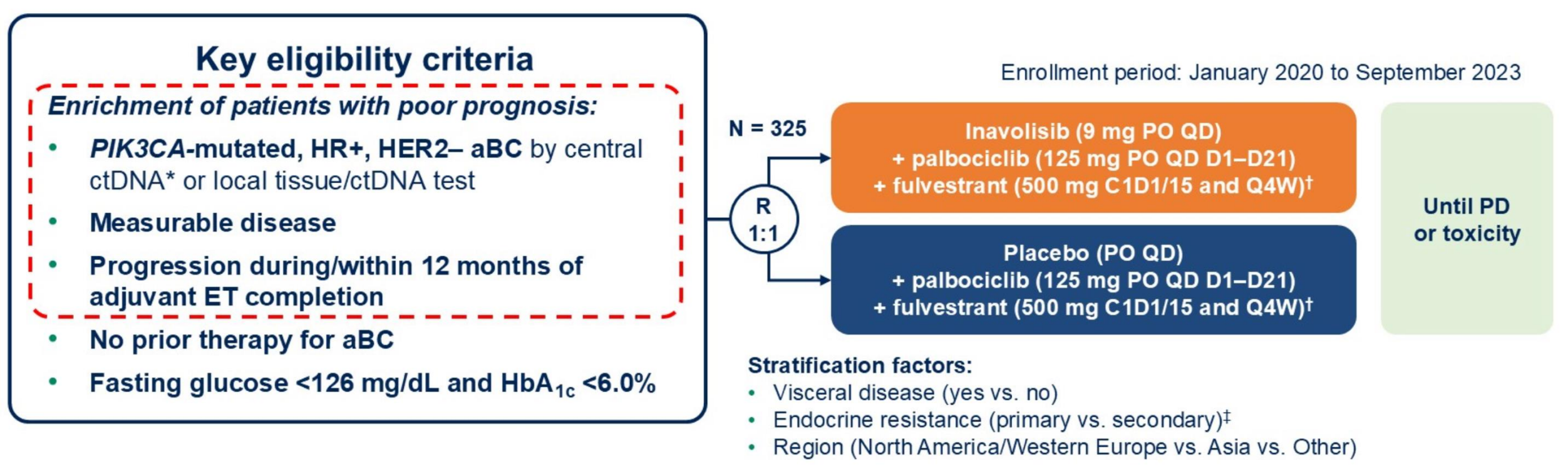
Camizestrant + CDK4/6i	157	138	105	82	55	41	26	11	9	7	6	0
AI + CDK4/6i	158	124	73	55	29	17	7	3	1	0	0	0

Bidard F-C et al. *N Engl J Med* June 1, 2025;[Online ahead of print]. Turner N et al. ASCO 2025;Abstract LBA4.

Key Endocrine/SERD Questions 2025

Eligibility for up-front inavolisib/palbociclib/fulvestrant (de novo? HbA1c?)

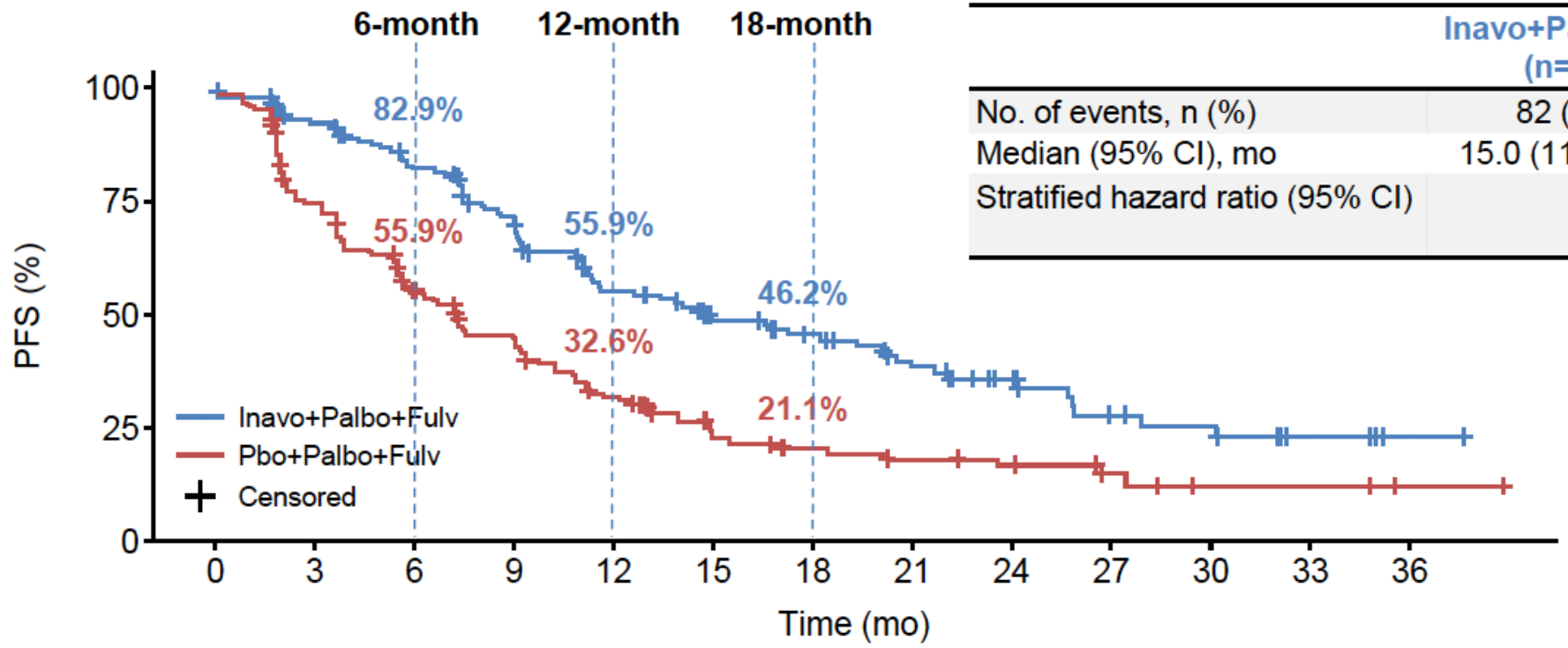
INAVO120 Study Design



ET = endocrine therapy; PD = disease progression

Turner N et al. ASCO 2025;Abstract 1003.

INAVO120: PFS Outcomes



	Inavo+Palbo+Fulv (n=161)	Pbo+Palbo+Fulv (n=164)
No. of events, n (%)	82 (50.9)	113 (68.9)
Median (95% CI), mo	15.0 (11.3, 20.5)	7.3 (5.6, 9.3)
Stratified hazard ratio (95% CI)	**0.43 (0.32, 0.59) p<0.0001**	

Patients at risk:

Inavo+Palbo+Fulv	161	134	111	92	66	48	41	31	22	13	11	5	1
Pbo+Palbo+Fulv	164	113	77	59	40	23	19	16	12	6	3	3	1

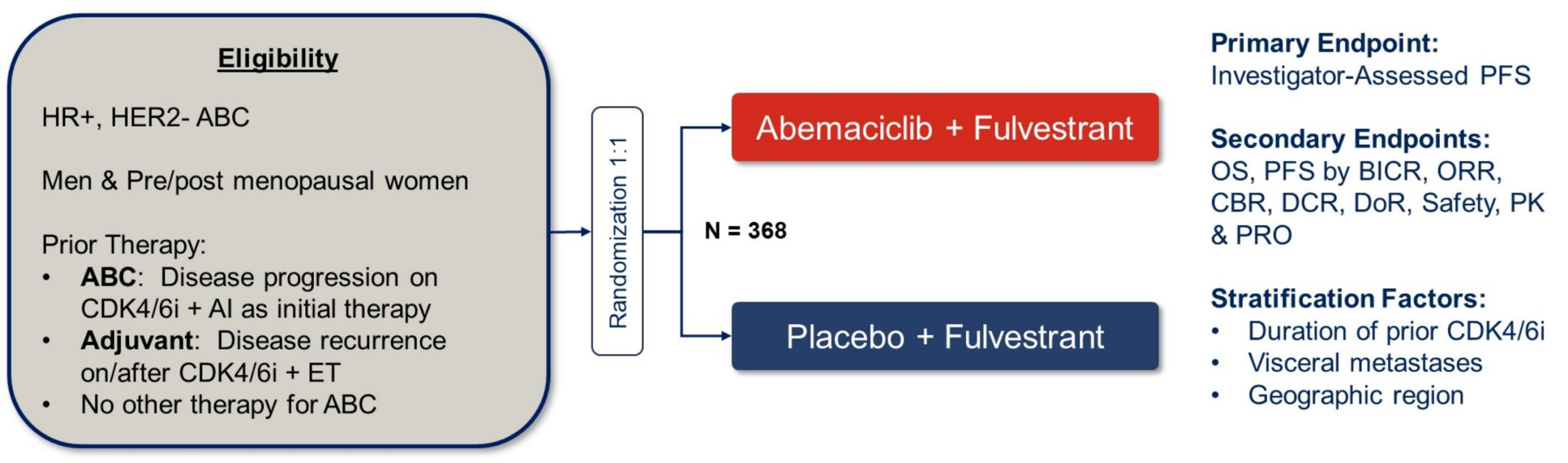
Median follow-up:
21.3 months

Jhaveri K et al. SABCS 2023;Abstract GS03-13.

Key Endocrine/SERD Questions 2025

Role of CDK inhibitor after CDK inhibitor? (abemaciclib)

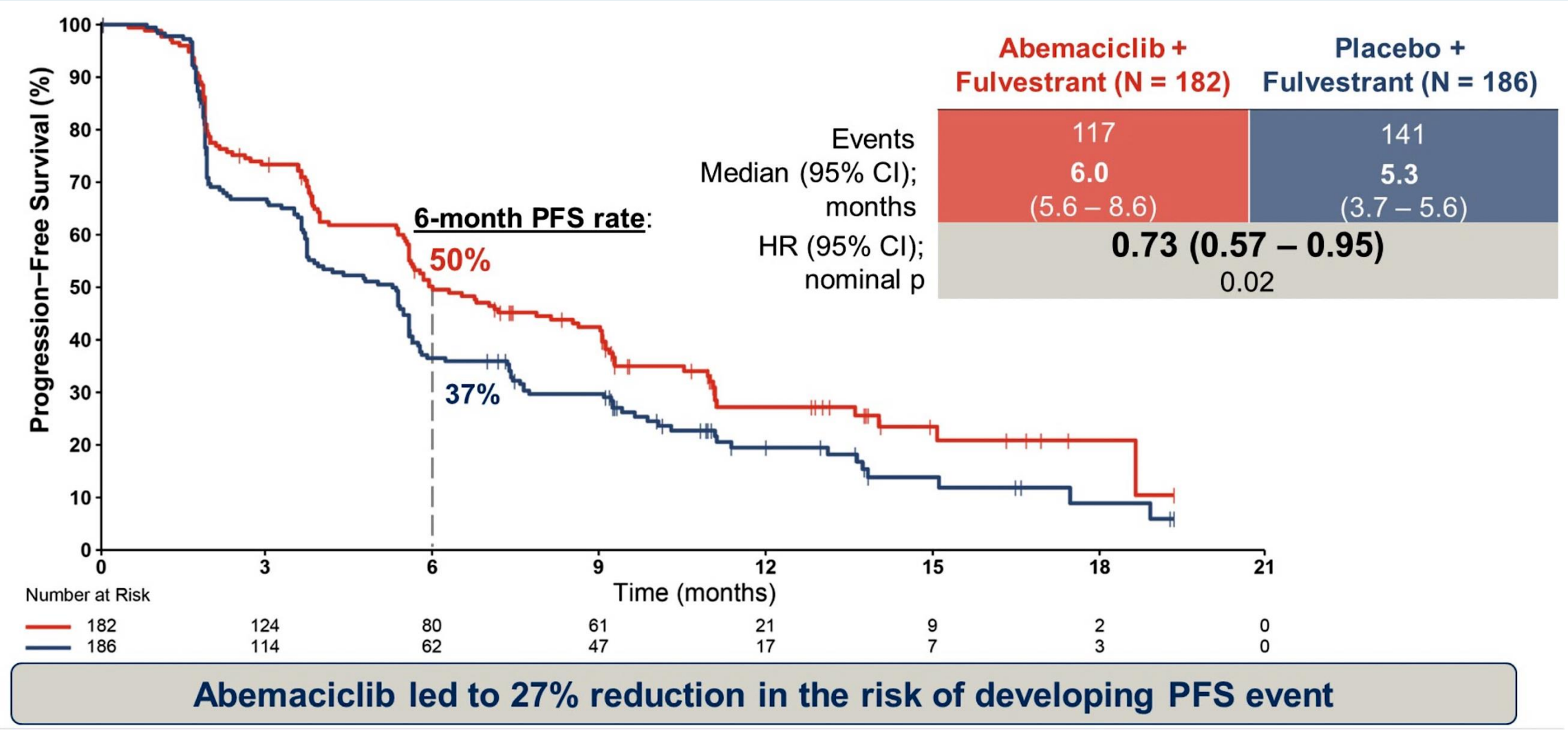
postMONARCH Study Design



ABC = advanced breast cancer; CDK4/6i = CDK4/6 inhibitor; AI = aromatase inhibitor; ET = endocrine therapy

Kalinsky K et al. ASCO 2024;Abstract LBA1001; *J Clin Oncol* 2025;43(9):1101-12.

postMONARCH: Progression-Free Survival (PFS) Outcomes



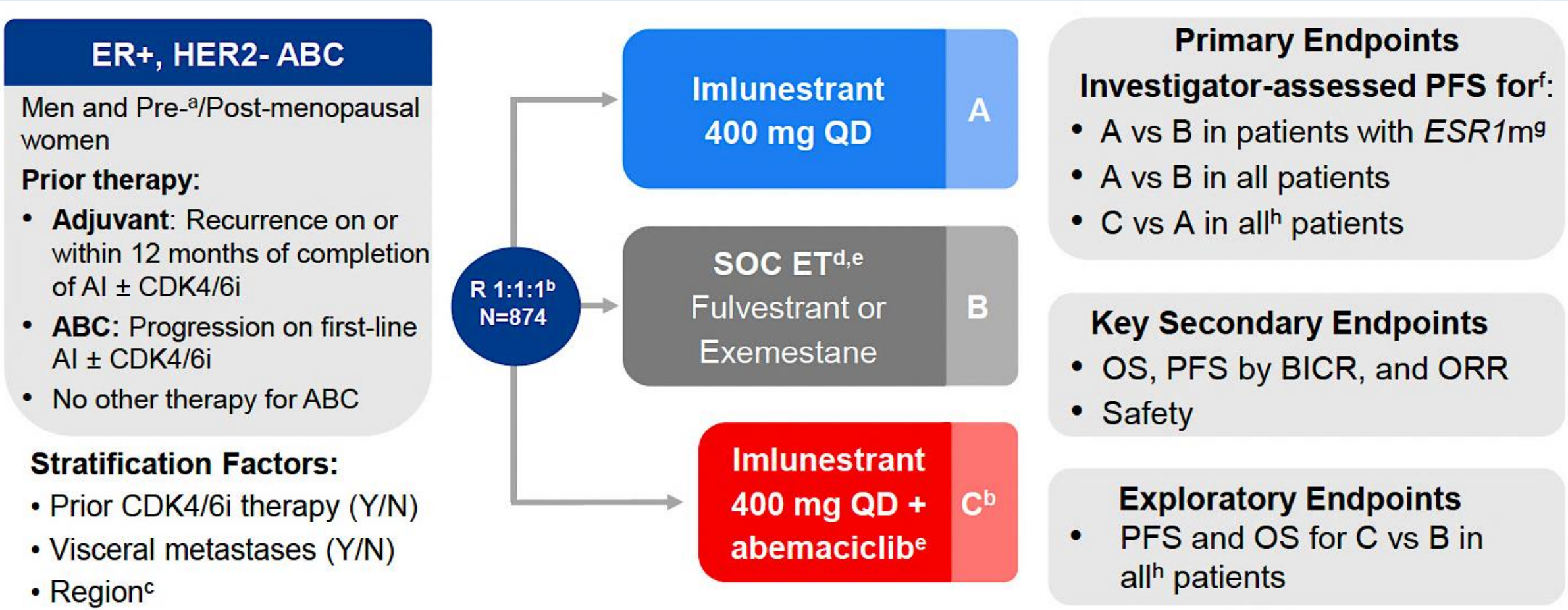
Abemaciclib led to 27% reduction in the risk of developing PFS event

Kalinsky K et al. ASCO 2024;Abstract LBA1001; *J Clin Oncol* 2025;43(9):1101-12.

Key Endocrine/SERD Questions 2025

Role of CDK inhibitor with SERD (abemaciclib/imlunestrant)

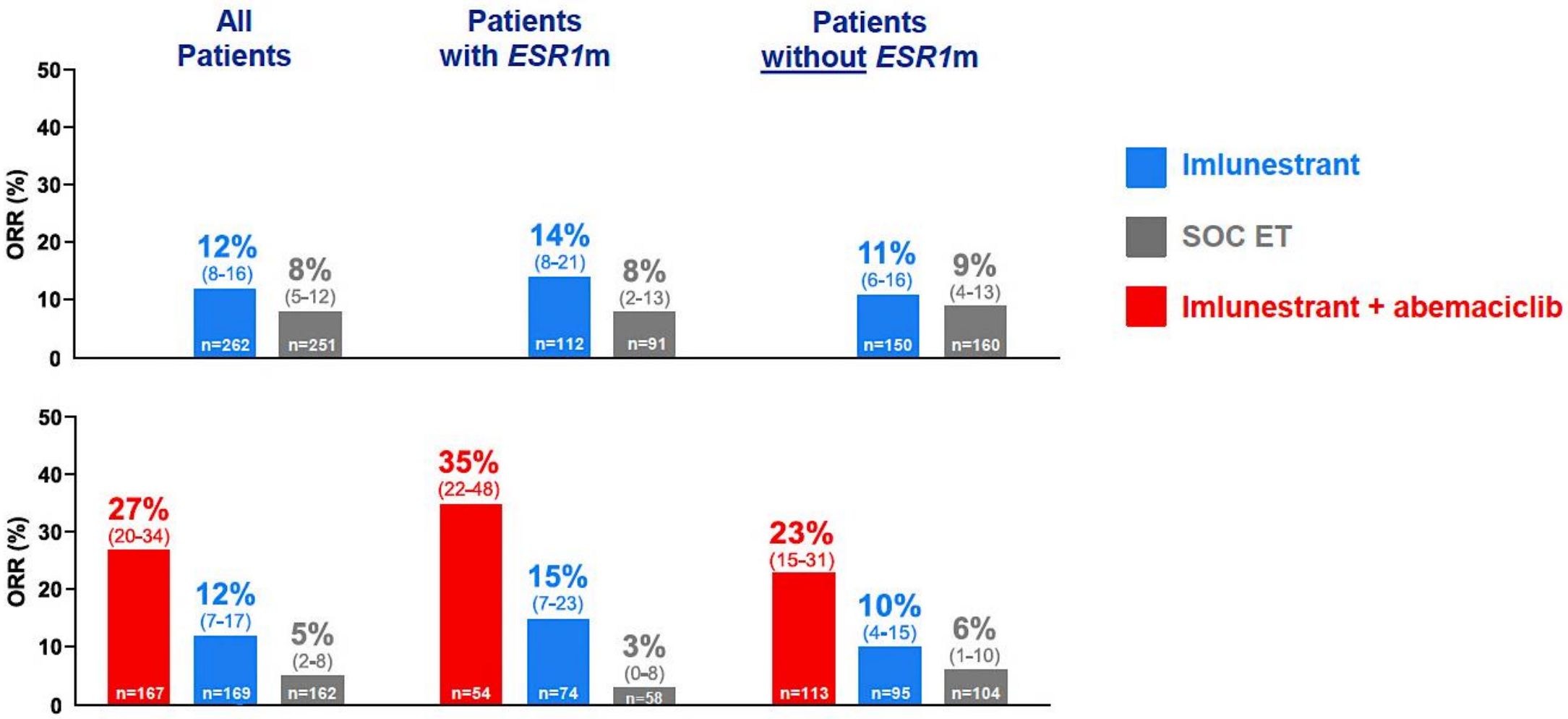
EMBER-3 Study Design



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. San Antonio Breast Cancer Symposium 2024;Abstract GS1-01.

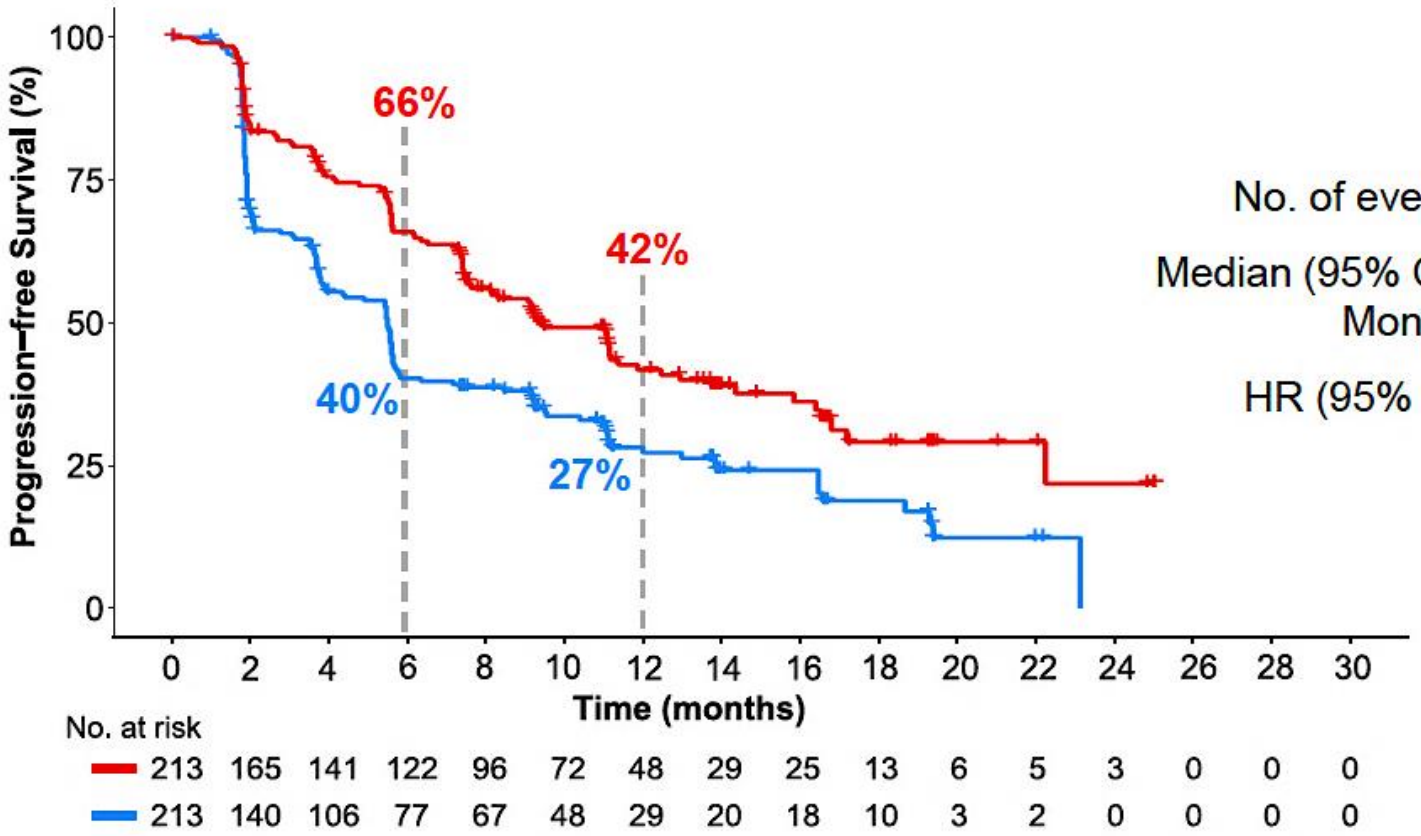
EMBER-3: Investigator-Assessed Objective Response Rate



*ESR1*m, *ESR1* mutation; ORR, objective response rate; SOC ET, standard of care endocrine therapy. Patients without *ESR1*m include those with unknown *ESR1*m status (top bars: imlunestrant, n=13; SOC ET, n=7; bottom bars: imlunestrant + abemaciclib, n=1; Imlunestrant, n=7; SOC ET, n=4). Bottom bars: analyses confined to the imlunestrant/SOC ET population concurrently randomized. The values indicated in parentheses represent the 95% confidence intervals.

Jhaveri KL et al. San Antonio Breast Cancer Symposium 2024;Abstract GS1-01.

EMBER-3: PFS with Imlunestrant and Abemaciclib for All Patients



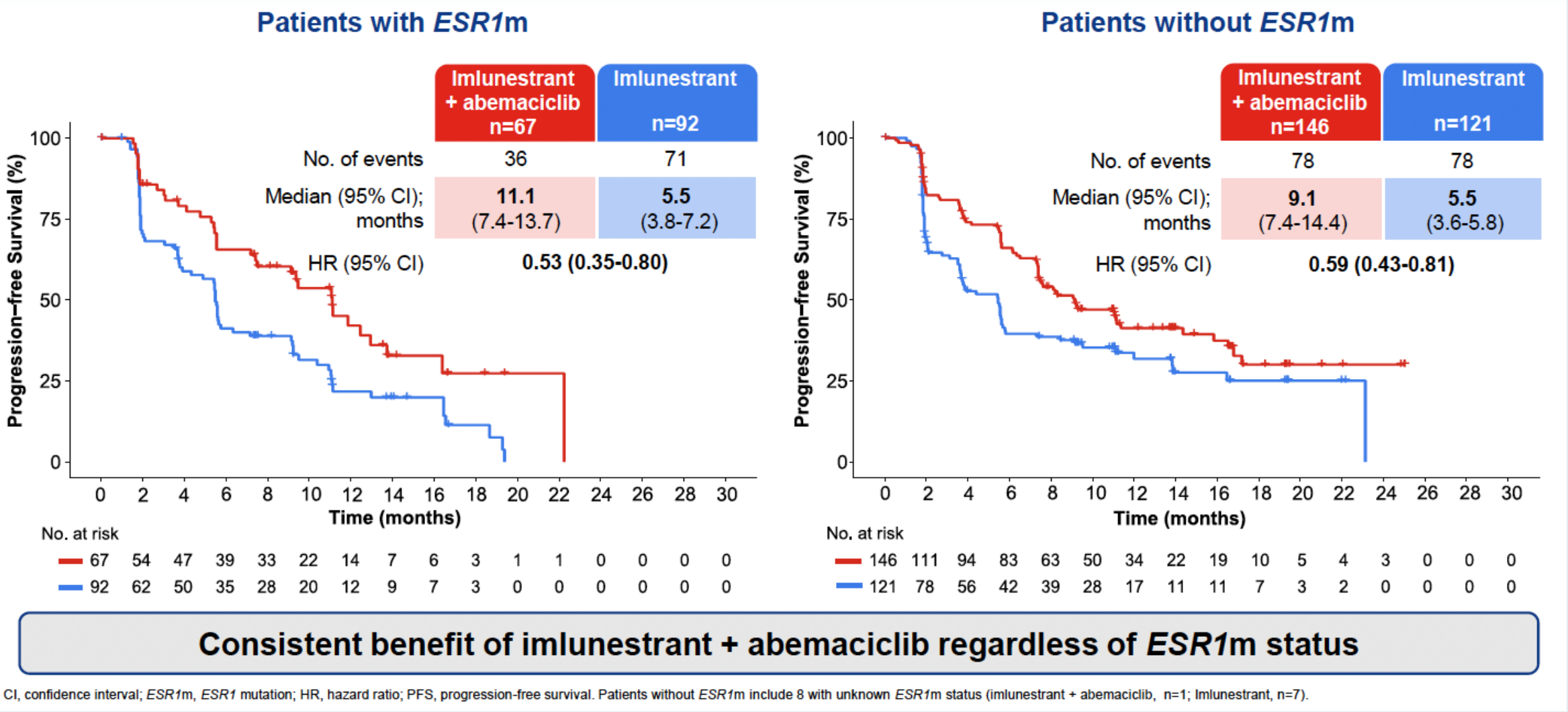
	Imlunestrant + abemaciclib n=213	Imlunestrant n=213[a]
No. of events	114	149
Median (95% CI); Months	**9.4** (7.5-11.9)	**5.5** (3.8-5.6)
HR (95% CI)	**0.57 (0.44-0.73)** *p*-value <0.001	

Imlunestrant + abemaciclib led to a 43% reduction in the risk of progression or death over imlunestrant alone in all patients

CI, confidence interval; HR, hazard ratio. [a]Efficacy analyses confined to the imlunestrant population concurrently randomized to imlunestrant + abemaciclib treatment arm. The median follow-up was 13.5 months in the imlunestrant + abemaciclib arm and 13.7 months in the imlunestrant arm.

Jhaveri KL et al. San Antonio Breast Cancer Symposium 2024;Abstract GS1-01.

EMBER-3: PFS with Imlunestrant and Abemaciclib by ESR1m Status



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

CI, confidence interval; *ESR1*m, *ESR1* mutation; HR, hazard ratio; PFS, progression-free survival. Patients without *ESR1*m include 8 with unknown *ESR1*m status (imlunestrant + abemaciclib, n=1; Imlunestrant, n=7).

Jhaveri KL et al. San Antonio Breast Cancer Symposium 2024;Abstract GS1-01.

Emerging treatment options for advanced, ER+ breast cancer

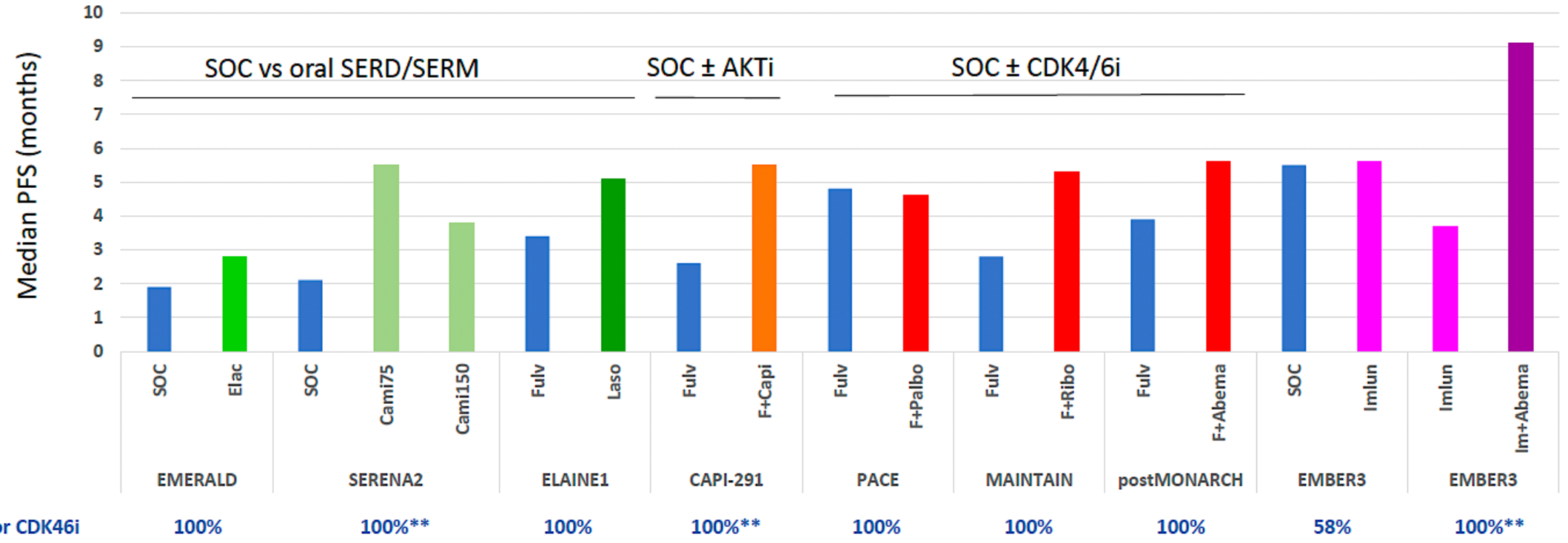
Harold J. Burstein, MD, PhD

Abstract GS1-01 Discussant, SABCS 2024

Dana-Farber Cancer Institute

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

Median PFS in Recent Randomized Trials of Endocrine Therapy: Outcomes Among Patients Who Received Prior CDK4/6 Inhibitor Treatment*



*there are a lot of problems with cross study comparisons, especially in unplanned subset analyses: extent/types of prior therapy, variable tumor genomics/biomarker profile, SOC options, sample size, exposure vs resistance, investigator vs BICR, etc.

** Denotes subset of larger study cohort

PFS = progression-free survival; SOC = standard of care; BICR = blinded independent central review

Burstein H. San Antonio Breast Cancer Symposium 2024;Abstract GS1-01 Discussant.

SERDs: Side Effects Encountered More Commonly Than with Fulvestrant in Randomized Clinical Trials

Side Effect	Elacestrant	Imlunestrant	Giredestrant	Camizestrant
Fatigue		X		X
Nausea	X	X	X	X
Vomiting	X	X	X	
Constipation	X			
Diarrhea	X	X		
Bradycardia			X	X
Photopsia				X
Transaminitis			X	
Hypertriglyceridemia	X			

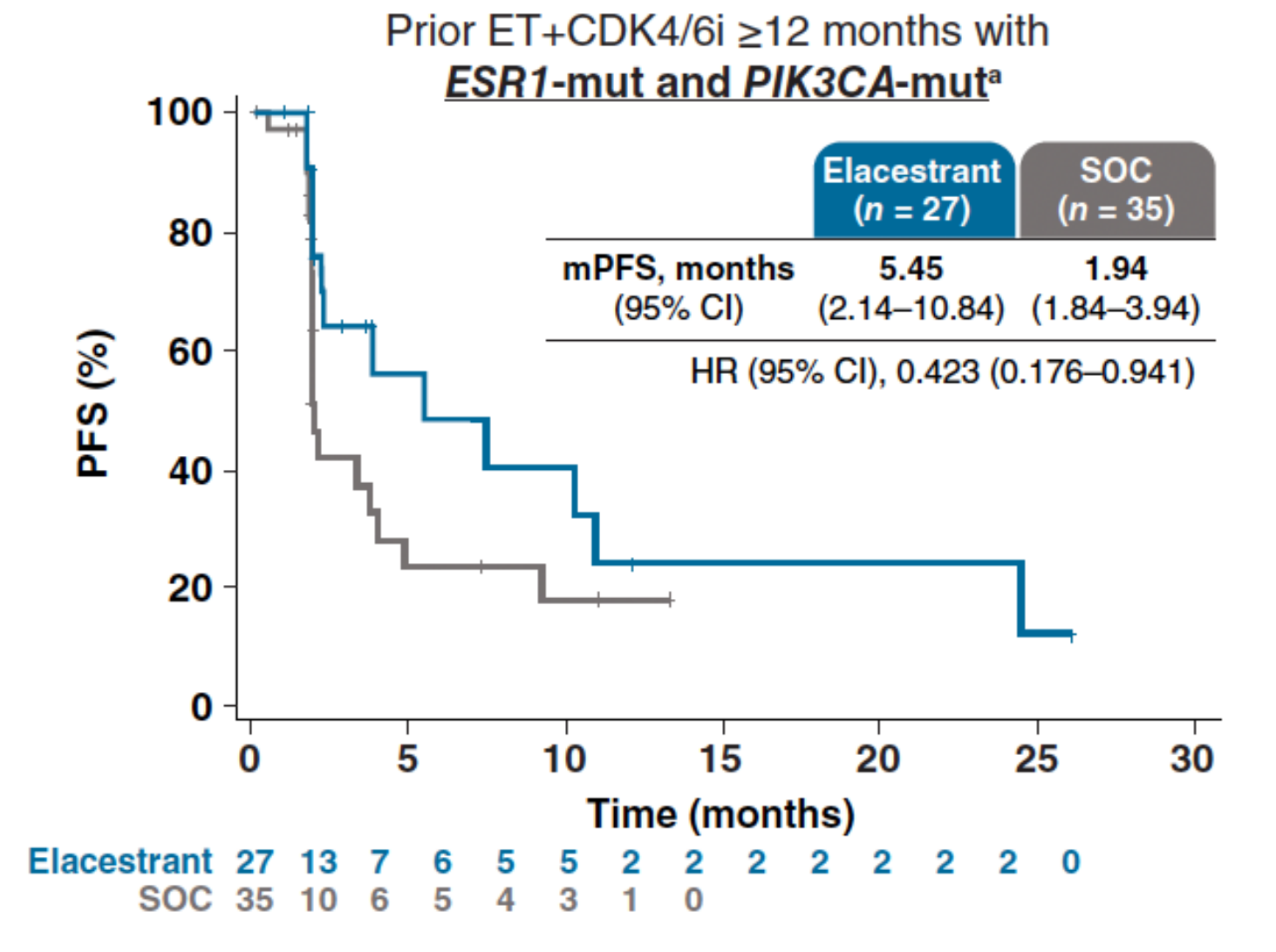
Burstein H. San Antonio Breast Cancer Symposium 2024;Abstract GS1-01 Discussant.

RTP RESEARCH TO PRACTICE

Key Endocrine/SERD Questions 2025

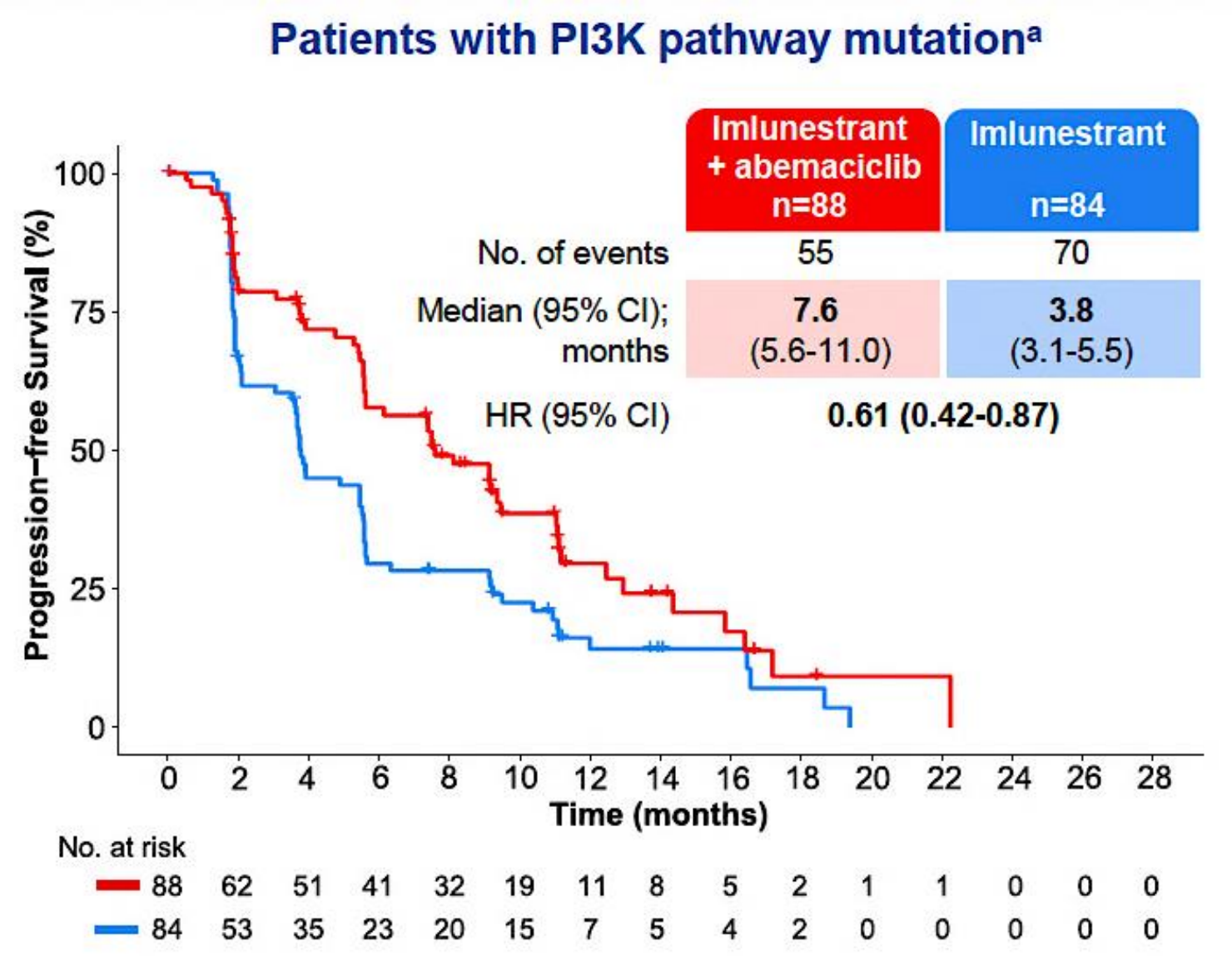
SERD after AKT inhibitor and reverse?

Elacestrant for Patients with PIK3CA-Mutated Disease



Bardia A et al. *Clin Cancer Res* 2024 August 1;[Online ahead of print].

Imlunestrant and Abemaciclib in PIK3CA-Mutated Disease

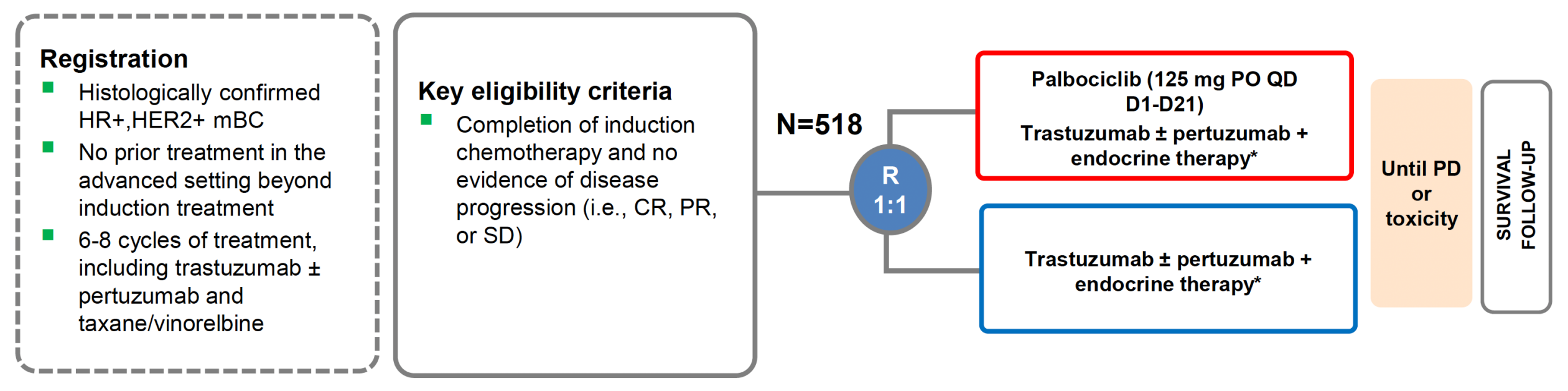


Jhaveri KL et al. San Antonio Breast Cancer Symposium 2024;Abstract GS1-01.

Key Endocrine/SERD Questions 2025

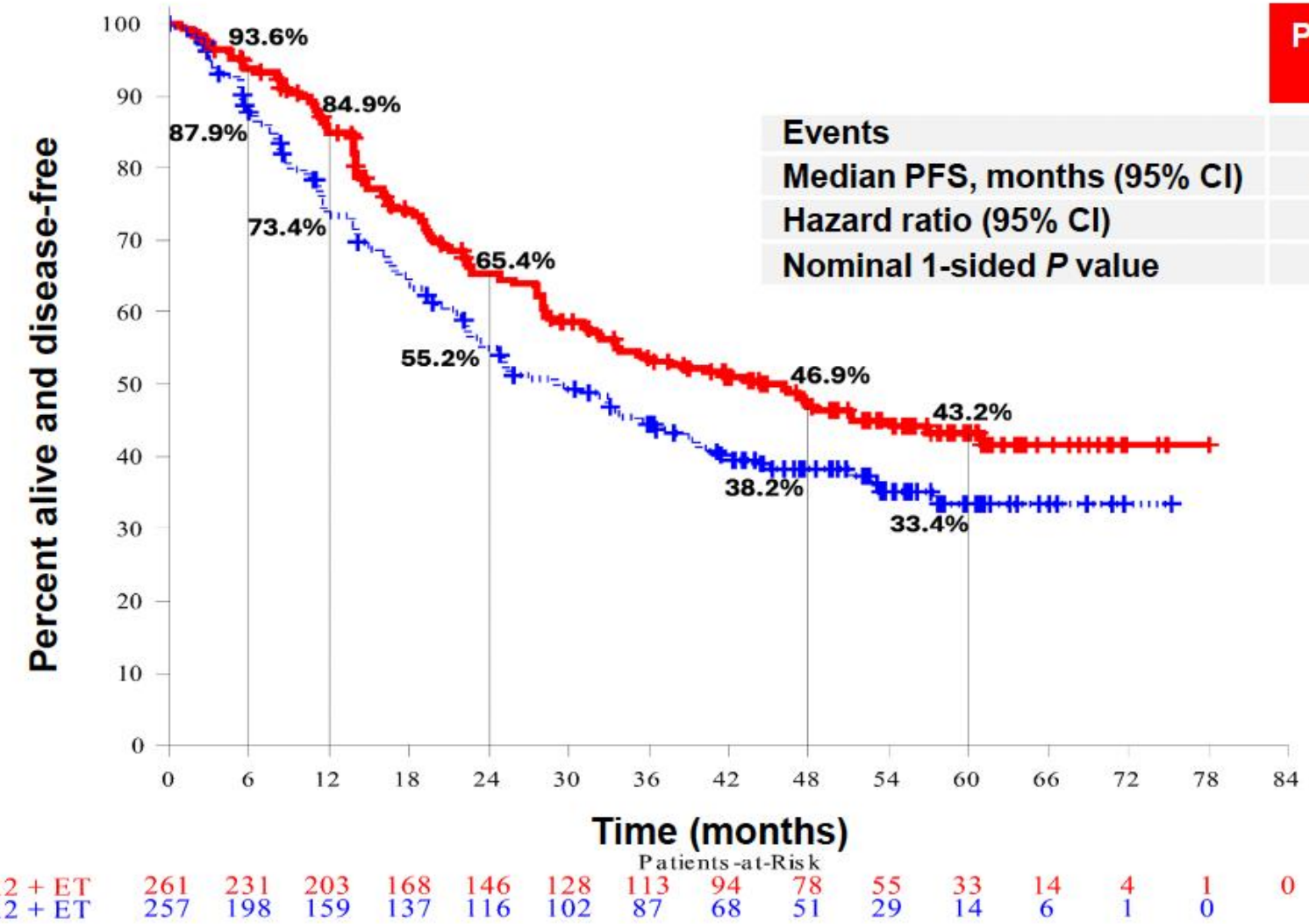
CDK inhibitor (palbociclib) after first-line T-DXd (ESR1+, HER2+)?

PATINA Study Design



Metzger O et al. SABCS 2024;Abstract P2-03-20.

PATINA: PFS Outcomes



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

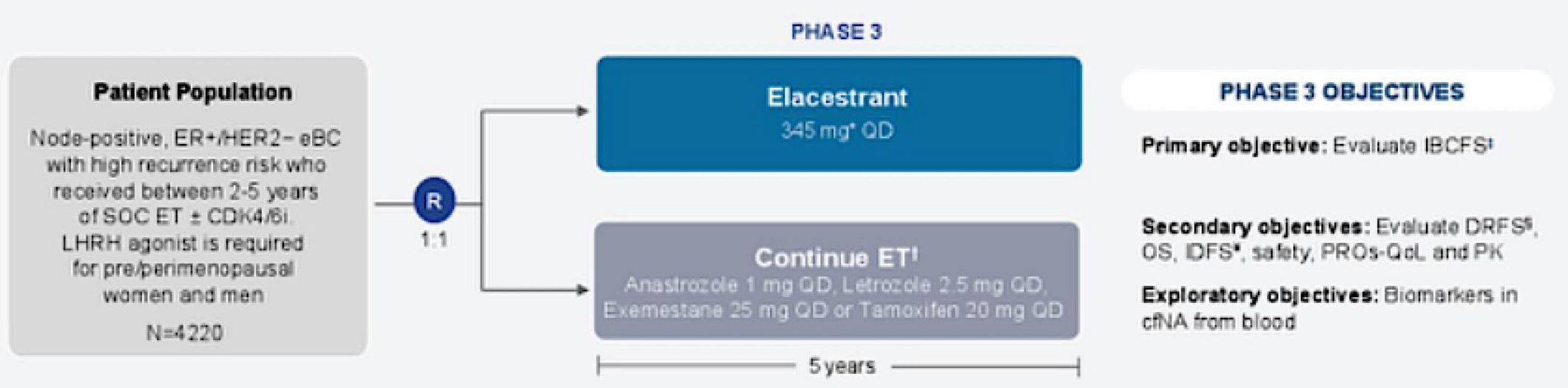
Median follow-up on patients who are alive and disease-free, 52.6 months

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

Metzger O et al. SABCS 2024;Abstract P2-03-20.

SERDs in ER-Positive, HER2-Negative Localized Breast Cancer

ELEGANT Study Design



IBCFS = invasive breast cancer-free survival; DRFS = distant relapse-free survival; OS = overall survival; IDFS = invasive disease-free survival; PK = pharmacokinetics; cfNA = cell-free nucleic acid

Bardia A et al. SABCS 2024;Abstract P2-08-21.

RESEARCH ARTICLE | OCTOBER 08 2024

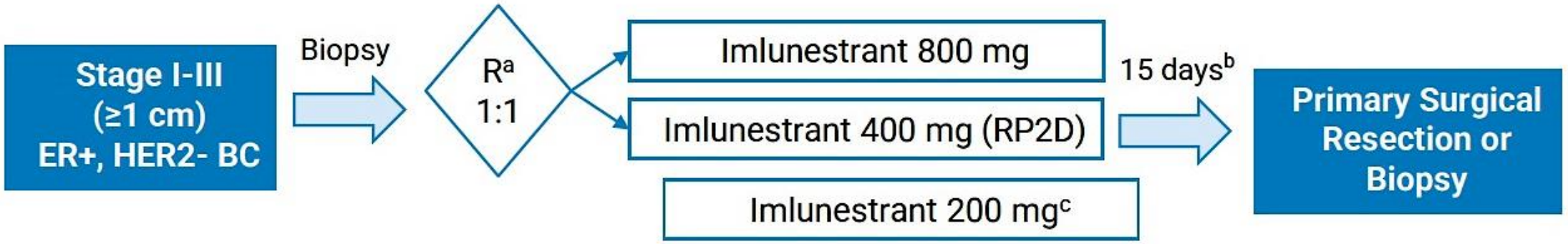
A preoperative window-of-opportunity study of oral SERD, imlunestrant, in newly diagnosed ER-positive, HER2-negative early breast cancer: Results from EMBER-2 Study.

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;[Online ahead of print].

EMBER-2 Study Design

- Key Inclusion criteria:
  - Post-menopausal women with stage I–III (≥1 cm), ER+ (>50% or Allred score >5), HER2-, Operable and untreated EBC



[a] Stratified by tumor histology (invasive ductal carcinoma [IDC] vs. invasive lobular carcinoma [ILC] vs. other)
[b] Treatment window was -2 to +7 days up to date of surgery/repeat biopsy
[c] 200 mg cohort was added in a protocol amendment, and opened after enrolment to the randomized cohorts was completed

- Imlunestrant was administered orally at 200 mg, 400 mg, or 800 mg QD for 15 days.[b]

EBC = early breast cancer

Primary Endpoint of EMBER-2: Relative Reduction of ER Expression

Relative reduction of ER, PR, and Ki-67 at week 2

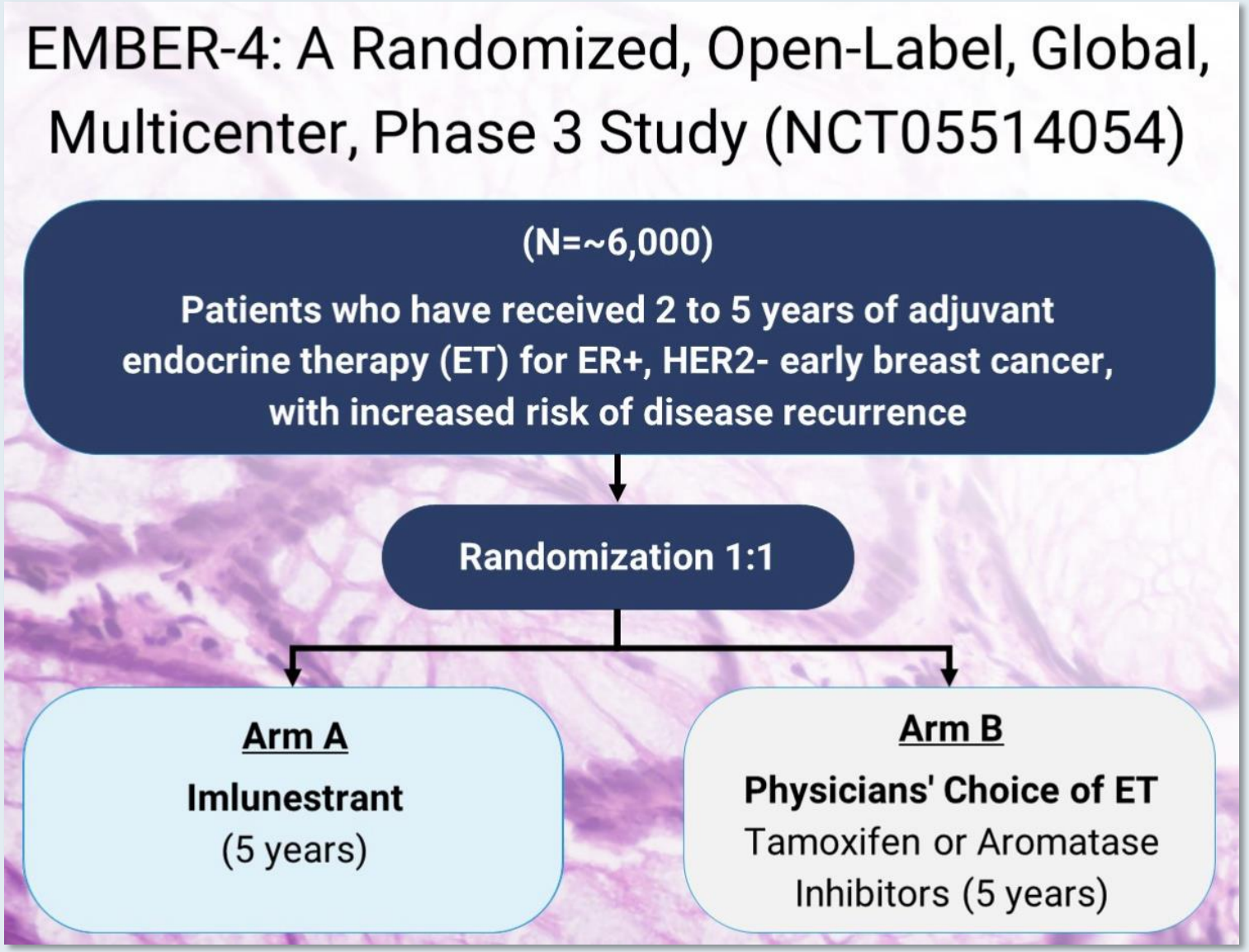
Geometric mean (90% CI) in PD biomarkers	200 mg N=22	400 mg N=27	800 mg N=26	Total N=75
ER[a]	-89% (-96%, -72%)	-82% (-91%, -60%)	-70% (-78%, -59%)	-81% (-87%, -72%)
PR[a]	-85% (-97%, -37%)	-76% (-90%, -38%)	-82% (-92%, -60%)	-81% (-89%, -66%)
Ki-67[a]	-69% (-79%, -54%)	-71% (-80%, -57%)	-72% (-81%, -59%)	-70% (-76%, -63%)
Baseline Ki-67 ≥5% n, %, (90% CI)	20 -70% (-80%, -56%)	22 -71% (-80%, -57%)	17 -78% (-84%, -70%)	59 -73% (-78%, -67%)
Baseline Ki-67 ≥15% n, %, (90% CI)	16 -73% (-83%, -56%)	13 -71% (-82%, -53%)	8 -75% (-83%, -63%)	37 -73% (-79%, -64%)
Baseline Ki-67 ≥20% n, %, (90% CI)	13 -77% (-87%, -59%)	12 -72% (-83%, -53%)	7 -78% (-84%, -68%)	32 -75% (-81%, -67%)
CCCA[b] (%)	3/20 (15%)	5/22 (23%)	6/17 (35%)	14/59 (24%)

[a] See Figure 1 for PD evaluable (mITT) population for each biomarker; [b] CCCA (complete cell cycle arrest among patients (n=59) with baseline Ki-67 ≥5%

Recommended Phase II dose (RP2D): 400 mg QD

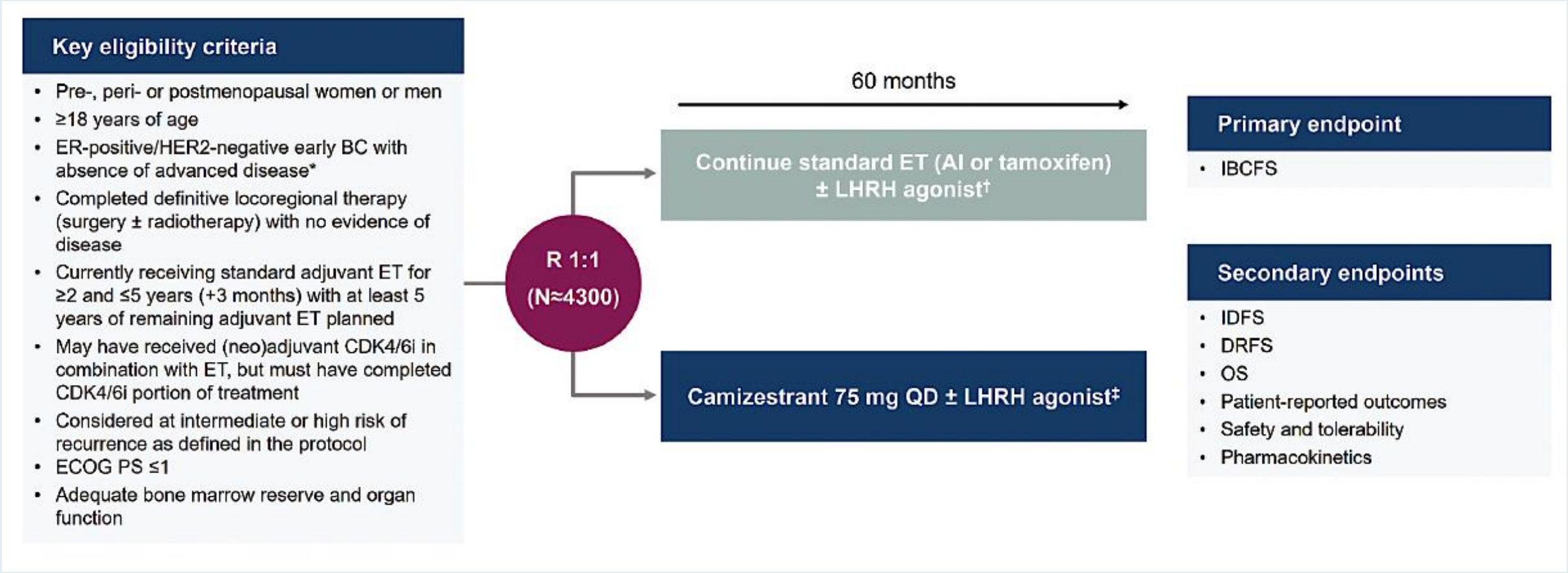
Neven P et al. *Clin Cancer Res* 2024;[Online ahead of print].

EMBER-4 Study Design



Jhaveri KL et al. San Antonio Breast Cancer Symposium 2022;Abstract OT1-01-02.

CAMBRIA-1 Study Design



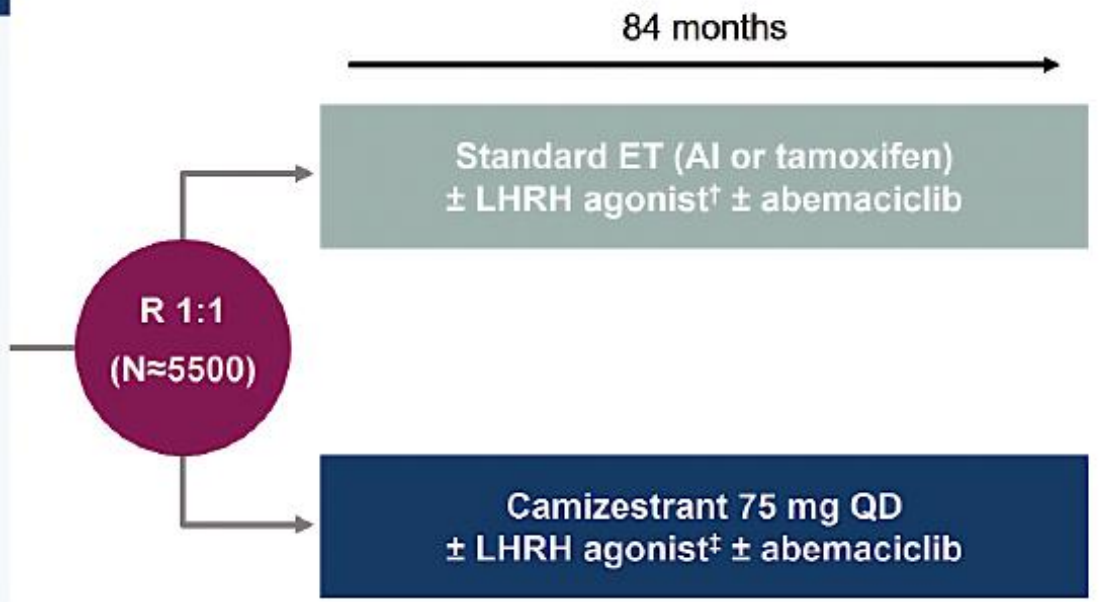
IBCFS = invasive breast cancer-free survival; IDFS = invasive disease-free survival; DRFS = distant relapse-free survival; OS = overall survival

Hamilton E et al. *Future Oncol* 2025;21(7):795-806.

CAMBRIA-2 Study Design

Key eligibility criteria

- Pre-, peri- or postmenopausal women or men
- ≥18 years of age
- ER-positive/HER2-negative early BC with absence of advanced disease*
- Completed definitive locoregional therapy (surgery ± radiotherapy) ± (neo)adjuvant systemic chemotherapy with no evidence of disease
- Patients should be randomized within the first 12 weeks after radiation or the last CT dose (whichever is last), and within 12 months of definitive breast surgery
- May have received up to 12 weeks of (neo)adjuvant ET prior to randomization
- Considered at intermediate–high or high risk of recurrence as defined in the protocol
- ECOG PS ≤1
- Adequate bone marrow reserve and organ function



Primary endpoint

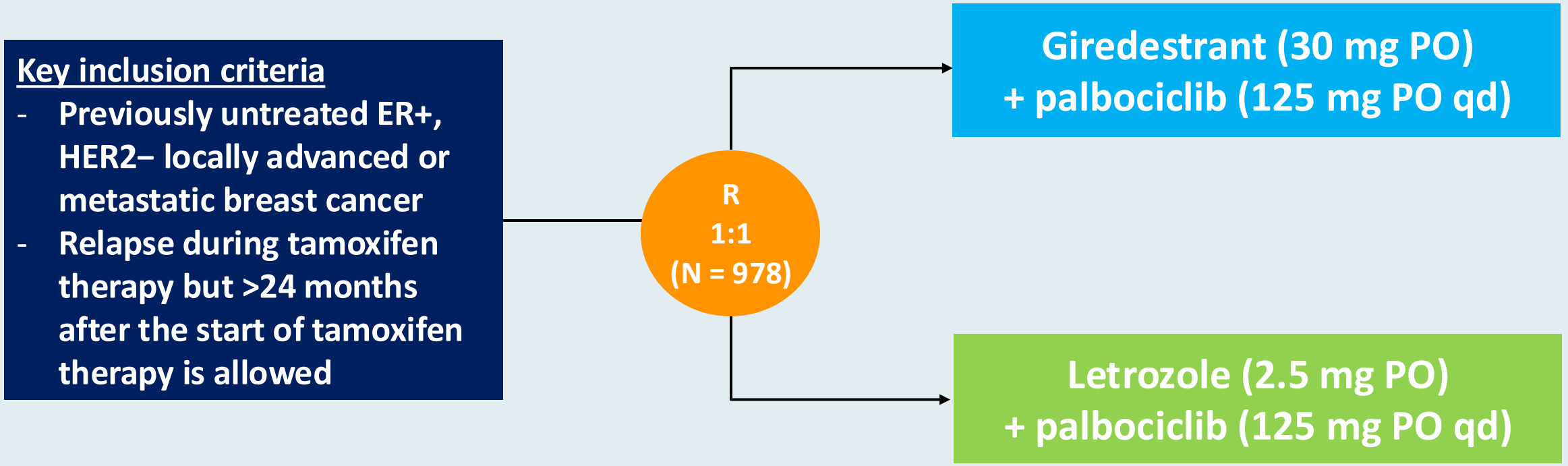
- IBCFS

Secondary endpoints

- IDFS
- DRFS
- OS
- Patient-reported outcomes
- Safety and tolerability
- Pharmacokinetics

Hamilton E et al. *Future Oncol* 2025;21(7):795-806.

persevERA Breast Cancer Study Design



Turner NC et al. ASCO 2021;Abstract TPS1103.

Questions from General Medical Oncologists

- What is your opinion on the future role of oral SERDs in earlier-stage breast cancer settings (eg, adjuvant or neoadjuvant use)?
- What strategies can I use to enhance adherence in patients on oral SERDs, especially in those with financial, cognitive, or logistical barriers?
- I got burned by using alpelisib due to it was causing DKA in my patient, with other -lisibs now, is there any reason for trying to give alpelisib again?
- Re PATINA trial, would you add palbociclib to the HP/AI regimen if a patient has been stable for years?

Agenda

Introduction: ER-Positive Metastatic Breast Cancer — Bringing Research Data into Practice

Module 1: Key Issues from GMO Survey

Module 2: Faculty Cases and GMO Questions

Dr Kaklamani – Case Presentation

- A 42-year-old premenopausal woman was diagnosed with invasive ductal carcinoma (IDC) of the left breast.
- ER: 80%; PR: 60%; HER2: 1+.
- She underwent breast-conserving surgery and was found to have a 2.5-cm IDC, grade 2, with 1+ axillary lymph nodes.
- She was given adjuvant chemotherapy with ACT (doxorubicin, cyclophosphamide, paclitaxel) and then was put on ovarian function suppression (OFS) and anastrozole for 5 years.

Dr Kaklamani – Case Presentation (cont'd)

- At 15 mo after discontinuing adjuvant endocrine therapy, she was found to have bone metastases.
- Biopsy showed IDC, with ER: 60%; PR: 60%; HER2: 1+.
- She was started on OFS with letrozole and ribociclib.
- After 26 months of therapy, she was found to have progression of disease with liver metastases.
- A liquid biopsy showed an *ESR1* mutation and no other actionable mutations.
- She was put on elacestrant and continued on it for 12 mo until progression.
- During treatment she complained of nausea grade 1 and was given ondansetron which she took PRN.

Dr Jhaveri – Case Presentation

- 57 year old postmenopausal woman presented with de novo ER+/HER2 – (IHC 1+) metastatic breast cancer to the bones (biopsy proven) in late 2019.
- She was started on Letrozole plus Palbociclib and after nearly 5 years progressed in the bones with 1 new liver metastases. LFTs were normal and she is asymptomatic. Guardant360® panel showed *ESR1*D538G mutation. Genetics testing was negative.
- What is the next best treatment option?
  A. Trastuzumab Deruxtecan
  B. Capecitabine
  C. Everolimus + Fulvestrant
  D. Fulvestrant
  E. Elacestrant

Dr Jhaveri – Case Presentation continued

- She started on Elacestrant in October of 2024 and recent imaging in June 2025 showed stable disease. Tolerating elacestrant very well with some intermittent grade 1 nausea and fatigue

Questions from General Medical Oncologists

- Optimal assay for ESR1 mutation?
- Tissue versus liquid genomic analysis?
- How often should liquid biopsies be done in the management of mBC?
- Should SERDs be considered in hormone-low tumors? What about triple-positive cases?
- Data for SERD in non-ESR patient?

Questions from General Medical Oncologists

- What advantages do oral SERDs offer over intramuscular fulvestrant?
- How do oral SERDs like elacestrant, imlunestrant, camizestrant, and giredestrant differ in their estrogen receptor degradation potency and selectivity?
- Which oral SERD is best tolerated and used in combination with other agents?
- What strategies should be used to mitigate/prevent nausea and vomiting that I have seen with my patients starting elacestrant?
- Unique side effects of oral SERDs and management strategies?

Dr Jhaveri – Case Presentation

- 53 year old postmenopausal woman presented with Stage 2 breast cancer. She is s/p lumpectomy and SLND and tumor size was 4.2 cm, grade 2, 0/3 LN ER80% PR 40% HER2 – (IHC 1+) and Oncotype RS of 27. She completed TC chemotherapy and adjuvant radiation and started letrozole. After 1 year of completing letrozole she developed back pain and workup led to a diagnosis of metastatic breast cancer to the bones and liver (biopsy proven; 3 lesions, largest 2.3 cm X 2.1 cm)) in June 2021. Liver biopsy confirmed ER 65% PR 30% and HER 2 (IHC 1+). Tissue NGS showed no actionable alterations. PMH significant for hypothyroidism controlled on levothyroxine.
- She was started on anastrazole plus palbociclib and tolerated it well without any need for dose modifications. In July of 2023, she was diagnosed with metastatic disease to the liver and bones (multiple mets in spine and ribs). Guardant360 panel was done and showed *ESR1Y537S and ESR1 380Q mutation*. Genetics testing was negative.
- What is the next best treatment option?
    A. Fulvestrant plus ribociclib
    B. Fulvestrant + Abemaciclib
    C. Capecitabine
    D. Everolimus + Fulvestrant
    E. Fulvestrant
    F. Elacestrant
    G. EMBER-3 trial

Dr Jhaveri – Case Presentation continued

- She was enrolled to EMBER-3 clinical trial and was randomized to Arm C- Imlunestrant + Abemaciclib
- She developed grade 1 diarrhea and fatigue but didn’t require dose reductions. Diarrhea was managed with Imodium and dietary modifications
- Remained on trial until July 2024; came off for progression in the bones and liver
- No new alterations seen on Guardant
- Started on capecitabine with progression in liver in Dec 2024
- Remains on Trastuzumab deruxtecan. Has some fatigue but tolerating it well with responding disease

Dr Kaklamani – Case Presentation

- A 56-year-old postmenopausal woman was diagnosed with IDC of the right breast.
- ER: 100%; PR: 80%; HER2: 2+ FISH-.
- She underwent breast-conserving surgery and was found to have 3.2-cm IDC, grade 3, without any axillary lymph node involvement.
- She had a 21-gene Recurrence Score® of 27 and was given adjuvant chemotherapy with docetaxel and cyclophosphamide (TC) x 4 and then was put on anastrozole.

Dr Kaklamani – Case Presentation (cont'd)

- At 4 years after initiation of adjuvant therapy, she was found to have bone and lung metastases.
- A biopsy showed IDC, with ER: 80%; PR: 40%; HER2: 1+.
- She was started on fulvestrant and palbociclib.
- After 18 months of therapy, she was found to have progression of disease with liver metastases.
- A liquid biopsy showed an *ESR1* mutation and no other actionable mutations.
- She enrolled on the EMBER-3 clinical trial and was randomly assigned to imlunestrant and abemaciclib
- During therapy she developed grade 2 diarrhea which required treatment with loperamide but no dose reduction.
- She continued on therapy for 15 months until disease progression.

Questions from General Medical Oncologists

- **Sequencing strategy if both ESR1 mutation and AKT1/PIK3CA/PTEN mutation are present?**
- **Why is imlunestrant still not available when the *NEJM* article was out in Dec 2024 showing impressive activity in combination with abemaciclib?**
- **Any situations where you would use imlunestrant/abemaciclib in first line treatment?**
- **Does it matter what the first CDK4/6i was in considering imlunestrant/ abemaciclib second line?**
- **Male breast cancer patient treatment?**

Questions from General Medical Oncologists

- SERDs with visceral crisis or high disease burden? Do you feel comfortable initiating endocrine therapy?
- Can you share a case where oral SERD therapy significantly altered the course of a patient's treatment plan or prognosis?
- How to pick between the PIK3CA/AKT meds?
- How to monitor the development of resistance to oral SERDs?

Questions from General Medical Oncologists

- How often to watch A1c and lipids on PIK3CA drugs?
- Based on recent ASCO presentation is vepdegestrant still being deemed HOPEFUL to replace oral SERD?
- PROTAC may not be as effective as imlunestrant, am I wrong here?
- This may be a shot in the dark but a single drug that would combine both SERM and SERD activity?

Dr Kaklamani – Case Presentation

- A 65-year-old postmenopausal woman was diagnosed with IDC of the right breast.
- ER: 80%; PR: 80%; HER2: 1+.
- At the time of diagnosis, she complained of lower back pain.
- Imaging revealed a lesion in her lumbar spine.
- She had a biopsy showing IDC, with ER: 60%; PR: 20%; HER2: 2+ consistent with her primary disease.

Dr Kaklamani – Case Presentation (cont'd)

- The patient was started on the nonsteroidal aromatase inhibitor letrozole and the CDK4/6 inhibitor abemaciclib.
- After 6 months of therapy, she enrolled on SERENA-6 and started having serial ctDNA testing.
- After an additional 9 months her ctDNA revealed an *ESR1* mutation. At the time her staging scans showed stable disease.
- She was randomly assigned to switch to camizestrant and continue abemaciclib.
- During therapy she developed photopsia grade 1 which did not require any dose reductions and continued on therapy for 15 months until radiologic disease progression.

Dr Jhaveri – Case Presentation

- 62 years old was diagnosed with stage IIA breast cancer s/p lumpectomy that revealed a 2.1 cm grade 2 node-negative tumor, ER 90% PR 90% and HER2 IHC 0, Onco*type* DX® RS 15, completed radiation and 5 years of adjuvant letrozole in 2021.
- In late summer of 2022 was diagnosed with metastatic disease to the bones, biopsy proven, ER/PR 80% HER2 IHC 1+. She started treatment with anastrozole with ribociclib in September of 2022 and tolerated it well without any need for dose modifications.
- After 8 months while on 1L therapy, she was enrolled to the SERENA-6 trial and started serial ctDNA monitoring. In April of ‘25, ESR1 mutation was detected. She remains asymptomatic and is continuing on the therapeutic portion of the trial.

Questions from General Medical Oncologists

- **Use of SERENA-6?**
- **Re the SERENA-6 trial, how do we know that overall survival will be longer with this approach rather than just waiting to switch to camizestrant when there is actual progression? Did the trial go over that or are we waiting for PFS2 data?**
- **Any CNS activity with SERDs?**
- **Beyond ESR1 mutation status, what patient-specific clinical factors (eg, prior CDK4/6i duration, visceral crisis, burden of disease) should guide the choice between an oral SERD or an ADC/chemotherapy in the post-CDK4/6i setting?**

Questions from General Medical Oncologists

- How do you choose between the ADCs that attack TROP2?
- Should you go from ADC to ADC or something in between?
- T-DXd and Dato-DXd sequencing
- Sequencing in HR+, HER2 low metastatic disease
- When to use T-DXd in HR+/HER2 ultralow
- How much pulmonary toxicity are investigators seeing in the real world with T-DXd?

RTP RESEARCH TO PRACTICE

Practical Perspectives: Experts Review
Actual Cases of Patients with Biliary Tract Cancers

A CME/MOC-Accredited Live Webinar

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

Faculty

Haley Ellis, MD
James J Harding, MD

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

Thank you for joining us!

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

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

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RESEARCH TO PRACTICE