What I Tell My Patients:
Integrating New Research Information into Current Clinical Care

A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress

Hormonal Therapy for Hormone Receptor-Positive Breast Cancer

Wednesday, April 24, 2024

6:00 PM – 8:00 PM

Faculty

Harold J Burstein, MD, PhD
Kelly Fischer, MSN, FNP-BC
Komal Jhaveri, MD, FACP
Melissa Rikal, FNP-BC, AOCNP

Moderator

Neil Love, MD

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Faculty

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Dana-Farber Cancer Institute
Professor of Medicine
Harvard Medical School
Boston, Massachusetts

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Dana-Farber Cancer Institute
Boston, Massachusetts

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
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New York, New York

Melissa Rikal, FNP-BC, AOCNP
Nurse Practitioner
Sarah Cannon Research Institute
Nashville, Tennessee

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

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Dr Burstein — Disclosures

No relevant conflicts of interest to disclose

Ms Fischer — Disclosures

No relevant conflicts of interest to disclose

Dr Jhaveri — Disclosures

Advisory Committees and Consulting Agreements	AbbVie Inc, AstraZeneca Pharmaceuticals LP, Blueprint Medicines, Bristol Myers Squibb, Daiichi Sankyo Inc, Eisai Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, Jounce Therapeutics, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Menarini Group, Novartis, Olema Oncology, Pfizer Inc, Scorpion Therapeutics, Seagen Inc, Stemline Therapeutics Inc, Sun Pharma Advanced Research Company, Taiho Oncology Inc
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Ms Rikal — Disclosures

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Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Lilly, and Stemline Therapeutics Inc.

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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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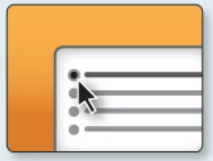
Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

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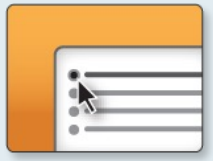
Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get NCPD Credit: An NCPD credit link will be provided in the chat room at the conclusion of the program.

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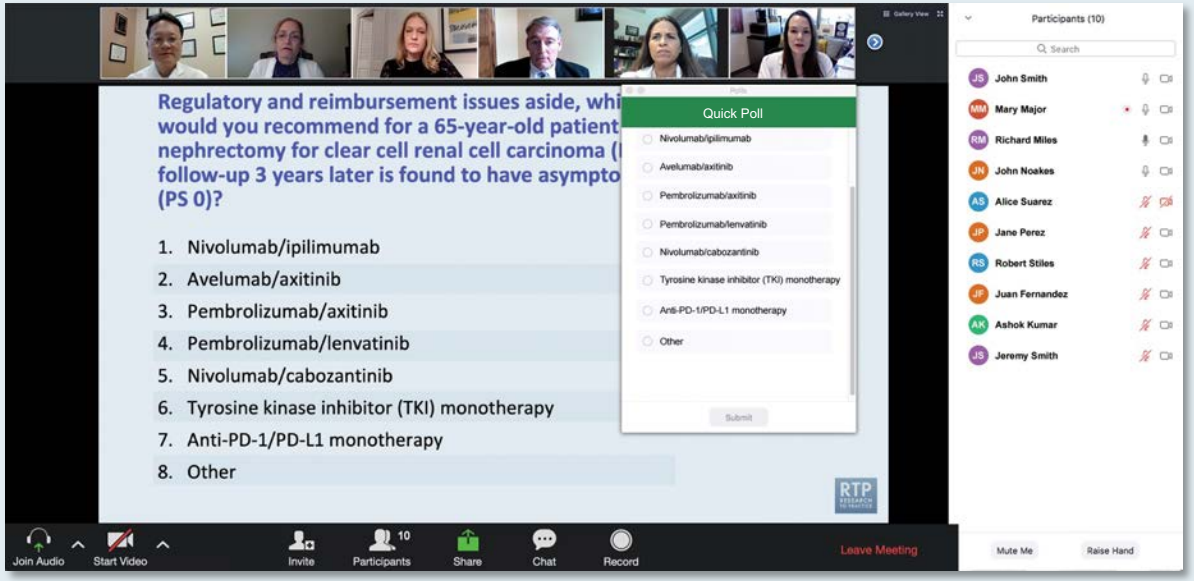
Clinicians, Please Complete the Pre- and Postmeeting Surveys



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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based video/PowerPoint program.
  An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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“What I Tell My Patients”
Sixteenth Annual RTP-ONS NCPD Symposium Series

Wednesday April 24	**Hormone Receptor–Positive Breast Cancer** 6:00 PM – 8:00 PM ET
Thursday April 25	**Endometrial Cancer** 6:00 AM – 7:30 AM ET
	Antibody–Drug Conjugates 12:15 PM – 1:45 PM ET
	Chronic Lymphocytic Leukemia and Bispecific Antibodies in Lymphoma 6:00 PM – 8:00 PM ET
Friday April 26	**Head and Neck Cancer** 6:00 AM – 7:30 AM ET
	Non–Small Cell Lung Cancer with an EGFR Mutation 12:15 PM – 1:45 PM ET
	Ovarian Cancer 6:00 PM – 7:30 PM ET
Saturday April 27	**Hepatobiliary Cancers** 6:00 AM – 7:30 AM ET
	Myelofibrosis 12:15 PM – 1:45 PM ET
	Gastroesophageal and Colorectal Cancers 6:00 PM – 8:00 PM ET
Wednesday, May 1	**LIVE WEBINAR — Prostate Cancer** 7:00 PM – 8:00 PM ET

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ONS 2024 Playlist

Hormonal Therapy for Hormone Receptor-Positive Breast Cancer
Knockin' On Heaven's Door — Bob Dylan, Bob Dylan, *Bob Dylan's Greatest Hits Volume 3*
Moses (Live in Sydney) — Coldplay, Guy Berryman, Jonny Buckland, Will Champion, Chris Martin, *Live 2003*
The Walker — Fitz and the Tantrums, *More Than Just a Dream*
Endometrial Cancer
Simple Man (Remastered) — Bad Company, Mick Ralphs, *Run with the Pack*
Still the Same — Bob Seger & The Silver Bullet Band, Bob Seger, *Stranger in Town*
Runnin' Down a Dream — Tom Petty, Tom Petty, Jeff Lynne, Mike Campbell, *Full Moon Fever*
Optimal Implementation of Antibody-Drug Conjugates
Are You Ready for the Country — Neil Young, Neil Young, *Harvest*
Jammin' Me — Tom Petty and the Heartbreakers, Tom Petty, Bob Dylan, Mike Campbell, *Let Me Up (I've Had Enough)*
Everybody I Love You — Crosby, Stills, Nash & Young, Stephen Stills, Neil Young, *Déjà Vu*
Chronic Lymphocytic Leukemia and Bispecific Antibodies in the Management of Lymphoma
Leaving You (Remastered) — Bad Company, Paul Rodgers, *Burnin' Sky (Deluxe)*
Clocks — Coldplay, Guy Berryman, Jonny Buckland, Will Champion, Chris Martin, *A Rush of Blood to the Head*
Feel Like a Number — Bob Seger & The Silver Bullet Band, Bob Seger, *Stranger in Town*

https://www.ResearchToPractice.com/ONS2024/Playlist

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Head and Neck Cancer
Jane — Jefferson Starship, David Freiberg, Jim McPherson, Craig Chaquico, Paul Kantner, *Freedom at Point Zero*
Sit Yourself Down — Stephen Stills, Stephen Stills, *Stephen Stills*
Brass in Pocket — Pretenders, Chrissie Hynde, James Honeyman-Scott, Pretenders, *The Best of the Pretenders*
Non-Small Cell Lung Cancer with an EGFR Mutation
So Far Away — Dire Straits, Mark Knopfler, *Private Investigations*
City of Blinding Lights — U2, *How to Dismantle an Atomic Bomb*
Victim of Love — Eagles, Don Felder, Don Henley, Glenn Frey, JD Souther, *Hotel California*
Ovarian Cancer
Like Water (Remastered) — Bad Company, Paul Bernard Rodgers, Machi Shimizu, *Burnin' Sky (Deluxe)*
Yellow — Coldplay, Chris Martin, Jonny Buckland, Guy Berryman, Will Champion, *Parachutes*
Almost Cut My Hair — Crosby, Stills, Nash & Young, David Crosby, *Déjà Vu*
Hepatobiliary Cancers
Gimme Shelter — Rolling Stones, Mick Jagger, Keith Richards, *Let It Bleed (50th Anniversary Edition)*
Magic Man — Heart, Ann Wilson, Nancy Wilson, *Dreamboat Annie*
Do — The White Stripes, Jack White, *The White Stripes*

https://www.ResearchToPractice.com/ONS2024/Playlist

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Myelofibrosis
Far Behind — Candlebox, *Candlebox*
Times Like These — Foo Fighters, Dave Grohl, Taylor Hawkins, Nate Mendel, Chris Shiflett, *Greatest Hits*
I'm Finding It Harder to Be a Gentleman — The White Stripes, Jack White, *White Blood Cells*
Gastroesophageal and Colorectal Cancers
Into the Fire — Thirteen Senses, Brendon James, Will South, Tom Welham, Adam Wilson, *The Invitation*
A Sky Full of Stars — Coldplay, Guy Berryman, Jonny Buckland, Will Champion, Chris Martin, Tim Bergling, *Ghost Stories*
Hold On, I'm Comin' — Sam & Dave, Isaac Hayes, David Porter, *Hold On, I'm Comin'*

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Hormonal Therapy for Hormone Receptor-Positive Breast Cancer Faculty

Harold J Burstein, MD, PhD
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Optimal Implementation of Antibody-Drug Conjugates Faculty

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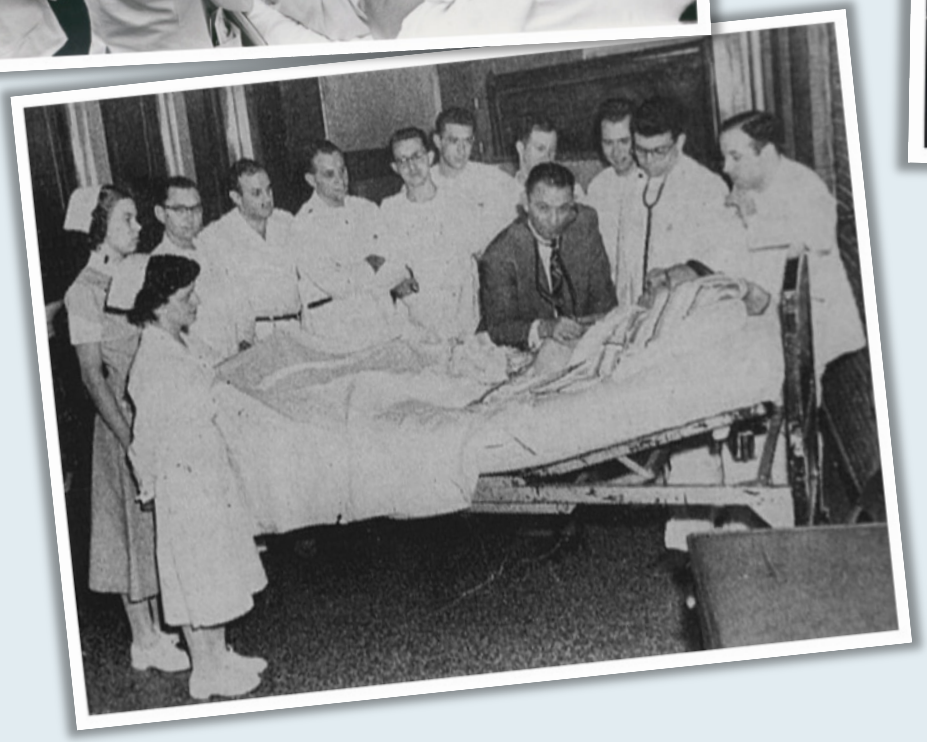

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The Core Oncology Triad
Developing an Individualized Oncology Strategy

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How was it different to take care of this patient versus another patient in the same oncologic setting?

What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

Consulting Nurse Faculty

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Oncology clinical trial terminology

- Waterfall plot
- Kaplan-Meier curve
- Overall survival
- Progression-free survival
- Disease-free survival
- Objective response rate
- Hazard ratio
- Phase I/II/III
- Minimal residual disease
- Circulating tumor DNA

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Neil Love, MD

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Agenda

Introduction

Module 1: The Utility of Genomic Assays in Treatment Decision-Making for HR-Positive, HER2-Negative Localized Breast Cancer

Module 2: The Role of CDK4/6 Inhibitors in Therapy for HR-Positive Breast Cancer

Module 3: Oral Selective Estrogen Receptor Degraders (SERDs) in the Management of HR-Positive Metastatic Breast Cancer (mBC)

Module 4: Alpelisib and Capivasertib in Treatment for HR-Positive mBC

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Consulting Nursing Faculty Comments

New diagnoses and introducing patients to cancer treatment

Sonia Glennie, ARNP, MSN, OCN

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The Utility of Genomic Assays in Treatment Decision-Making for HR-Positive, HER2-Negative Localized Breast Cancer

Dr Burstein
Boston, Massachusetts

Dr Jhaveri
New York, New York

- **Clinicopathologic factors affecting the decision to consult a genomic assay for patients with HR-positive, HER2-negative localized breast cancer**
- **Key studies informing the use of the 21-gene Recurrence Score® to guide neoadjuvant and adjuvant treatment decision-making**
- **Practical interpretation of 21-gene Recurrence Score results**
- **Current clinical utility, if any, of other genomic assays in treating HR-positive localized breast cancer**

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Genomic Assays

Available assays

- Onco*type* DX®
- MammaPrint®
- Prosigna®
- PAM50
- Breast Cancer Index®

Key issues

- Benefit of adding chemotherapy to endocrine therapy for premenopausal and postmenopausal patients

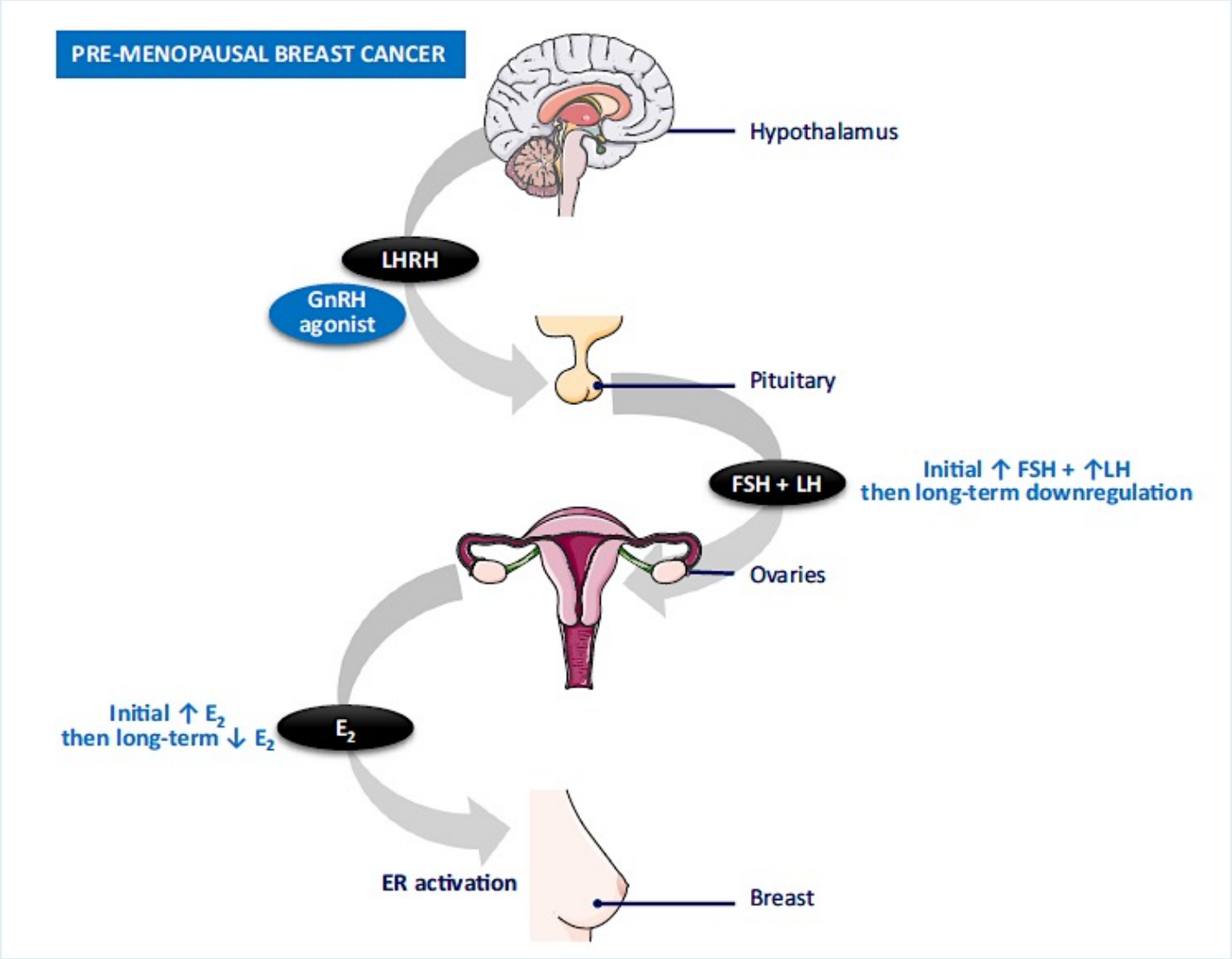
Mechanisms of Action of Hormonal Therapy; Adjuvant Hormonal Therapy for Premenopausal Patients with HR-Positive Breast Cancer

Dr Burstein
Boston, Massachusetts

Dr Jhaveri
New York, New York

- **Individualized selection of an adjuvant hormonal therapy approach for premenopausal patients with breast cancer**
- **Identification of appropriate candidates for ovarian function suppression (OFS)/ablation**
- **Utility of OFS as a means to preserve fertility in premenopausal patients**
- **Frequency and severity of common side effects with various hormonal therapy approaches**

GnRH Agonist Mode of Action in Premenopausal Breast Cancer



McCann KE et al. *NPJ Breast Cancer* 2024;10(1):8.

Kelly Fischer, MSN, FNP-BC

What I tell my patients about to begin various classic hormonal therapies (eg, tamoxifen, aromatase inhibitors, ovarian function suppression)

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Melissa Rikal, FNP-BC, AOCNP

What I tell my patients about the possibility of taking a break from adjuvant hormonal therapy to become pregnant

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Module 4: Alpelisib and Capivasertib in Treatment for HR-Positive mBC

CDK4/6 Inhibitors as Adjuvant Therapy

Dr Burstein
Boston, Massachusetts

Dr Jhaveri
New York, New York

- **Long-term findings with the addition of abemaciclib to adjuvant hormonal therapy for patients with HR-positive, HER2-negative breast cancer at high risk for recurrence**
- **Published data with the addition of ribociclib to adjuvant endocrine therapy for localized HR-positive breast cancer**
- **Identification of candidates for adjuvant CDK4/6 inhibitors**
- **Ongoing studies evaluating CDK4/6 inhibitors as a component of neoadjuvant or adjuvant therapy**

Clinical Trial Updates

Adjuvant Abemaciclib Plus Endocrine Therapy for Hormone Receptor–Positive, Human Epidermal Growth Factor Receptor 2–Negative, High-Risk Early Breast Cancer: Results From a Preplanned monarchE Overall Survival Interim Analysis, Including 5-Year Efficacy Outcomes

Priya Rastogi, MD[1]; Joyce O'Shaughnessy, MD[2]; Miguel Martin, MD[3]; Frances Boyle, MD[4]; Javier Cortes, MD[5]; Hope S. Rugo, MD[6]; Matthew P. Goetz, MD[7]; Erika P. Hamilton, MD[8]; Chiun-Sheng Huang, MD[9]; Elzbieta Senkus, MD[10]; Alexey Tryakin, MD[11]; Irfan Cicin, MD[12]; Laura Testa, MD[13]; Patrick Neven, MD[14]; Jens Huober, MD[15]; Zhimin Shao, MD[16]; Ran Wei, PhD[17]; Valérie André, PhD[17]; Maria Munoz, PhD[17]; Belen San Antonio, PhD[17]; Ashwin Shahir, MD[17]; Nadia Harbeck, MD[18]; and Stephen Johnston, MD[19]

J Clin Oncol 2024;42(9):987-93.

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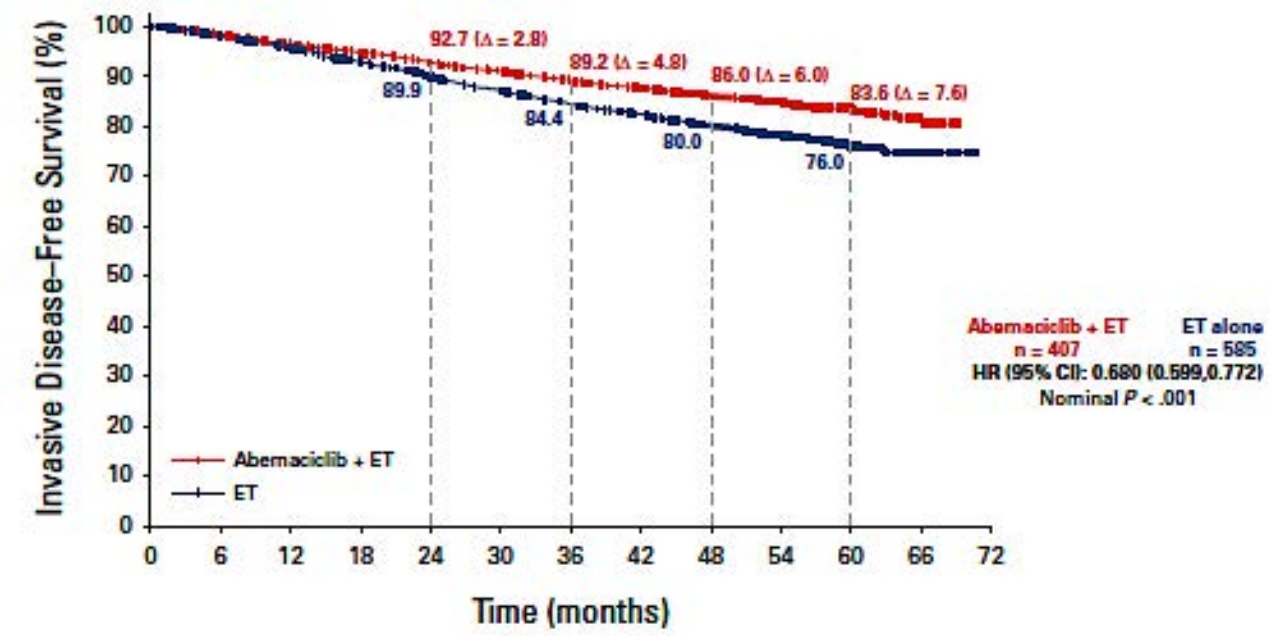
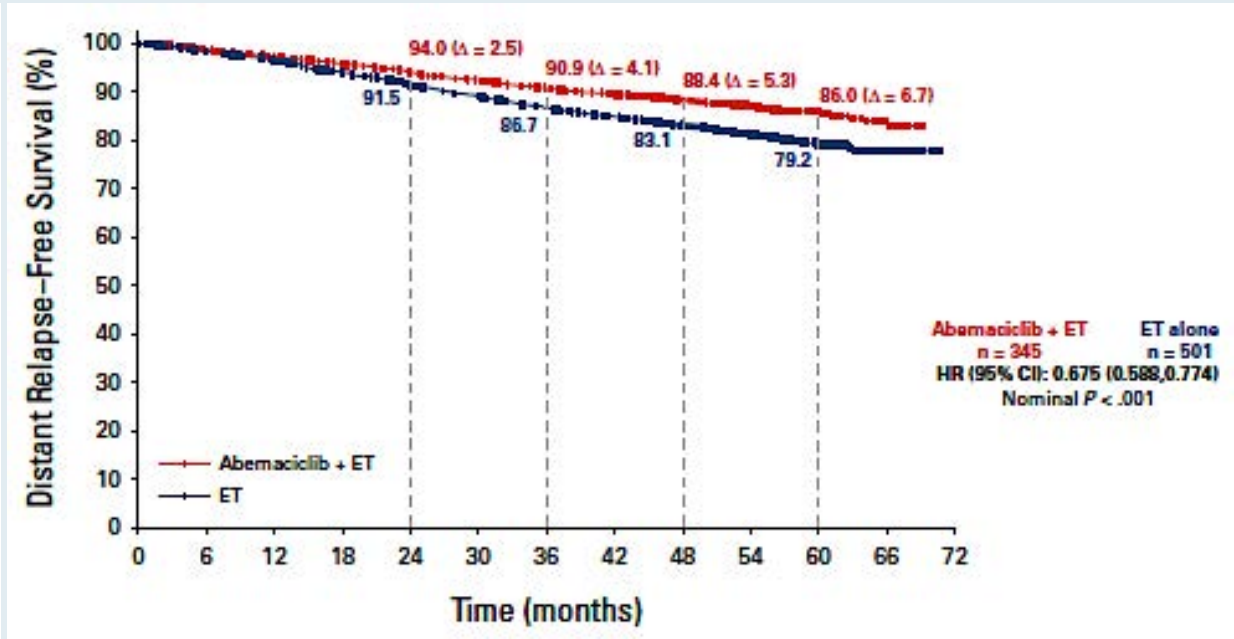
monarchE Trial: Invasive Disease-Free Survival and Distant Relapse-Free Survival

IDFS



DRFS



ET = endocrine therapy

Rastogi P et al. *J Clin Oncol* 2024;42(9):987-93.

monarchE: Adverse Events in ≥10% of Patients

Abemaciclib + ET (N = 2791)			ET alone (N = 2800)	
n (%)	Any Grade	Grade ≥3	Any grade	Grade ≥3
Diarrhea	2331 (83.5)	219 (7.8)	242 (8.6)	6 (0.2)
Infections	1429 (51.2)	155 (5.6)	1102 (39.4)	83 (3.0)
Neutropenia	1278 (45.8)	546 (19.6)	157 (5.6)	23 (0.8)
Fatigue	1133 (40.6)	80 (2.9)	499 (17.8)	4 (0.1)
Nausea	824 (29.5)	14 (0.5)	252 (9.0)	2 (0.1)
Anemia	681 (24.4)	57 (2.0)	104 (3.7)	10 (0.4)
Headache	546 (19.6)	8 (0.3)	421 (15.0)	5 (0.2)
Vomiting	491 (17.6)	15 (0.5)	130 (4.6)	3 (0.1)
Stomatitis	385 (13.8)	4 (0.1)	151 (5.4)	0 (0.0)
Thrombocytopenia	373 (13.4)	36 (1.3)	52 (1.9)	4 (0.1)
Decreased appetite	329 (11.8)	16 (0.6)	68 (2.4)	2 (0.1)
Alopecia	313 (11.2)	N/A	75 (2.7)	0 (0.0)
ALT	343 (12.3)	77 (2.8)	157 (5.6)	19 (0.7)
AST	330 (11.8)	52 (1.9)	137 (4.9)	15 (0.5)
Rash	312 (11.2)	11 (0.4)	127 (4.5)	0 (0.0)
ILD	**89 (3.2)**	**11 (0.4)**	**37 (1.3)**	**1 (0.0)**

Rugo HS et al. *Ann Oncol.* 2022; 33: 616-627

CDK4/6 Inhibitors

Agent	Current indications and usage for ER-positive, HER2-negative breast cancer
Palbociclib	• With an aromatase inhibitor (AI) as initial endocrine-based therapy for advanced or metastatic disease • With fulvestrant for advanced or metastatic disease after disease progression on endocrine therapy
Ribociclib	• With an AI as initial endocrine-based therapy for pre/peri/postmenopausal women or men with advanced or metastatic disease • With fulvestrant as initial endocrine-based therapy or after disease progression on endocrine therapy for postmenopausal women or men with advanced or metastatic disease
Abemaciclib	• **With endocrine therapy as adjuvant treatment for node-positive localized breast cancer at high risk of recurrence** • As monotherapy for advanced or metastatic disease with disease progression after endocrine therapy and prior chemotherapy in the metastatic setting • With fulvestrant after disease progression on endocrine therapy for adult patients with advanced or metastatic disease • With an AI as initial endocrine-based therapy for postmenopausal women and men with advanced or metastatic disease

RTP RESEARCH TO PRACTICE

Consulting Nursing Faculty Comments

The patient with disease relapse after adjuvant treatment

Ronald Stein, JD, MSN, NP-C, AOCNP

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RESEARCH
TO PRACTICE

CDK4/6 Inhibitors for Metastatic Breast Cancer (mBC)

Dr Burstein
Boston, Massachusetts

Dr Jhaveri
New York, New York

- **Long-term follow-up data, including overall survival findings, with abemaciclib, palbociclib and ribociclib for patients with HR-positive mBC**
- **Factors affecting the selection of a CDK4/6 inhibitor and an endocrine partner for premenopausal and postmenopausal patients**
- **Role of CDK4/6 inhibitors in treatment for unique patient populations, such as those with aggressive visceral disease or central nervous system metastases**
- **Available data on the utility of continuing CDK4/6 inhibitors beyond progression or rechallenge in later lines of therapy; current clinical role of this strategy**

Side Effects of CDK4/6 Inhibitors

Dr Burstein
Boston, Massachusetts

Dr Jhaveri
New York, New York

- **Spectrum and frequency of clinically relevant hematologic and nonhematologic toxicities, including cytopenias, gastrointestinal (GI) events, interstitial lung disease/pneumonitis and venous thromboembolic events, with CDK4/6 inhibitors**
- **Optimal monitoring for and management of CDK4/6 inhibitor-associated toxicities**
- **Role of switching between CDK4/6 inhibitors for patients experiencing tolerability issues**
- **Comparative tolerability of CDK4/6 inhibitors in the adjuvant versus metastatic settings; appropriate threshold for dose reduction/delay or treatment discontinuation for patients undergoing potentially curative therapy**

Kelly Fischer, MSN, FNP-BC

What I tell my patients about to begin treatment with a CDK4/6 inhibitor

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Agenda

Introduction

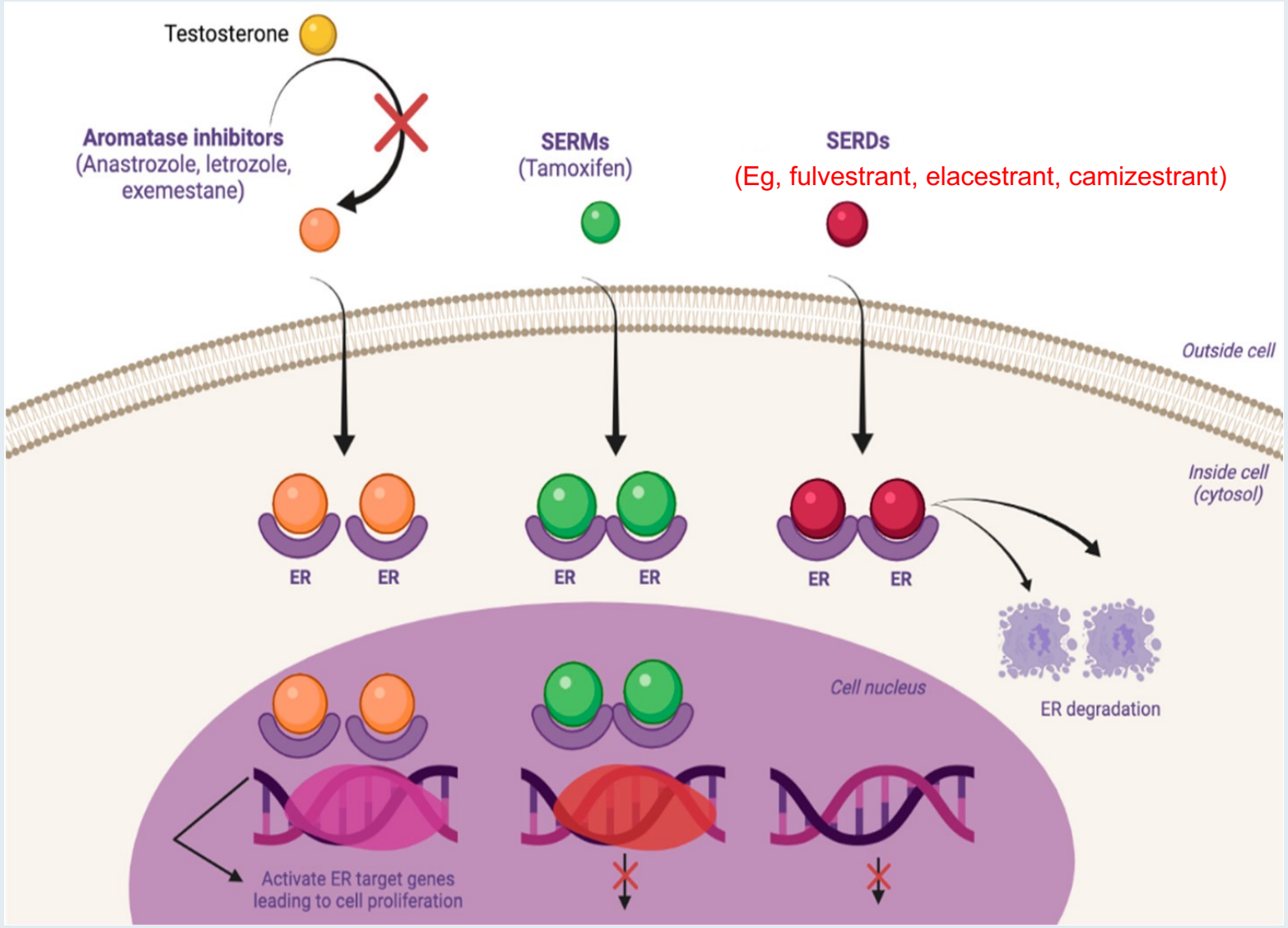
Module 1: The Utility of Genomic Assays in Treatment Decision-Making for HR-Positive, HER2-Negative Localized Breast Cancer

Module 2: The Role of CDK4/6 Inhibitors in Therapy for HR-Positive Breast Cancer

Module 3: Oral Selective Estrogen Receptor Degraders (SERDs) in the Management of HR-Positive Metastatic Breast Cancer (mBC)

Module 4: Alpelisib and Capivasertib in Treatment for HR-Positive mBC

Mechanism of Action of Different Endocrine Therapies



Hernando C et al. *Int J Mol Sci* 2021;22:7812.

RTP RESEARCH TO PRACTICE

Oral Selective Estrogen Receptor Degraders (SERDs) in the Management of HR-Positive mBC

Dr Burstein
Boston, Massachusetts

Dr Jhaveri
New York, New York

- **Prevalence of ESR1 mutations in HR-positive mBC; optimal timing and approach to testing**
- **Major findings with elacestrant versus endocrine monotherapy for pretreated HR-positive, HER2-negative mBC; outcomes among patients with and without ESR1 mutations**
- **FDA approval of elacestrant for postmenopausal patients with HR-positive, HER2-negative mBC with an ESR1 mutation; optimal incorporation into current management algorithms**
- **Available findings with and ongoing evaluation of other oral SERDs, such as camizestrant and imlunestrant, alone and in combination with other systemic therapies for advanced HR-positive, HER2-negative breast cancer**

Elacestrant

Mechanism of action

- **Oral SERD (selective estrogen receptor degrader)**

Indication

- **For postmenopausal women or adult men with ER-positive, HER2-negative, advanced or metastatic breast cancer with an ESR1 mutation and disease progression after at least 1 line of endocrine therapy**

Recommended dose

- **One 345-mg tablet po qd, with food**

Elacestrant package insert, 11/2023.

Camizestrant

Mechanism of action

- **Oral SERD**

Indication

- **Investigational**

Key clinical trial

- **Phase II SERENA-2 trial evaluating camizestrant in postmenopausal women with locally advanced or metastatic ER-positive, HER2-negative breast cancer previously treated with endocrine therapy**

Oliveira M et al. SABCS 2022;Abstract GS3-02.

Imlunestrant

Mechanism of action

- **Oral SERD**

Indication

- **Investigational**

Key clinical trial

- **Phase Ia/Ib EMBER trial evaluating imlunestrant monotherapy for patients with ER-positive, HER2-negative advanced breast cancer**
- **Phase III EMBER-3 trial evaluating imlunestrant, investigator's choice of endocrine therapy, and imlunestrant with abemaciclib for patients with ER-positive, HER2-negative advanced breast cancer**

Jhaveri KL et al. *JCO* 40, 1021-1021(2022). Jhaveri K et al. SABCS 2021;Abstract OT2-11-01.

RTP RESEARCH TO PRACTICE

Tolerability/Toxicity Profile of Oral SERDs

Dr Burstein
Boston, Massachusetts

Dr Jhaveri
New York, New York

- **Spectrum and incidence of common adverse events observed with oral SERDs; comparative side-effect profiles of approved and investigational agents in this class**
- **Pathophysiology of the hyperlipidemia observed with elacestrant; optimal monitoring of lipid profiles and other laboratory values in patients receiving oral SERDs**
- **Recommended prophylaxis for and management of GI toxicities associated with elacestrant**
- **Strategies to encourage adherence among patients with HR-positive, HER2-negative mBC receiving oral SERDs**

Melissa Rikal, FNP-BC, AOCNP

What I tell my patients about to begin treatment with elacestrant

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Agenda

Introduction

Module 1: The Utility of Genomic Assays in Treatment Decision-Making for HR-Positive, HER2-Negative Localized Breast Cancer

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Module 3: Oral Selective Estrogen Receptor Degraders (SERDs) in the Management of HR-Positive Metastatic Breast Cancer (mBC)

Module 4: Alpelisib and Capivasertib in Treatment for HR-Positive mBC

RTP RESEARCH TO PRACTICE

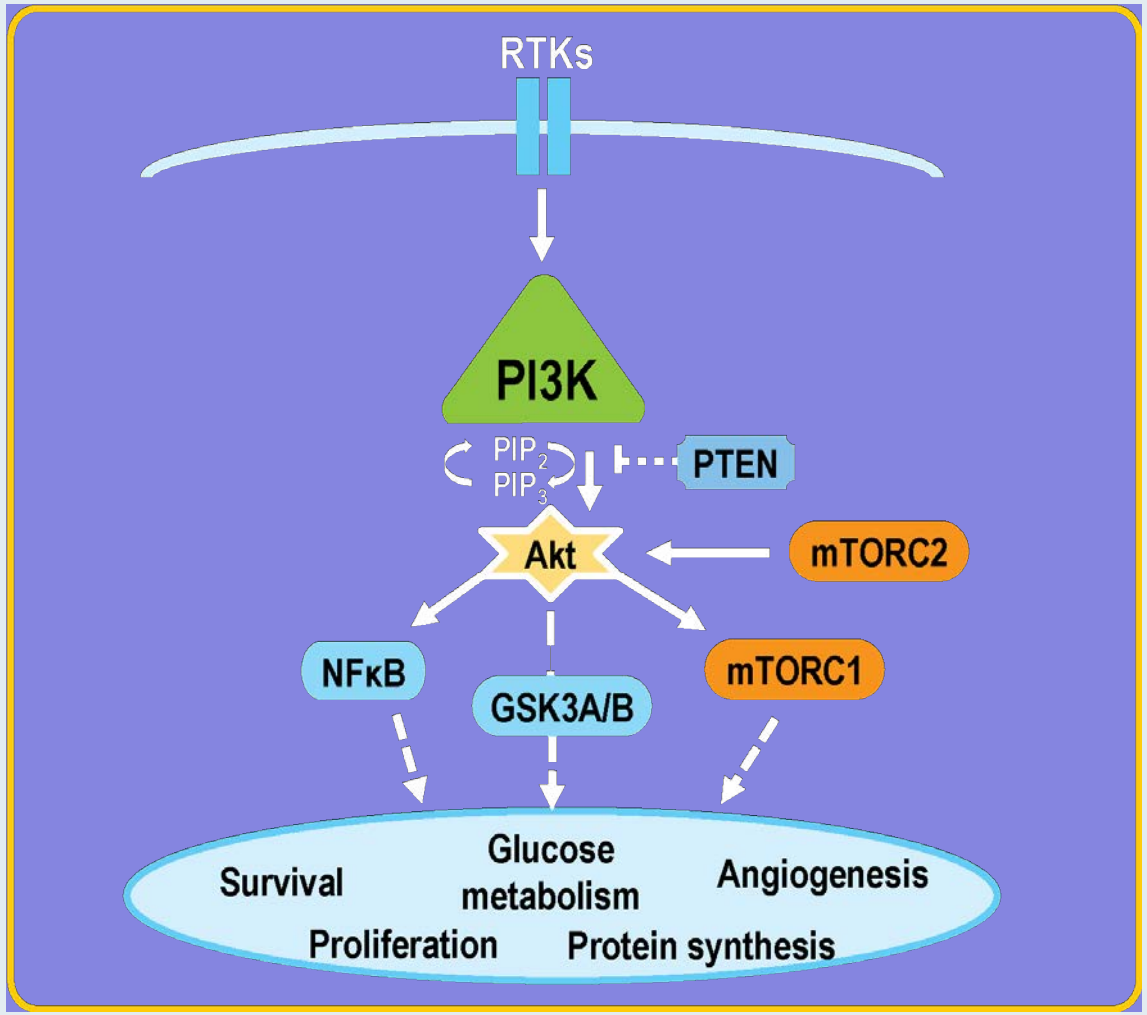
Role of Alpelisib in Treatment for HR-Positive mBC

Dr Burstein
Boston, Massachusetts

Dr Jhaveri
New York, New York

- **Prevalence of PIK3CA mutations in HR-positive mBC; published research findings with alpelisib-based therapy in this population**
- **Optimal incorporation of alpelisib-based therapy into current management algorithms**
- **Incidence and severity of common toxicities associated with alpelisib, such as hyperglycemia, GI-related adverse events (AEs) and cutaneous AEs**
- **Appropriate strategies to monitor for, prevent and manage alpelisib-related toxicities**

PI3 Kinase Inhibitors: Mechanism of Action



- PI3K is involved in the activation of AKT.
- Hyperactivation of the PI3K pathway is implicated in malignant transformation, cancer progression and endocrine therapy resistance.
- PIK3CA encodes the alpha isoform of the PI3K catalytic subunit.
- Around 40% of patients with HR-positive, HER2-negative breast cancer present with an activating PIK3CA tumor mutation.
- Alpelisib is a specific inhibitor of the PI3K alpha isoform.

André F et al. ESMO 2018;Abstract LBA3_PR.

Alpelisib

Mechanism of action

- **PI3K inhibitor**

Indication

- **In combination with fulvestrant for adults with HR-positive, HER2-negative, PIK3CA-mutated advanced or metastatic breast cancer as detected by an FDA-approved test after disease progression on or after an endocrine-based regimen**

Recommended dose

- **300 mg (two 150-mg tablets) taken orally once daily with food**

Alpelisib package insert, 1/2024.

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Kelly Fischer, MSN, FNP-BC

What I tell my patients about to begin treatment with alpelisib

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Inavolisib Combination Reduces the Risk of Disease Progression by 57% in People With Advanced Hormone Receptor-Positive, HER2-Negative Breast Cancer With a PIK3CA Mutation

Press Release – December 8, 2023

"[The manufacturer] presented today positive results from the Phase III INAVO120 study evaluating inavolisib in combination with palbociclib and fulvestrant as a first-line treatment for people with *PIK3CA*-mutated, hormone receptor (HR)-positive, HER2-negative, endocrine-resistant, locally advanced or metastatic breast cancer.

The inavolisib combination reduced the risk of disease worsening or death (progression-free survival; PFS) by 57% compared to palbociclib and fulvestrant alone. The benefit was consistent across subgroups. Overall survival (OS) data were immature at this time, but a clear positive trend has been observed. Follow-up for OS will continue to the next analysis. Data available for other secondary endpoints at this analysis showed clinically meaningful increases in objective response rate, duration of response and clinical benefit rate.

The inavolisib combination was well tolerated and adverse events were consistent with the known safety profiles of the individual study treatments, with no new safety signals observed.

Inavolisib, an investigational oral therapy, is currently being investigated in three Phase III clinical studies in people with PIK3CA-mutated locally advanced or metastatic breast cancer (INAVO120, INAVO121, INAVO122). Data from the INAVO120 study will be submitted to health authorities with the view of bringing this potential treatment option to patients as soon as possible."

https://finance.yahoo.com/news/genentech-inavolisib-combination-reduces-risk-164500740.html

Capivasertib and Its Use in the Management of HR-Positive mBC

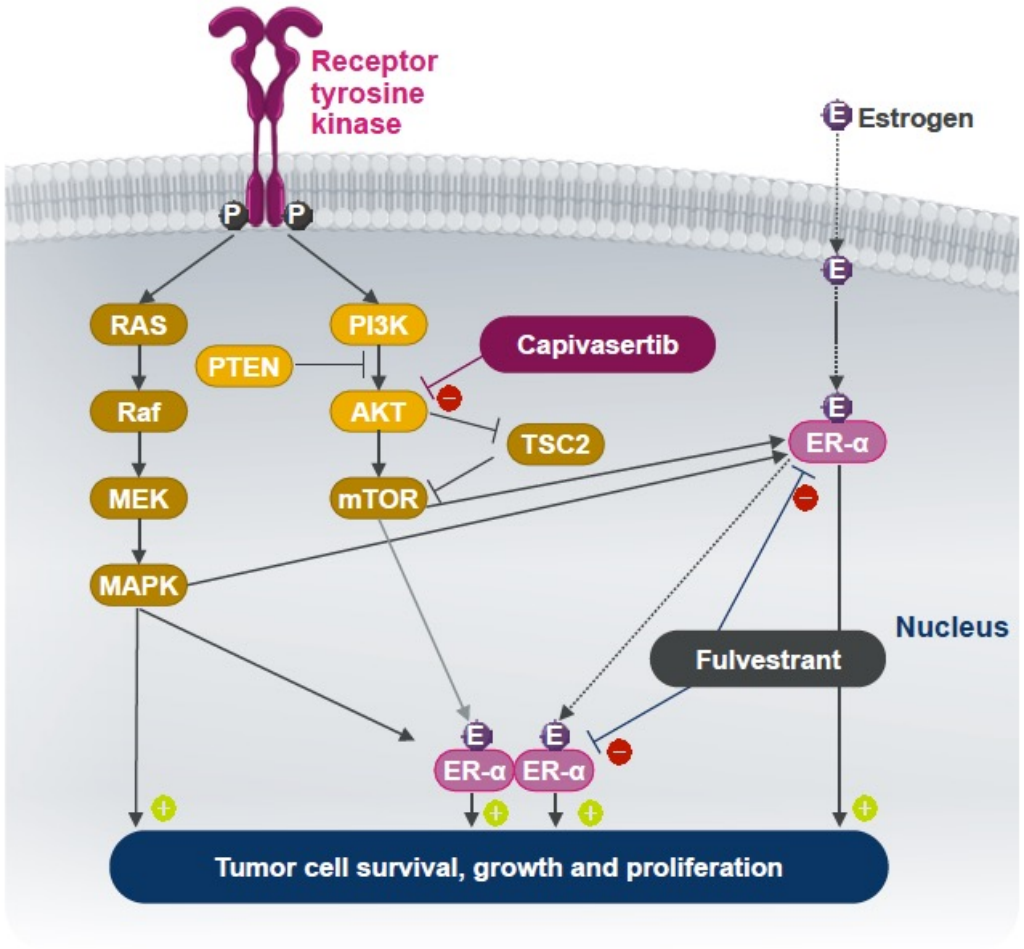
Dr Burstein
Boston, Massachusetts

Dr Jhaveri
New York, New York

- **Biological rationale for inhibiting AKT in HR-positive mBC; mechanism of action of capivasertib**
- **Key efficacy and safety data with capivasertib/fulvestrant for recurrent HR-positive, HER2-negative mBC**
- **FDA approval of capivasertib/fulvestrant for patients with HR-positive, HER2-negative locally advanced or metastatic breast cancer with 1 or more PIK3CA/AKT1/PTEN alterations who experience disease progression on at least 1 endocrine-based regimen in the metastatic setting or recurrence on or within 12 months of completing adjuvant therapy**
- **Optimal approach to PIK3CA/AKT1/PTEN testing and integration of capivasertib/fulvestrant into current treatment algorithms**

Capivasertib Mechanism of Action

- AKT pathway activation occurs in many HR+/HER2– ABC through alterations in *PIK3CA, AKT1 and PTEN*, but may also occur in cancers without those genetic alterations.[1,2] AKT signalling is also implicated in the development of resistance to endocrine therapy[2]
- Capivasertib is a potent, selective inhibitor of all three AKT isoforms (AKT1/2/3)



Turner NC et al. SABCS 2022;Abstract GS3-04.

Capivasertib

Mechanism of action

- **AKT inhibitor**

Indication

- **In combination with fulvestrant for patients with HR-positive, HER2-negative locally advanced or metastatic breast cancer with 1 or more PIK3CA/AKT1/PTEN alterations, as detected by an FDA-approved test, after disease progression on at least 1 endocrine-based regimen in the metastatic setting or recurrence on or within 12 months of completing adjuvant therapy**

Recommended dose

- **400 mg PO BID, with or without food, for 4 days followed by 3 days off**

Capivasertib package insert, 11/2023.

RTP RESEARCH TO PRACTICE

FDA Approves Capivasertib with Fulvestrant for Breast Cancer

Press Release – November 16, 2023

"… the Food and Drug Administration approved capivasertib with fulvestrant for adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer with one or more PIK3CA/AKT1/PTEN-alterations, as detected by an FDA-approved test, following progression on at least one endocrine-based regimen in the metastatic setting or recurrence on or within 12 months of completing adjuvant therapy.

FDA also approved the FoundationOne®CDx assay as a companion diagnostic device to identify patients with breast cancer for treatment with capivasertib with fulvestrant.

Efficacy was evaluated in CAPItello-291 (NCT04305496), a randomized, double-blind, placebo-controlled, multicenter trial in 708 patients with locally advanced or metastatic HR-positive, HER2-negative breast cancer, of which 289 patients had tumors with PIK3CA/AKT1/PTEN-alterations. All patients were required to have progression on aromatase inhibitor-based treatment. Patients could have received up to two prior lines of endocrine therapy and up to 1 line of chemotherapy for locally advanced or metastatic disease."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-capivasertib-fulvestrant-breast-cancer

RTP RESEARCH TO PRACTICE

Side Effects and Other Practical Considerations with Capivasertib

Dr Burstein
Boston, Massachusetts

Dr Jhaveri
New York, New York

- **Spectrum, frequency and severity of toxicities associated with capivasertib**
- **Incidence of hyperglycemia in patients receiving capivasertib; indications for blood glucose monitoring and role, if any, in treatment for those with preexisting diabetes**
- **Recommending monitoring and treatment strategies for patients experiencing diarrhea while receiving capivasertib**
- **Pathophysiology, spectrum and optimal treatment of cutaneous adverse reactions with capivasertib**
- **Dose, schedule and recommended approach to dose reductions with capivasertib**

Melissa Rikal, FNP-BC, AOCNP

What I tell my patients about to begin treatment with capivasertib

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What I Tell My Patients: Integrating New Research Information into Current Clinical Care

A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress

Optimal Implementation of Antibody-Drug Conjugates

Thursday, April 25, 2024
12:15 PM – 1:45 PM

Faculty

Jamie Carroll, APRN, MSN, CNP
Kelly EH Goodwin, MSN, RN, ANP-BC
Erika Hamilton, MD
Hope S Rugo, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Consulting Nursing Faculty Comments

Preventing professional burnout

Jessica Mitchell, APRN, CNP, MPH

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APPENDIX

The Utility of Genomic Assays in Treatment Decision-Making for HR-Positive, HER2-Negative Localized Breast Cancer

RTP
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San Antonio Breast Cancer Symposium – December 6-10, 2022

Trial Assigning IndividuaLized Options for TReatment (TAILORx): An Update Including 12-Year Event Rates

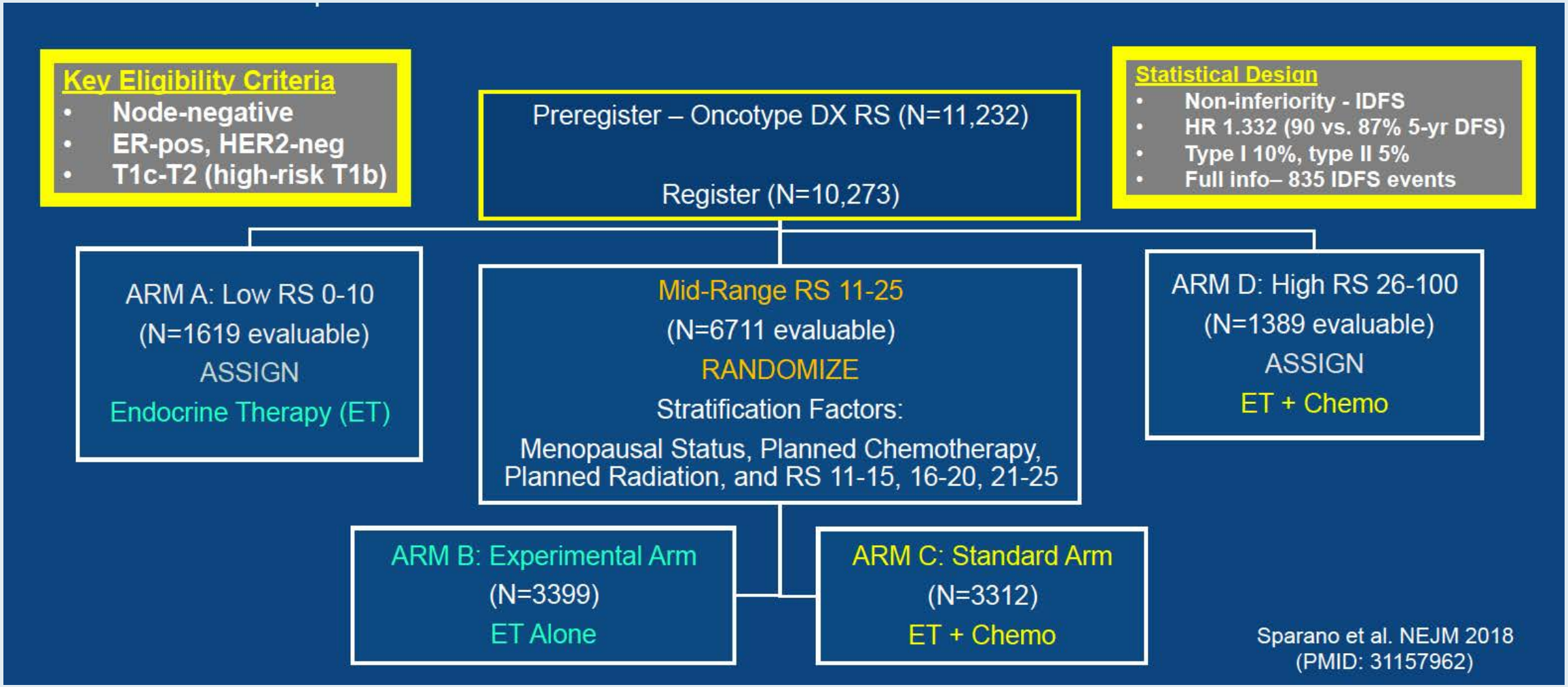
Abstract GS1-05

Joseph A. Sparano, Robert J. Gray, Della F. Makower, Kathy S. Albain, Daniel F. Hayes, Charles E. Geyer, Elizabeth Claire Dees, Matthew P. Goetz, John A. Olson, Jr., Tracy G. Lively, Sunil Badve, Thomas J. Saphner, Timothy J. Whelan, Virginia Kaklamani, & George W. Sledge, Jr.

on behalf of the TAILORx Investigators

Funding: U.S. NIH/NCI U10CA180820, U10CA180794, UG1CA189859, UG1CA190140, UG1CA233160, UG1CA23337, UG1CA189869; U.S. Postal Service Breast Cancer Stamp Fund; Canadian Cancer Society Research Institute grants 015469, 021039; Breast Cancer Research Foundation, Komen Foundation.

TAILORx Study Design: Treatment Assignment and Randomization



RS = Recurrence Score

Sparano JA et al. SABCS 2022;Abstract GS1-05.

RTP RESEARCH TO PRACTICE

TAILORx Updated Analysis: Conclusions

- Longer median followup and more events in randomized group
  - Median 11.0 vs. 7.5 years
  - IDFS (1295 vs. 836) and DRFI (375 vs. 250) events
- Main study findings unchanged for RS 11-25 arms (primary objective)
  - ET non-inferior to CET for IDFS (primary endpoint) and DRFI (secondary endpoint)
  - RFI and OS also similar between treatment arms (exploratory endpoints)
- Other exploratory key study findings also similar to original analysis
  - Chemotherapy benefit for women ≤ 50 with RS 21-25
  - Some chemotherapy benefit for women ≤ 50 with RS 16-20 and high clinical risk
- New findings of updated analyses (exploratory)
  - Late recurrences > 5 years exceed early recurrence
  - Racial disparities for black women associated with early but not late recurrence

Sparano JA et al. SABCS 2022;Abstract GS1-05.

San Antonio Breast Cancer Symposium®, December 7-10, 2021

Abstract GS2-07

RxPONDER: A Clinical Trial Rx for Positive Node, Endocrine Responsive Breast Cancer

Updated results from a phase 3 randomized clinical trial in participants (pts) with 1-3 positive lymph nodes, hormone receptor-positive (HR+) and HER2-negative breast cancer with recurrence score of 25 or less: SWOG S1007

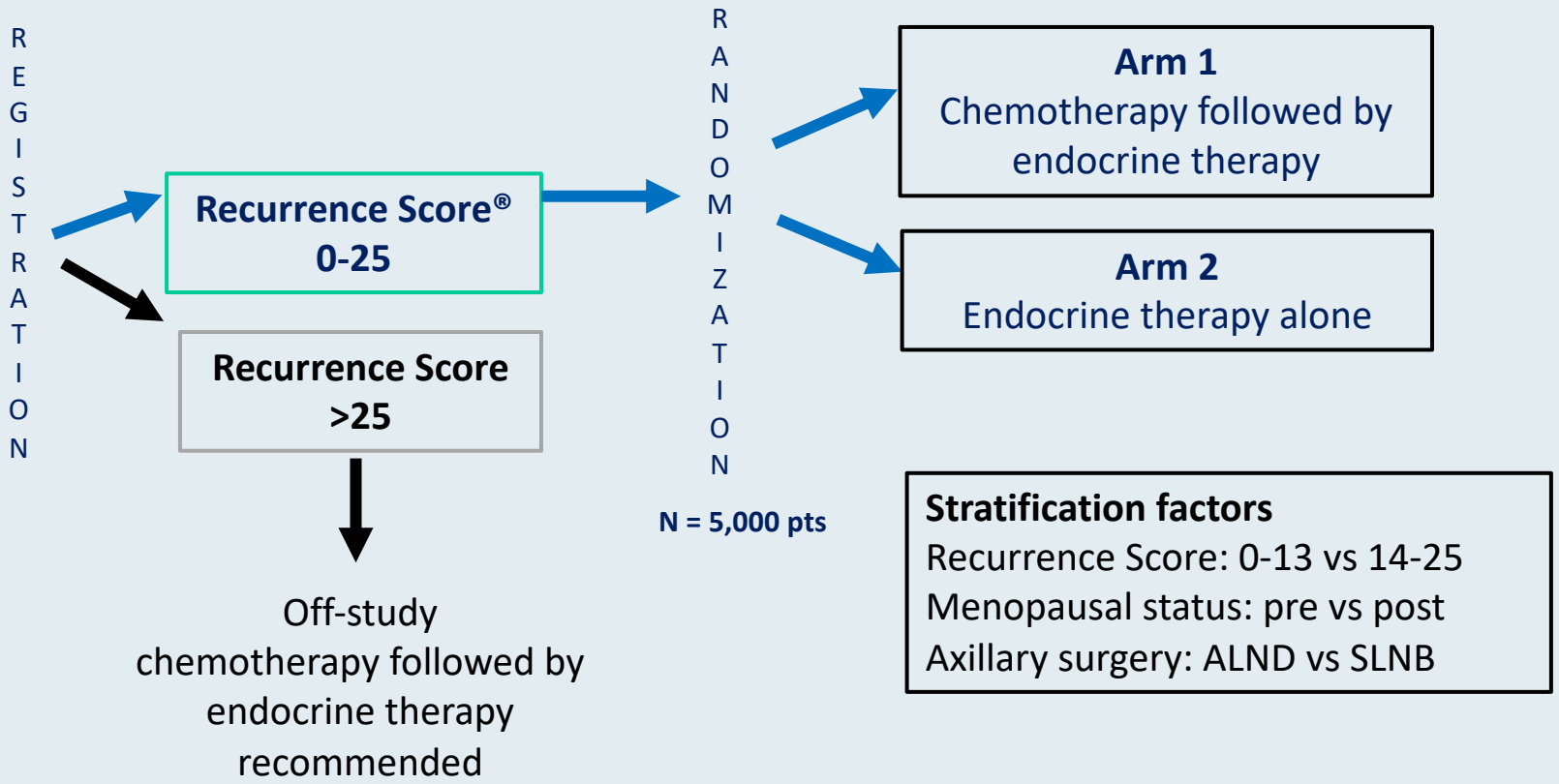
Kevin Kalinsky, William E Barlow, Julie R Gralow, Funda Meric-Bernstam, Kathy S Albain, Daniel F Hayes, Nancy U Lin, Edith A Perez, Lori J Goldstein, Stephen K Chia, Sukhbinder Dhesy-Thind, Priya Rastogi, Emilio Alba, Suzette Delaloge, Miguel Martin, Catherine M Kelly, Manuel Ruiz-Borrego, Miguel Gil Gil, Claudia Arce-Salinas, Etienne G.C. Brain, Eun Sook Lee, Jean-Yves Pierga, Begoña Bermejo, Manuel Ramos-Vazquez, Kyung Hae Jung, Jean-Marc Ferrero, Anne F. Schott, Steven Shak, Priyanka Sharma, Danika L. Lew, Jieling Miao, Debasish Tripathy, Lajos Pusztai, Gabriel N. Hortobagyi

On Behalf of the RxPonder Investigators

RxPONDER Trial Schema

Key Entry Criteria

- Women age ≥18
- ER and/or PR ≥1%, HER2-negative breast cancer with 1*-3 positive LN without distant metastasis
- Ability to receive adjuvant taxane and/or anthracycline-based chemotherapy†
- Axillary staging by SLNB or ALND



LN = lymph nodes; SLNB = sentinel lymph node biopsy; ALND = axillary lymph node dissection

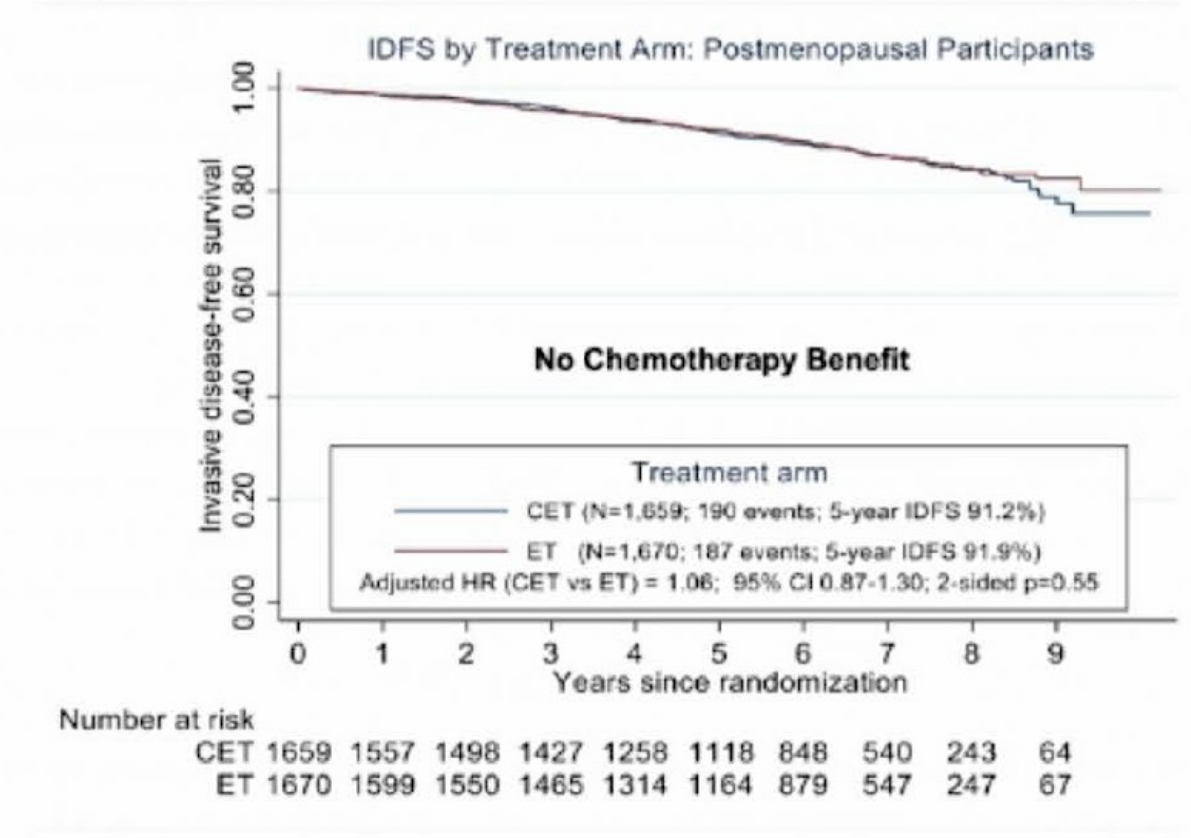
* After randomization of 2,493 pts, the protocol was amended to exclude enrollment of pts with pN1mic as only nodal disease.

† Approved chemotherapy regimens included TC, FAC (or FEC), AC/T (or EC/T), FAC/T (or FEC/T). AC alone or CMF not allowed.

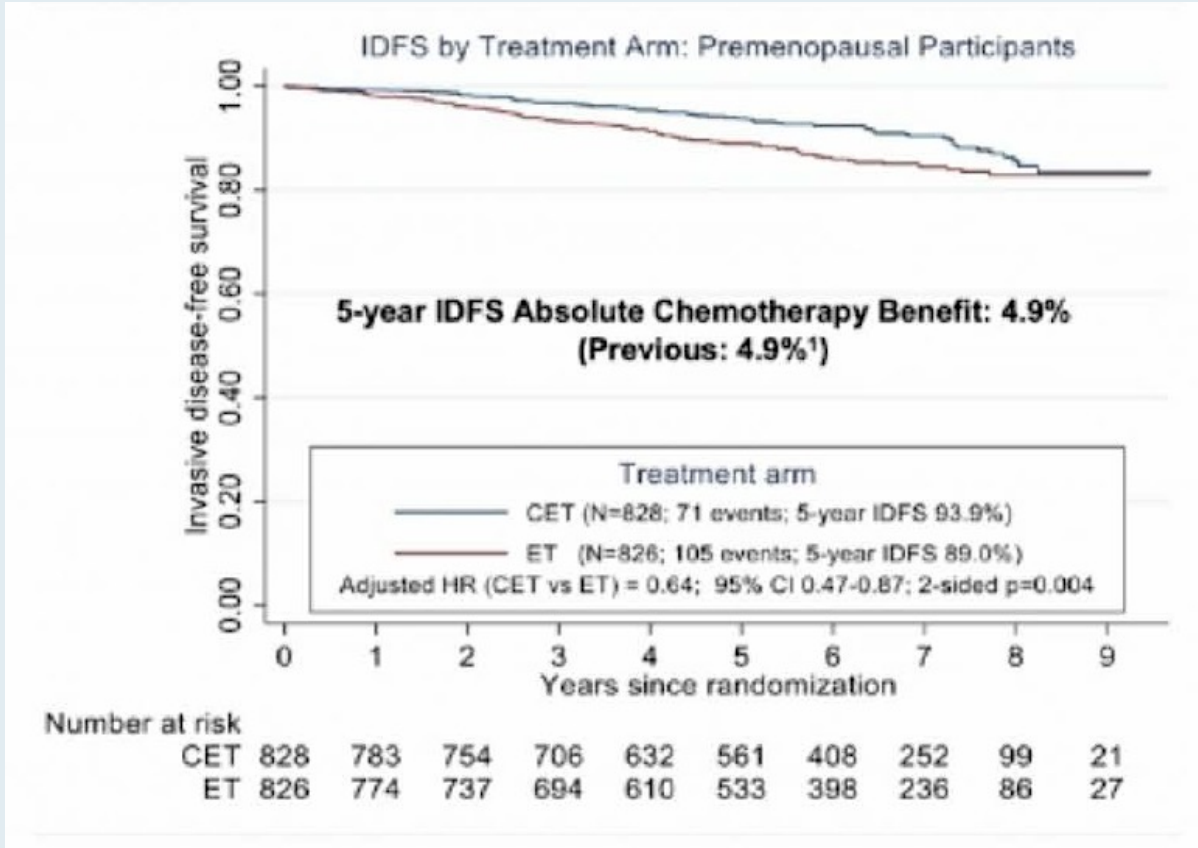
Kalinsky K et al. SABCS 2020;Abstract GS3-00.

RxPONDER Updated Analysis: IDFS Stratified by Menopausal Status

Postmenopausal



Premenopausal



IDFS = invasive disease-free survival; CET = chemotherapy followed by endocrine therapy; ET = endocrine therapy

Kalinsky K et al. SABCS 2021;Abstract GS2-07.

RTP RESEARCH TO PRACTICE

J Clin Oncol 2022;40(16):1816-37.

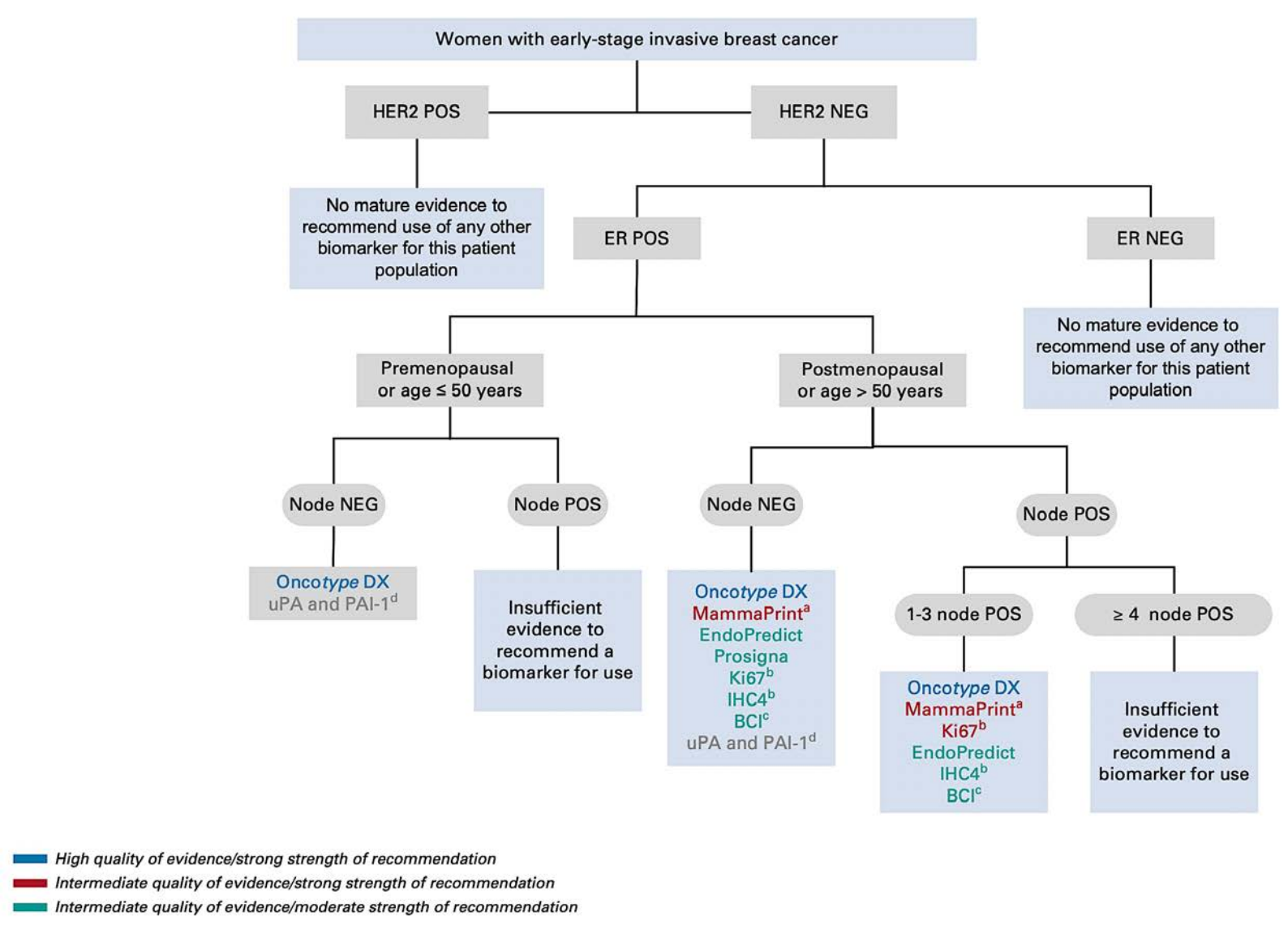
ASCO special articles

Biomarkers for Adjuvant Endocrine and Chemotherapy in Early-Stage Breast Cancer: ASCO Guideline Update

Fabrice Andre, MD[1]; Nofisat Ismaila, MD, MSc[2]; Kimberly H. Allison, PhD[3]; William E. Barlow, PhD[4]; Deborah E. Collyar, BSc[5]; Senthil Damodaran, MD, PhD[6]; N. Lynn Henry, MD, PhD[7]; Komal Jhaveri, MD[8,9]; Kevin Kalinsky, MD, MS[10]; Nicole M. Kuderer, MD[11]; Anya Litvak, MD[12]; Erica L. Mayer, MD, MPH[13]; Lajos Pusztai, MD[14]; Rachel Raab, MD[15]; Antonio C. Wolff, MD[16]; and Vered Stearns, MD[16]

RTP RESEARCH TO PRACTICE

Biomarkers for Adjuvant Endocrine Therapy and Chemotherapy in Localized Breast Cancer: ASCO Guideline Update



Andre F et al. *J Clin Oncol* 2022;40(16):1816-37.

RTP RESEARCH TO PRACTICE

NCCN Guidelines: Gene Expression Assays for Consideration of Adjuvant Systemic Therapy

Assay	Predictive	Prognostic	NCCN Category of Preference	NCCN Category of Evidence and Consensus
21-gene (Onco*type* DX®) (for pN0)	Yes	Yes	Preferred	1
21-gene (Onco*type* DX®) for pN1 (1–3 positive nodes)[c]	Yes	Yes	Postmenopausal: Preferred	1
			Premenopausal: Other	2A
70-gene (MammaPrint®) for pN0 and pN1 (1–3 positive nodes)	Not determined	Yes	Other	1
50-gene (Prosigna®) for pN0 and pN1 (1–3 positive nodes)	Not determined	Yes	Other	2A
12-gene (EndoPredict®) for pN0 and pN1 (1–3 positive nodes)	Not determined	Yes	Other	2A
Breast Cancer Index® (BCI)	Predictive of benefit of extended adjuvant endocrine therapy	Yes	Other	2A

National Comprehensive Cancer Network (NCCN®). NCCN clinical practice guidelines in oncology. Breast cancer — Version 2.2024. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed April 2024.

RTP RESEARCH TO PRACTICE

Oral Selective Estrogen Receptor Degraders (SERDs) in the Management of HR-Positive Metastatic BC (mBC)

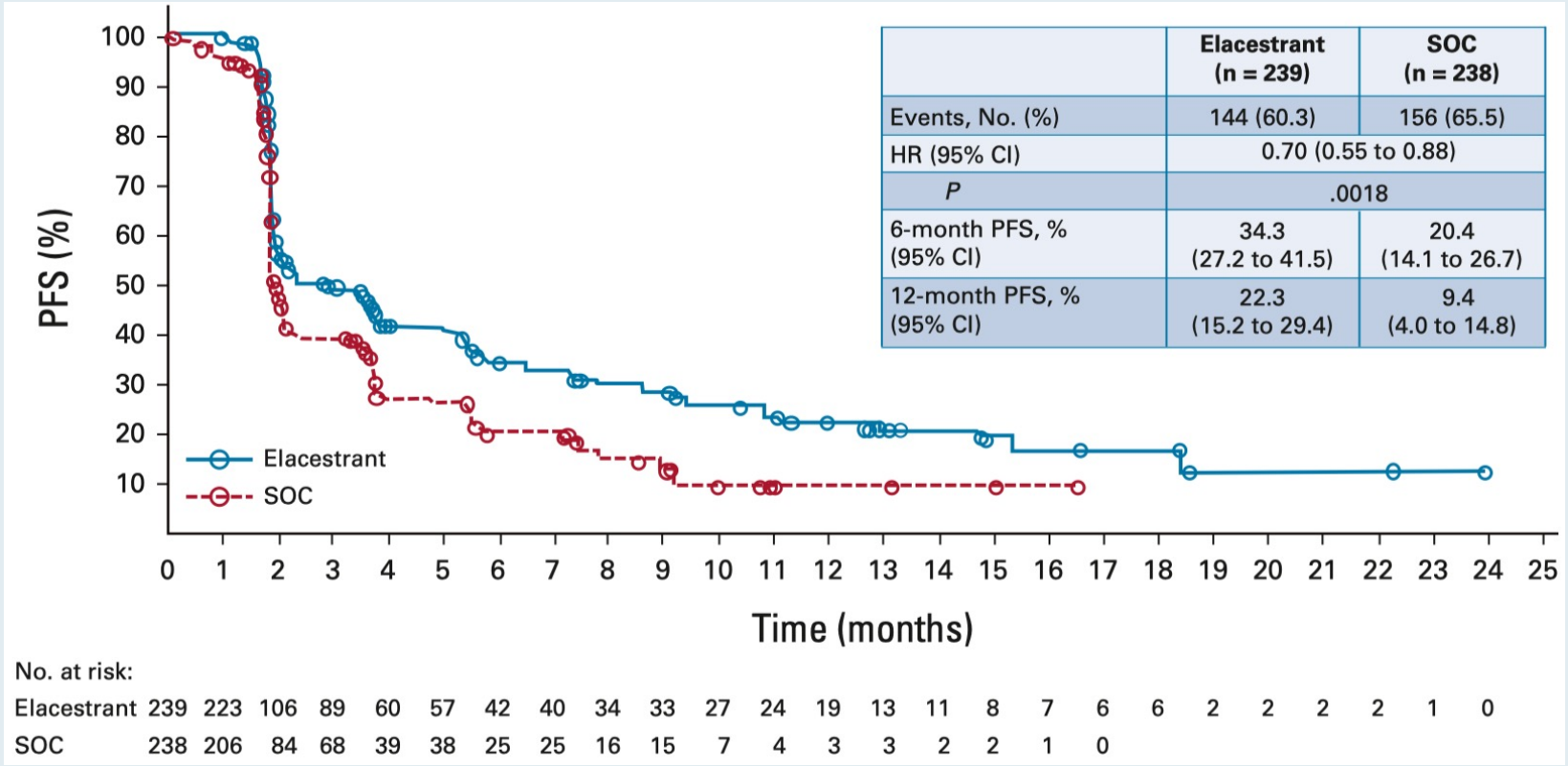
J Clin Oncol 2022;40(28):3246-56.

original reports

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

Francois-Clement Bidard, MD[1,2]; Virginia G. Kaklamani, MD[3]; Patrick Neven, MD[4]; Guillermo Streich, MD[5]; Alberto J. Montero, MD[6]; Frédéric Forget, MD[7]; Marie-Ange Mouret-Reynier, MD[8]; Joo Hyuk Sohn, MD[9]; Donatienne Taylor, MD[10]; Kathleen K. Harnden, MD[11]; Hung Khong, MD[12]; Judit Kocsis, MD[13]; Florence Dalenc, MD[14]; Patrick M. Dillon, MD[15]; Sunil Babu, MD[16]; Simon Waters, MD[17]; Ines Deleu, MD[18]; José A. García Sáenz, MD[19]; Emilio Bria, MD[20]; Marina Cazzaniga, MD[21]; Janice Lu, MD[22]; Philippe Aftimos, MD[23]; Javier Cortés, MD[24,25,26,27]; Shubin Liu, MS[28]; Giulia Tonini, PhD[29]; Dirk Laurent, MD[30]; Nassir Habboubi, MD[31]; Maureen G. Conlan, MD[32]; and Aditya Bardia, MD[33]

EMERALD Trial: Progression-Free Survival (PFS) with Elacestrant versus Standard Therapy by BICR in ITT Population



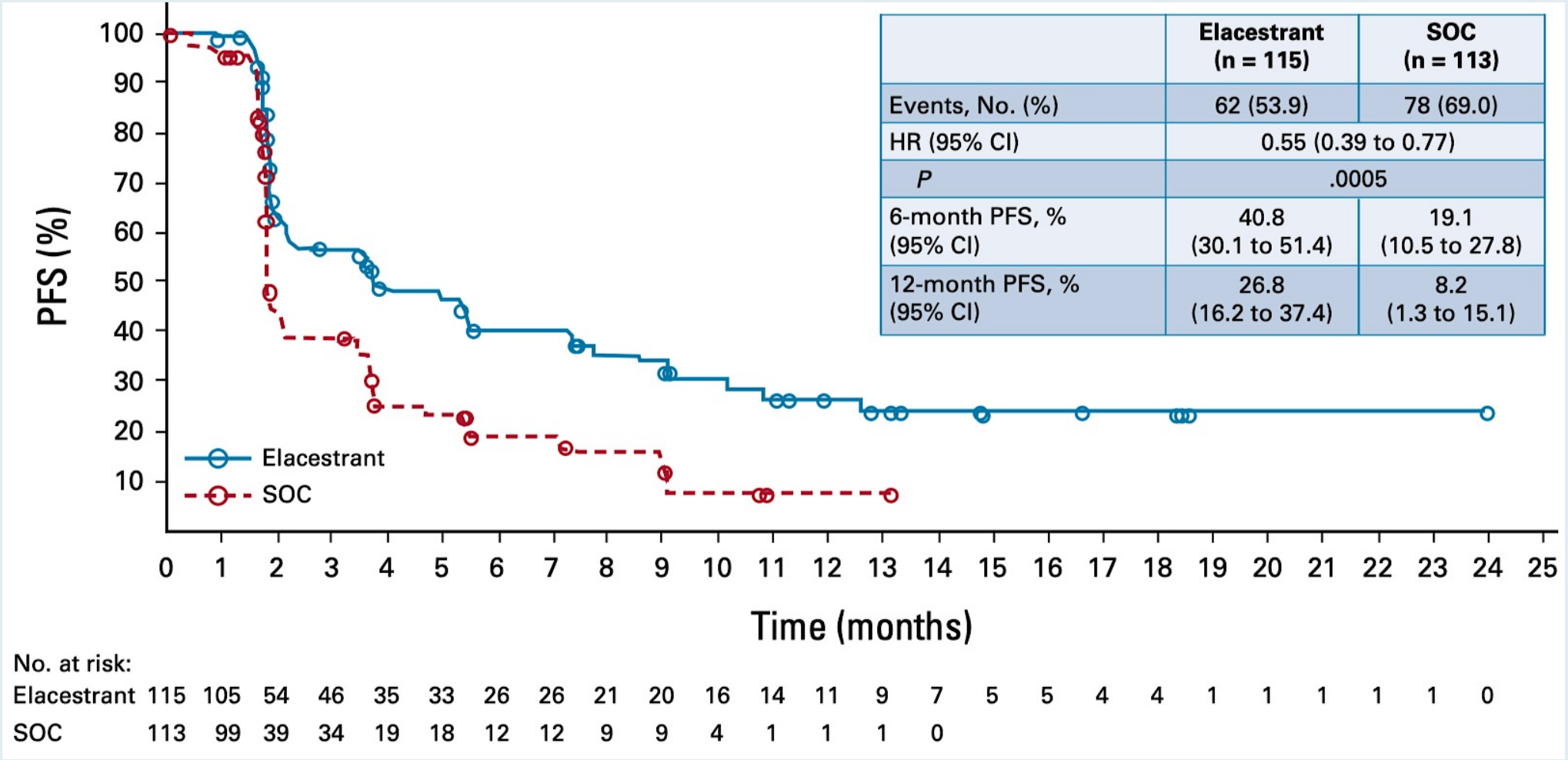
	Elacestrant (n = 239)	SOC (n = 238)
Events, No. (%)	144 (60.3)	156 (65.5)
HR (95% CI)	0.70 (0.55 to 0.88)	
P	.0018	
6-month PFS, % (95% CI)	34.3 (27.2 to 41.5)	20.4 (14.1 to 26.7)
12-month PFS, % (95% CI)	22.3 (15.2 to 29.4)	9.4 (4.0 to 14.8)

BICR = blinded independent central review; ITT = intent to treat; SOC = standard of care

Bidard F-C et al. *J Clin Oncol* 2022;40(28):3246-56.

RTP RESEARCH TO PRACTICE

EMERALD: Progression-Free Survival with Elacestrant versus Standard Therapy in ESR1 Mutation Population

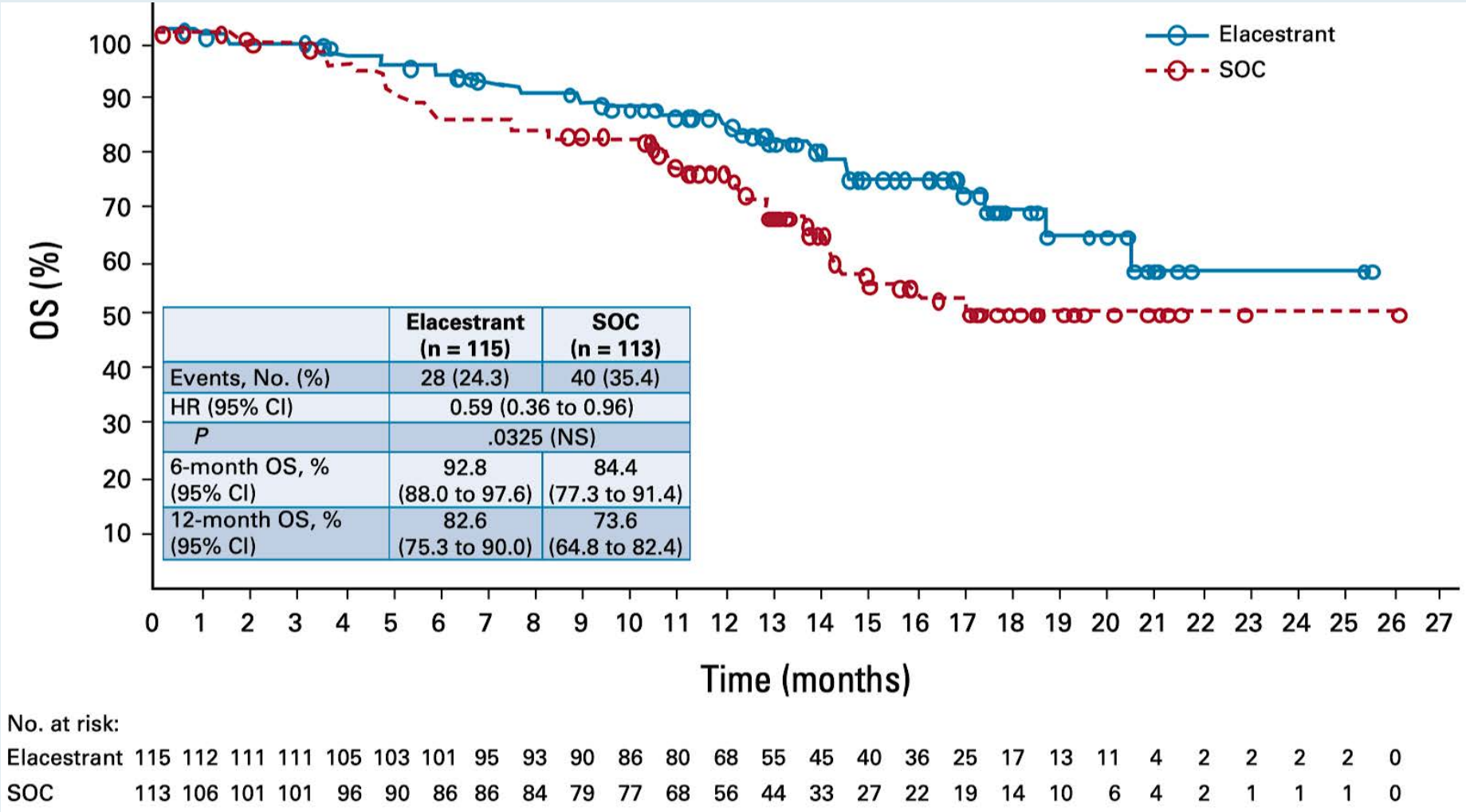


	Elacestrant (n = 115)	SOC (n = 113)
Events, No. (%)	62 (53.9)	78 (69.0)
HR (95% CI)	0.55 (0.39 to 0.77)	
P	.0005	
6-month PFS, % (95% CI)	40.8 (30.1 to 51.4)	19.1 (10.5 to 27.8)
12-month PFS, % (95% CI)	26.8 (16.2 to 37.4)	8.2 (1.3 to 15.1)

Bidard F-C et al. *J Clin Oncol* 2022;40(28):3246-56.

RTP RESEARCH TO PRACTICE

EMERALD: Interim Overall Survival with Elacestrant versus Standard Therapy in ESR1 Mutation Population



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

No. at risk:

Elacestrant	115	112	111	111	105	103	101	95	93	90	86	80	68	55	45	40	36	25	17	13	11	4	2	2	2	2	0
SOC	113	106	101	101	96	90	86	86	84	79	77	68	56	44	33	27	22	19	14	10	6	4	2	1	1	1	0

Bidard F-C et al. *J Clin Oncol* 2022;40(28):3246-56.

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EMERALD: Adverse Events

Event	Elacestrant (n = 237)	SOC		
		Total (n = 229)	Fulvestrant (n = 161)	AI (n = 68)
Any AE	218 (92.0)	197 (86.0)	144 (89.4)	53 (77.9)
Grade 3 and 4[a]	64 (27.0)	47 (20.5)	33 (20.5)	14 (20.6)
Grade 5[b]	4 (1.7)	6 (2.6)	5 (3.1)	1 (1.5)
Leading to dose reduction	7 (3.0)	0	0	Not applicable
Leading to study drug discontinuation	15 (6.3)	10 (4.4)	6 (3.7)	4 (5.9)

AEs[c] Occurring in ≥ 10% of Patients in Any Arm	Elacestrant		Total		Fulvestrant		AI	
	All Grades	Grade 3/4	All Grades	Grade 3/4	All Grades	Grade 3/4	All Grades	Grade 3/4
Nausea	83 (35.0)[d]	6 (2.5)	43 (18.8)	2 (0.9)	26 (16.1)	0	17 (25.0)	2 (2.9)
Fatigue	45 (19.0)	2 (0.8)	43 (18.8)	2 (0.9)	35 (21.7)	1 (0.6)	8 (11.8)	1 (1.5)
Vomiting	45 (19.0)[e]	2 (0.8)	19 (8.3)	0	12 (7.5)	0	7 (10.3)	0
Decreased appetite	35 (14.8)	2 (0.8)	21 (9.2)	1 (0.4)	12 (7.5)	0	9 (13.2)	1 (1.5)
Arthralgia	34 (14.3)	2 (0.8)	37 (16.2)	0	28 (17.4)	0	9 (13.2)	0
Diarrhea	33 (13.9)	0	23 (10.0)	2 (0.9)	14 (8.7)	1 (0.6)	9 (13.2)	1 (1.5)
Back pain	33 (13.9)	6 (2.5)	22 (9.6)	1 (0.4)	16 (9.9)	1 (0.6)	6 (8.8)	0
AST increased	31 (13.1)	4 (1.7)	28 (12.2)	2 (0.9)	20 (12.4)	2 (1.2)	8 (11.8)	0
Headache	29 (12.2)	4 (1.7)	26 (11.4)	0	18 (11.2)	0	8 (11.8)	0
Constipation	29 (12.2)	0	15 (6.6)	0	10 (6.2)	0	5 (7.4)	0
Hot flush	27 (11.4)	0	19 (8.3)	0	15 (9.3)	0	4 (5.9)	0
Dyspepsia	24 (10.1)	0	6 (2.6)	0	4 (2.5)	0	2 (2.9)	0
ALT increased	22 (9.3)	5 (2.1)	23 (10.0)	1 (0.4)	17 (10.6)	0	6 (8.8)	1 (1.5)

Bidard F-C et al. *J Clin Oncol* 2022;40(28):3246-56.

RTP RESEARCH TO PRACTICE

San Antonio Breast Cancer Symposium®, December 6-10, 2022

Abstract GS3-02

Camizestrant, a next-generation oral SERD *vs* fulvestrant in post-menopausal women with advanced ER-positive HER2-negative breast cancer: Results of the randomized, multi-dose Phase 2 SERENA-2 trial

Mafalda Oliveira, MD, PhD[1], Denys Pominchuk, PhD[2], Zbigniew Nowecki MD[3], Erika Hamilton, MD[4], Yaroslav Kulyaba, MD[5], Timur Andabekov, PhD[6], Yevhen Hotko, MD[7], Tamar Melkadze, MD[8], Gia Nemsadze, MD, PhD[9], Patrick Neven, MD[10], Yuriy Semegen, MD[11], Vladimir Vladimirov, MD[12], Claudio Zamagni, MD[13], Hannelore Denys, MD, PhD[14], Frédéric Forget, MD[15], Zsolt Horvath, MD, PhD[16], Alfiya Nesterova, MD, PhD[17], Maxine Bennett, PhD[18], Bistra Kirova, MBChB, MSc[19], Teresa Klinowska, PhD[20], Justin P O Lindemann, MBChB, MB[18], Delphine Lissa, PharmD, PhD[18], Alastair Mathewson, PhD[18], Christopher J Morrow, PhD[18], Zuzana Traugottova, MD[21], Ruaan van Zyl, PhD[22], Ekaterine Arkania, MD[23]

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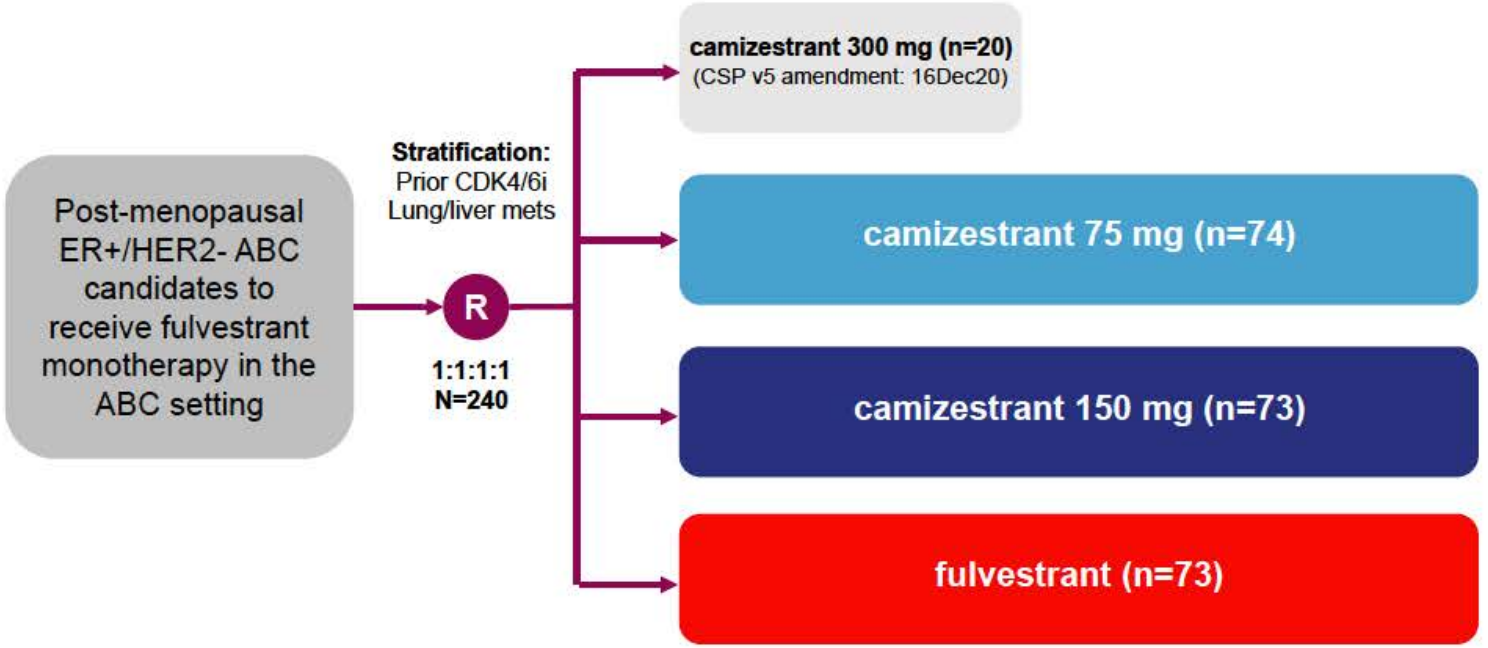
SERENA-2 Phase III Study Design

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

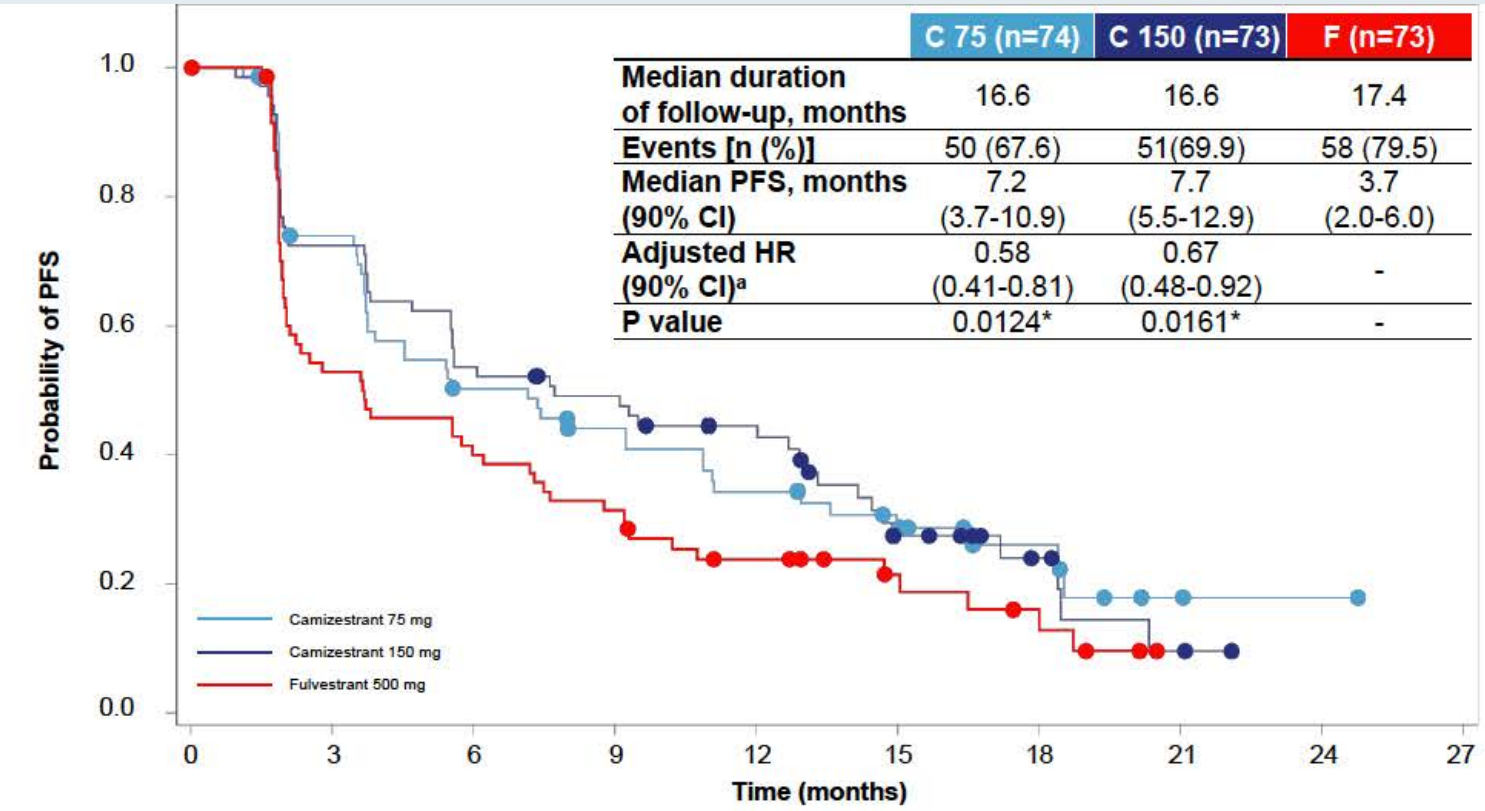


- **Primary endpoint:** PFS (investigator assessment*)
- **Secondary endpoints:** CBR24, ORR, OS, safety
- **Translational endpoints:** serial ctDNA analysis including *ESR1*m, serial CTCs analysis

*disease progression assessed by the Investigator and defined using RECIST, version 1.1
ABC: advanced breast cancer; CBR24: clinical benefit rate at 24 weeks; CDK4/6i: CDK4/6 inhibitor; CT: chemotherapy; CTC: circulating tumor cells; ctDNA: circulating tumor DNA; ER: estrogen receptor; *ESR1*m: mutation in estrogen receptor 1 gene; ET: endocrine therapy; HER2: human epidermal growth factor; PFS: progression-free survival; R: randomization; RECIST: Response Evaluation Criteria for Solid Tumors; SERD: selective estrogen receptor degrader

Oliveira M et al. SABCS 2022;Abstract GS3-02.

SERENA-2 Primary Endpoint: PFS by Investigator Assessment



	C 75 (n=74)	C 150 (n=73)	F (n=73)
Median duration of follow-up, months	16.6	16.6	17.4
Events [n (%)]	50 (67.6)	51(69.9)	58 (79.5)
Median PFS, months (90% CI)	7.2 (3.7-10.9)	7.7 (5.5-12.9)	3.7 (2.0-6.0)
Adjusted HR (90% CI)[a]	0.58 (0.41-0.81)	0.67 (0.48-0.92)	-
P value	0.0124*	0.0161*	-

C 75	74	50	33	27	21	14	7	2	1	0
C 150	73	50	37	32	25	12	6	2	0	
F	73	37	28	22	14	8	5	0		

*Statistically significant; [a]HRs adjusted for prior use of CDK4/6i and liver/lung metastases

CDK4/6i: CDK4/6 inhibitor; CI: confidence interval; HR: hazard ratio; PFS: progression-free survival

In the overall population, camizestrant produces a statistically significant and clinically meaningful improvement in PFS for both 75 and 150 mg camizestrant doses over fulvestrant

Oliveira M et al. SABCS 2022;Abstract GS3-02.

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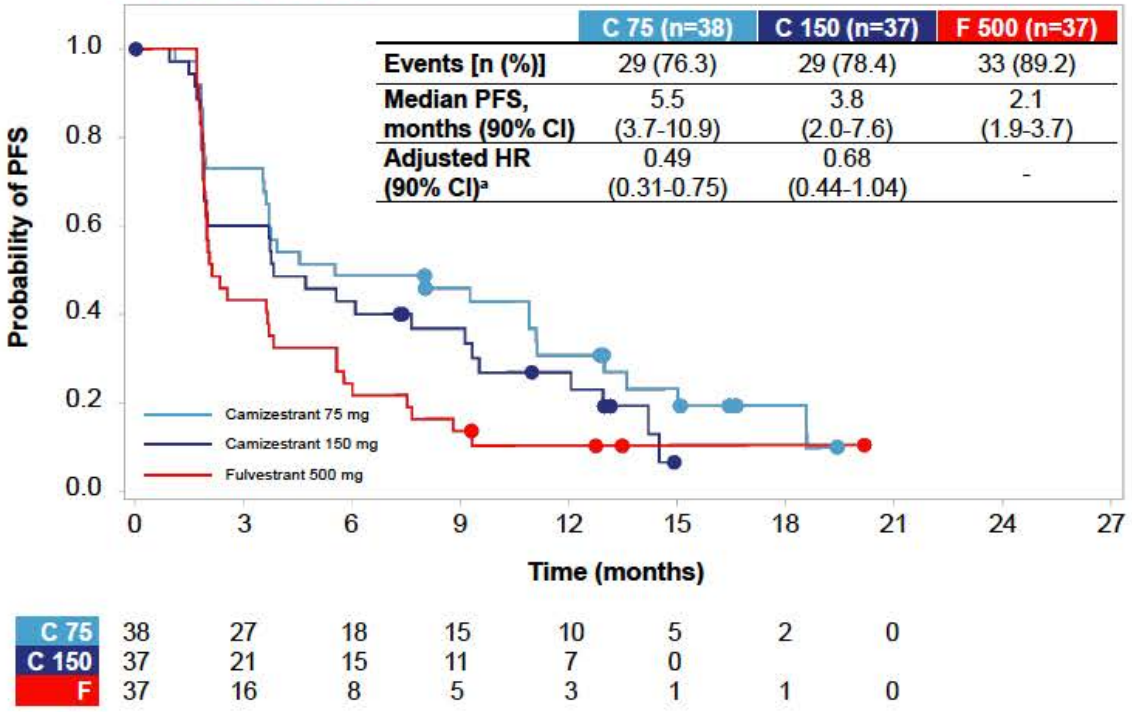
SERENA-2: PFS by Prior CDK4/6 Inhibitor Use

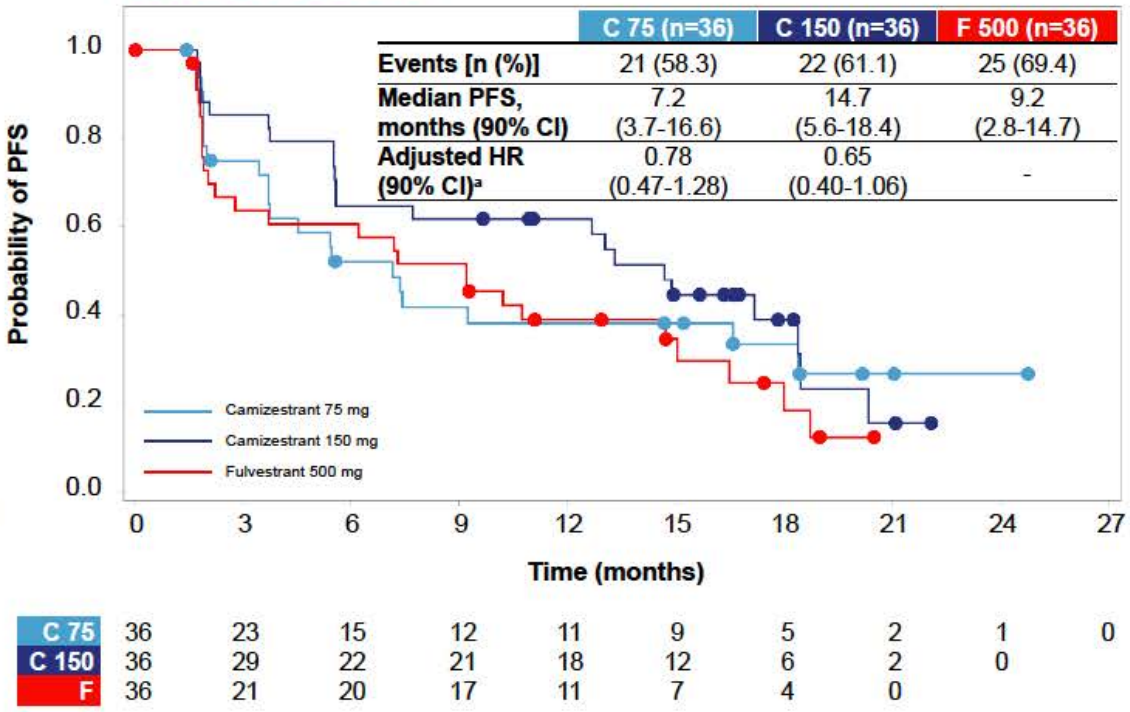
Prior CDK4/6i



	C 75 (n=38)	C 150 (n=37)	F 500 (n=37)
Events [n (%)]	29 (76.3)	29 (78.4)	33 (89.2)
Median PFS, months (90% CI)	5.5 (3.7-10.9)	3.8 (2.0-7.6)	2.1 (1.9-3.7)
Adjusted HR (90% CI)[a]	0.49 (0.31-0.75)	0.68 (0.44-1.04)	-

C 75	38	27	18	15	10	5	2	0
C 150	37	21	15	11	7	0		
F	37	16	8	5	3	1	1	0

No prior CDK4/6i



	C 75 (n=36)	C 150 (n=36)	F 500 (n=36)
Events [n (%)]	21 (58.3)	22 (61.1)	25 (69.4)
Median PFS, months (90% CI)	7.2 (3.7-16.6)	14.7 (5.6-18.4)	9.2 (2.8-14.7)
Adjusted HR (90% CI)[a]	0.78 (0.47-1.28)	0.65 (0.40-1.06)	-

C 75	36	23	15	12	11	9	5	2	1	0
C 150	36	29	22	21	18	12	6	2	0	
F	36	21	20	17	11	7	4	0		

- In the sub-population of patients previously treated with CDK4/6i + endocrine therapy, camizestrant at both doses produces a clinically meaningful improvement in PFS over fulvestrant

[a]HRs adjusted for liver/lung metastases

CI: confidence interval; CDK4/6i: CDK4/6 inhibitor; HR: hazard ratio; PFS: progression-free survival

Oliveira M et al. SABCS 2022;Abstract GS3-02.

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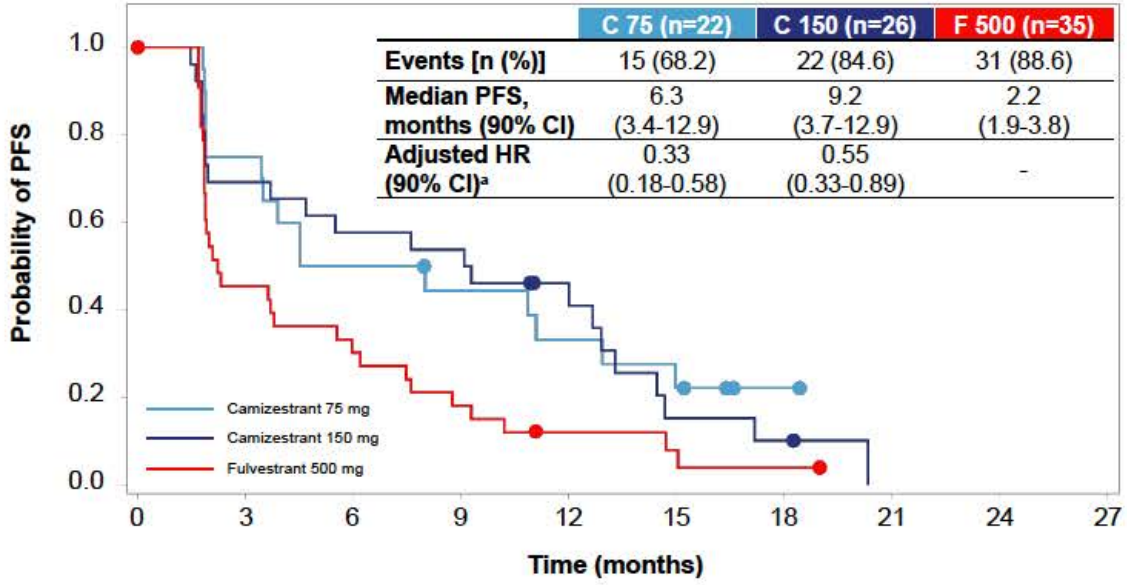
SERENA-2: PFS by Detectable ESR1 Mutation

*ESR1*m detectable at baseline

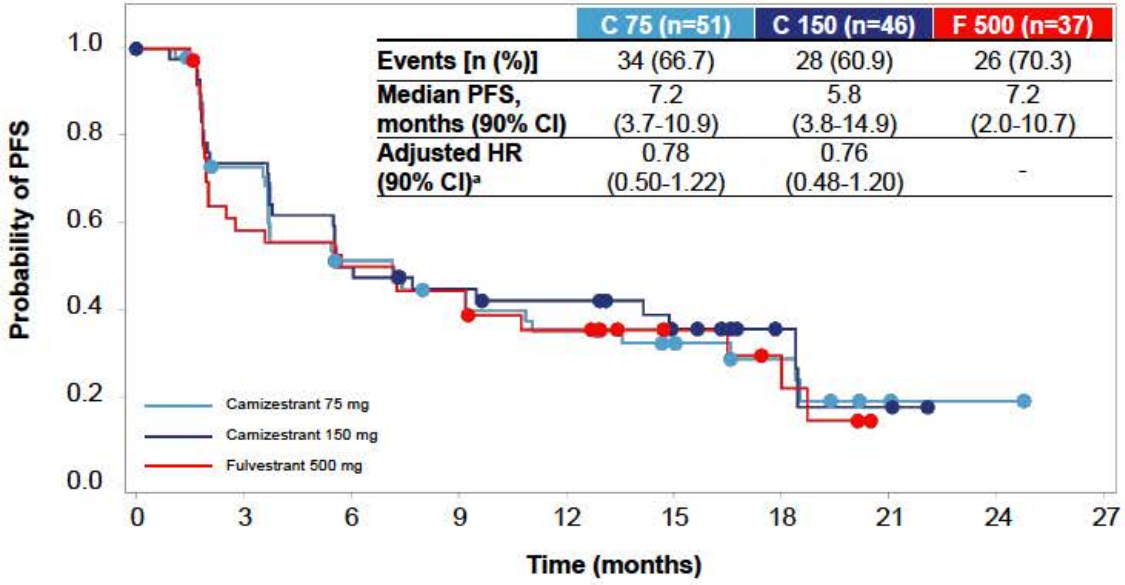
	C 75 (n=22)	C 150 (n=26)	F 500 (n=35)
Events [n (%)]	15 (68.2)	22 (84.6)	31 (88.6)
Median PFS, months (90% CI)	6.3 (3.4-12.9)	9.2 (3.7-12.9)	2.2 (1.9-3.8)
Adjusted HR (90% CI)[a]	0.33 (0.18-0.58)	0.55 (0.33-0.89)	-



C 75	22	15	10	8	6	4	1	0
C 150	26	18	15	14	9	3	2	0
F	35	15	10	6	3	2	1	0

*ESR1*m not detectable at baseline

	C 75 (n=51)	C 150 (n=46)	F 500 (n=37)
Events [n (%)]	34 (66.7)	28 (60.9)	26 (70.3)
Median PFS, months (90% CI)	7.2 (3.7-10.9)	5.8 (3.8-14.9)	7.2 (2.0-10.7)
Adjusted HR (90% CI)[a]	0.78 (0.50-1.22)	0.76 (0.48-1.20)	-



C 75	51	34	23	19	15	10	6	2	1	0
C 150	46	31	21	17	15	9	4	2	0	
F	37	21	18	16	11	6	4	1	0	

- In the sub-population of patients with detectable *ESR1*m at baseline, camizestrant at both doses produces a clinically meaningful improvement in PFS over fulvestrant

[a]HRs adjusted for prior use of CDK4/6i and liver/lung metastases

CI: confidence interval; CDK4/6i: CDK4/6 inhibitor; ESR1m: mutation in estrogen receptor 1 gene; HR: hazard ratio; PFS: progression-free survival

Oliveira M et al. SABCS 2022;Abstract GS3-02.

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SERENA-2: Treatment-Emergent Adverse Events

AE, n (%)	C 75 (n=74)		C 150 (n=73)		C 300 (n=20)		F 500 (n=73)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
Any AE	57 (77.0)	9 (12.2)	66 (90.4)	16 (21.9)	19 (95.0)	3 (15)	50 (68.5)	10 (13.7)
Photopsia	9 (12.2)	0	18 (24.7)	0	7 (35.0)	0	0	0
(Sinus) bradycardia	4 (5.4)	0	19 (26.0)	0	8 (40.0)	0	0	0
Fatigue	4 (5.4)	0	13 (17.8)	1 (1.4)	4 (20.0)	0	3 (4.1)	0
Anemia	8 (10.8)	0	11 (15.1)	1 (1.4)	1 (5.0)	0	5 (6.8)	2 (2.7)
Asthenia	6 (8.1)	0	11 (15.1)	0	2 (10.0)	0	4 (5.5)	0
Arthralgia	3 (4.1)	0	9 (12.3)	1 (1.4)	2 (10.0)	0	2 (2.7)	0
AST increased	2 (2.7)	0	6 (8.2)	0	2 (10.0)	0	5 (6.8)	1 (1.4)
ALT increased	1 (1.4)	0	6 (8.2)	1 (1.4)	3 (15.0)	0	4 (5.5)	1 (1.4)
Covid-19	4 (5.4)	0	4 (5.5)	0	3 (15.0)	0	3 (4.1)	0
Diarrhea	4 (5.4)	0	4 (5.5)	0	3 (15.0)	1 (5.0)	2 (2.7)	1 (1.4)
Pain in extremity	1 (1.4)	0	4 (5.5)	1 (1.4)	2 (10.0)	0	3 (4.1)	0
Dyspepsia	1 (1.4)	0	3 (4.1)	0	2 (10.0)	0	1 (1.4)	0
Insomnia	1 (1.4)	0	3 (4.1)	0	2 (10.0)	0	1 (1.4)	0
Hyponatremia	0	0	3 (4.1)	1 (1.4)	2 (10.0)	0	1 (1.4)	1 (1.4)
Blood pressure increased	2 (2.7)	1 (1.4)	1 (1.4)	1 (1.4)	2 (10.0)	1 (5.0)	0	0
Cataract	2 (2.7)	0	0	0	2 (10.0)	0	0	0
Vitreous floaters	2 (2.7)	0	0	0	2 (10.0)	0	0	0

Oliveira M et al. SABCS 2022;Abstract GS3-02.

SERENA-2: Conclusions

- SERENA-2 met its primary objective: camizestrant at both 75 and 150 mg doses improves PFS over fulvestrant in post-menopausal women with ER+/HER2- ABC
- Camizestrant delivers statistically significant and clinically meaningful PFS benefit at both 75 and 150 mg doses over fulvestrant in the overall population
  - A clinically meaningful PFS benefit was observed across the pre-specified subgroups of unmet medical need (post-CDK4/6i, lung/liver metastases, *ESR1*m and evidence of ER-driven disease)
- Both camizestrant doses are well tolerated, with infrequent Grade ≥3 TRAEs, dose reductions and discontinuations
- The results of SERENA-2 support the further development of camizestrant in ER+ BC
- Recruitment to two Phase 3 studies of camizestrant in ABC, SERENA-4[a] and SERENA-6[b], continues

Oliveira M et al. SABCS 2022;Abstract GS3-02.

RTP RESEARCH TO PRACTICE

Select Ongoing Phase III Trials of Oral SERDs in Development for HR-Positive Advanced Breast Cancer (ABC)

Trial	N	Randomization	Setting	Est primary completion
SERENA-4	1,370	• Camizestrant + palbociclib • Anastrozole + palbociclib	Untreated ABC	August 2026
persevERA	992	• Giredestrant + palbociclib • Letrozole + palbociclib	Untreated ABC	March 2025
SERENA-6	300	• Camizestrant + (palbociclib, ribociclib or abemaciclib) • (Anastrozole or letrozole) + (palbociclib, ribociclib or abemaciclib)	Detectable ESR1 mutation, no PD during first-line AI + CDK4/6i	January 2025
EMBER-3	860	• Imlunestrant • Imlunestrant + abemaciclib • Investigator's choice of ET	ABC previously treated with ET ± CDK4/6i	April 2024
evERA	320	• Giredestrant + everolimus • Investigator's choice of ET + everolimus	ABC previously treated with ET + CDK4/6i	October 2024
heredERA	812	• Giredestrant + pertuzumab/trastuzumab/hyaluronidase-zzxf • Pertuzumab/trastuzumab/hyaluronidase-zzxf	Untreated ER+, HER2+ ABC after first-line pertuzumab/trastuzumab/ hyaluronidase-zzxf + taxane	August 2026

PD = disease progression; AI = aromatase inhibitor; CDK4/6i = CDK4/6 inhibitor

www.clinicaltrials.gov. Accessed April 2024.

Alpelisib and Capivasertib in Treatment for HR-Positive mBC

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ASCO Rapid Recommendations

Endocrine and Targeted Therapy for Hormone Receptor–Positive, Human Epidermal Growth Factor Receptor 2–Negative Metastatic Breast Cancer—Capivasertib-Fulvestrant: ASCO Rapid Recommendation Update

Harold J. Burstein, MD, PhD[1]; Angela DeMichele, MD[2]; Lesley Fallowfield, DPhil[3]; Mark R. Somerfield, PhD[4]; and N. Lynn Henry, MD, PhD[5]; for the Biomarker Testing and Endocrine and Targeted Therapy in Metastatic Breast Cancer Expert Panels

J Clin Oncol 2024;42:1450-53.

RTP RESEARCH TO PRACTICE

Treatment Options According to Prior Endocrine Therapy

Line of Therapy	Tumor Genomic Findings	Prior Endocrine Therapy[a]	
		None, tamoxifen only, or no prior recent AI therapy (anastrozole, exemestane, letrozole)	Recurrence on or within recent exposure to AI therapy
First-line treatment		AI + CDK4/6 inhibitor	Fulvestrant + CDK4/6 inhibitor
Tumor genomic testing[b]			
Second-line treatment	No targetable mutations	Fulvestrant or fulvestrant + everolimus	Fulvestrant + everolimus, or chemotherapy
	ESR1 mutation	Elacestrant, or fulvestrant + everolimus	Elacestrant
	PIK3CA mutation	Fulvestrant + capivasertib, fulvestrant + alpelisib,[d] or fulvestrant	Fulvestrant + capivasertib, or fulvestrant + alpelisib[d]
	AKT1 mutation or *PTEN* inactivation	Fulvestrant + capivasertib, or fulvestrant	Fulvestrant + capivasertib
Third-line treatment and beyond[c]	No targetable mutations or targeted therapy already given	Chemotherapy or further endocrine-based treatments	Chemotherapy or further endocrine-based treatments
	ESR1 mutation	Elacestrant[e] or chemotherapy	Elacestrant[e] or chemotherapy
	PIK3CA mutation	Fulvestrant + capivasertib,[e] or fulvestrant + alpelisib,[d,e] or chemotherapy	Fulvestrant + capivasertib,[e] or fulvestrant + alpelisib,[d,e] or chemotherapy
	AKT1 mutation or *PTEN* inactivation	Fulvestrant + capivasertib,[e] or chemotherapy	Fulvestrant + capivasertib,[e] or chemotherapy

Burstein HJ et al. *J Clin Oncol* 2024;42:1450-53.

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

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

ORIGINAL ARTICLE

Capivasertib in Hormone Receptor–Positive Advanced Breast Cancer

N.C. Turner, M. Oliveira, S.J. Howell, F. Dalenc, J. Cortes, H.L. Gomez Moreno, X. Hu, K. Jhaveri, P. Krivorotko, S. Loibl, S. Morales Murillo, M. Okera, Y.H. Park, J. Sohn, M. Toi, E. Tokunaga, S. Yousef, L. Zhukova, E.C. de Bruin, L. Grinsted, G. Schiavon, A. Foxley, and H.S. Rugo, for the CAPItello-291 Study Group*

CAPItello-291 Phase III Study Design

Patients with HR+/HER2– ABC

- Men and pre-/post-menopausal women
- Recurrence or progression while on or <12 months from end of adjuvant AI, or progression while on prior AI for ABC
- ≤2 lines of prior endocrine therapy for ABC
- ≤1 line of chemotherapy for ABC
- Prior CDK4/6 inhibitors allowed (at least 51% required)
- No prior SERD, mTOR inhibitor, PI3K inhibitor, or AKT inhibitor
- HbA1c <8.0% (63.9 mmol/mol) and diabetes not requiring insulin allowed
- FFPE tumor sample from the primary/recurrent cancer available for retrospective central molecular testing

R1:1 (N=708)

Stratification factors:
- Liver metastases (yes/no)
- Prior CDK4/6 inhibitor (yes/no)
- Region*

Capivasertib	400 mg twice daily, 4 days on, 3 days off	43.7% altered
Fulvestrant	500 mg: cycle 1, days 1 & 15; then every 4 weeks	
Placebo	Twice daily, 4 days on, 3 days off	37% altered
Fulvestrant	500 mg: cycle 1, days 1 & 15; then every 4 weeks	

Dual primary endpoints

PFS by investigator assessment
- Overall
- AKT pathway-altered tumors (≥1 qualifying *PIK3CA*, *AKT1*, or *PTEN* alteration)

Secondary endpoints

Overall survival
- Overall
- AKT pathway-altered tumors

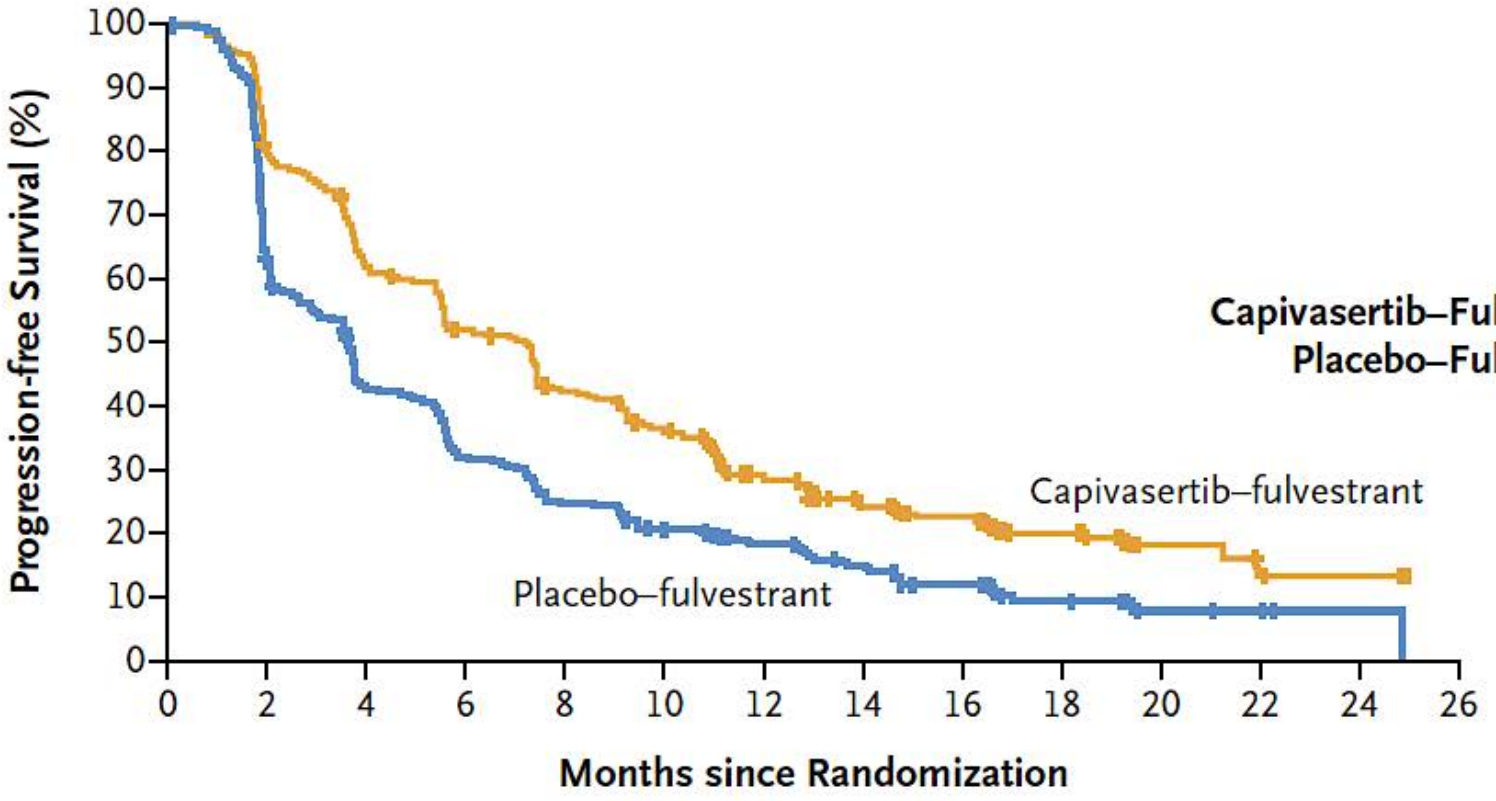
Objective response rate
- Overall
- AKT pathway-altered tumors

Summary of Demographics

- Median age ~59
- Asian 26%, Black 1%
- Primary ET resistance ~38%
- Visceral metastases ~68%
- One line of prior ET for mBC ~75%
- Prior CDK4/6i for mBC ~70%
- Chemotherapy for ABC ~18%

Turner NC et al. SABCS 2022;Abstract GS3-04.

CAPItello-291 Dual-Primary Endpoint: Investigator-Assessed PFS in the Overall Population



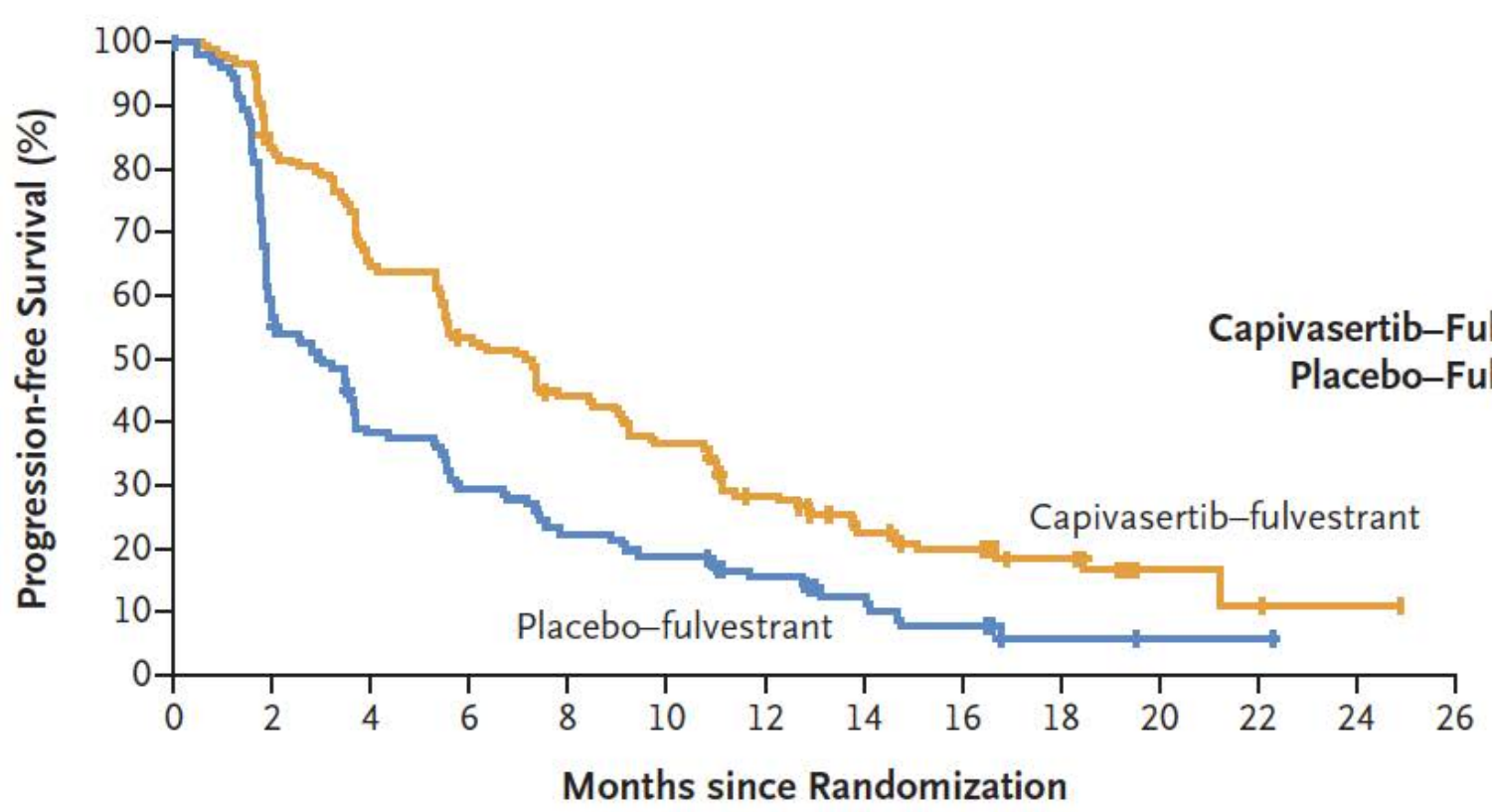
	No. of Patients	No. of Events	Median Progression-free Survival (95% CI)
			mo
Capivasertib–Fulvestrant	355	258	7.2 (5.5–7.4)
Placebo–Fulvestrant	353	293	3.6 (2.8–3.7)

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

Turner NC et al. *N Engl J Med* 2023 June 1;388(22):2058-70.

RTP RESEARCH TO PRACTICE

CAPItello-291 Dual-Primary Endpoint: Investigator-Assessed PFS in the AKT Pathway-Alteration Population



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

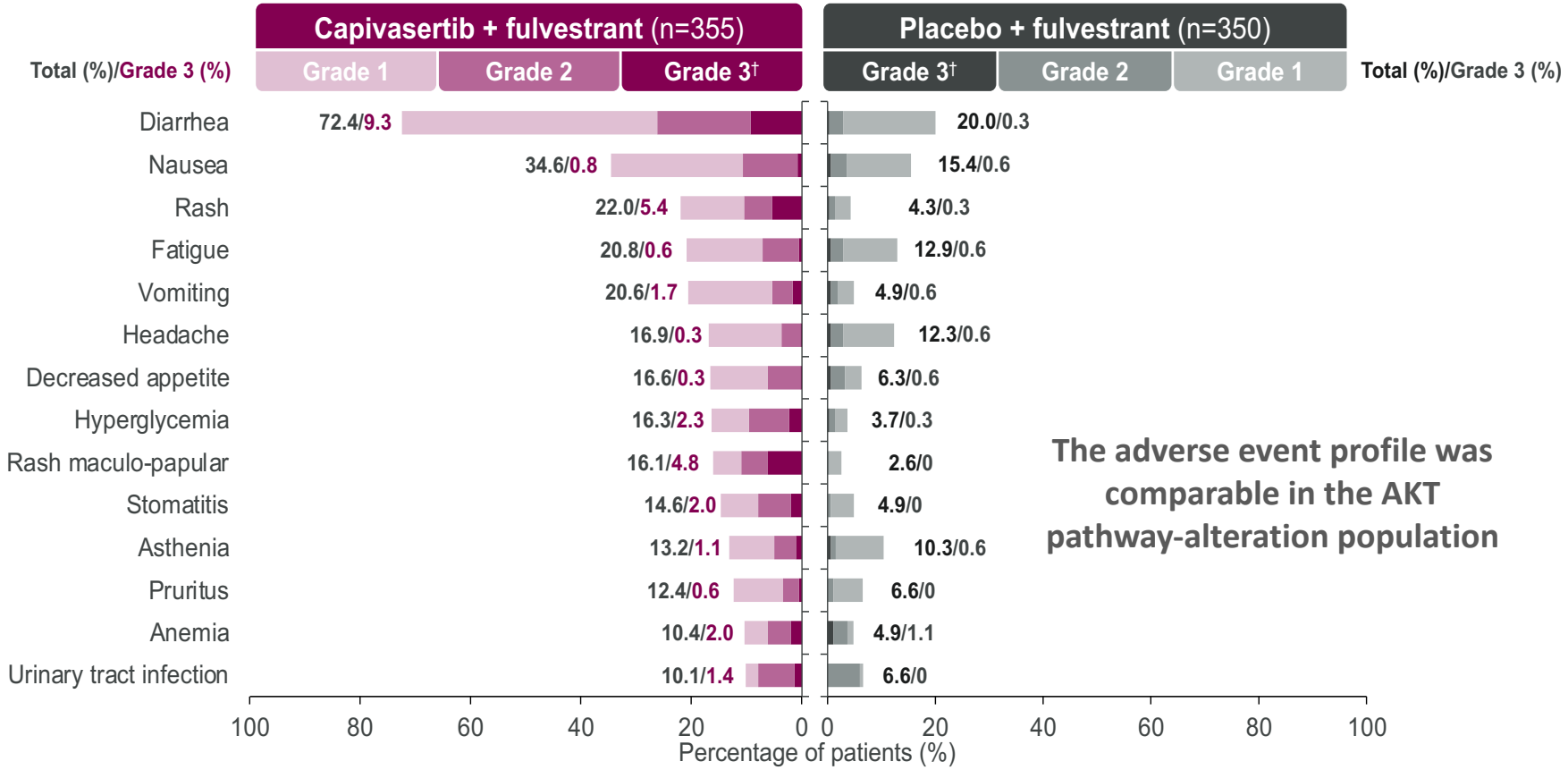
Adjusted hazard ratio for disease progression or death, 0.50 (95% CI, 0.38–0.65)
P<0.001

Turner NC et al. *N Engl J Med* 2023 June 1;388(22):2058-70.

RTP RESEARCH TO PRACTICE

CAPItello-291: Safety

Adverse events (>10% of patients) – overall population



Adverse events of any grade related to rash (group term including rash, rash macular, maculo-papular rash, rash papular and rash pruritic) were reported in 38.0% of the patients in the capivasertib + fulvestrant arm (grade ≥3 in 12.1%) and in 7.1% of those in the placebo + fulvestrant group (grade ≥3 in 0.3%). †All events shown were Grade 3 except one case of Grade 4 hyperglycemia in the capivasertib + fulvestrant arm.

Turner NC et al. *N Engl J Med* 2023 June 1;388(22):2058-70; SABCS 2022;Abstract GS3-04.

RTP RESEARCH TO PRACTICE

What I Tell My Patients:
Integrating New Research Information into Current Clinical Care

A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress

Hormonal Therapy for Hormone Receptor-Positive Breast Cancer

Wednesday, April 24, 2024

6:00 PM – 8:00 PM

Faculty

Harold J Burstein, MD, PhD
Kelly Fischer, MSN, FNP-BC
Komal Jhaveri, MD, FACP
Melissa Rikal, FNP-BC, AOCNP

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

What I Tell My Patients: Integrating New Research Information into Current Clinical Care

A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress

Endometrial Cancer

Thursday, April 25, 2024
6:00 AM – 7:30 AM

Faculty

Jennifer Filipi, MSN, NP
Kathryn M Lyle, MSN, WHNP-BC, AGNP-C
David M O'Malley, MD
Shannon N Westin, MD, MPH, FASCO, FACOG

Moderator

Neil Love, MD

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

To Claim NCPD Credit

In-person attendees: Please refer to the program syllabus for the NCPD credit link or QR code.

Virtual attendees: The NCPD credit link is posted in the chat room.

NCPD/ONCC credit information will be emailed to each participant within 1 to 2 business days.

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