

FDA is committed to ensuring digital accessibility for people with disabilities. We are continually improving the user experience for everyone and applying the relevant accessibility standards. At the time of initial posting on **April 30, 2026**, the attached **Event Materials** may not be fully accessible to users using assistive technology. A fully accessible version of the **Event Materials** is in preparation and will be posted as soon as it is ready. We regret any inconvenience that this may cause our readers.

Please let us know if you encounter accessibility barriers by contacting **Division of Advisory Committee and Consultant Management (DACCM)** at:

- ODAC@fda.hhs.gov



Camizestrant + CDK4/6i for
Treatment of HR-positive,
HER2-negative Advanced
Breast Cancer Upon Emergence
of *ESR1* Mutation During
First-Line Endocrine-Based Therapy

United States Food and Drug Administration
Oncologic Drugs Advisory Committee

April 30, 2026



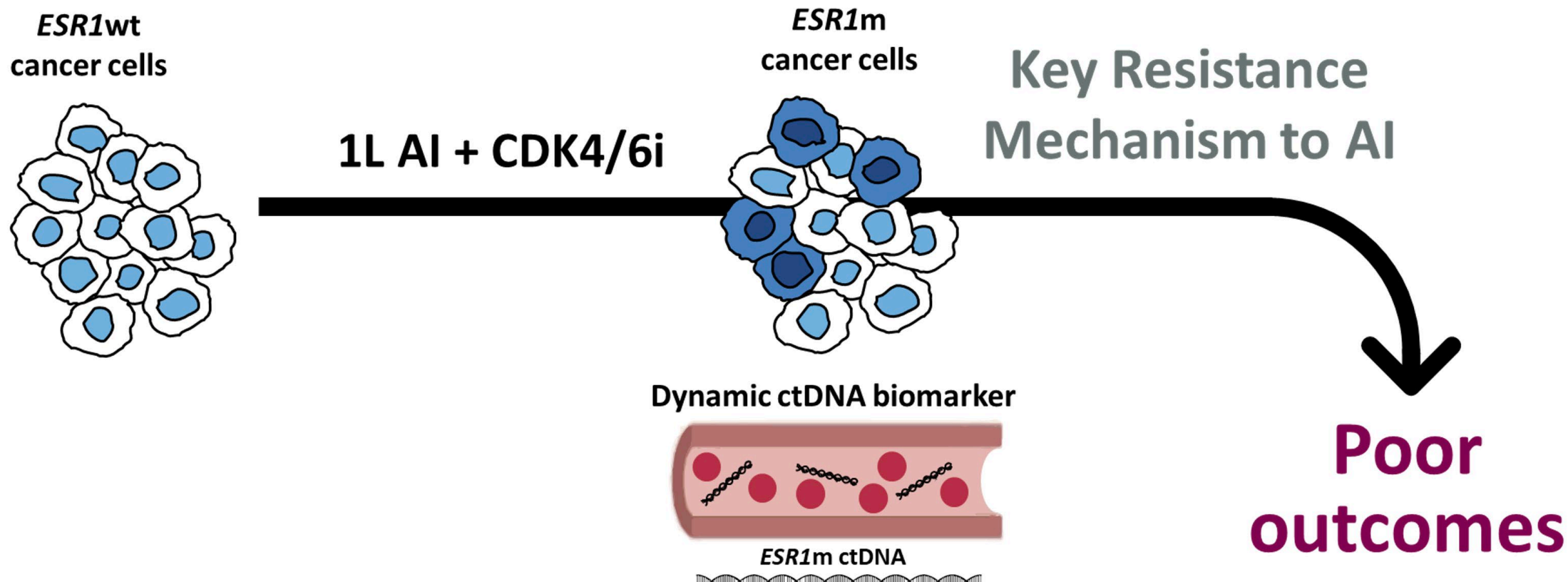
Introduction

Ingrid Mayer, MD, MSCI

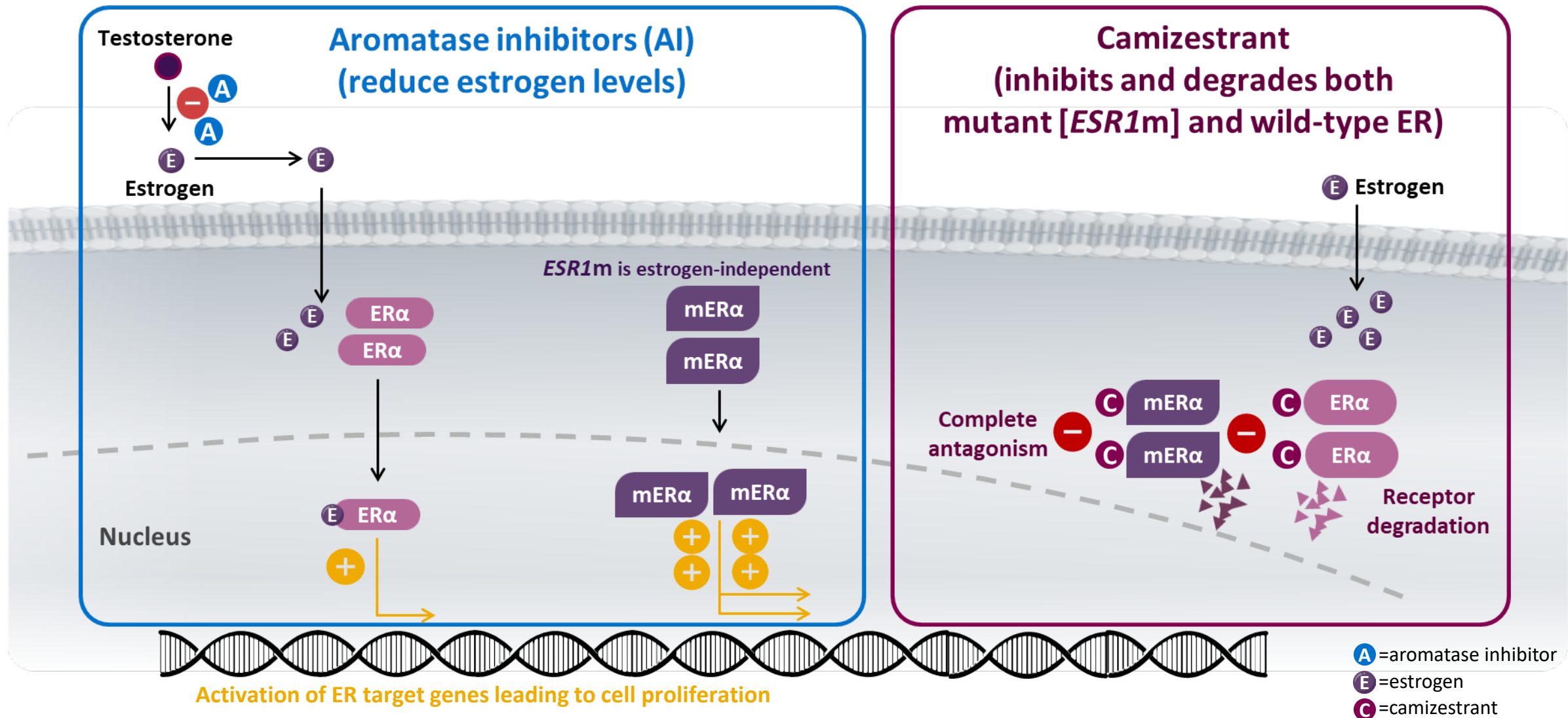
VP, Global Clinical Strategy Head, Breast/GYN Cancers
Late Development Oncology, Research & Development
AstraZeneca



ESR1 Mutation Clonal Evolution Drives Clinical Progression During First-Line AI + CDK4/6i Therapy for HR+ aBC



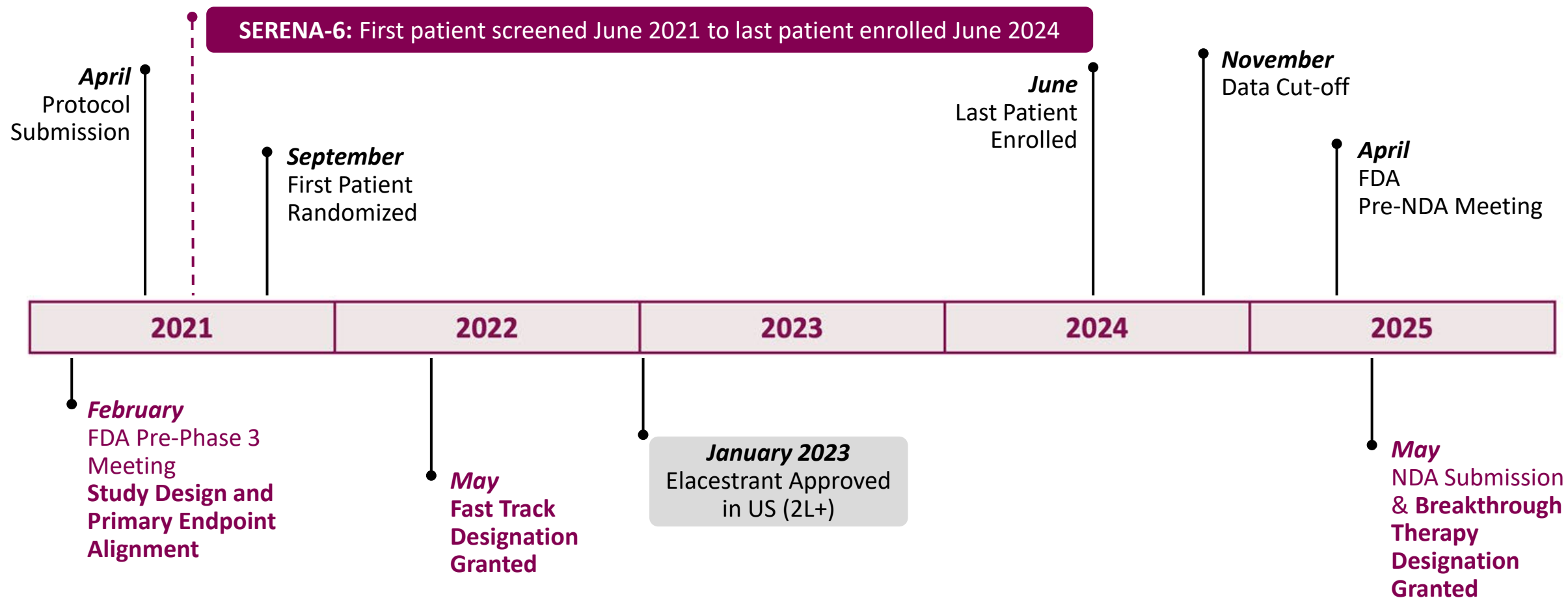
Camizestrant Is a Potent Oral SERD and Complete ER Antagonist



Proposed Indication

Camizestrant in combination with a CDK4/6 inhibitor (palbociclib, ribociclib, or abemaciclib) for the treatment of adult patients with HR-positive, HER2-negative, locally advanced or metastatic breast cancer, **upon emergence of *ESR1* mutation during first-line endocrine-based therapy**, based on an FDA approved test.

SERENA-6 Key Regulatory Milestones: Breakthrough Therapy Designation in May 2025



Current Treatment Paradigm for *ESR1*m HR+ aBC



DELAY 1L PROGRESSION (2017+)

Approved 1L ET-Based Therapy	HR	Δ PFS (months)
ET Replacement ¹ (AI → fulvestrant)	0.8	2-3
Add-On ²⁻⁵ (AI + CDK4/6i)	0.54-0.57	9-13

REACT AFTER 1L PROGRESSION (2023+)

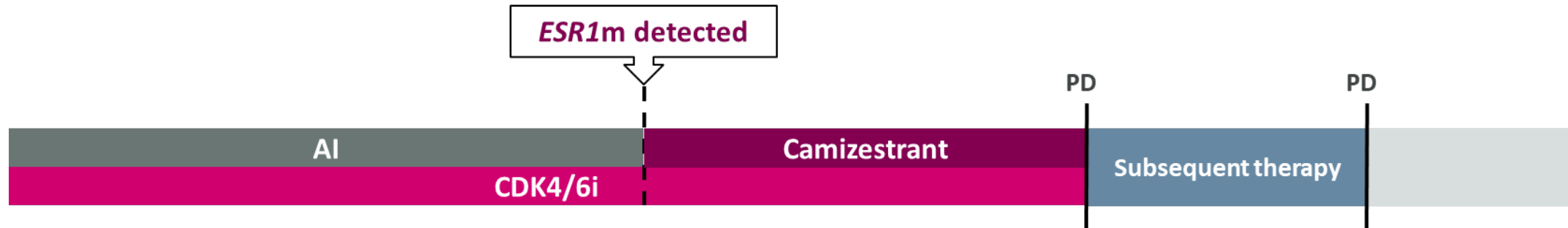
Approved 2L ET-Based Therapy	HR	Δ PFS (months)
ET Replacement ⁶⁻⁹ (elacestrant, imlunestrant)	0.55-0.72	<2
Add-On ¹⁰⁻¹² (fulv/exe + targeted Tx)	0.43-0.62	3-5

PD=clinical/radiological disease progression.

1. Robertson JFR, et al. *Lancet*. 2016;388:2997-3005; 2. Finn RS, et al. *N Engl J Med*. 2016;375:1925-1936; 3. Hortobagyi GN, et al. *Ann Oncol*. 2018;29:1541-1547; 4. Tripathy D, et al. *Lancet Oncol*. 2018;19(7):904-915; 5. Johnston S, et al. *NPJ Breast Cancer*. 2019;5:5; 6. Bidard F-C, et al. *J Clin Oncol*. 2022;40(28):3246-3256; 7. Jhaveri KL, et al. *N Engl J Med*. 2025;392(12):1189-1202; 8. Jhaveri KL, et al. *Ann Oncol*. 2026;37(4):532-543; 9. [Inluriyo EMA Summary of Product Characteristics](#); 10. Oliveira M, et al. *ESMO Open*. 2024; Abstract 1870; 11. De Laurentiis M, et al. *Clin Cancer Res*. 2026;32(4 suppl). Abstract RF7-02; 12. Baselga J, et al. *N Engl J Med*. 2012;366:520-529.

SERENA-6: A New Treatment Paradigm for *ESR1*m HR+ aBC

Hypothesis: Replacing AI with camizestrant at emergence of *ESR1*m suppresses resistant clones, maximizing the benefit of first-line ET + CDK4/6i by delaying disease progression



INTERCEPT 1L RESISTANCE

AI → Camizestrant	HR	Δ PFS (months)
ET Replacement ¹ (<i>ESR1</i> m)	0.44	7

Camizestrant at *ESR1*m Emergence in 1L: Positive Benefit/Risk

Benefit for Camizestrant + CDK4/6i Replacement Strategy	
PFS^a	Delays disease progression (HR=0.44; primary endpoint) Allows patients to get subsequent endocrine-based therapy
PFS2^b	Positive benefit is preserved through subsequent line of therapy (HR=0.63)
OS^b	No detriment (HR=0.87)
Chemotherapy/ADC-free survival^b	Prolongs chemotherapy/ADC-free survival (HR=0.64) and time on ET
Camizestrant + CDK4/6i Is Patient-Centric	
PRO	Maintains QoL
Risk for Camizestrant + CDK4/6i	
Adverse event rate	Well-tolerated
Discontinuation rate	1%
Impact on activities of daily living	None or minimal impact

a. Data cut-off 1 (DCO1).

b. DCO3.

What You Will Hear Today



Disease Background & Unmet Need

Massimo Cristofanilli, MD, FACP

Scientific Director of the Englander Institute of Precision Medicine
Weill-Cornell Medicine and NY Presbyterian



SERENA-6 Efficacy and PROs

Cynthia Huang-Bartlett, MD

Global Clinical Head – Camizestrant
AstraZeneca



SERENA-6 Clinical Safety

Andrew Walding, MSc

Global Safety Head – Camizestrant
AstraZeneca



Clinical Perspective

Kevin Kalinsky, MD, MS, FASCO

Emory University School of Medicine
Director of the Glenn Family Breast Center at Winship Cancer Center



Concluding Remarks

Ingrid Mayer, MD, MSCI

VP, Global Clinical Strategy Head, Breast/GYN Cancers Late Development Oncology, Research & Development
AstraZeneca

External Experts Available to Address Your Questions



Patient-Reported Outcomes

David Cella, PhD

Associate Director for Cancer Prevention, Control, and Survivorship
Robert H. Lurie Comprehensive Cancer Center
Northwestern University



Ophthalmology

Ranya Habash, MD

Board Certified Ophthalmologist
Bascom Palmer Eye Institute
University of Miami



Cardiology

Anju Nohria, MD, MSc

Cardio-Oncology Site-Director
New York University Langone Medical Center

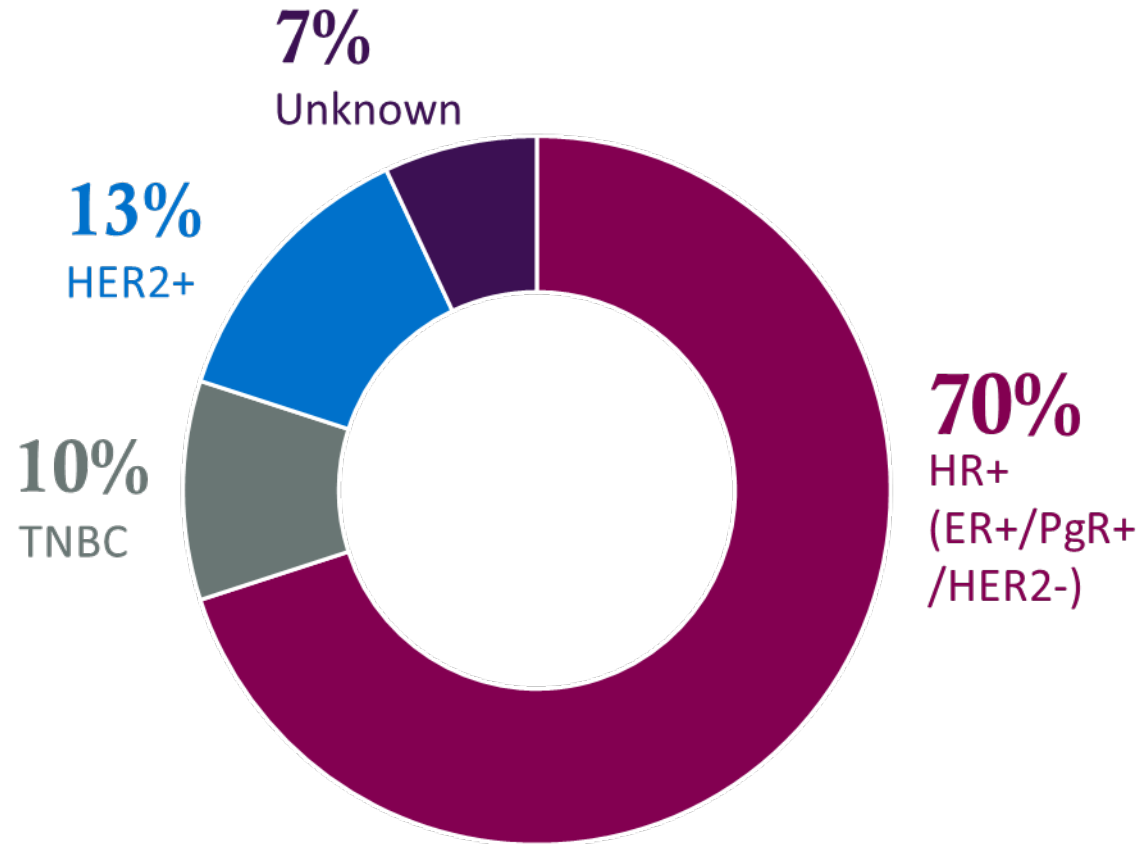
Disease Background & Unmet Need

Massimo Cristofanilli, MD, FACP

Scientific Director of the Englander Institute of Precision Medicine
Weill-Cornell Medicine and NY Presbyterian



Hormone-Receptor Positive Advanced Breast Cancer Is Incurable



In the US, >150,000 people living with metastatic breast cancer (mBC)¹

- >105,000 living with HR+ mBC
- ~29,000 die from HR+ mBC annually²

Goal of systemic treatment:

- Extend disease control
- Improve symptoms
- Maintain quality of life

ER=estrogen receptor; HER2=human epidermal growth factor receptor-2; HR=hormone receptor; PgR=progesterone receptor; TNBC=triple-negative breast cancer.

Advanced breast cancer includes locally advanced breast cancer treated without curative intent and metastatic breast cancer.

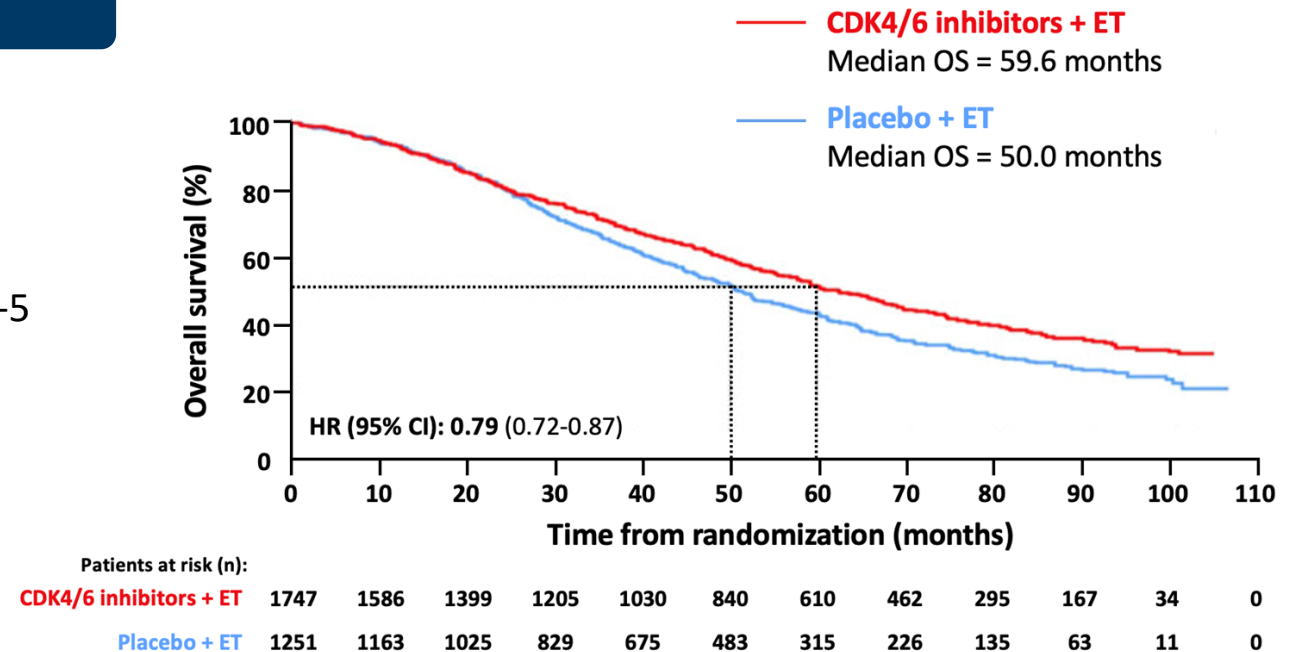
[American Cancer Society Cancer, Breast Cancer Facts & Figures 2024-2025](#). 1. Gallicchio L, et al. *J Natl Cancer Inst*. 2022;114(11):1476-1483. 2. [National Cancer Institute SEER statistics](#).

First-line Treatment With ET + CDK4/6i Is Highly Effective for ER-Signaling–Dependent Disease and Is Well-Tolerated

1L SoC AI + CDK4/6i
mPFS: ~25-34 months

- Longest PFS in the HR+ aBC treatment journey¹⁻⁴
- Prolonged QoL with good tolerability¹⁻⁵
- Dependency on ER-signaling is greatest in this setting⁶

1L ET + CDK4/6i prolongs OS⁷

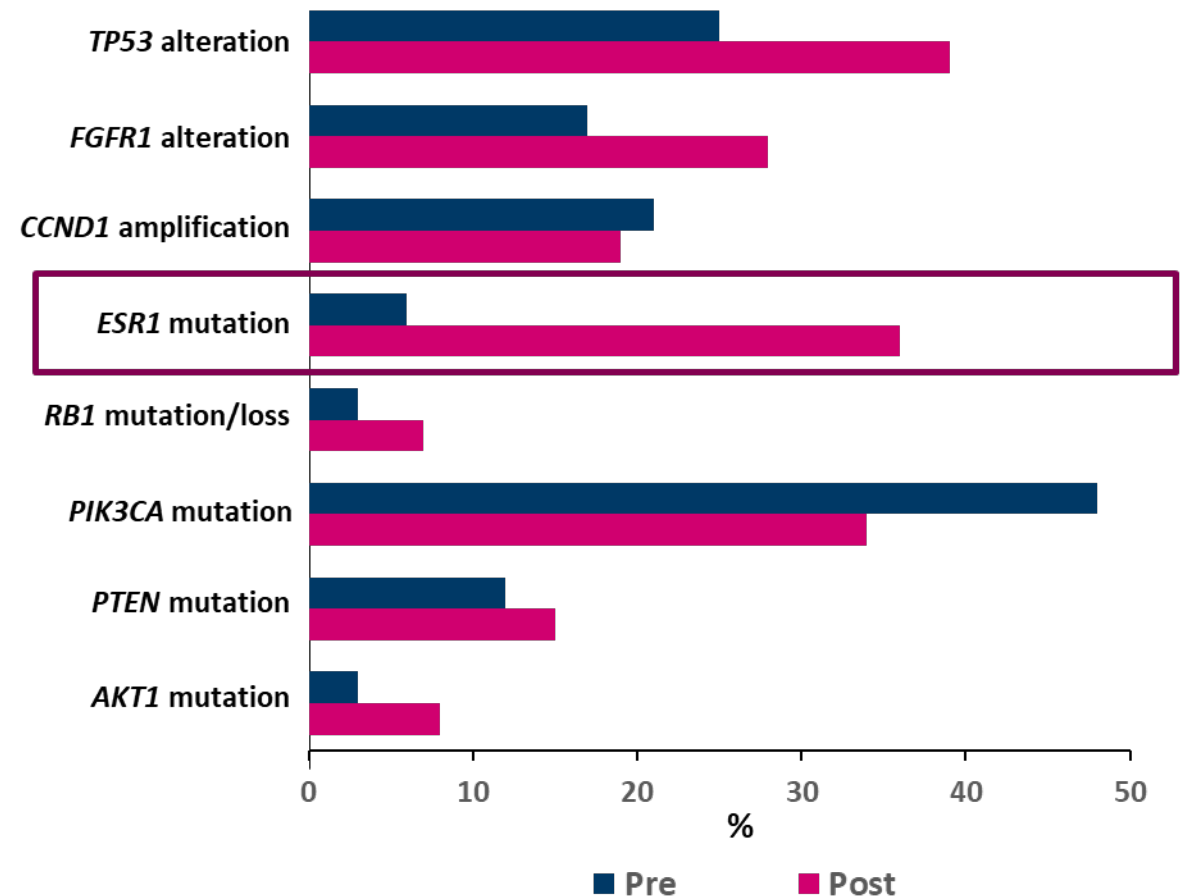


After Progression on AI + CDK4/6i, Disease Becomes Harder to Treat Due to Endocrine Resistance

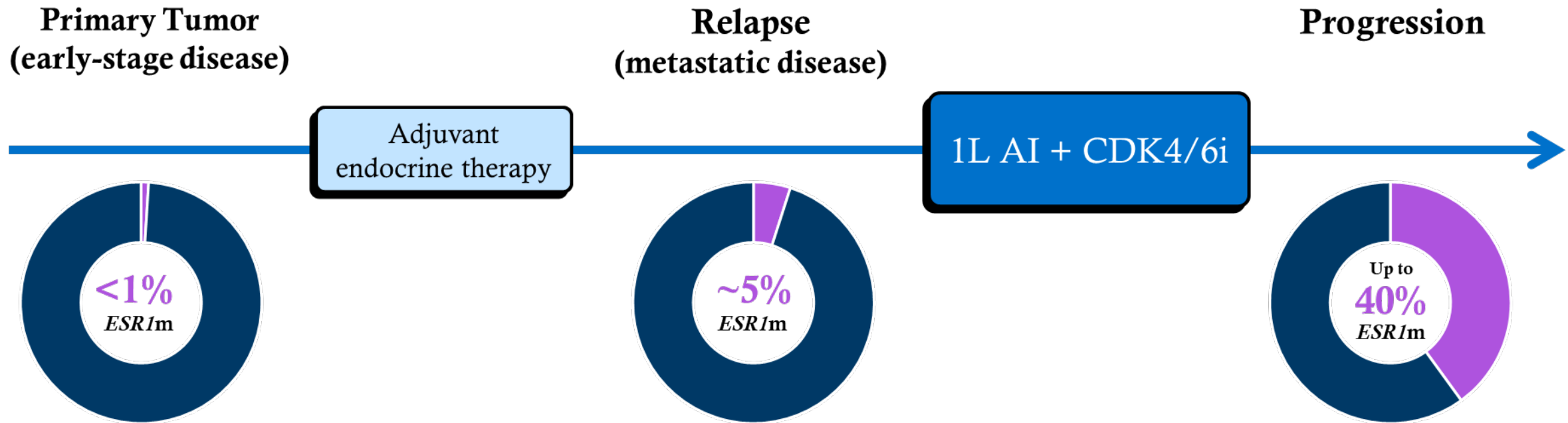
Progression is associated with

- Increased disease burden
- Worsening symptoms
- Deterioration in QoL
- Greater tumor heterogeneity

Prevalence (%) of genomic alterations
pre- and post-treatment with 1L AI + CDK4/6i
in a cohort of 508 patients¹

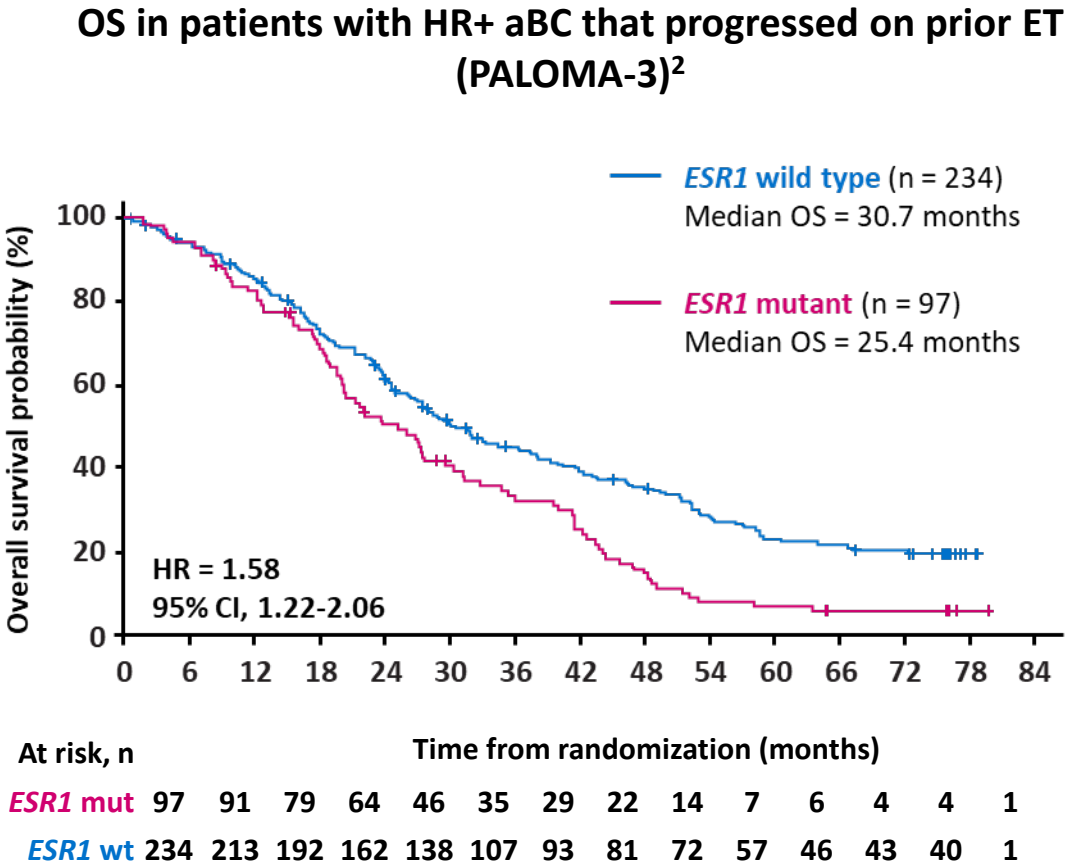
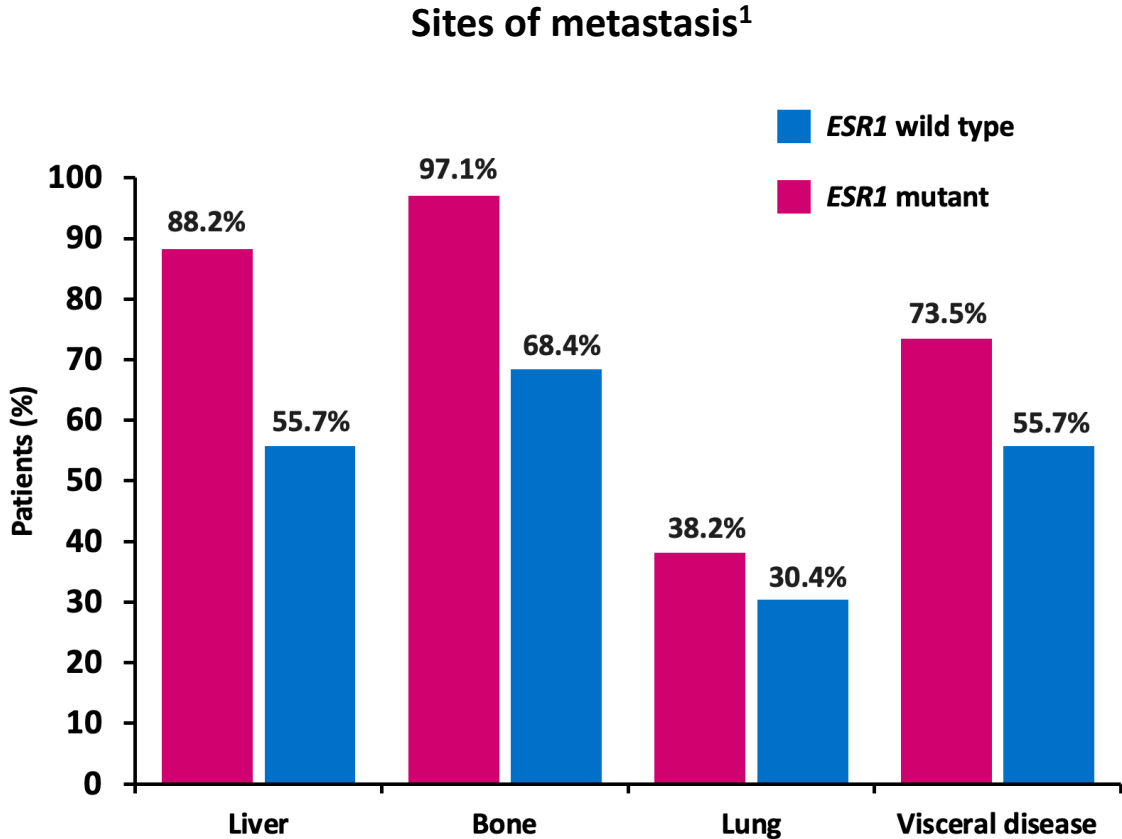


ESR1 Mutations Emerge Under Selective Pressure of Aromatase Inhibition



ESR1m Is a Key Mechanism of Resistance to Traditional Endocrine Therapy in HR+ aBC

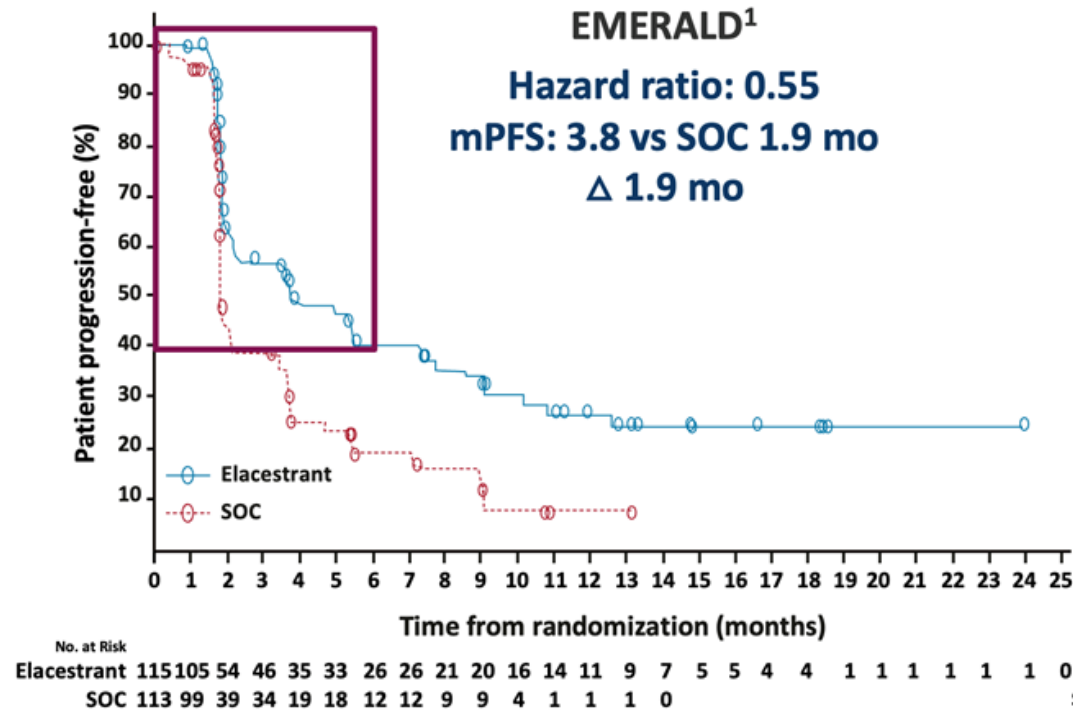
ESR1m is associated with more aggressive disease biology and worse clinical outcomes



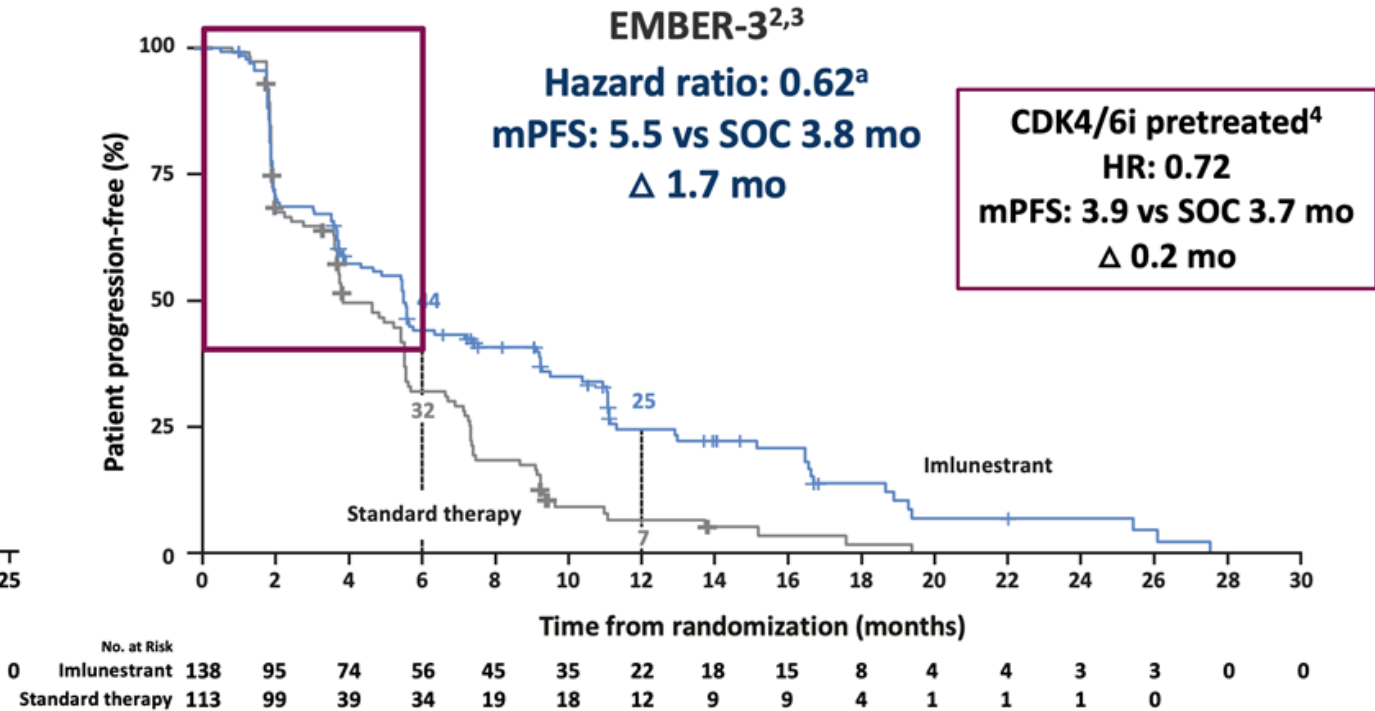
1. Kuang Y, et al. *NPJ Breast Cancer*. 2018;4:22; 2. Reprinted from *Clin Cancer Res*, 2022, 28(16), 3433-3442, Cristofanilli M, et al, Overall survival with palbociclib and fulvestrant in women with HR/HER2⁻ aBC: updated exploratory analyses of PALOMA-3, a double-blind, phase III randomized study, with permission from AACR.

Targeting *ESR1m* After Progression on AI + CDK4/6i Has Limited Benefit

Elacestrant FDA approved in 2023



Imlunestrant FDA approved in 2025



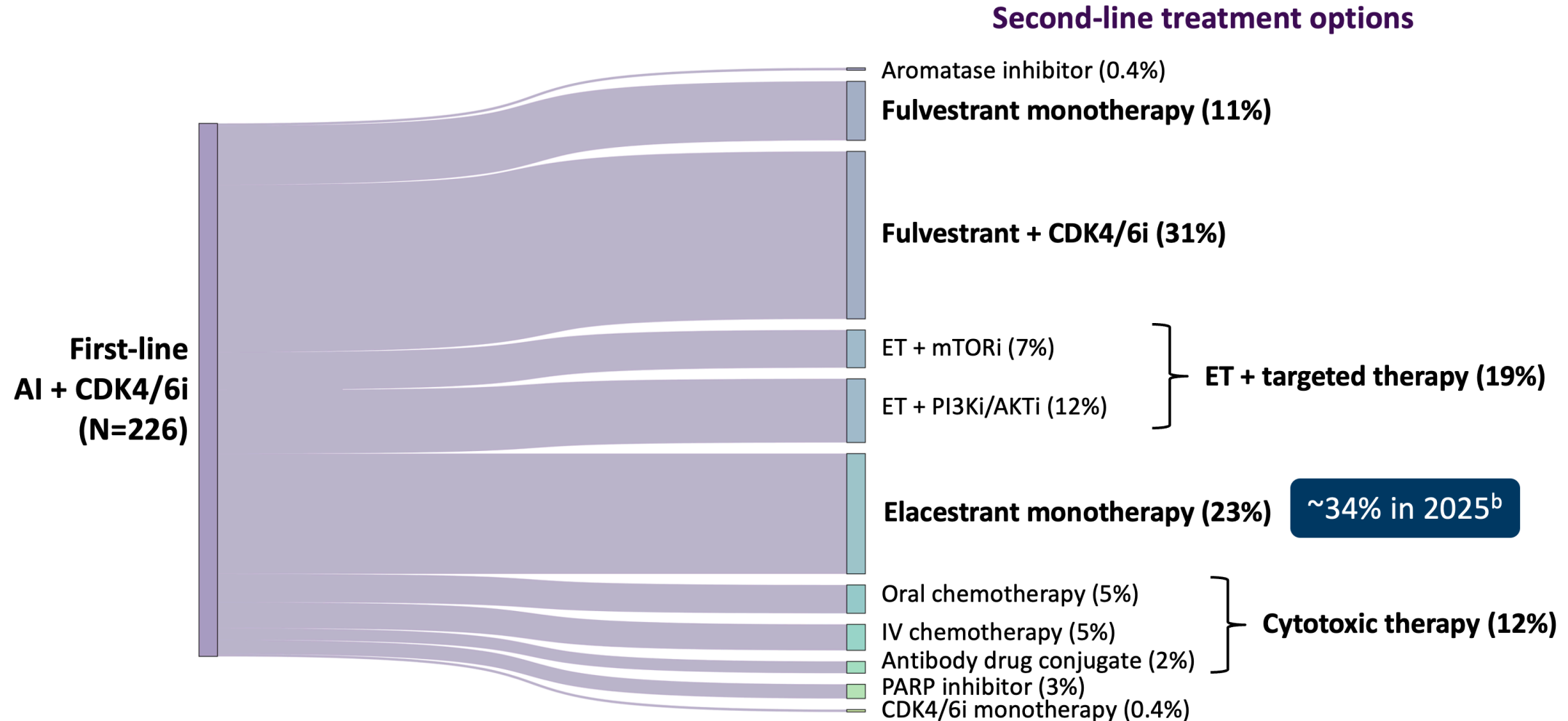
- Despite activity against *ESR1m*, median PFS remains under 6 months after progression on ET + CDK4/6i
- ~60% of patients with an *ESR1m* progress within 6 months

a. 30% of patients in this cohort were CDK4/6i naive.

1. Bidard F-C, et al. Elacestrant (oral selective estrogen receptor degrader) versus standard endocrine therapy for estrogen receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer: results from the randomized phase III EMERALD trial. *J Clin Oncol* (an American Society of Clinical Oncology journal). 2022;40(28):3246-3256, https://ascopubs.org/doi/10.1200/JCO.22.00338?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed; 2. Reprinted from *N Engl J Med*. Jhaveri KL, et al. Imlunestrant with or without abemaciclib in advanced breast cancer: updated efficacy results from the phase III EMBER-3 trial, 392(12), 1189-1202, Copyright 2025 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society; 3. Jhaveri KL, et al. *Ann Oncol*. 2026;37(4):532-543; 4. Inluriyo EMA Summary of Product Characteristics.

Complexity of 2L Treatment Options in Patients With *ESR1m* After AI + CDK4/6i

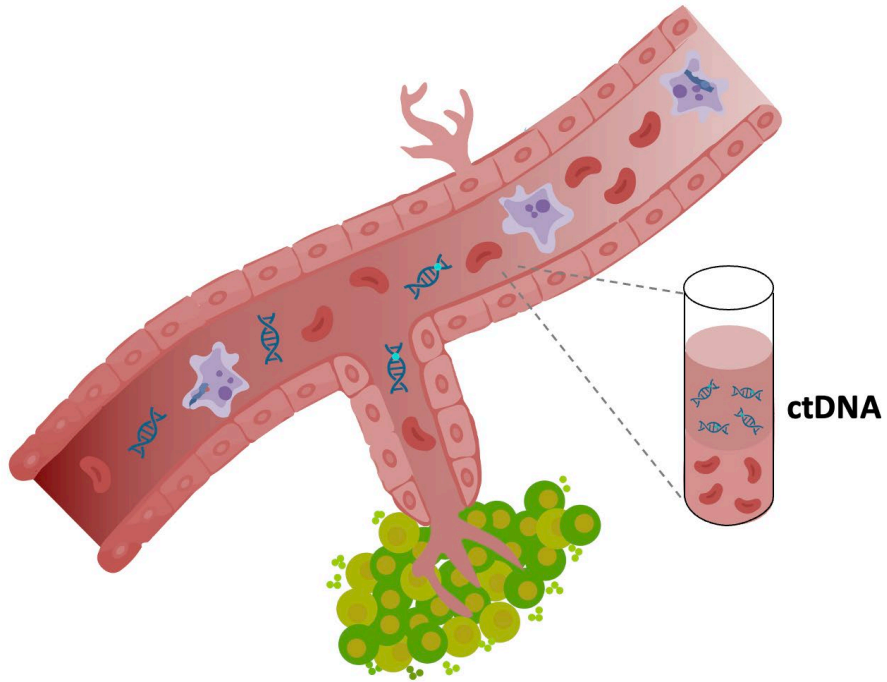
Real-World US Treatment Patterns^a



a. Flatiron Health Research Database; patients diagnosed with HR+/HER2- *ESR1m* mBC from 2015 to 2025 with positive *ESR1m* test at initiation of second-line therapy.

b. As of 2025 RWE, elacestrant usage was ~34% (AstraZeneca data on file).

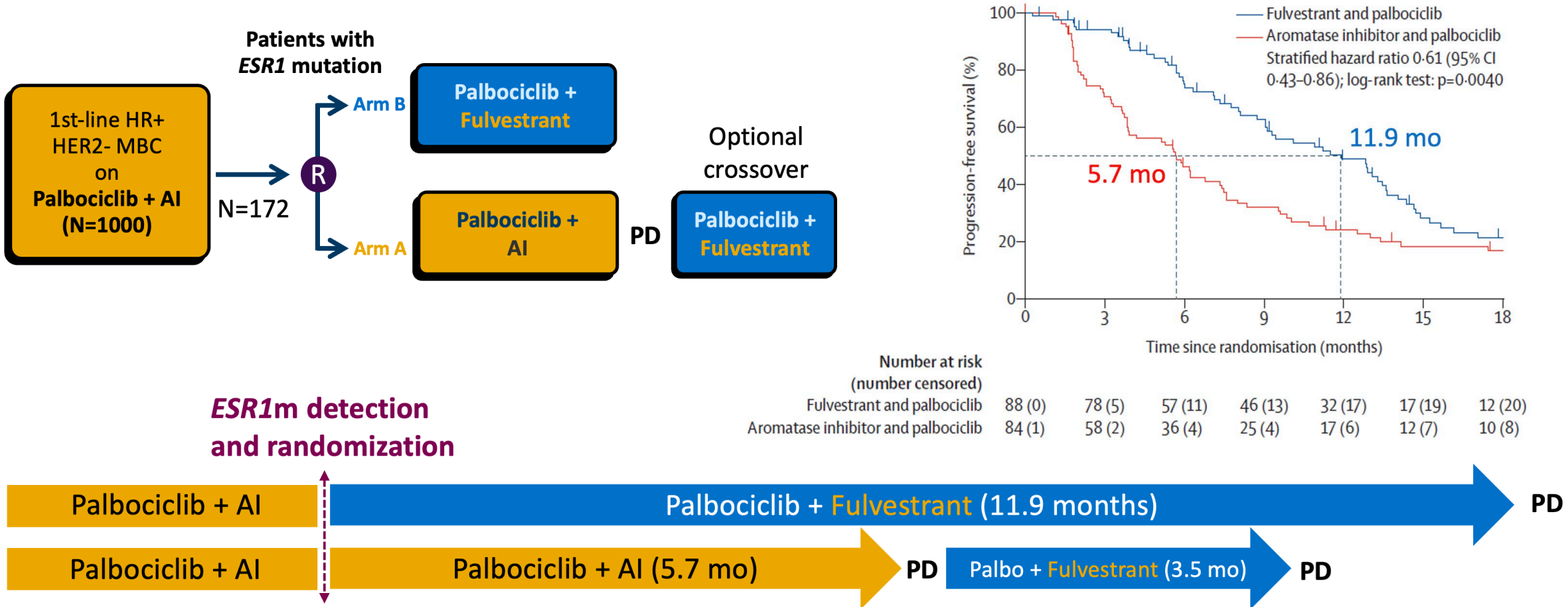
ESR1m Can Be Detected in ctDNA, Which Is Routinely Used in Clinical Practice



Blood-based ctDNA profiling

- Does not require invasive tissue biopsy
- Representative of predominant cancer clone(s)
- Assesses tumor clonal evolution → aids treatment decisions
- **Ideal test to detect *ESR1m*¹**

PADA-1 Demonstrated Significant Improvement in PFS



Reprinted from *The Lancet Oncol*, 23(11), Bidard FC, et al, Switch to fulvestrant and palbociclib versus no switch in advanced breast cancer with rising *ESR1* mutation during aromatase inhibitor and palbociclib therapy (PADA-1): a randomised, open-label, multicentre, phase 3 trial, 1367-1377, Copyright 2022, with permission from Elsevier.

Unmet Need Summary

Target Resistance and Keep Patients on 1L ET + CDK4/6i Longer

- **Resistance leading to disease progression in 1L invariably occurs, and disease becomes harder to treat**
 - Increased tumor burden and genomic complexity
 - Worsening symptoms and QoL
- ***ESR1m* is a key acquired mechanism of resistance to aromatase inhibitors**
 - Associated with poor outcomes
 - Endocrine sensitivity decreases and patients' needs are heterogeneous
 - Real-world choices of 2L therapy yield modest benefit
 - ~34% of US patient population with *ESR1m* HR+ aBC received an oral SERD in 2025
- ***ESR1m* ctDNA monitoring during AI + CDK4/6i therapy offers opportunity to replace the ineffective AI ahead of clinical/radiographic disease progression**
 - Allows patients to remain on well-tolerated 1L ET + CDK4/6i longer



SERENA-6

Efficacy and PROs

Cynthia Huang-Bartlett, MD

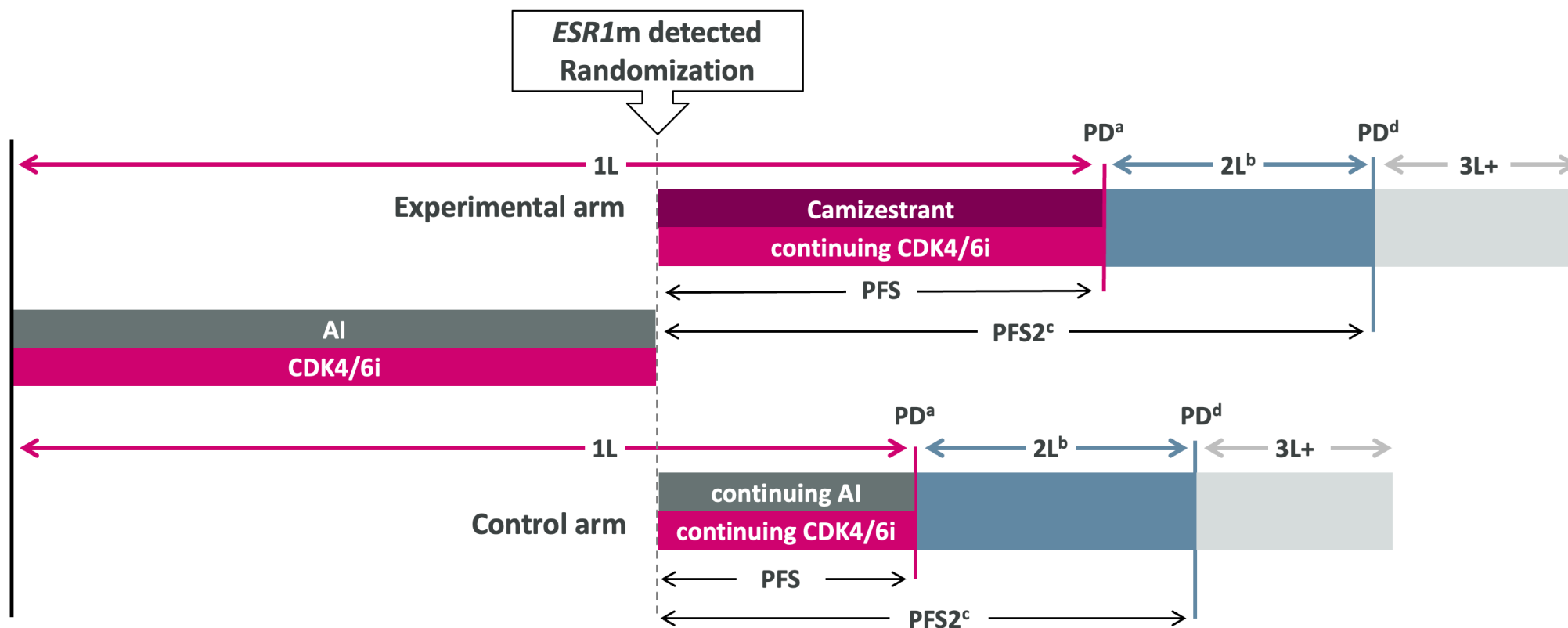
Global Clinical Head – Camizestrant

AstraZeneca



SERENA-6 Hypothesis

Replacing AI with camizestrant at emergence of *ESR1m* suppresses resistant clones, maximizing the benefit of first-line ET + CDK4/6i by delaying disease progression



a. PD per RECIST 1.1 by investigator assessment.

b. 2L treatment options per SoC and physician's preference (include endocrine mono- or combination with targeted therapy, or chemotherapy or ADCs).

c. PFS2 defined per EMA guideline on the evaluation of anticancer medicinal products in man.

d. Clinical or objective PD; 170 patients had a second progression event (PFS2) at DCO3.

SERENA-6: Two-Step Design

STEP 1: *ESR1m* detection phase

STEP 2: Randomized treatment phase

HR+ /HER2-
aBC on 1L
AI + CDK4/6i
≥6 months

ctDNA blood test
every 2-3 months
with routine tumor scans



ESR1m assessed at global
central lab

ESR1m
detected, no
radiographic
or clinical
progression



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

315 Randomized 1:1

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

Primary Endpoint
PFS by investigator
assessment
(RECIST v1.1)

Secondary Endpoints

- PFS^a
- OS^a
- Safety
- Patient-reported outcomes

Stratification factors

- Visceral vs non-visceral disease
- *ESR1m* detection at first test vs at subsequent test
- Time from initiation of AI + CDK4/6i to randomization (<18 vs ≥18 months)
- Palbociclib vs ribociclib vs abemaciclib

SERENA-6 Statistical Considerations

Planned enrollment: 300 patients

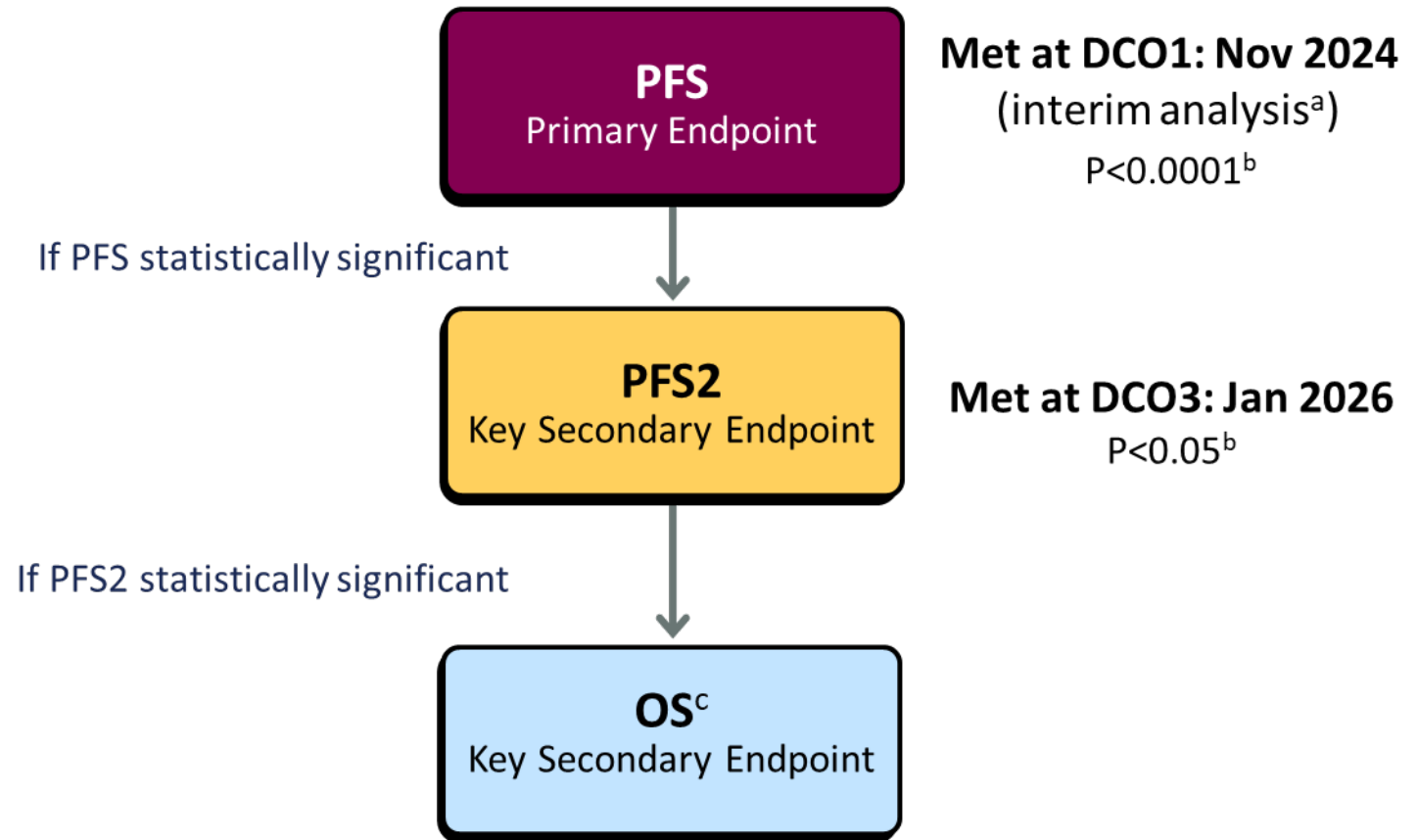
Power for PFS:

93%, assuming HR=0.61
at ~5% two-sided significance

Power for PFS2:

77%, assuming HR=0.65
at ~5% two-sided significance

Multiple Testing Procedure



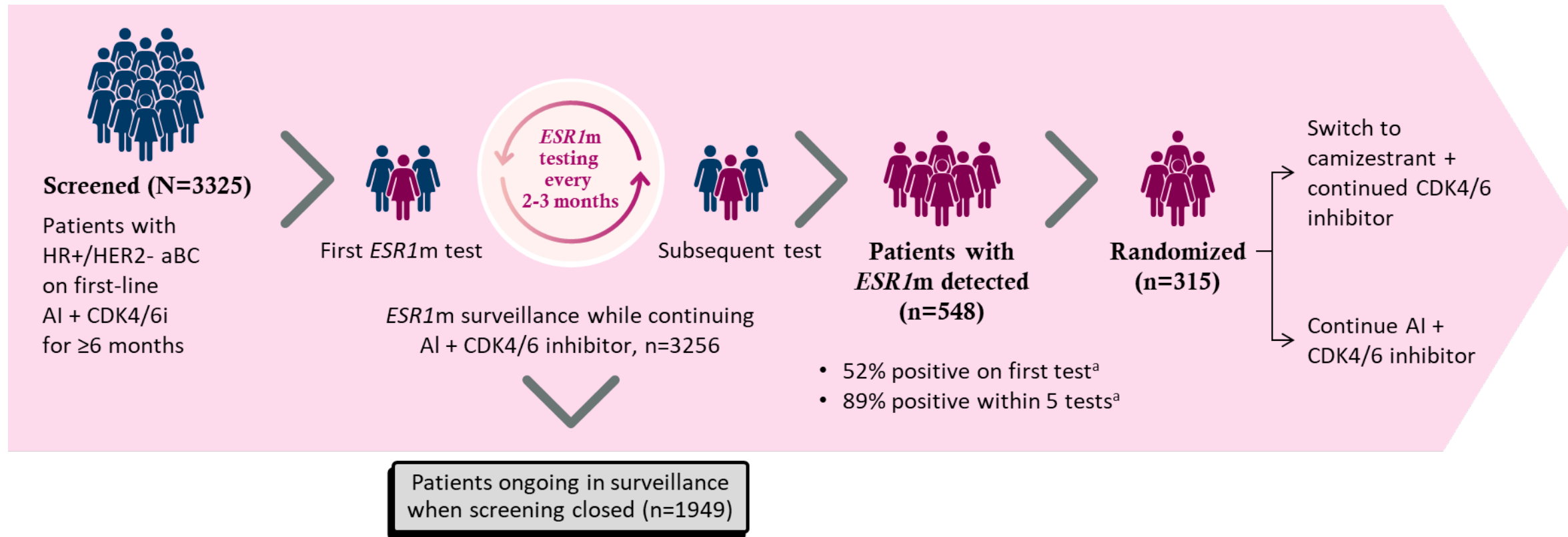
DCO=data cutoff.

a. Interim analysis was triggered by 135 PFS events and all randomized patients had at least 1 tumor assessment (actual number of events is 171).

b. 2-sided alpha using Haybittle-Peto boundary.

c. Primary OS analysis planned at DCO4.

SERENA-6 Patient Flow



Crude rate of *ESR1m* positive = 548 positive for *ESR1m*/1949 who completed surveillance (42%).

a. Number of tests obtaining a positive *ESR1m* test result based on N=548 patients.

Baseline Demographics & Disease Characteristics Well Balanced

SERENA-6

Characteristic		Camizestrant + CDK4/6i (N=157)	AI + CDK4/6i (N=158)
Median age (range), years		61.0 (29-81)	60.5 (35-89)
Female, n (%)		157 (100)	155 (98)
Race, n (%)	White	97 (62)	102 (65)
	Asian	39 (25)	34 (22)
	Other/Not reported	21 (13)	22 (14)
Postmenopausal status, n (%)		123 (78)	127 (80)
ECOG performance-status score, n (%) ^a	0	107 (68)	98 (62)
	1	48 (31)	56 (35)
Most common <i>ESR1</i> m at baseline, n (%) ^b	D538G	70 (45)	82 (52)
	Y537S	61 (39)	60 (38)
	Y537N	29 (19)	25 (16)
Region, n (%)	Asia	40 (25)	39 (25)
	Europe	89 (57)	91 (57)
	North America [US/Canada]	22 (14)/6 (4)	23 (15)/5 (3)

a. Data missing for 2 patients in the camizestrant + CDK4/6i arm and 3 patients in the AI + CDK4/6i arm. One patient in the AI + CDK4/6i arm had an ECOG performance status score of 2, which was a protocol deviation.

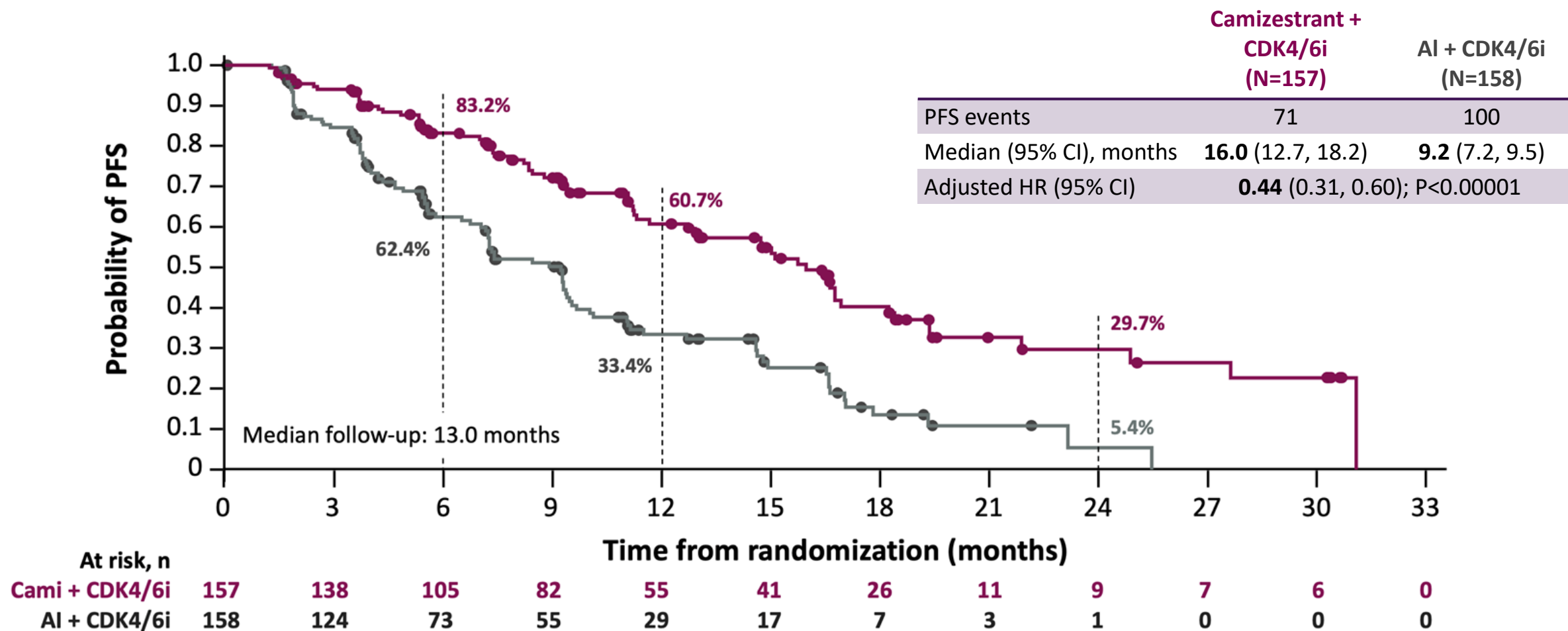
b. The 3 most prevalent *ESR1*m detected of the 11 qualifying mutations. Patients may have had more than 1 *ESR1*m.

Stratification Factors

SERENA-6

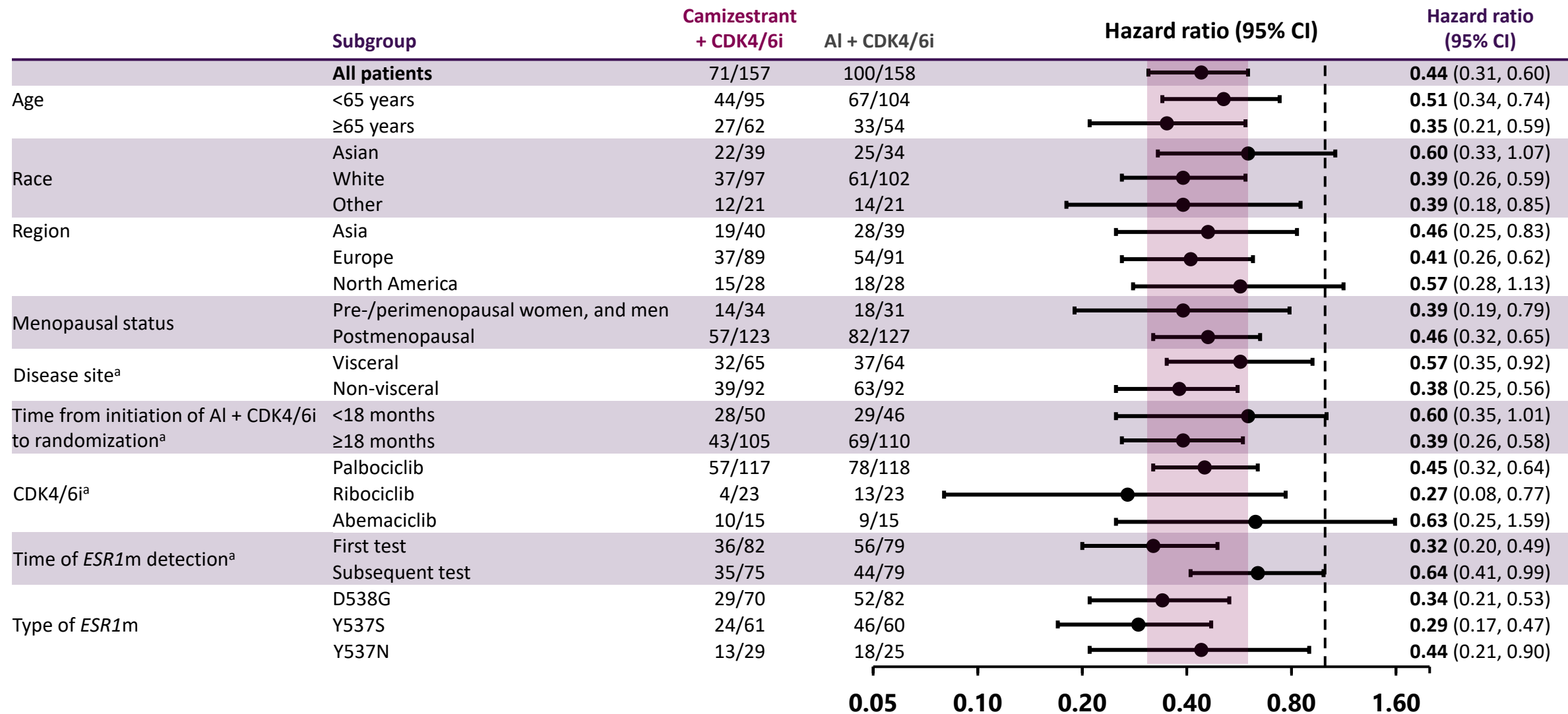
Stratification Factor		Camizestrant + CDK4/6i (N=157)	AI + CDK4/6i (N=158)
Sites of metastases, n (%)	Visceral	66 (42)	71 (45)
	Non-visceral	91 (58)	87 (55)
Time of <i>ESR1</i> m detection, n (%)	At first test	84 (54)	84 (53)
	At a subsequent test	73 (47)	74 (47)
Time from initiation of AI + CDK4/6i to randomization	≥18 months, n (%)	97 (62)	100 (63)
	<18 months, n (%)	60 (38)	58 (37)
	Median (range), months	23 (7-96)	23 (6-96)
CDK4/6i continued at randomization, n (%)	Palbociclib	119 (76)	119 (75)
	Ribociclib	24 (15)	23 (15)
	Abemaciclib	14 (9)	16 (10)

SERENA-6 Met Primary Endpoint (DCO1): Statistically Significant and Clinically Meaningful PFS Benefit



Consistent PFS Benefit Across All Key Subgroups

SERENA-6 (DCO1)

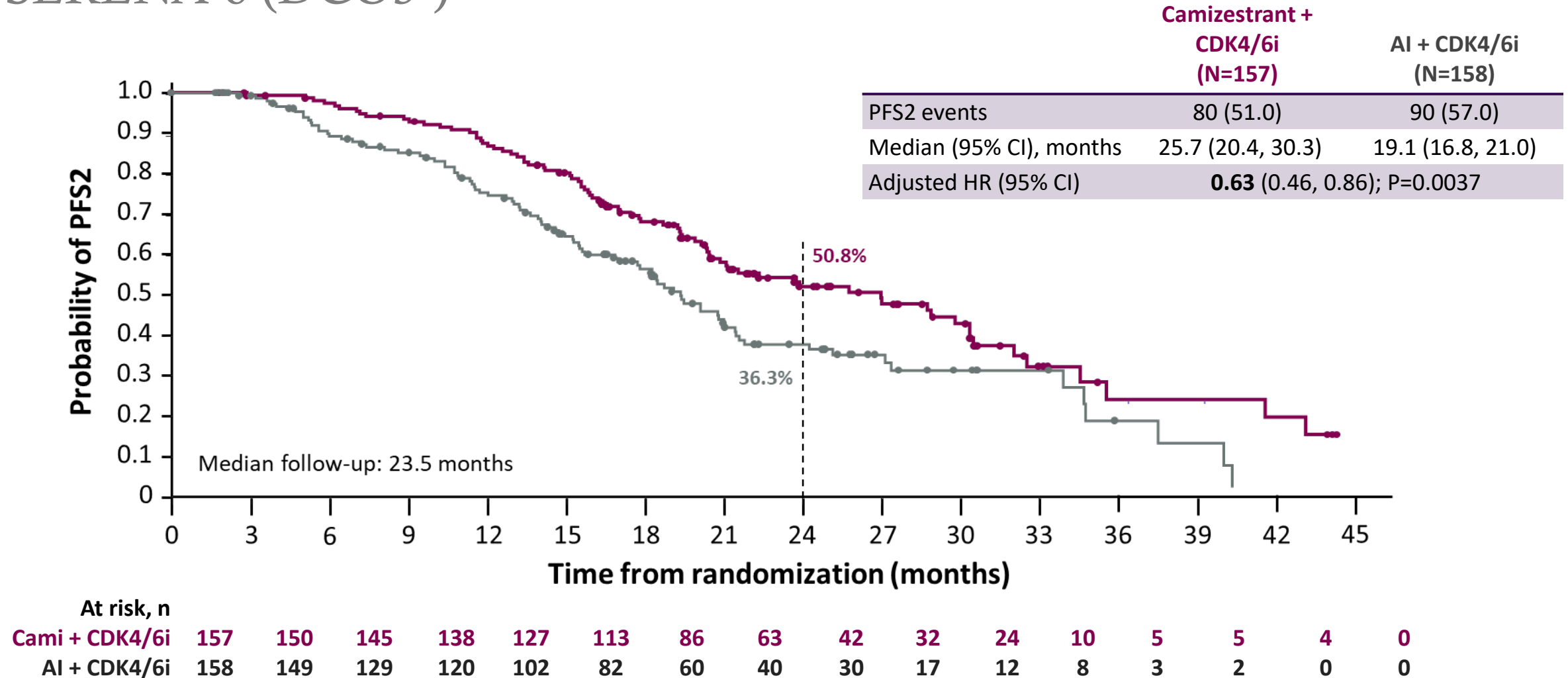


a. Stratification factor.

Reprinted with permission from Massachusetts Medical Society.

Reprinted from *N Engl J Med*, Bidard F-C, et al. First-line camizestrant for emerging *ESR1*-mutated advanced breast cancer, 393, 569-580, Copyright 2025 Massachusetts Medical Society.

Statistically Significant and Clinically Meaningful PFS2 Demonstrating Sustained Benefit SERENA-6 (DCO3^a)

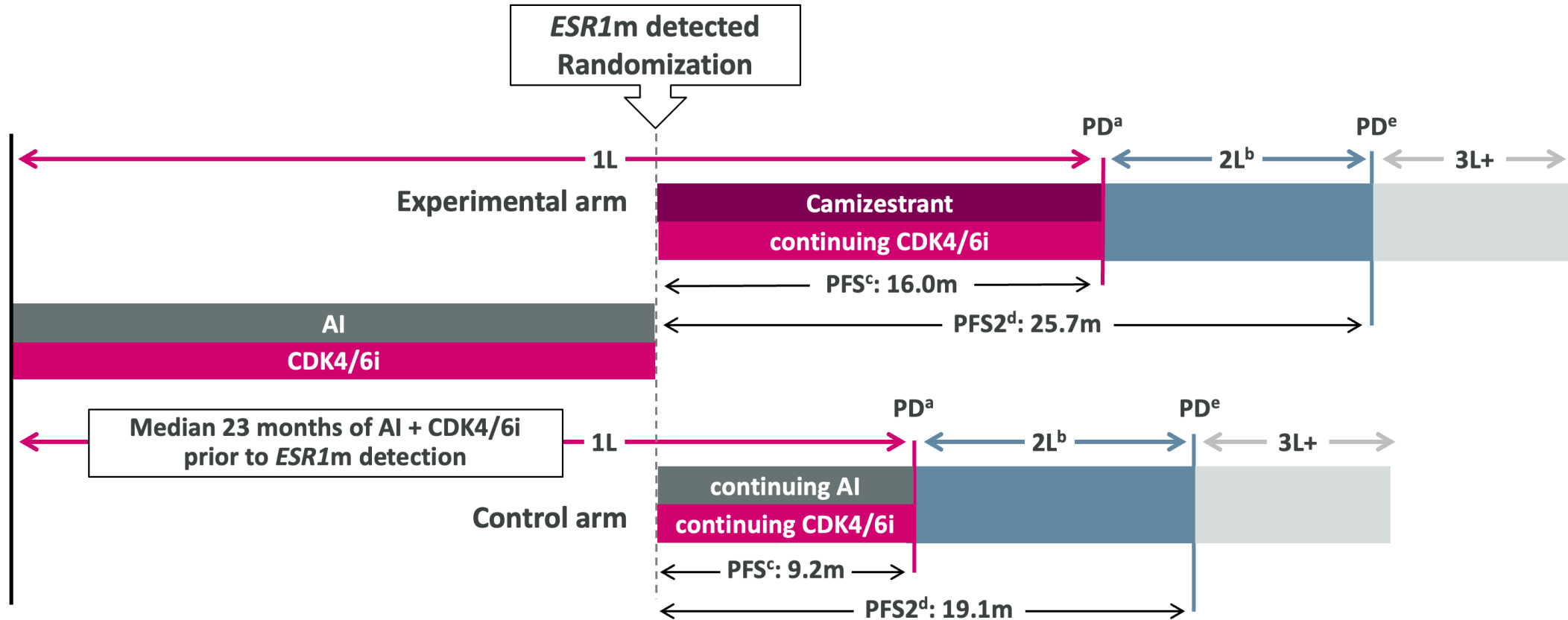


a. DCO3 is the data cutoff for the prespecified primary analysis of PFS2, per protocol.

Prespecified Analysis of PFS2 by RECIST Criteria Is Consistent With Primary PFS2 Analysis SERENA-6 (DCO3)

	Camizestrant + CDK4/6i (N=157)	AI + CDK4/6i (N=158)
PFS2 events per RECIST 1.1, n	69	78
Median (95% CI), months	27.7 (22.3, 30.5)	20.8 (17.7, 25.1)
Adjusted HR (95% CI)	0.64 (0.46, 0.90)	
Nominal P value	0.00939	

PFS Benefit Is Sustained Through PFS2



a. First progression per RECIST 1.1 by investigator assessment.

b. 2L treatment options per SoC and physician's preference (include endocrine mono- or combination with targeted therapy, or chemotherapy or ADCs).

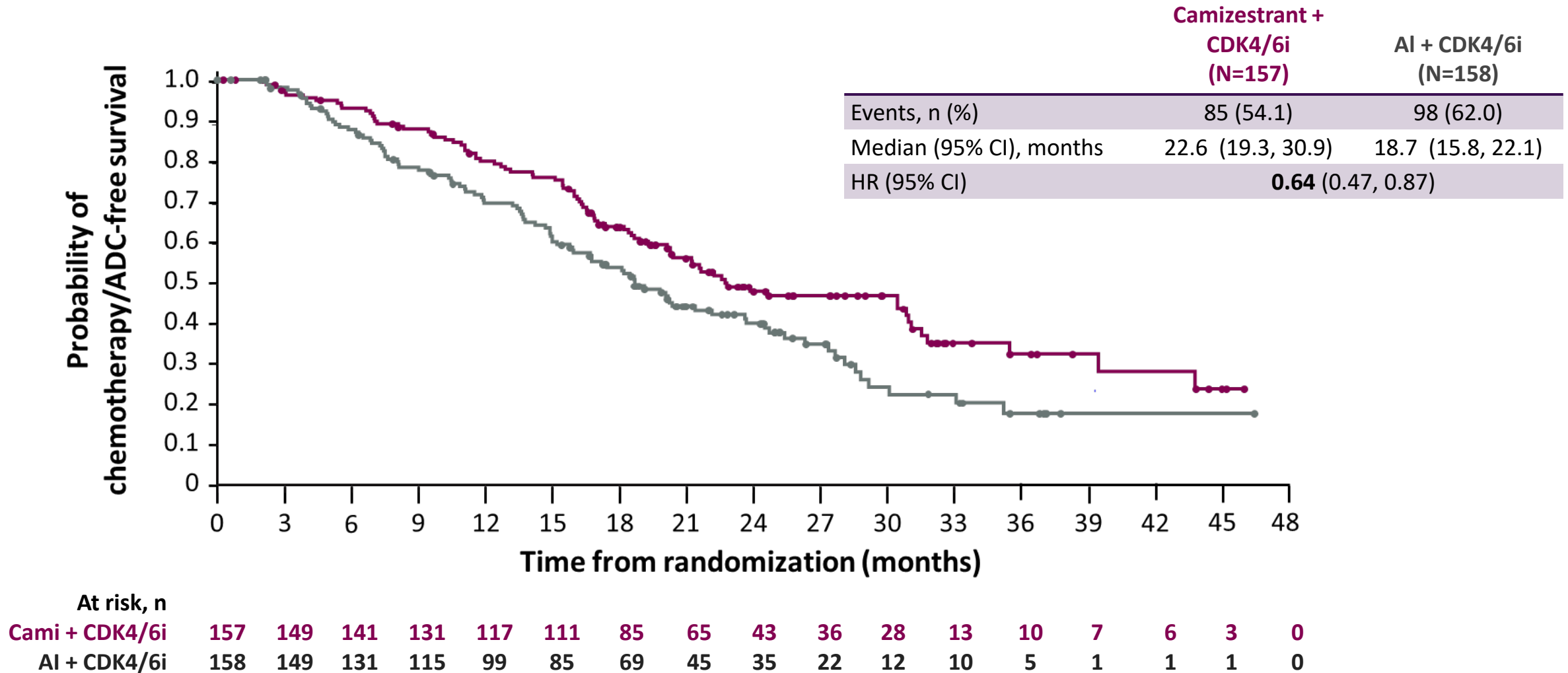
c. Primary analysis at DCO1.

d. PFS2 defined per EMA guideline on the evaluation of anticancer medicinal products in man, primary analysis at DCO3.

e. Clinical or objective PD; 170 patients had a second progression event (PFS2) at DCO3.

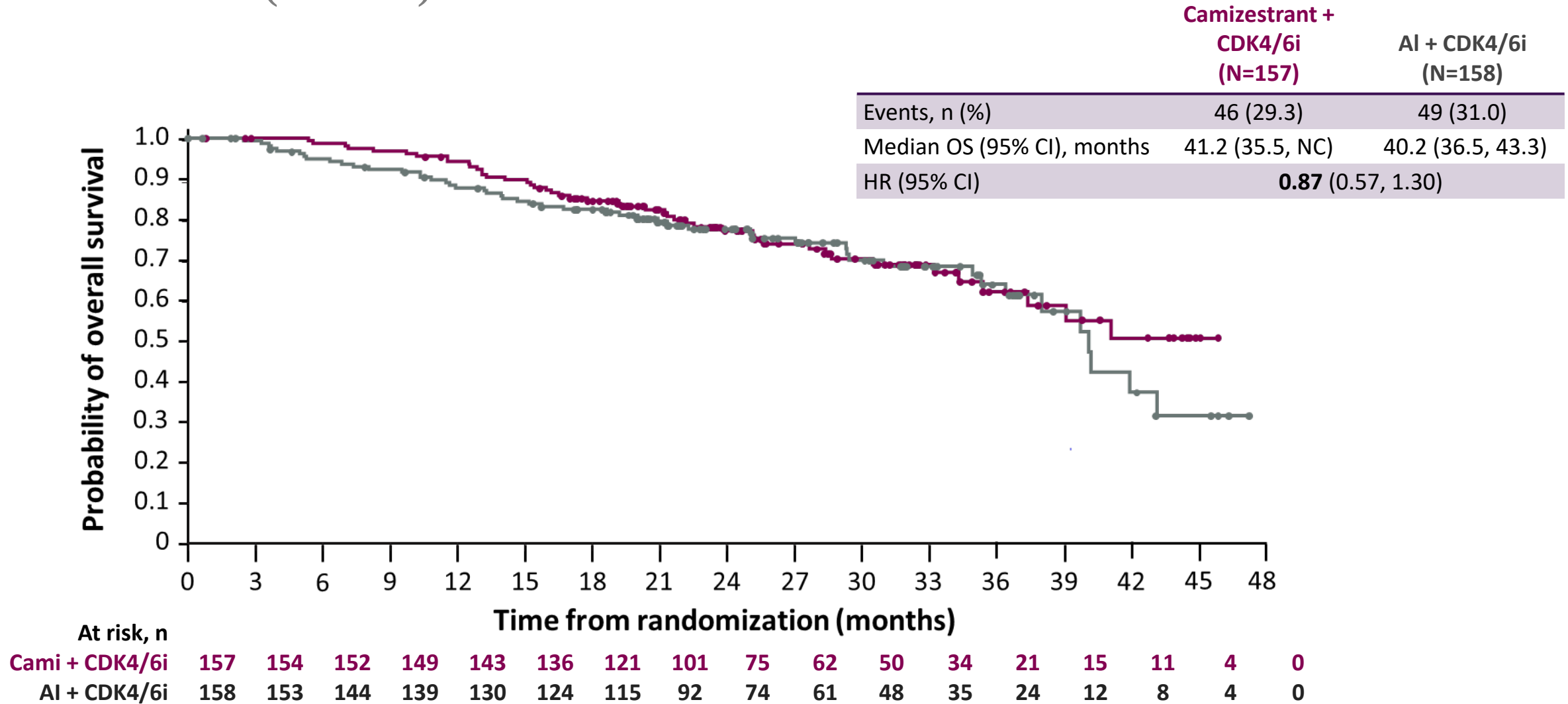
Chemotherapy/ADC-Free Survival Is Prolonged

SERENA-6 (DCO3)

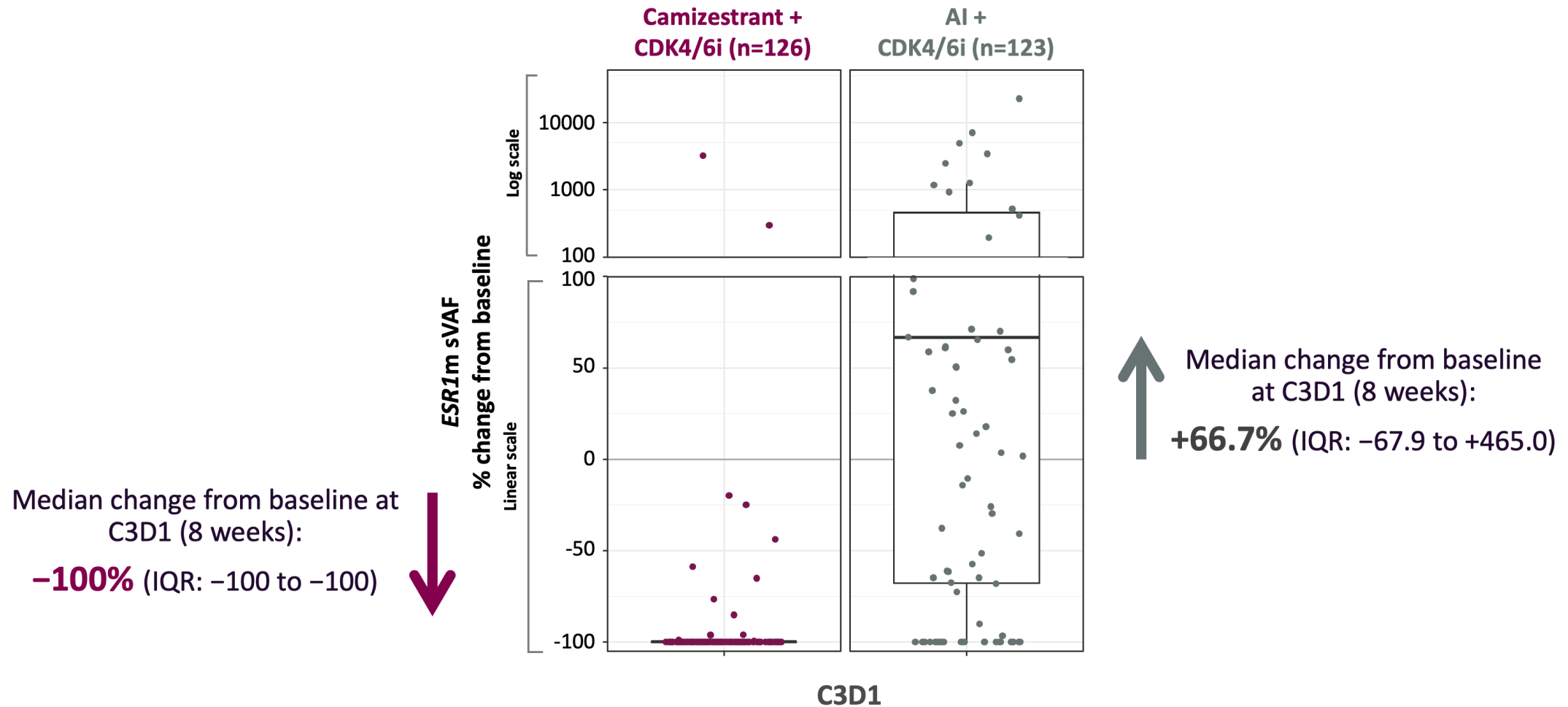


Overall Survival

SERENA-6 (DCO3)

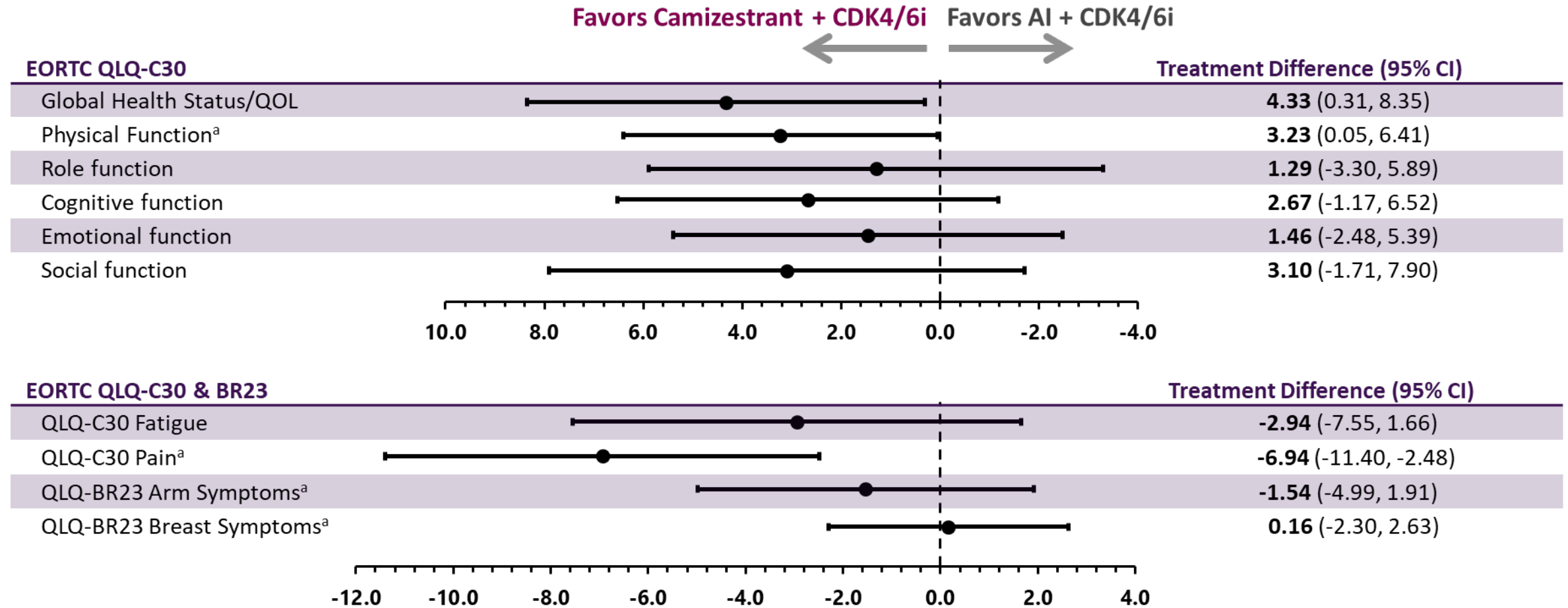


Camizestrant + CDK4/6i Profoundly Reduces *ESR1*m ctDNA



Patient-Reported Outcomes Favor Camizestrant

Model-Adjusted Mean Change From Baseline Over First 28 Weeks



a. Prespecified secondary endpoints.

Estimates were obtained using a mixed model repeated measures (MMRM) analysis, including treatment, visit, and treatment-by-visit interaction as exploratory variables and the baseline score and the baseline score by visit interaction as covariates. Reprinted from *Ann Oncol*, 37(2), Mayer EL, et al. Patient-reported outcomes in the SERENA-6 trial of camizestrant plus CDK4/6 inhibitor in patients with advanced breast cancer and emergent ESR1 mutations during first-line endocrine-based therapy, 180-193, Copyright 2026, with permission from Elsevier.

Summary

- SERENA-6 is an innovative study using cutting-edge technology
 - Design was aligned with the FDA and global health authorities
- Switching to camizestrant with continued CDK4/6i upon *ESR1m* detection demonstrated
 - Statistically significant and clinically meaningful 56% reduction in the risk of progression or death compared with AI + CDK4/6i (HR=0.44, P<0.00001)
 - Consistent PFS benefit across subgroups
 - Statistically significant and clinically meaningful PFS2 results (HR=0.63, P=0.0037)
 - No OS detriment (HR=0.87)
- PRO data further support the positive benefit/risk assessment



SERENA-6 Clinical Safety

Andrew Walding, MSc

Global Safety Head – Camizestrant

AstraZeneca



Safety Profile of Camizestrant 75 mg Is Well-Characterized

Completed studies provide a robust supportive safety pool (N=380)

	Camizestrant + CDK4/6i combination	Camizestrant monotherapy
Total	263	117
SERENA-1	108 ^a	24 ^b
SERENA-2		74
SERENA-6	155	
Japan Phase I		7
China Phase I		12

- >6000 patients exposed to camizestrant across early and advanced breast cancer
- Over 3000 patients with >1 yr exposure to camizestrant, including some with >4 yrs

SERENA-6 safety pool is of sufficient size to enable characterization of AEs

a. SERENA-1 parts C, D, G, H, K, and L.

b. SERENA-1 parts A and B.

Exposure and Dose Intensity

SERENA-6

	Camizestrant + CDK4/6i (N=155)	AI + CDK4/6i (N=155)
Median treatment exposure, months		
Camizestrant/AI	10.1	6.3
CDK4/6i	9.8	6.1
Median relative dose intensity,^a %		
Camizestrant/AI	99.6	99.7
CDK4/6i	98.8	99.5

60% longer median exposure in camizestrant arm; no impact on the CDK4/6i dose intensity

a. Relative dose intensity is the percentage of the actual dose intensity delivered relative to the intended dose intensity through to treatment discontinuation.

Overview of Safety Profile

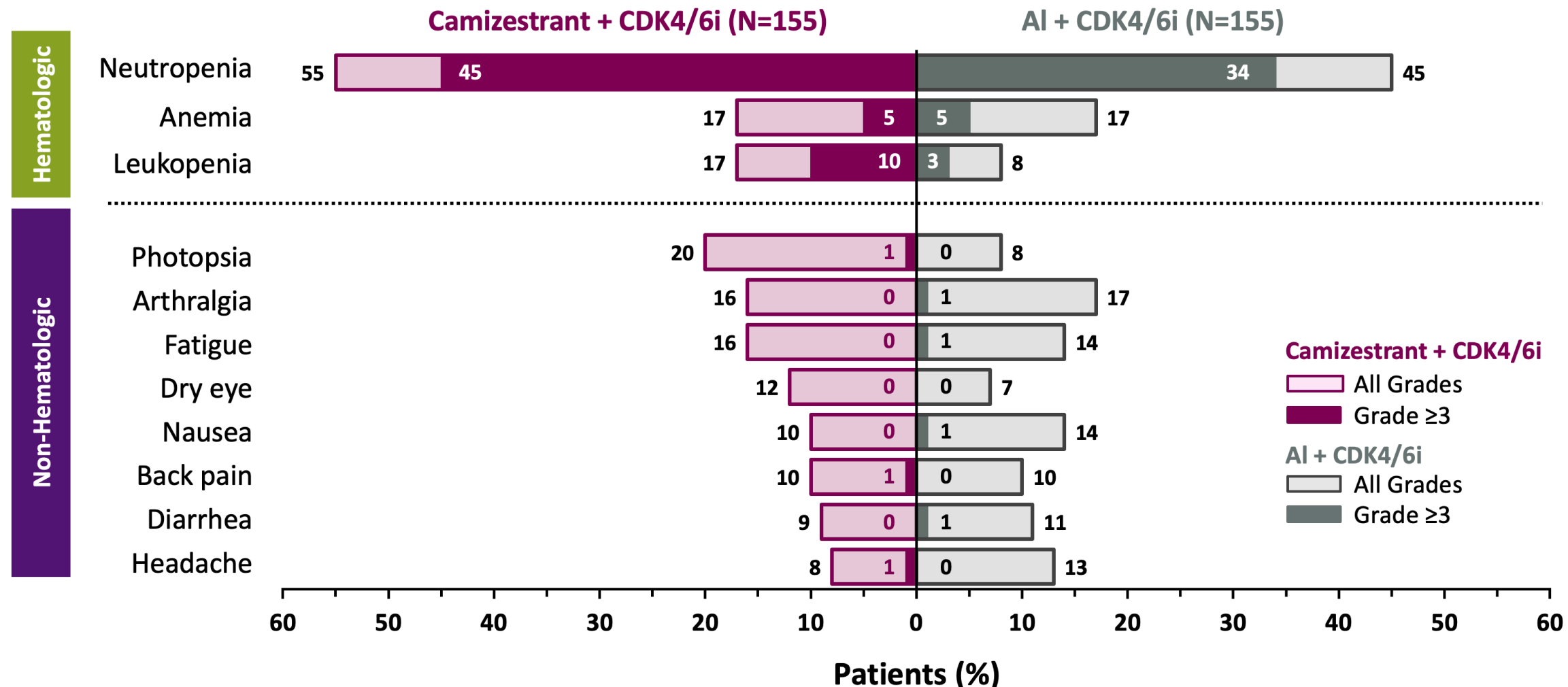
SERENA-6

	Patients, n (%)	
	Camizestrant + CDK4/6i (N=155)	AI + CDK4/6i (N=155)
Any adverse event (AE)	145 (94)	135 (87)
AEs of CTCAE Grade ≥ 3	93 (60)	71 (46)
Serious AEs	16 (10)	19 (12)
AEs leading to death	2 (1)	1 (1)
AEs leading to discontinuation		
Camizestrant/AI	2 (1)	3 (2)
CDK4/6i	2 (1)	2 (1)
AEs leading to dose reduction		
Camizestrant/AI ^a	9 (6)	2 (1)
CDK4/6i	18 (12)	17 (11)
AEs leading to dose interruption		
Camizestrant/AI	34 (22)	22 (14)
CDK4/6i	75 (48)	53 (34)

a. Dose reductions in the AI arm apply to camizestrant placebo.

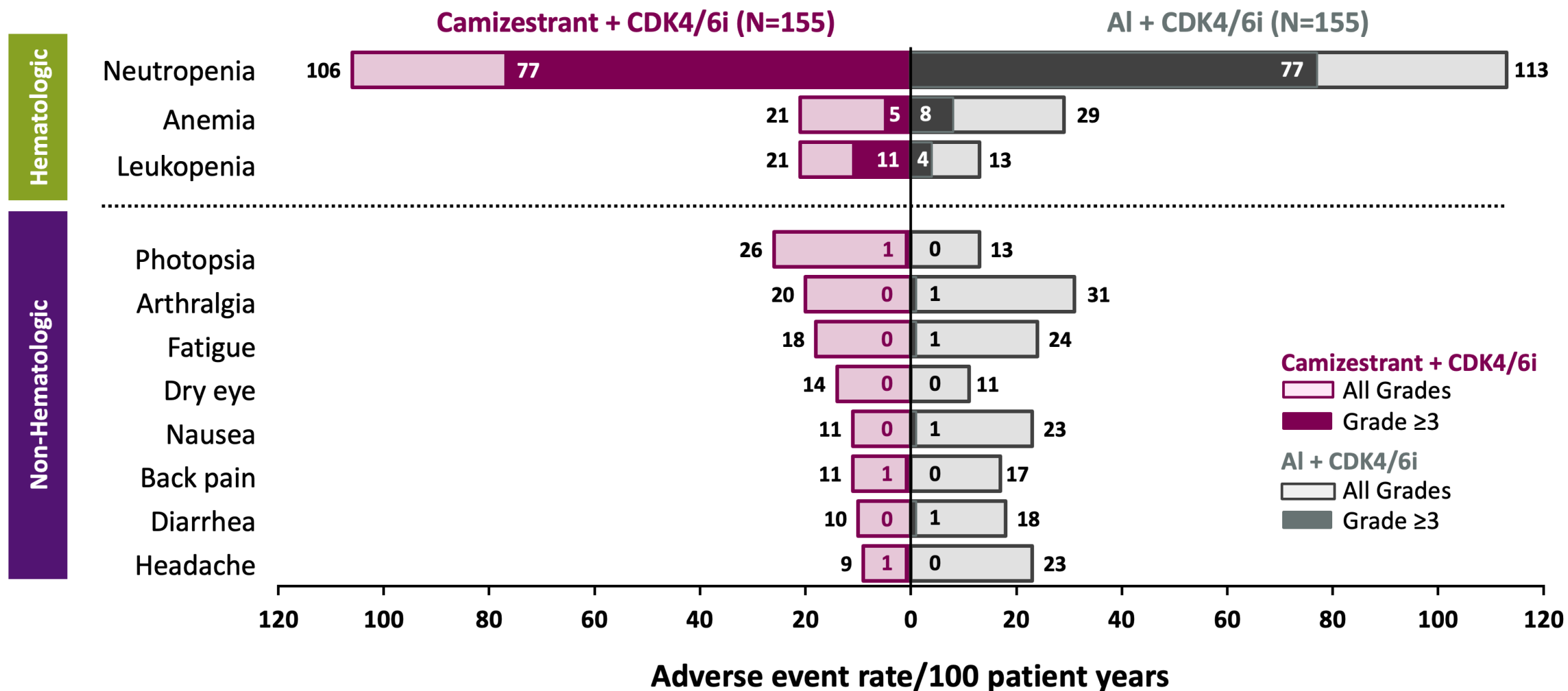
Most Common Adverse Events ($\geq 10\%$ of Patients) by Grade

SERENA-6



Exposure-Adjusted Incidence of AEs by Grade

SERENA-6



Exposure-adjusted incidence rates were calculated as the total number of patients who had an AE reported, divided by the total number of days at risk for AEs across all subjects in each arm, multiplied by 365.25 and then by 100.

ADR: Reversible, Sinus Rhythm Bradycardia

Grouped term/preferred term ^a	Patients, n (%)	
	Camizestrant + CDK4/6i (N=155)	AI + CDK4/6i (N=155)
Bradycardia^b	12 (7.7)	0
Bradycardia	8 (5.2)	0
Sinus bradycardia	4 (2.6)	0

- Camizestrant lowers heart rate through HCN4 “pacemaker channel” in the sinoatrial node
- Median decrease in heart rate of 14 bpm from baseline to Day 15, reaching a stable nadir at that time
 - Magnitude of effect is dependent on baseline heart rate (ie, small effect for those with low baseline heart rate)
 - Heart rate recovered to baseline at the safety follow-up

a. MedDRA preferred term coded from investigator verbatim reported term.

b. Adverse Drug Reaction grouping.

Camizestrant + Ribociclib Combination

- Camizestrant monotherapy has no independent effect on QT interval at clinically relevant doses
 - High-quality clinical QTc study using 24-hr Holter monitoring, in line with international guidelines
- Mechanisms of camizestrant-mediated bradycardia and ribociclib-mediated QTc prolongation are distinct
- Camizestrant + ribociclib studied in 83 patients in SERENA-1 and SERENA-6
 - No significant QTc prolongation or arrhythmias in SERENA-6
 - 1 Grade 4 QT prolongation AE in SERENA-1
 - Event heavily confounded; ribociclib not interrupted when QTcF >550 ms, contrary to ribociclib dose-modification requirements

ADR: Reversible, Transient Peripheral Visual Effects

Grouped term/preferred term	Patients, n (%)	
	Camizestrant + CDK4/6i (N=155)	AI + CDK4/6i (N=155)
Visual effects^a	49 (31.6)	25 (16.1)
Photopsia	31 (20.0)	12 (7.7)
Vision blurred	11 (7.1)	11 (7.1)
Visual impairment	6 (3.9)	3 (1.9)
Diplopia	3 (1.9)	2 (1.3)
Photophobia	3 (1.9)	0
Visual perseveration	2 (1.3)	0

- Mostly (~90%) Grade 1 with few (2.6%) dose interruptions
- Early onset, reversible, non-structural effect
- Comprehensive ocular exams^b showed
 - No evidence of structural effects on the eye
 - No change in visual acuity or visual fields attributed to camizestrant

a. Adverse Drug Reaction grouping.

b. Comprehensive visual exams included assessment of visual field, best corrected distance visual acuity, intraocular pressure, optical coherence tomography (OCT), and funduscopy.

Summary of Safety

- Camizestrant + CDK4/6 inhibitor demonstrated a favorable safety profile
- Well-tolerated, with a low treatment discontinuation rate due to AEs
- Safety profile of camizestrant + CDK4/6 inhibitor combination is consistent with clinical experience of camizestrant and each CDK4/6 inhibitor
- Despite longer exposure on the camizestrant arm, patients report that AEs were not bothersome, with no or minimal impact of AEs on activities of daily living

Clinical Perspective

Kevin Kalinsky, MD, MS, FASCO

Emory University School of Medicine

Director of the Glenn Family Breast Center at Winship Cancer Center



Patient Case



45-year-old female diagnosed with *de novo* metastatic breast cancer to bone only

June 2021

- **Bone biopsy:**
ER 99% PgR 79%
HER2-negative

- **ctDNA at baseline:**
no actionable mutation

Lupron + letrozole +
ribociclib + denosumab

June 2024

- **Clinical progression:**

New back pain with T4 lesion, received xRT for 5 fractions

- **ctDNA at progression:**
ESR1 mutation



Several options discussed:

- Single-agent oral SERD
- Fulvestrant + everolimus
- Fulvestrant + abemaciclib

She opted for fulvestrant + abemaciclib

Patient Concerns and Treatment Goals

“

I have been checking monthly tumor markers (CEA, CA15-3, CA27-29), but these always remained normal for me.

“

I was doing scans every 3-4 months.

“

What other tests could I have done to detect a change before I developed back pain?

Treatment goals important to my patients

- Delay disease progression
- Palliate disease symptoms
- Delay need for chemotherapy
- Prolong survival
- Maintain good quality of life

Why I Would Incorporate the SERENA-6 Approach

SERENA-6 is a positive study, demonstrating a favorable benefit/risk

Disease Biology

- *ESR1m* is a key driver of AI resistance and is actionable
- Tumors are most sensitive to endocrine therapy before clinical progression

Extend Benefit of 1L Therapy

- 56% reduction in risk of progression/death
- Extended benefit of 1L ET + CDK4/6i
- Maximizes time on well-tolerated endocrine therapy

Delay IV Treatment

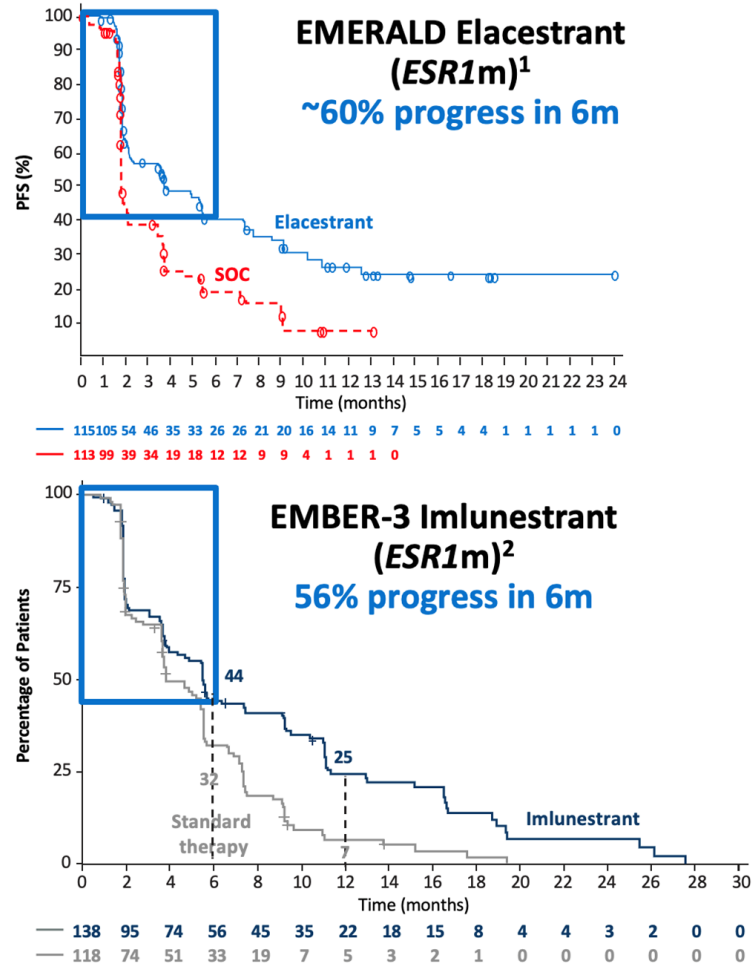
- Chemotherapy and ADC often more toxic
- Time in the infusion center can be burdensome

Maintain QoL

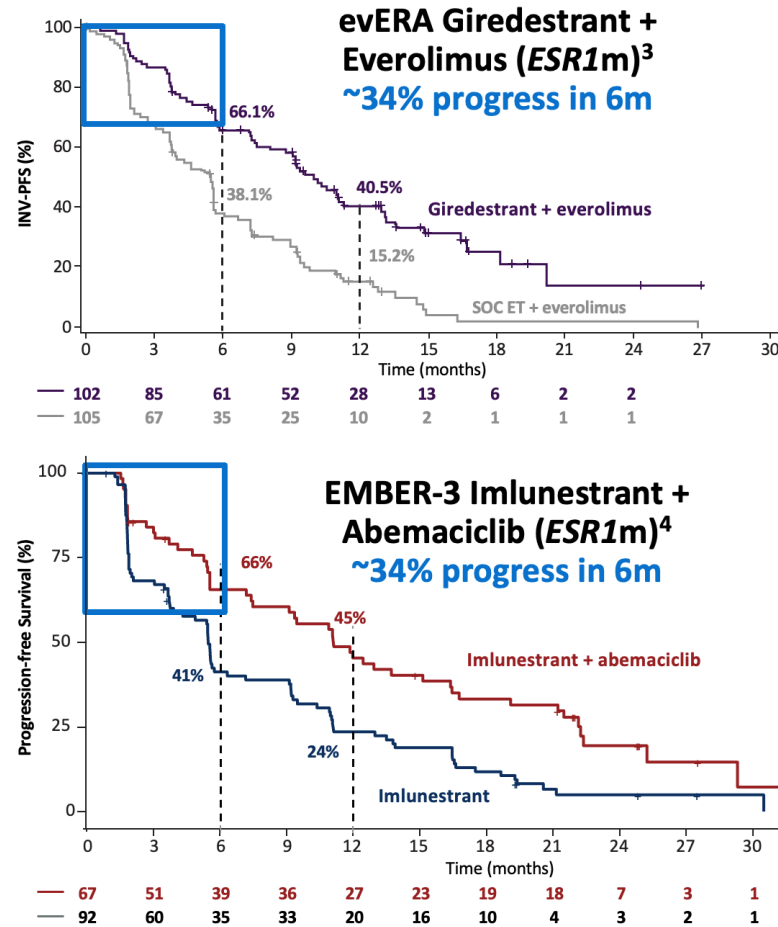
- Delayed onset of disease-related symptoms (eg, pain) and decline in physical function and emotional well-being

Disease Biology: Tumors Most Sensitive to ET Before Clinical Progression

Approved 2L Novel SERD MonoTx

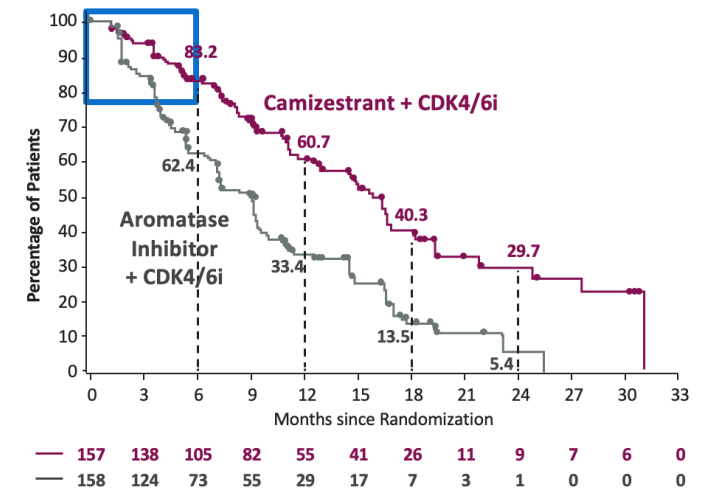


Data from 2L Novel SERD Combos (Unapproved)



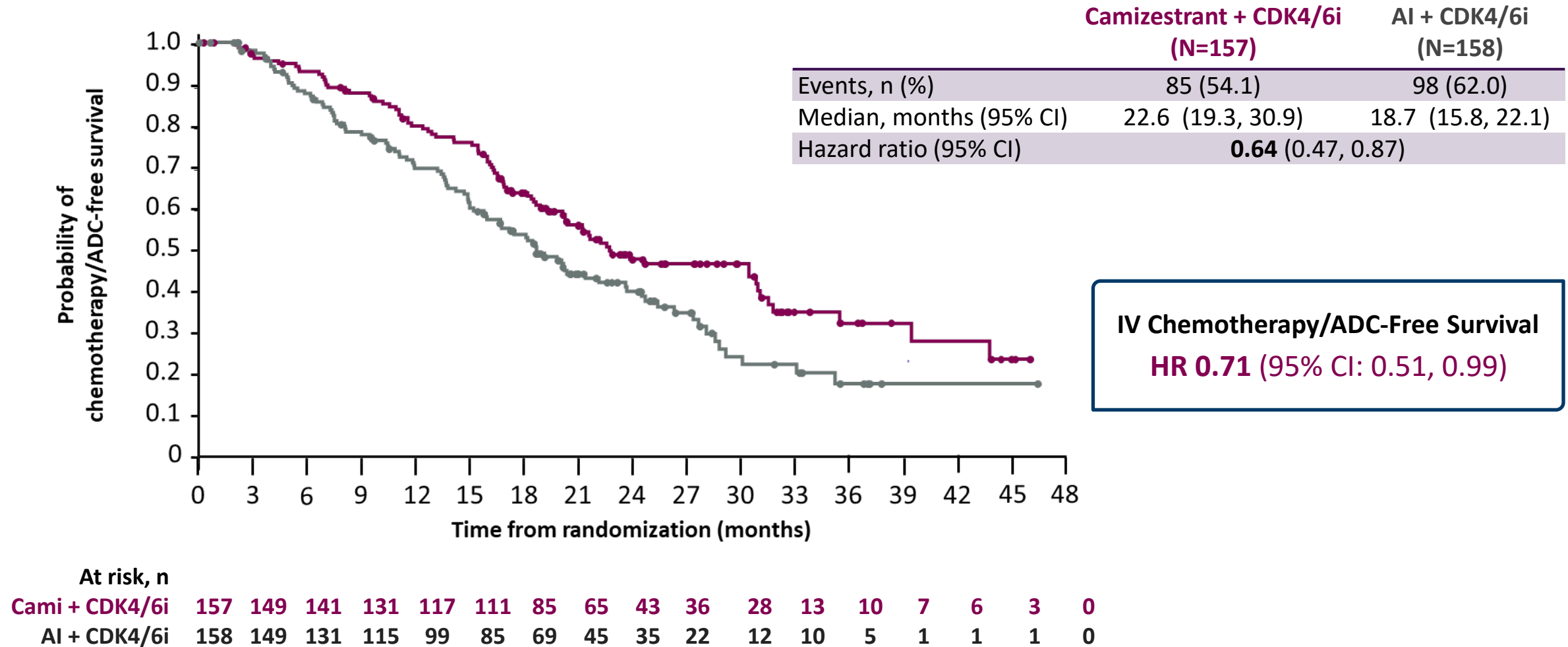
1L ET-Switch to camizestrant

SERENA-6 Camizestrant + CDK4/6i (*ESR1m*)⁵ 17% progress in 6m

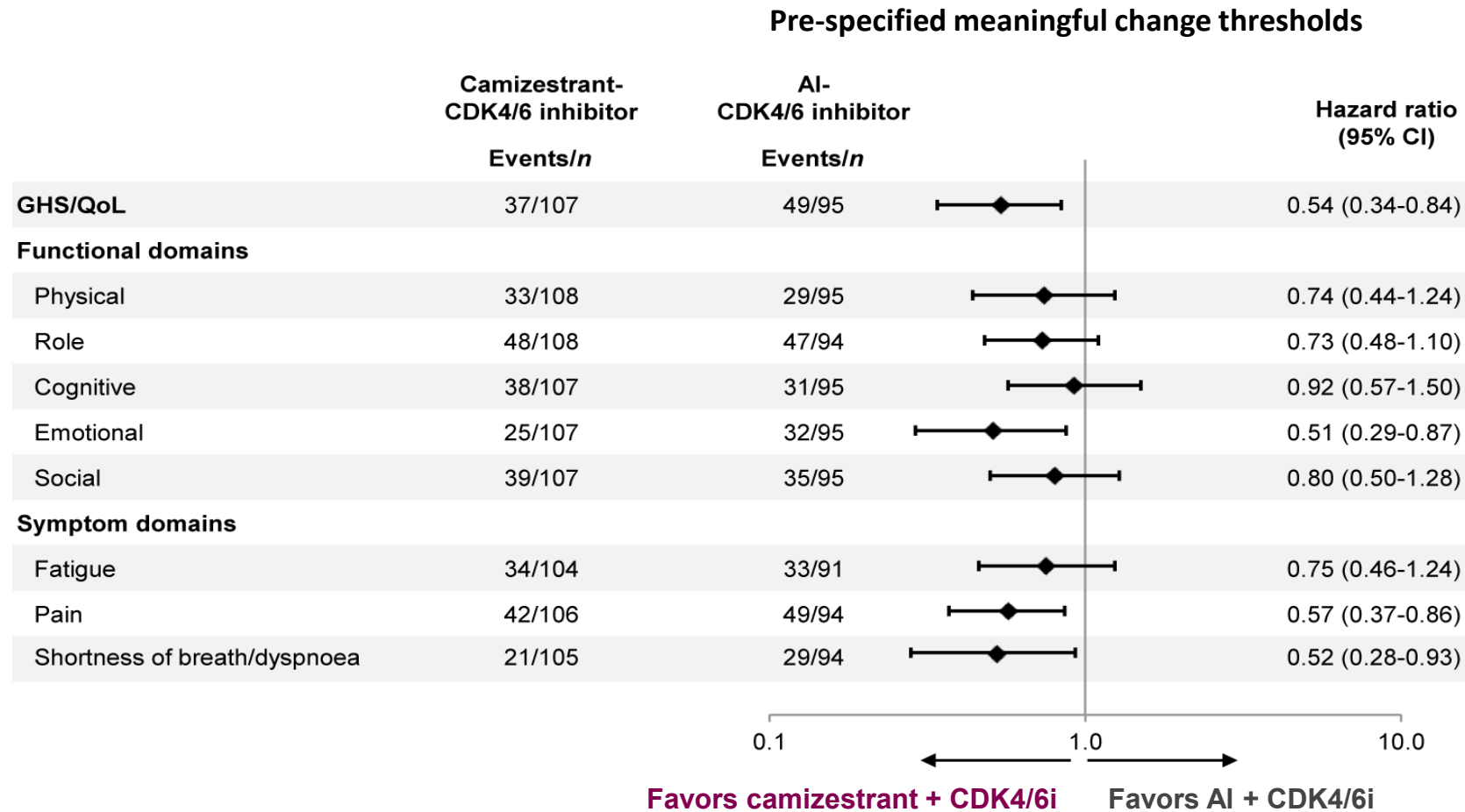


1. Bidard F-C, et al. Elacestrant (oral selective estrogen receptor degrader) versus standard endocrine therapy for estrogen receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer: results from the randomized phase III EMERALD trial. *J Clin Oncol* (an American Society of Clinical Oncology journal). 2022;40(28):3246-3256, https://ascopubs.org/doi/10.1200/JCO.22.00338?url_ver=Z39.88-2003&rft_id=ori:rid:crossref.org&rft_dat=cr_pub%20%20pubmed; 2. Reprinted from *N Engl J Med*. Jhaveri KL, et al. Imlunestrant with or without abemaciclib in advanced breast cancer: updated efficacy results from the phase III EMBER-3 trial, 392(12), 1189-1202, Copyright 2025 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society; 3. Reprinted with permission from Mayer E, et al. ESMO 2025. Abstract LBA16; 4. Reprinted from *Ann Oncol*, 37(4), Jhaveri KL, et al. Imlunestrant with or without abemaciclib in advanced breast cancer: updated efficacy results from the phase III EMBER-3 trial, 532-543, Copyright 2026, with permission from Elsevier; 5. Reprinted from *N Engl J Med*, Bidard F-C, et al. First-line camizestrant for emerging ESR1-mutated advanced breast cancer, 393, 569-580, Copyright 2025 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

Prolonging Chemotherapy/ADC-Free Survival

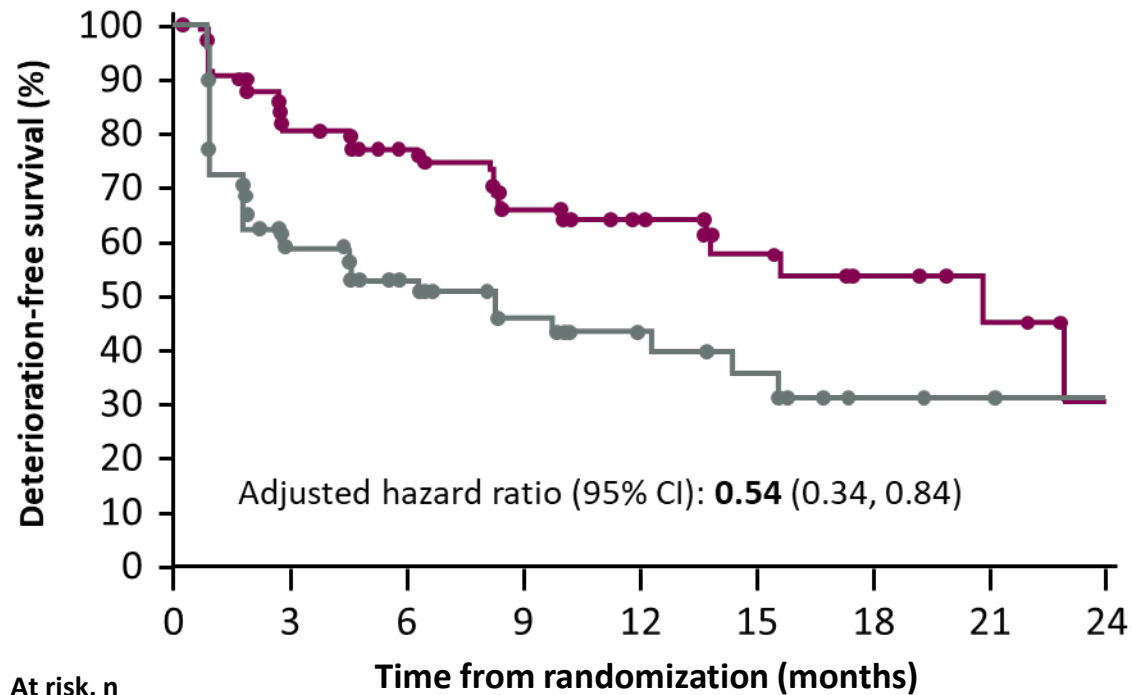


Delaying Time to Deterioration in Patient-Reported EORTC QLQ-C30 Symptoms, Function, and QoL

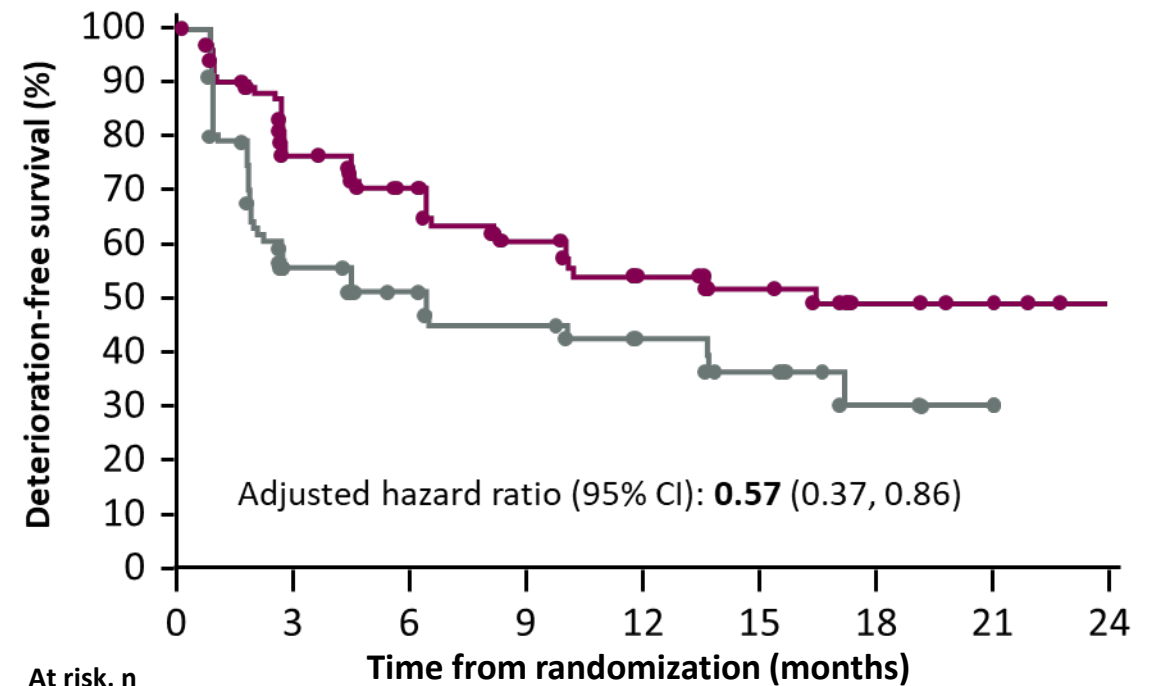


Delaying Time to Deterioration in Patient-Reported EORTC QLQ-C30 Global Health Status/QoL and Pain

Global Health Status/QoL

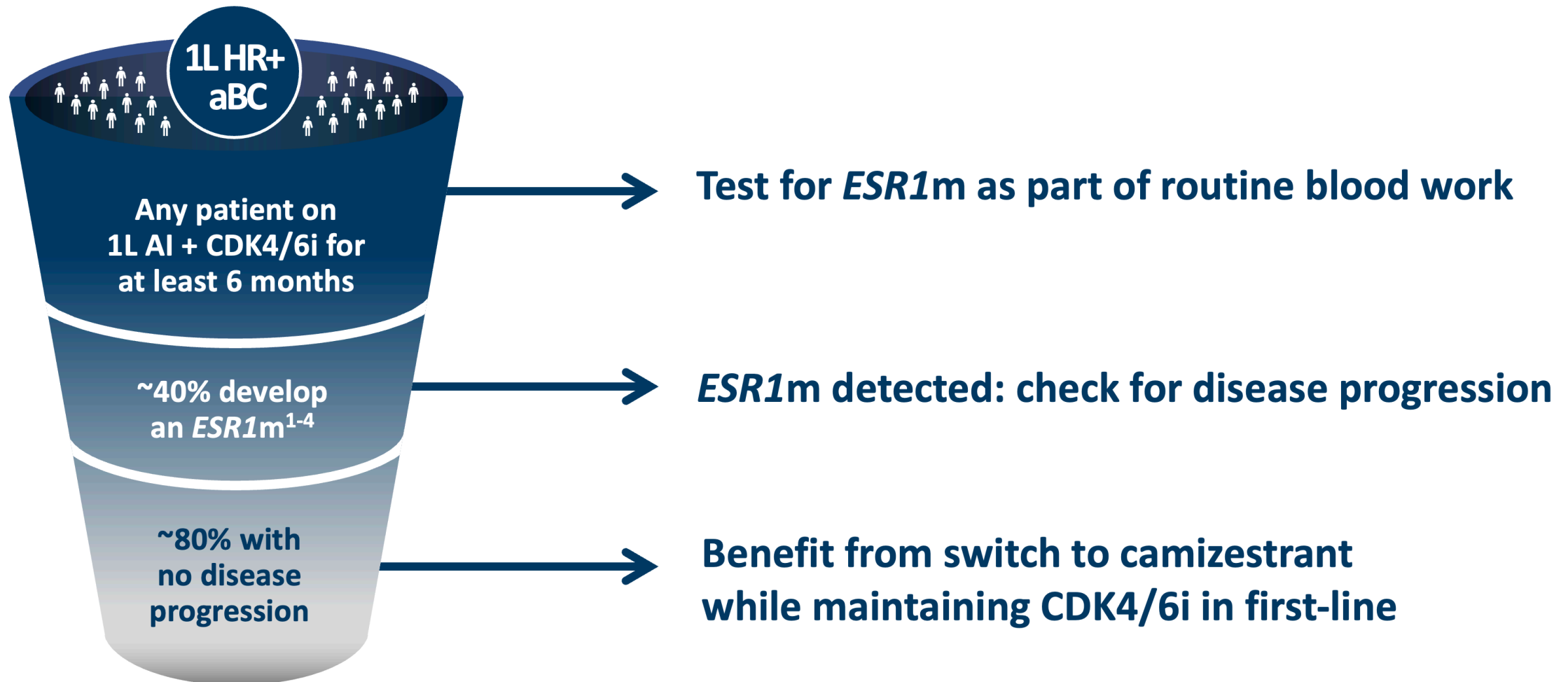


Pain



The analysis population is a subset of the full analysis set and includes all randomized patients with a baseline score that would allow deterioration, plus at least 1 evaluable post-baseline assessment. Reprinted from *Ann Oncol*, 37(2), Mayer EL, et al. Patient-reported outcomes in the SERENA-6 trial of camizestrant plus CDK4/6 inhibitor in patients with advanced breast cancer and emergent ESR1 mutations during first-line endocrine-based therapy, 180-193, Copyright 2026, with permission from Elsevier.

Taking Action to Stay Ahead of Progression in Patients Suitable for the SERENA-6 Approach



I Would Recommend the SERENA-6 Approach to My Patients

**SERENA-6 trial demonstrated a positive benefit/risk,
and this paradigm shift addresses patients' treatment goals**

**Switching to camizestrant + CDK4/6i
at emergence of *ESR1m***

- ✓ Prolongs 1L ET+CDK4/6i by 7 months
- ✓ 1/3 pts progression-free at 2 years
- ✓ Extends overall time on endocrine therapies
- ✓ Delays need for chemotherapy/ADCs
- ✓ Delays deterioration in QoL
- ✓ Well-tolerated

**Encourages more active
patient engagement**

- Easy to implement
- Empowers patients to adjust treatment before disease progression or worsening symptoms



Concluding Remarks

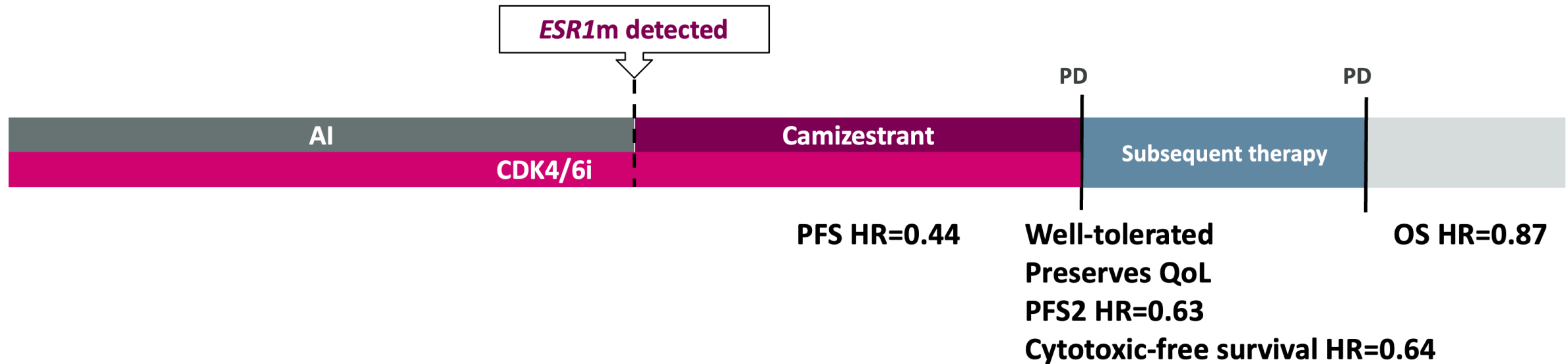
Ingrid Mayer, MD, MSCI

VP, Global Clinical Strategy Head, Breast/GYN Cancers
Late Development Oncology, Research & Development
AstraZeneca



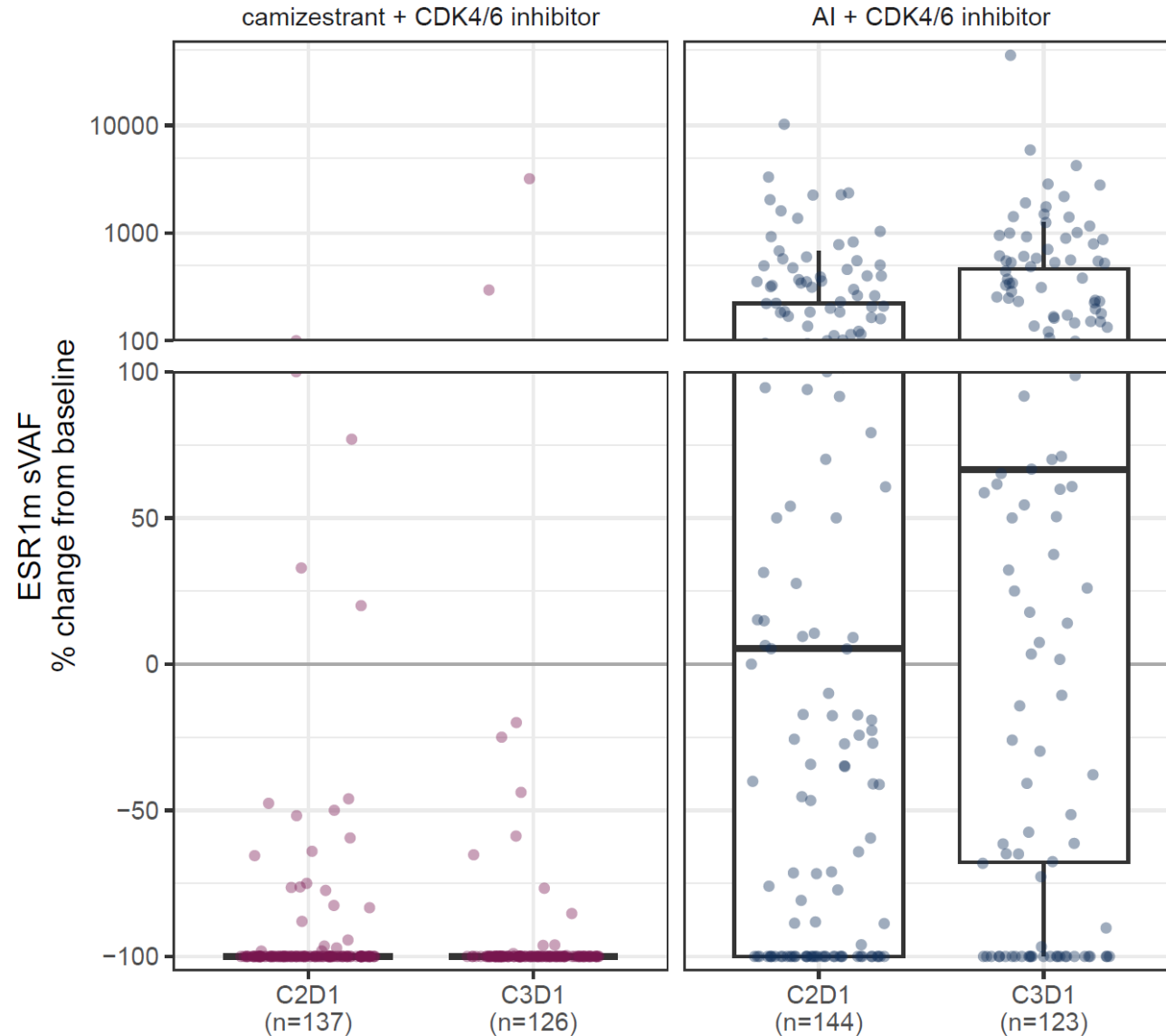
SERENA-6: A New Treatment Paradigm for *ESR1*m HR+ HER2- Advanced Breast Cancer

Positive Benefit/Risk for Patients



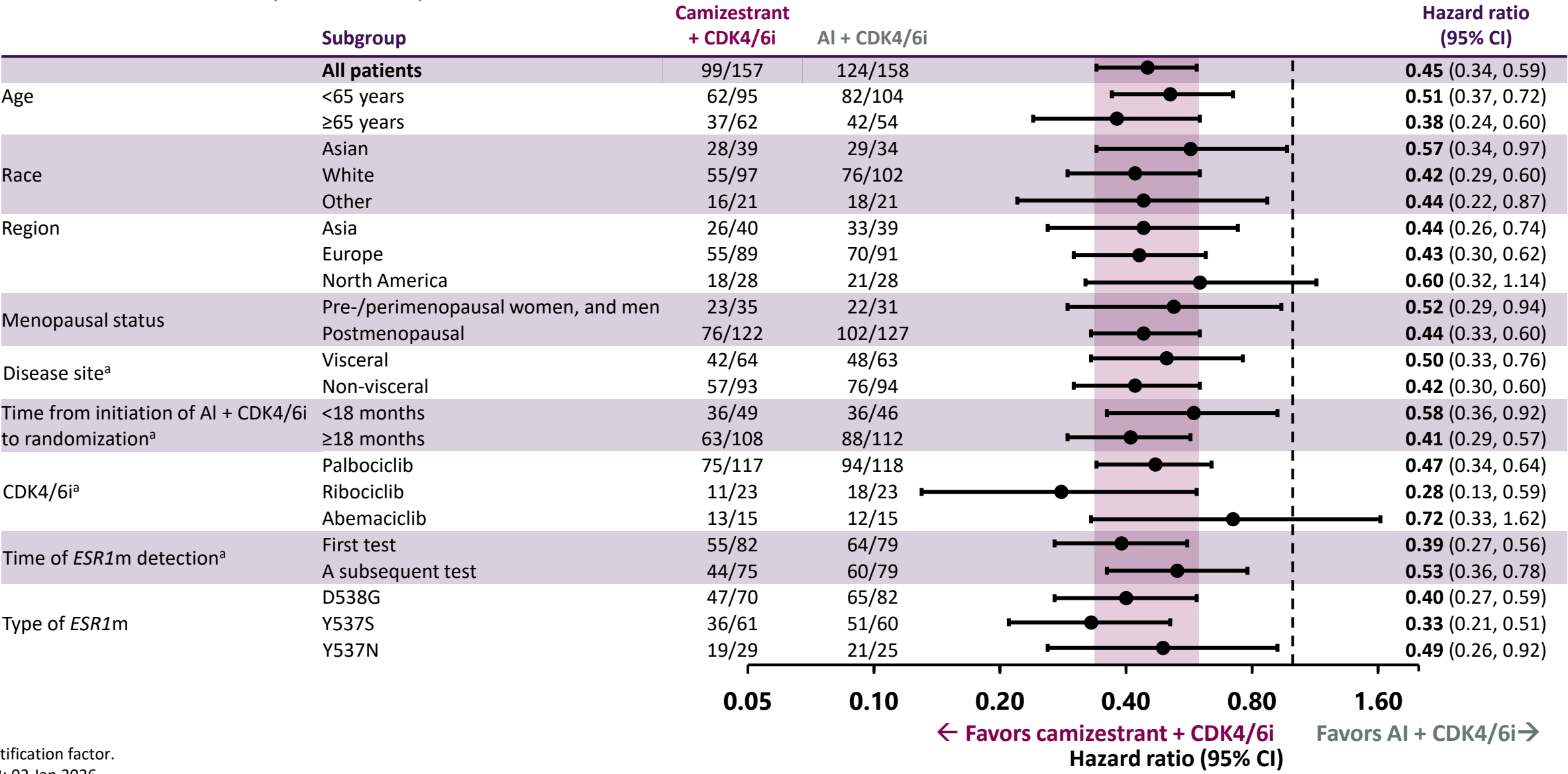
Backup Slides Presented

Equivalent Reduction in *ESR1m* Seen at C2D1 and C3D1 on the Camizestrant Arm



Consistent PFS Benefit Across All Key Subgroups

SERENA-6 (DCO3)



^a Stratification factor.
DCO3: 02 Jan 2026

PFS Outcome in Patients with *ESR1*m and Commonly Mutated Genes Alterations Detected or Not Detected

DCO1

Co-occurring alteration		Camizestrant + CDK4/6i [PFS events/n (%)]	AI + CDK4/6i [PFS events/n (%)]	Median PFS months (95% CI) in camizestrant + CDK4/6i	Median PFS months (95% CI) in AI + CDK4/6i	HR (95% CI)
PIK3CA	Present	26/64 (40.6%)	39/66 (59.1%)	16.62 (11.30, 21.88)	9.66 (7.16, 11.14)	0.45 (0.27, 0.74)
	Absent	45/93 (48.4%)	61/92 (66.3%)	15.97 (11.14, 18.40)	7.26 (5.59, 9.26)	0.45 (0.30, 0.66)
GATA3	Present	17/27 (63.0%)	15/21 (71.4%)	12.91 (5.36, 15.97)	6.74 (3.71, 14.92)	0.63 (0.31, 1.28)
	Absent	54/130 (41.5%)	85/137 (62.0%)	16.62 (14.72, 21.88)	9.26 (7.26, 9.66)	0.41 (0.29, 0.58)
TP53	Present	21/43 (48.8%)	25/37 (67.6%)	11.30 (7.23, 19.35)	5.59 (3.78, 9.30)	0.44 (0.24, 0.79)
	Absent	50/114 (43.9%)	75/121 (62.0%)	16.43 (13.01, 18.40)	9.26 (7.23, 11.07)	0.44 (0.30, 0.63)

Switching to camizestrant + CDK4/6i upon emergence of *ESR1*m provided consistent PFS benefit over remaining on AI + CDK4/6i regardless of whether alterations in *PIK3CA*, *GATA3* or *TP53* were detected or not

Time to Treatment Strategy Failure by K-M Method: From Randomization to the End of Endocrine Therapy

	Camizestrant + CDK4/6i N=157	AI + CDK4/6i N=158
Median, months	18.76	15.57
95% CI	(16.6, 21.3)	(13.29, 18.29)
Hazard ratio	0.77 (0.59, 1.0)	

Calculation based on the KM technique
Event – Endocrine therapy end date before starting chemotherapy, or no other subsequent therapy or death.