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

Localized HR-Positive Breast Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, May 6, 2026
5:00 PM – 6:00 PM ET

Faculty

Harold J Burstein, MD, PhD
Joyce O'Shaughnessy, MD

Moderator

Neil Love, MD

RTP Year in Review 2026

Faculty

Harold J Burstein, MD, PhD
Director of Academic Partnerships
Institute Physician
Dana-Farber Cancer Institute
Professor of Medicine
Harvard Medical School
Boston, Massachusetts

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

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Commercial Support

This activity is supported by educational grants from Biotheranostics Inc, A Hologic Company, Exact Sciences Corporation, Genentech, a member of the Roche Group, Lilly, and Novartis.

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Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Dr Love — Disclosures

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Dr Burstein — Disclosures

No relevant financial relationships to disclose.

Dr O'Shaughnessy — Disclosures

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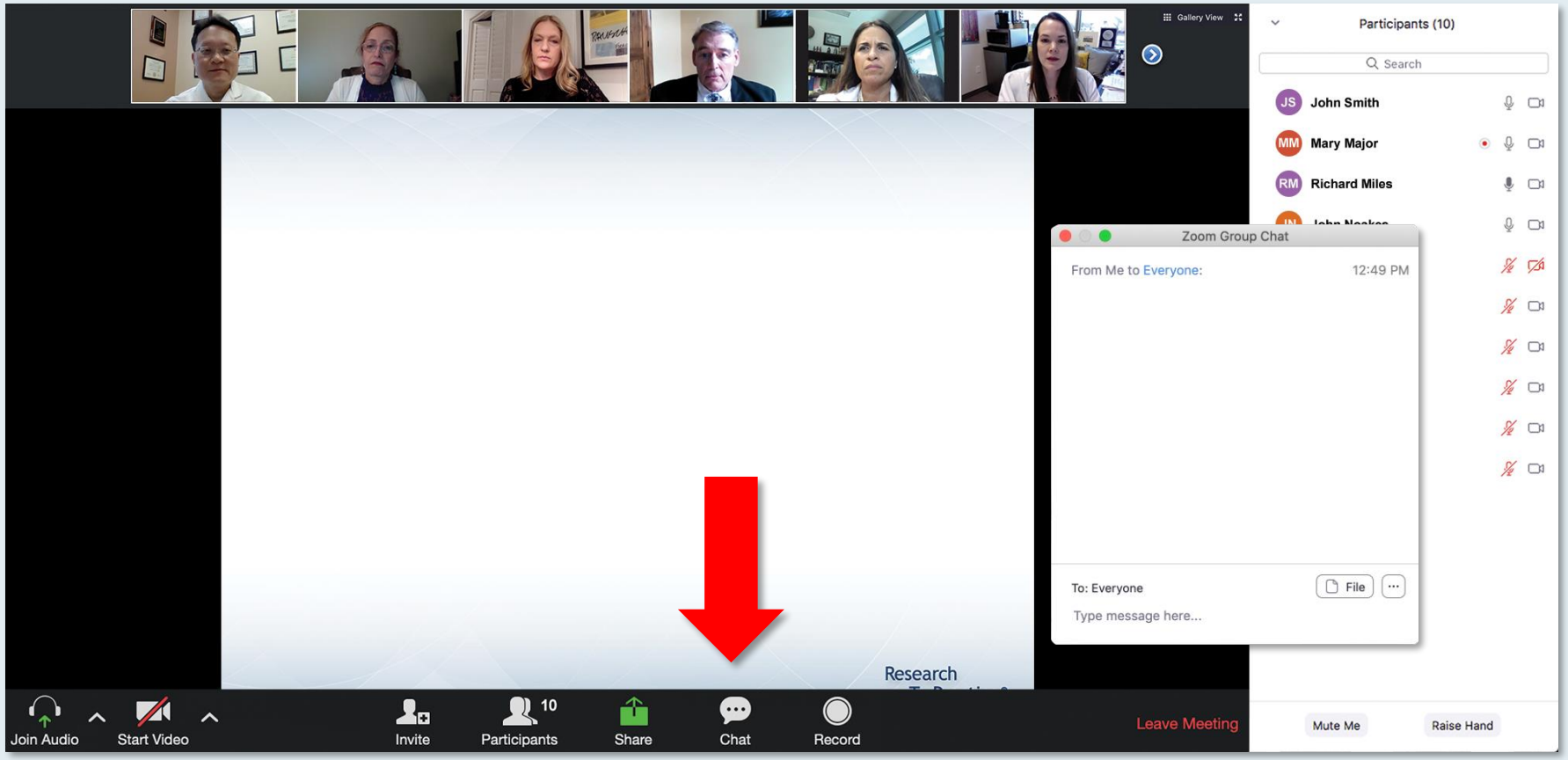
We Encourage Clinicians in Practice to Submit Questions



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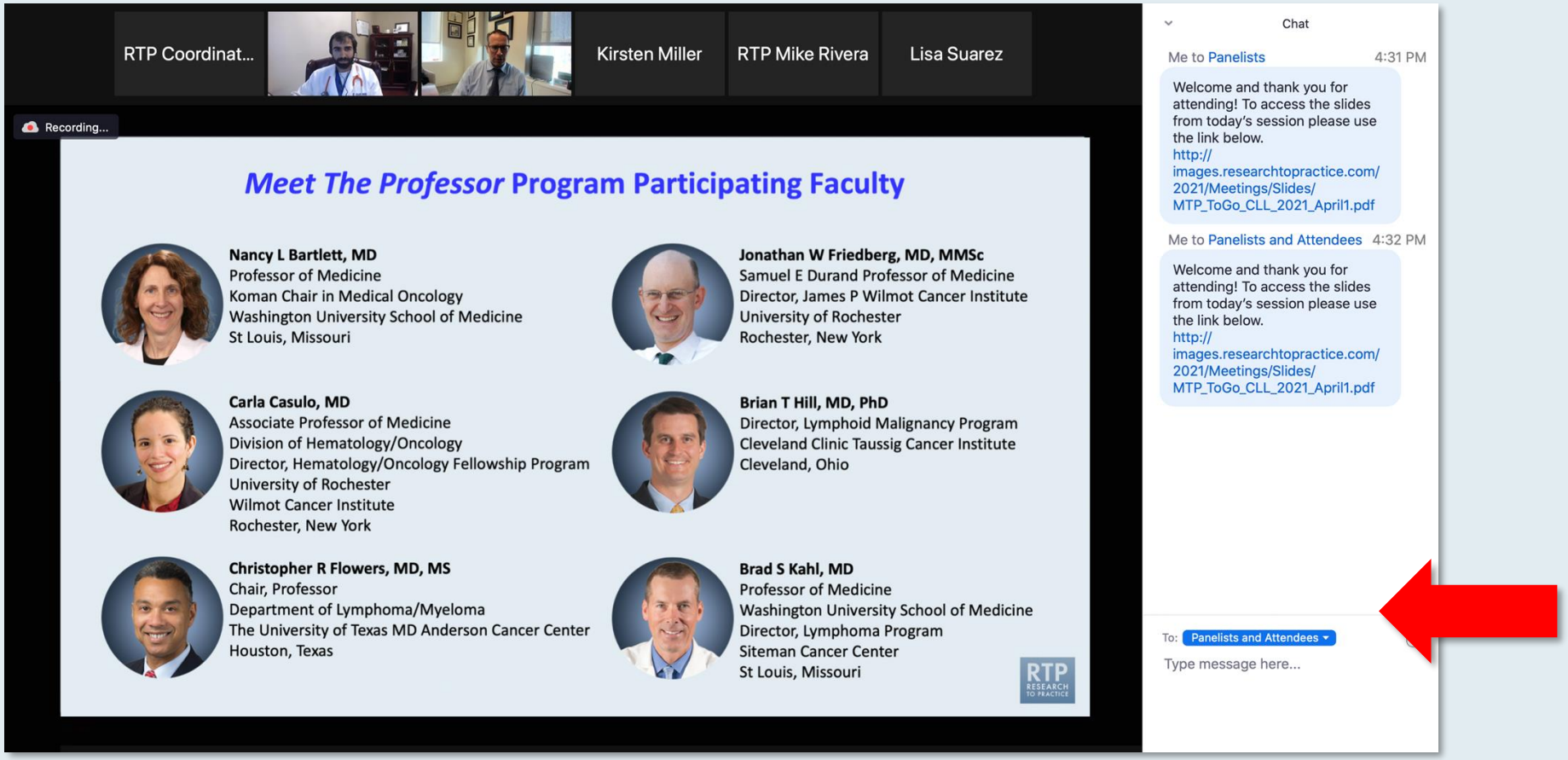

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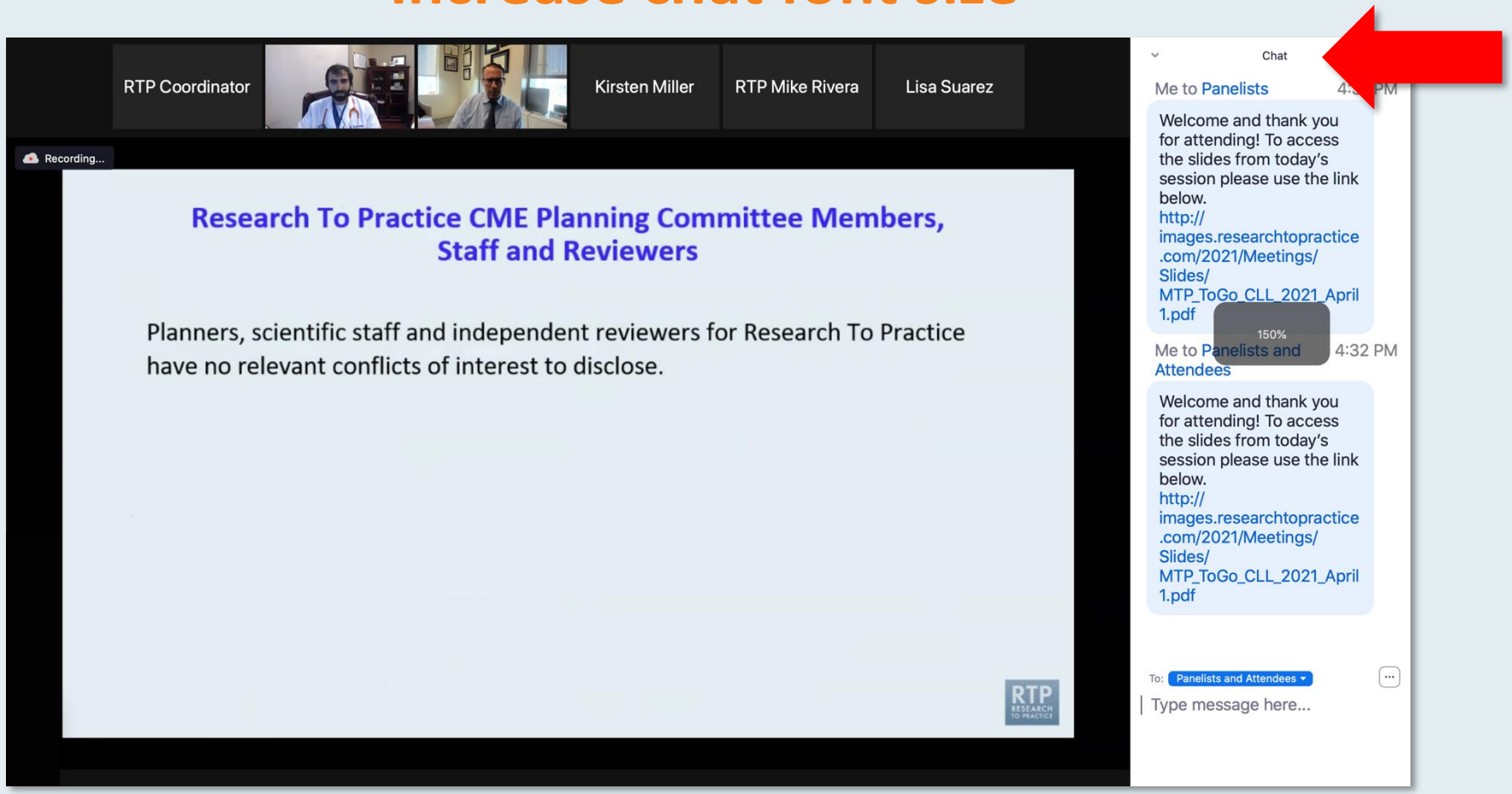

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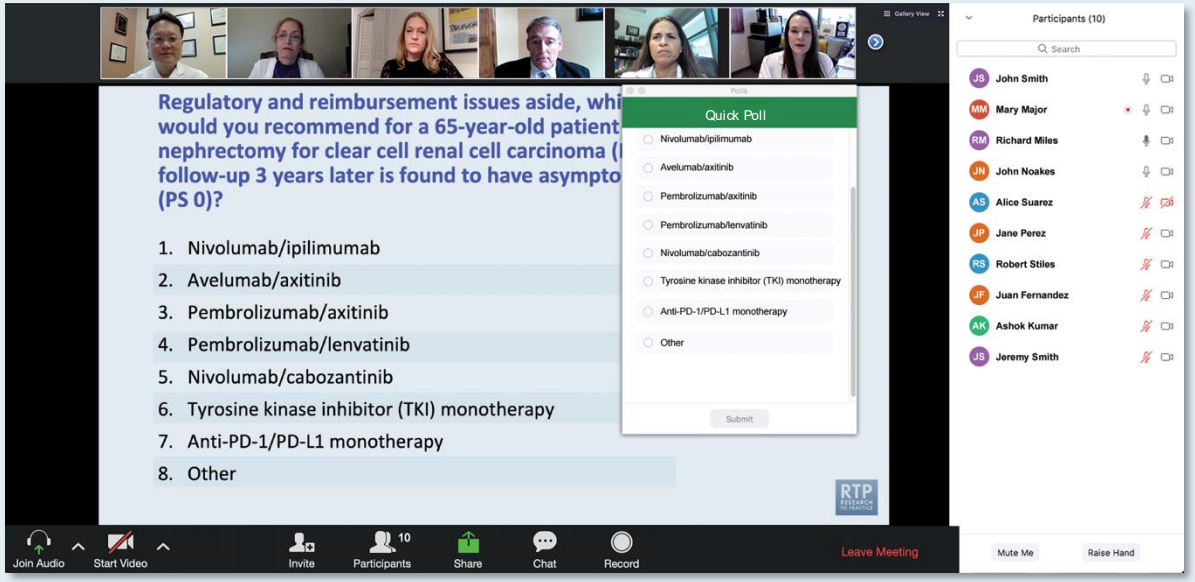

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WITH DR NEIL LOVE

HR-Positive Metastatic Breast Cancer — An Interview with Dr Seth Wander on Optimizing Biomarker Assessment and Related Treatment Decision-Making

SETH WANDER, MD, PHD
MASSACHUSETTS GENERAL HOSPITAL

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Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse

A Complimentary NCPD Symposium Series Held During the 51st Annual ONS Congress May 13-16

San Antonio Marriott Rivercenter | San Antonio, Texas

Antibody-Drug Conjugates

Wednesday, May 13, 2026 | 11:15 AM – 12:45 PM CT

Prostate Cancer

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Renal Cell Carcinoma

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MODULE 3: Premenopausal Patients

MODULE 4: Duration of Adjuvant Endocrine Treatment

MODULE 5: Genomic Predictors of Chemotherapy Benefit

MODULE 6: Neoadjuvant Treatment

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Thank you for joining us!

Please take a moment to complete the survey currently up on Zoom.
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Information on how to obtain CME, ABIM MOC and ABS credit will be provided in the Zoom chat room.
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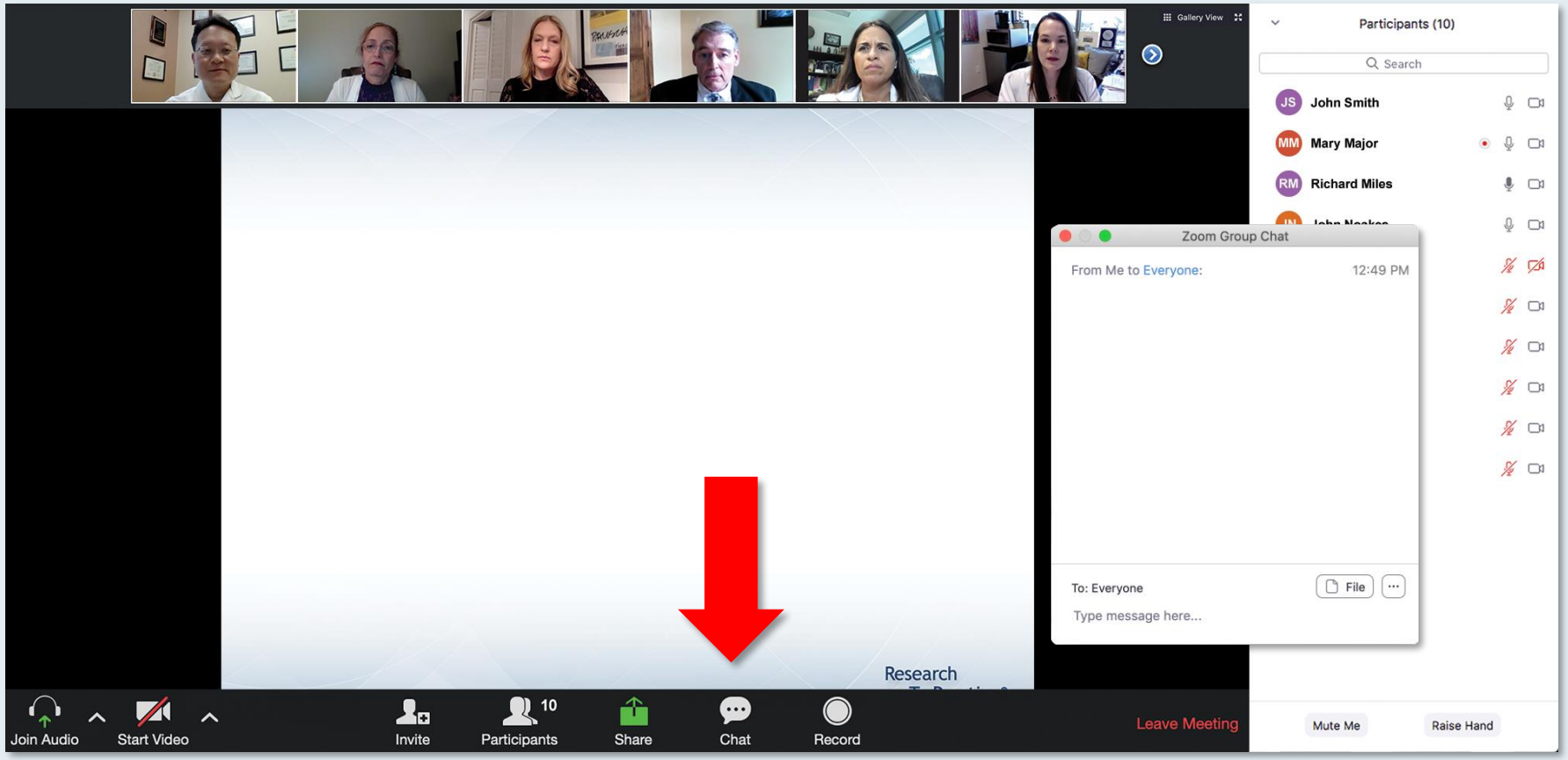

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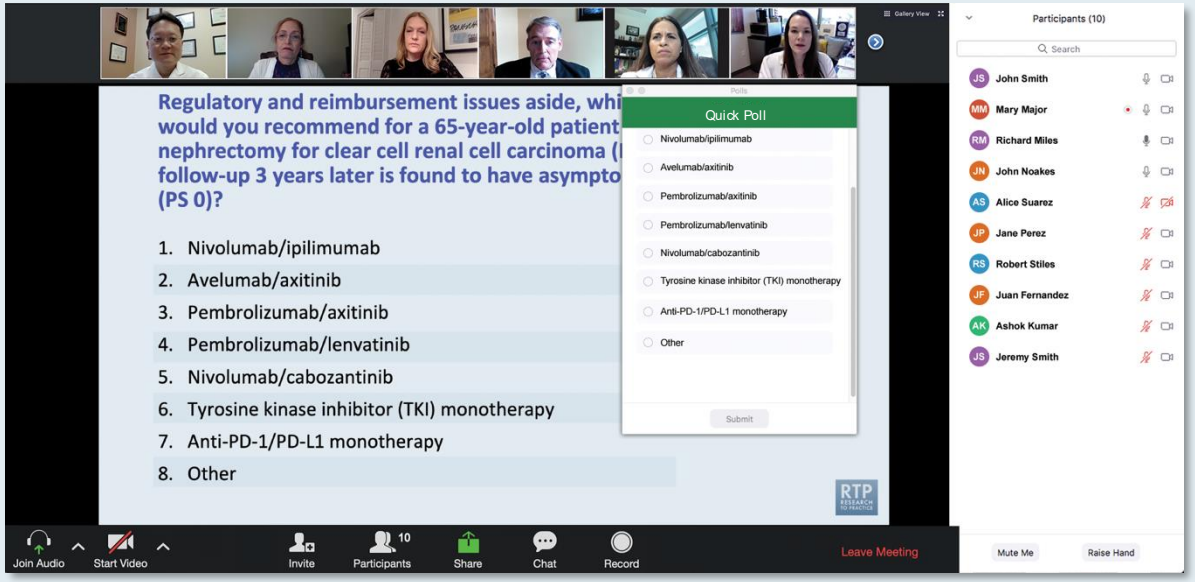

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Year in Review
Advances in the Use of Endocrine Therapy for Localized HR-positive Breast Cancer

Harold J Burstein
Dana-Farber Cancer Institute
Harvard Medical School

Year in Review
Genomic Evaluation for Treatment Decision-Making in Localized HR-Positive Breast Cancer

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

RTP Year in Review 2026

Key Datasets

Joyce O'Shaughnessy, MD

- Abdou Y et al. Race and clinical outcomes in hormone receptor-positive, HER2-negative, node-positive breast cancer in the randomized RxPONDER trial. *J Natl Cancer Inst* 2025;117(5):889-97.
- Hwang RF et al. Sentinel lymph node biopsy and clinical outcome of patients with node-positive breast cancer in the RxPONDER trial (S1007). San Antonio Breast Cancer Symposium 2025;Abstract PD12-05.
- Pusztai L et al. Development and validation of the RSClinN+ tool to predict prognosis and chemotherapy benefit for hormone receptor-positive, node-positive breast cancer. *J Clin Oncol* 2025;43(8):919-28.
- Mamounas E et al. A phase III trial evaluating addition of adjuvant chemotherapy to ovarian function suppression + endocrine therapy in premenopausal women with pN0-1, HR+/HER2- breast cancer (BC) and Onco*type* Recurrence Score (RS) ≤25 (OFSET): NRG-BR009. ASCO 2025;Abstract TPS615.
- Sparano JA et al. Multimodal artificial intelligence (AI) models integrating image, clinical, and molecular data for predicting early and late breast cancer recurrence in TAILORx. San Antonio Breast Cancer Symposium 2025;Abstract GS1-08.
- Samiian L et al. Molecular insights into HR+/HER2+ early-stage breast cancer: Neoadjuvant therapy responses by MammaPrint® and BluePrint® genomic subtypes. ASCO 2025;Abstract 605.

Key Datasets

Joyce O'Shaughnessy, MD (continued)

- Brufsky AM et al. MammaPrint predicts chemotherapy benefit in HR+HER2- early breast cancer: FLEX Registry real-world data. *JNCI Cancer Spectr* 2025;9(5).
- O'Shaughnessy J et al. Improved 3-year IDFS with anthracycline-based therapy for patients with 70-gene signature High 2, Luminal B, HR+HER2- early-stage breast cancer. San Antonio Breast Cancer Symposium 2025;Abstract PS2-07-03.
- Sanft T et al. Prospective decision impact study of the Breast Cancer Index: Results from the BCI Registry study. ASCO 2025;Abstract 531.
- O'Regan R et al. Assessment of adjuvant endocrine therapy with ovarian function suppression by breast cancer index. *JAMA Netw Open* 2025;8(11).
- O'Regan R et al. Identifying premenopausal patients with early-stage hormone receptor-positive breast cancer at minimal risk of distant recurrence by breast cancer index. *Breast* 2026;86:104714.
- Mamounas E et al. Evaluation of the Sensitivity to Endocrine Therapy (SET ER/PR) assay to predict benefit from extended endocrine therapy in the NRG/NSABP B-42 trial. San Antonio Breast Cancer Symposium 2025;Abstract GS3-05.

Key Datasets

Harold J Burstein, MD, PhD

- Francis P et al. 15-year outcomes for women with premenopausal hormone receptor-positive early breast cancer (BC) in the SOFT and TEXT trials assessing benefits from adjuvant exemestane (E) + ovarian function suppression (OFS) or tamoxifen (T)+OFS. ASCO 2025;Abstract 505.
- Johnston S et al. Overall survival with abemaciclib in early breast cancer. *Ann Oncol* 2026;37(2):155-65.
- Martin M et al. MonarchE: Evaluation of prognostic and predictive value of Ki-67 index pre and post neoadjuvant chemotherapy (NAC) and changes following NAC. ESMO 2025;Abstract 295MO.
- Cortes J et al. monarchE: Subgroup analysis of adjuvant abemaciclib + endocrine therapy for HR+, HER2-, high-risk early breast cancer by nodal status. San Antonio Breast Cancer Symposium 2025;Abstract PS1-08-08.
- Mayer E et al. TRADE: A phase II trial to assess the tolerability of abemaciclib dose escalation in early-stage HR-positive/HER2-negative breast cancer. *Ann Oncol* 2026 January;37(1):117-24.
- Schlam I et al. Trade: 6-month abemaciclib tolerability after initial dose escalation in early HR+/HER2- breast cancer. San Antonio Breast Cancer Symposium 2025;Abstract PD1-08.
- Crown J et al. Adjuvant ribociclib plus nonsteroidal aromatase inhibitor therapy in patients with HR-positive/HER2-negative early breast cancer: 5-year follow-up of NATALEE efficacy outcomes and updated overall survival. *ESMO Open* 2025;10(11):105858.

Key Datasets

Harold J Burstein, MD, PhD (continued)

- Hurvitz S et al. Five-year analysis of distant disease-free survival (DDFS) across key subgroups from the phase 3 NATALEE trial of ribociclib (RIB) plus a nonsteroidal aromatase inhibitor (NSAI) in patients with HR+/HER2− early breast cancer (EBC). San Antonio Breast Cancer Symposium 2025;Abstract PS3-09-08.
- McAndrew NP et al. Impact of neoadjuvant chemotherapy (NACT) response on clinical outcomes with ribociclib (RIB) in HR+/HER2− EBC: A subgroup analysis from the phase 3 NATALEE trial. ESMO 2025;Abstract 366P.
- Cottu PH et al. Risk of recurrence (ROR) after neoadjuvant ribociclib plus ET in clinically high-risk ER+/HER2− BC: Preliminary analysis of the SOLTI-RIBOLARIS trial. ESMO 2025;Abstract 296O.
- Martín M et al. Neoadjuvant abemaciclib plus letrozole versus chemotherapy in patients with HR+/HER2- highly proliferative breast cancer. *Clin Cancer Res* 2026 March 2;32(5):850-8.
- Bardia A et al. Giredestrant vs standard-of-care endocrine therapy as adjuvant treatment for patients with estrogen receptor-positive, HER2-negative early breast cancer: Results from the global phase III lidERA Breast Cancer trial. San Antonio Breast Cancer Symposium 2025;Abstract GS1-10.
- Cussac AL et al. Preoperative window-of-opportunity study with giredestrant or tamoxifen (tam) in premenopausal women with estrogen receptor-positive (ER+)/human epidermal growth factor receptor 2-negative (HER2-) and Ki67≥10% early breast cancer (EBC): The EMPRESS study. ESMO 2025;Abstract 294MO.

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MODULE 1: Adjuvant CDK4/6 Inhibitors

MODULE 2: Adjuvant Oral Selective Estrogen Receptor Degraders

MODULE 3: Premenopausal Patients

MODULE 4: Duration of Adjuvant Endocrine Treatment

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Oncologic Drugs Advisory Committee Meeting: April 30, 2026

- "The morning session focused on the results of the **SERENA-6** trial, which was intended to support a new drug application (NDA) for camizestrant, an oral selective estrogen receptor degrader (SERD), for the treatment of patients with HR+/HER2- metastatic breast cancer. The committee evaluated whether a novel treatment-switching paradigm—where patients receiving an aromatase inhibitor (AI) and CDK4/6 inhibitor switched to camizestrant upon detection of an ESR1 mutation, rather than at radiographic progression—provided adequate evidence of clinically meaningful benefit on camizestrant.

- The afternoon session focused on the results of the **CAPItello-281** trial, intended to support a supplemental NDA (sNDA) for the addition of capivasertib, a pan-AKT kinase inhibitor, to abiraterone and prednisone. The committee considered whether the trial demonstrated that the benefits outweigh the risks for patients with PTEN-deficient metastatic hormone-sensitive prostate cancer (mHSPC)."

https://friendsofcancerresearch.org/blog/stakeholder-connect-insights-from-the-april-30-odac-meeting/

Oncologic Drugs Advisory Committee Meeting: April 30, 2026

- **“The committee voted 6-3 that the SERENA-6 trial did not demonstrate clinically meaningful benefit for camizestrant treatment.** Those in favor cited the magnitude of PFS improvement, the favorable early OS trend, and plausibility of the early treatment switching approach. Those opposed pointed to the trial’s inability to determine whether earlier treatment switching improves patient outcomes, particularly in the absence of a statistically significant OS benefit or a crossover design to isolate treatment timing. Thus, the committee concluded that, although camizestrant appears active, the trial design could not establish whether the observed PFS gain represents a real, clinically meaningful benefit from the earlier treatment switching.

- **The committee voted (7-1, 1 abstain) that the benefits of adding capivasertib to abiraterone and prednisone treatment outweighed the risks for the proposed indication.** Members voting ‘yes’ cited the unmet need in PTEN-deficient aggressive disease, manageable toxicity with appropriate monitoring infrastructure, the importance of patient choice, and the biological plausibility reinforced by the biomarker dose-response signal. The ‘no’ voter cited marginal magnitude of benefit relative to the toxicity burden and duration.”

https://friendsofcancerresearch.org/blog/stakeholder-connect-insights-from-the-april-30-odac-meeting/

Rana R McKay, MD, FASCO
May 5, 2026

RTP Year in Review 2026

Year in Review:
Localized HR-Positive Breast Cancer

INTRODUCTION: ODAC – April 30, 2026

MODULE 1: Adjuvant CDK4/6 Inhibitors

MODULE 2: Adjuvant Oral Selective Estrogen Receptor Degraders

MODULE 3: Premenopausal Patients

MODULE 4: Duration of Adjuvant Endocrine Treatment

MODULE 5: Genomic Predictors of Chemotherapy Benefit

MODULE 6: Neoadjuvant Treatment

RTP Year in Review 2026

Select Key Datasets
Adjuvant CDK4/6 Inhibitors

- Johnston S et al. Overall survival with abemaciclib in early breast cancer. *Ann Oncol* 2026;37(2):155-65.
- Martin M et al. MonarchE: Evaluation of prognostic and predictive value of Ki-67 index pre and post neoadjuvant chemotherapy (NAC) and changes following NAC. ESMO 2025;Abstract 295MO.
- Cortes J et al. monarchE: Subgroup analysis of adjuvant abemaciclib + endocrine therapy for HR+, HER2-, high-risk early breast cancer by nodal status. San Antonio Breast Cancer Symposium 2025;Abstract PS1-08-08.
- Mayer E et al. TRADE: A phase II trial to assess the tolerability of abemaciclib dose escalation in early-stage HR-positive/HER2-negative breast cancer. *Ann Oncol* 2026 January;37(1):117-24.

Select Key Datasets
Adjuvant CDK4/6 Inhibitors

- Schlam I et al. Trade: 6-month abemaciclib tolerability after initial dose escalation in early HR+/HER2- breast cancer. San Antonio Breast Cancer Symposium 2025;Abstract PD1-08.
- Hurvitz S et al. Five-year analysis of distant disease-free survival (DDFS) across key subgroups from the phase 3 NATALEE trial of ribociclib (RIB) plus a nonsteroidal aromatase inhibitor (NSAI) in patients with HR+/HER2− early breast cancer (EBC). San Antonio Breast Cancer Symposium 2025;Abstract PS3-09-08.
- McAndrew NP et al. Impact of neoadjuvant chemotherapy (NACT) response on clinical outcomes with ribociclib (RIB) in HR+/HER2− EBC: A subgroup analysis from the phase 3 NATALEE trial. ESMO 2025;Abstract 366P.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY DRIVING INNOVATION IN ONCOLOGY

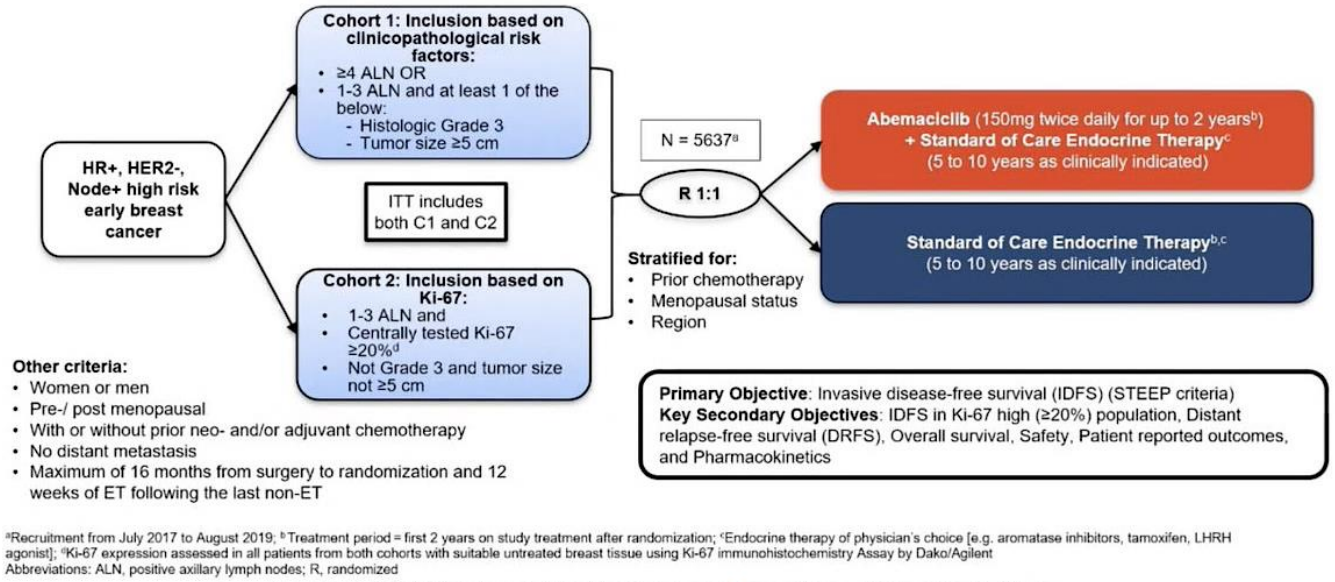
ORIGINAL ARTICLE

Overall survival with abemaciclib in early breast cancer☆

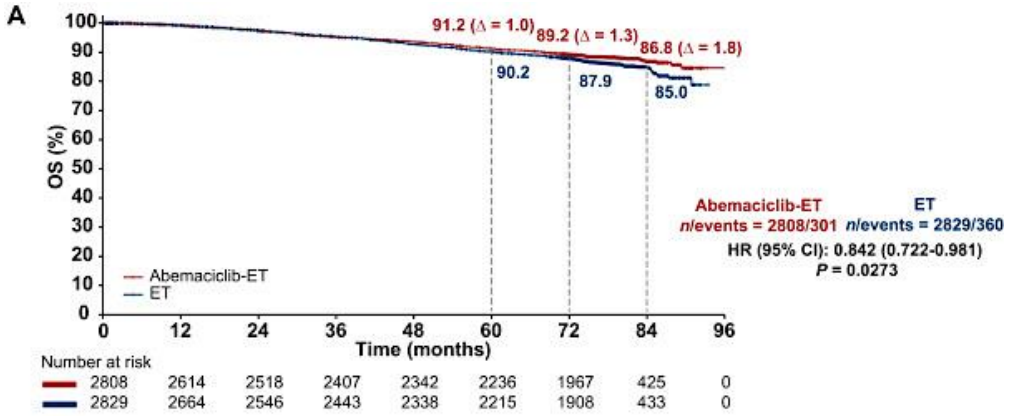
S. Johnston[1*], M. Martin[2], J. O'Shaughnessy[3], R. Hegg[4], S. M. Tolaney[5], V. Guarneri[6,7], L. Del Mastro[8,9], M. Campone[10], J. Sohn[11], F. Boyle[12], J. Cortes[13], H. S. Rugo[14,15], M. P. Goetz[16], E. P. Hamilton[17], C.-S. Huang[18], E. Senkus[19,20], I. Cicin[21], L. Testa[22], P. Neven[23], J. Huober[24], Z. Shao[25], R. Wei[26], M. Munoz[26], B. San Antonio[26], A. Shahir[26], P. Rastogi[27] & N. Harbeck[28]

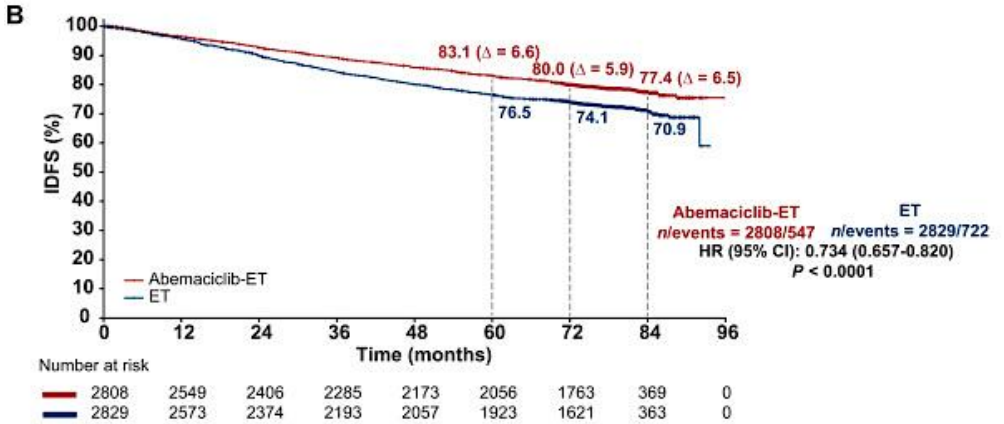
2026;37(2):155-65

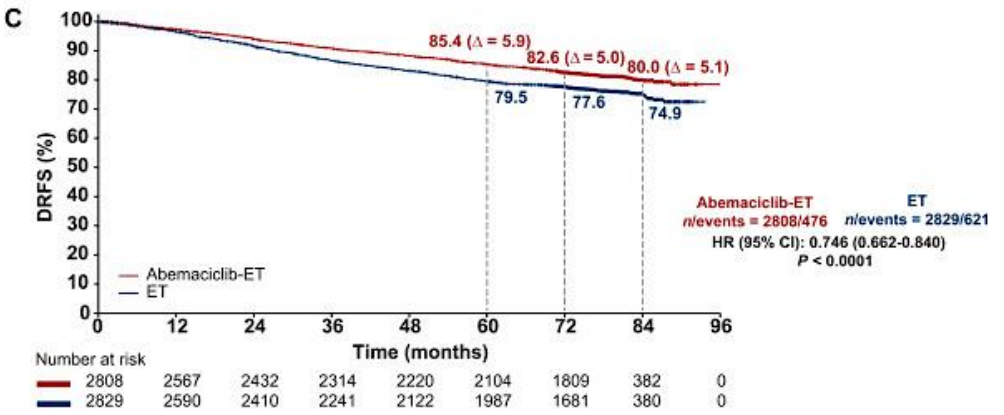
MONARCH-E



[a]Recruitment from July 2017 to August 2019; [b]Treatment period = first 2 years on study treatment after randomization; [c]Endocrine therapy of physician's choice [e.g. aromatase inhibitors, tamoxifen, LHRH agonist]; [d]Ki-67 expression assessed in all patients from both cohorts with suitable untreated breast tissue using Ki-67 immunohistochemistry Assay by Dako/Agilent
Abbreviations: ALN, positive axillary lymph nodes; R, randomized







Johnston S, et al. *Ann Oncol* 2026:37:155

Dana-Farber Cancer Institute

TRADE: Adjuvant Abemaciclib Tolerability at 6 Months After Initial Dose Escalation in Early HR+/HER2- Breast Cancer

HARVARD MEDICAL SCHOOL

Presentation Number: PD1-08

Abstract Number: 1009

Ilana Schlam[1], Dario Trapani[2], Se-Eun Kim[1], Meredith Faggen[1], Natalie Sinclair[1], Pedro Sanz-Altamira[1], Chiara Battelli[3], Shana Berwick[4], Steve Lo[5], Jose Acevedo[6], Sarah Sinclair[7], Alys Malcolm[1], Leticia Varella[1], Sarah Sammons[1], Susan Schumer[1], Philip D. Poorvu[1], Erin Wallace[1], Esther Pasternak[1], Nabihah Tayob[1], Sara M. Tolaney[1], Erica L. Mayer[1]

[1]Dana-Farber Cancer Institute, Boston MA; [2]European Institute of Oncology, IRCCS, Milan; [3]New England Cancer Specialists, Portland ME; [4]Beth Israel Deaconess Medical Center, Boston MA; [5]Stamford Health, Stamford, CT; [6]Boston Medical Center, Boston MA; [7]Northern Light Health, Brewer ME

SABCS 2025; Abstract PD1-08

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY DRIVING INNOVATION IN ONCOLOGY

ORIGINAL ARTICLE

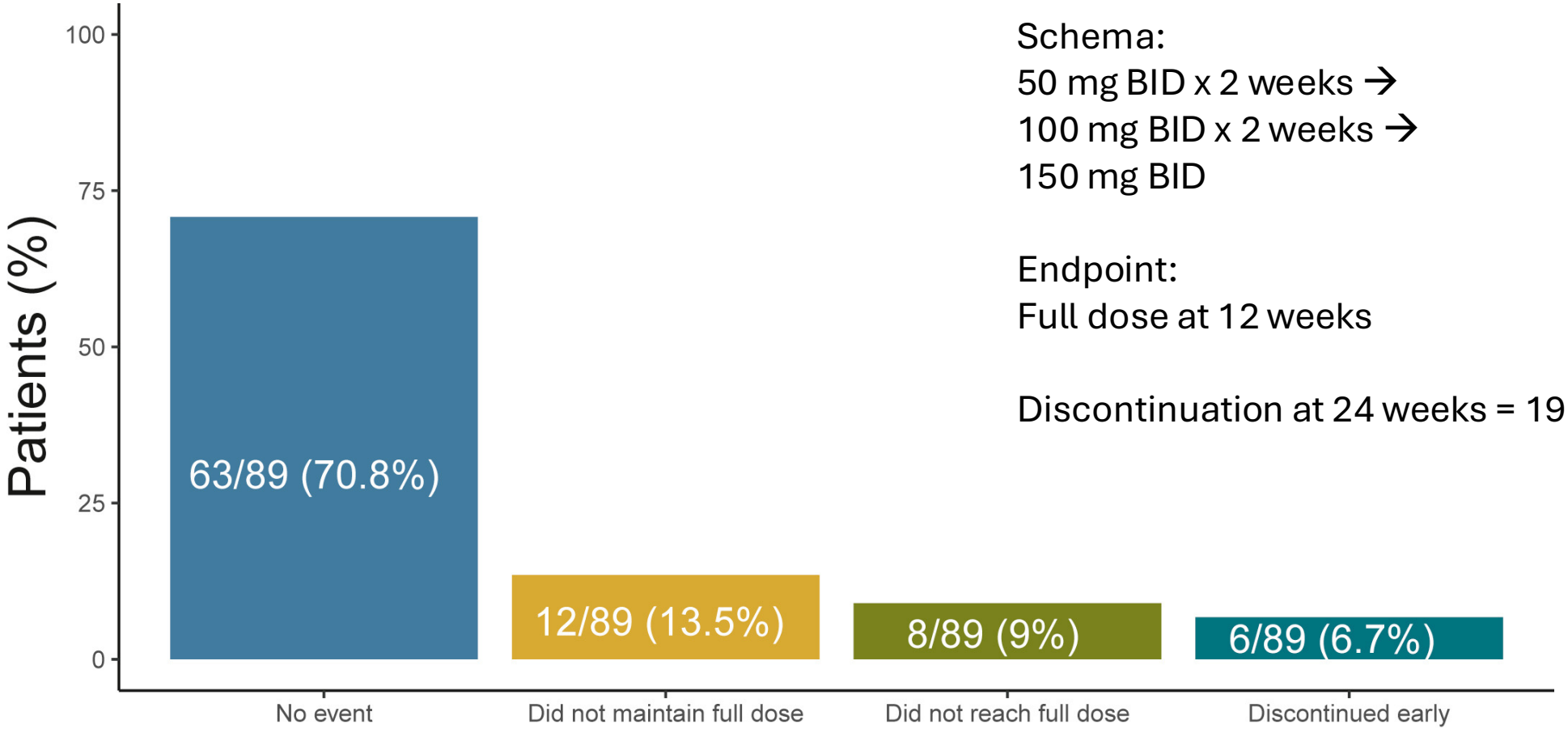
TRADE: a phase II trial to assess the tolerability of abemaciclib dose escalation in early-stage HR-positive/HER2-negative breast cancer☆

E. L. Mayer[1,2*], D. Trapani[3,4], S.-E. Kim[1], M. Faggen[1], N. Sinclair[1], P. Sanz-Altamira[1], C. Battelli[5], S. Berwick[6], S. Lo[7], J. Acevedo[8], S. Sinclair[9], A. Malcolm[1], L. Varella[1,2], S. Sammons[1,2], S. Schumer[1,2], P. D. Poorvu[1,2], E. Wallace[1], E. Pasternak[1], N. Tayob[1,2] & S. M. Tolaney[1,2]

2026;37(1):117-24

RTP Year in Review 2026

TRADE Study: Feasibility of Abemaciclib Dose Escalation



Schema:
50 mg BID x 2 weeks →
100 mg BID x 2 weeks →
150 mg BID

Endpoint:
Full dose at 12 weeks

Discontinuation at 24 weeks = 19%

Mayer EL, et al. *Ann Oncol* 2026; Schlamm I, et al. SABCS 2025

Poster# PS3-09-08

SABCS 2025

Sara A. Hurvitz | shurvitz@fredhutch.org

Five-Year Analysis of Distant Disease-Free Survival Across Key Subgroups From The Phase 3 NATALEE Trial of Ribociclib Plus a Nonsteroidal Aromatase Inhibitor in Patients with HR+/HER2− Early Breast Cancer

Sara Hurvitz,[1] Michal Jarzab,[2] Alistair Ring,[3] Priyanka Sharma,[4] Ionut Temciuc,[5] Huilin Hu,[6] Murat Akdere,[7] Juan Pablo Zarate,[8] Denise A. Yardley[8]

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

ORIGINAL ARTICLE

Adjuvant ribociclib plus nonsteroidal aromatase inhibitor therapy in patients with HR-positive/HER2-negative early breast cancer: 5-year follow-up of NATALEE efficacy outcomes and updated overall survival☆

J. Crown[1*], D. Stroyakovskii[2], D. A. Yardley[3], C.-S. Huang[4], P. A. Fasching[5], A. Bardia[6,7], S. Chia[8], S.-A. Im[9], M. Martin[10], B. Xu[11], C. H. Barrios[12], M. Untch[13], R. Moroose[14], S. A. Hurvitz[15], G. N. Hortobagyi[16], D. J. Slamon[6], F. Visco[17], G. Spera[18], J. P. Zarate[19], D. Halligan[20], Z. Li[19] & S. Loi[21]

2025;10(11):105858

RTP Year in Review 2026

NATALEE: Subset Outcomes with 5 years of follow-up

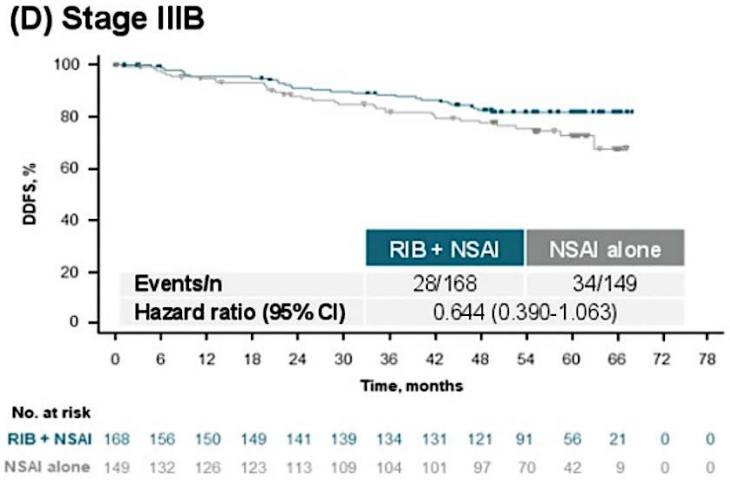


Table 2. Absolute DDFS Benefit by Anatomical Stage

Stage	3-y DDFS rate, %		3-y abs. benefit	5- DDFS rate, %		5-year abs. benefit
	RIB + NSAI	NSAI alone		RIB + NSAI	NSAI alone	
IIA	97.5	95.0	**Δ2.5**	95.9	89.7	**Δ6.2**
IIB	93.2	92.4	**Δ0.8**	90.2	89.0	**Δ1.2**
IIIA	91.6	88.5	**Δ3.1**	85.9	82.0	**Δ3.9**
IIIB	88.5	81.7	**Δ6.8**	81.7	72.8	**Δ8.9**
IIIC	84.6	81.8	**Δ2.8**	75.5	69.5	**Δ6.0**

Table 3. Absolute DDFS Benefit by Nodal Status

Subgroup	3-y DDFS rate, %		3-y abs. benefit	5-y DDFS rate, %		5-y abs. benefit
	RIB + NSAI	NSAI alone		RIB + NSAI	NSAI alone	
Nodal status						
N0	94.6	91.5	**Δ3.1**	91.6	85.8	**Δ5.8**
N1-N3	91.3	88.8	**Δ2.5**	86.1	82.0	**Δ4.1**

DDFS by Menopausal Status, Ki67 Status, Age Group, and Prior ET Duration

- RIB + NSAI showed consistent DDFS benefits regardless of menopausal status, Ki67 status, age, and prior duration of ET, with increasing absolute benefits from 3 to 5 years across most subgroups (**Table 4**)

Table 4. DDFS by Menopausal Status, Ki67 Status, Age Group, and Prior ET Duration in NATALEE

Subgroup	Events/n		3-y DDFS rate, %		3-y abs. benefit	5-y DDFS rate, %		5-y abs. benefit	HR (95% CI)
	RIB + NSAI	NSAI alone	RIB + NSAI	NSAI alone		RIB + NSAI	NSAI alone		
Menopausal status									
Premenopausal[a]	110/1126	147/1132	92.8	90.0	**Δ2.8**	88.5	84.4	**Δ4.1**	0.685 (0.535-0.877)
Postmenopausal	179/1423	228/1420	90.7	88.4	**Δ2.3**	85.4	81.0	**Δ4.4**	0.725 (0.596-0.882)
Ki67 score									
≤20	118/1200	166/1241	92.8	90.5	**Δ2.3**	88.5	84.2	**Δ4.3**	0.691 (0.545-0.875)
>20	126/919	157/932	89.9	87.3	**Δ2.6**	84.6	79.8	**Δ4.8**	0.725 (0.572-0.918)
Age									
<40 y	31/250	44/293	92.3	86.8	**Δ5.5**	85.5	80.5	**Δ5.0**	0.650 (0.409-1.032)
≥40 y	258/2299	331/2259	91.6	89.4	**Δ2.2**	86.9	82.7	**Δ4.2**	0.717 (0.610-0.844)
<65 y	237/2142	298/2186	91.8	89.7	**Δ2.1**	87.2	83.7	**Δ3.5**	0.743 (0.626-0.881)
≥65 y	52/407	77/366	90.8	85.7	**Δ5.1**	84.7	75.4	**Δ9.3**	0.572 (0.402-0.815)
Prior ET									
<12 weeks	78/748	102/718	92.4	89.7	**Δ2.7**	87.7	83.2	**Δ4.5**	0.664 (0.494-0.893)
≥12 but <26 weeks	79/651	92/664	91.4	89.3	**Δ2.1**	85.4	83.4	**Δ2.0**	0.813 (0.601-1.099)
≥26 weeks	40/358	55/353	92.5	89.5	**Δ3.0**	87.5	80.7	**Δ6.8**	0.666 (0.401-1.005)

[a] Also includes men.

Hurvitz S et al. SABCS 2025, abstract PS3-09-08

Poster # 366P

ESMO 2025

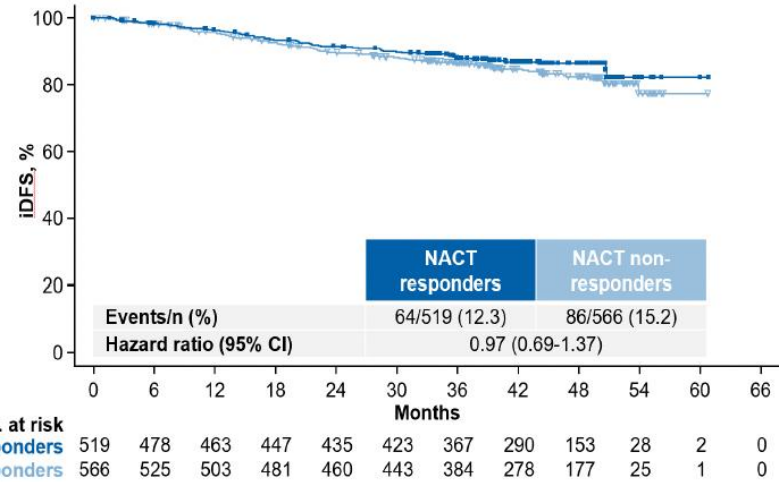
Nicholas McAndrew | NMcAndrew@mednet.ucla.edu

Impact of neoadjuvant chemotherapy response on adjuvant ribociclib benefit in HR+/HER2− EBC: a NATALEE analysis

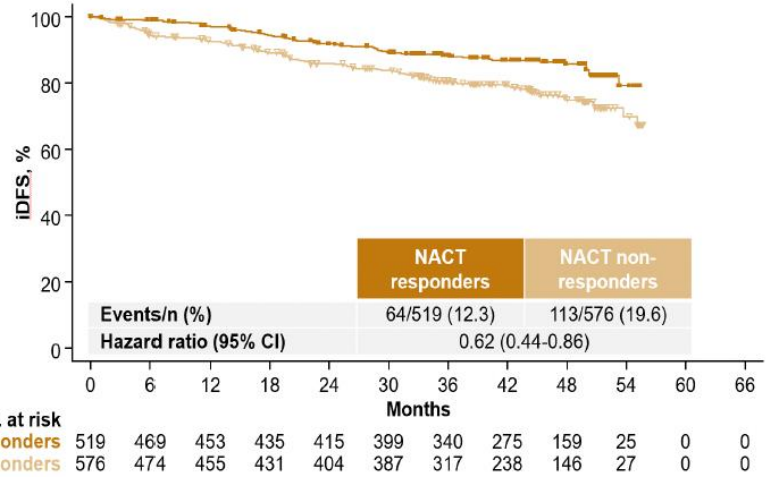
Nicholas McAndrew,[1] Stephen Chia,[2] Fabio Puglisi,[3] Yann Izarzugaza,[4] Christian Schem,[5] Binghe Xu,[6] Fanny Le Du,[7] Priyanka Sharma,[8] Peter A. Fasching,[9] Alejandro Rodriguez,[10] Murat Akdere,[11] Yogesh Chattar,[12] Juan Pablo Zarate,[13] Aditya Bardia[1]

NATALEE: Outcomes as a Function of NACT Response

A. iDFS for NACT Responders vs Non-Responders in the Ribociclib + NSAI Arm



B. iDFS for NACT Responders vs Non-Responders in the NSAI-Alone Arm



McAndrew NP, et al. ESMO 2025, abstract 366 P

Summary

- Long-term follow-up for MonarchE and NATALEE show durable benefits
- In the reports for MonarchE, there is now a survival benefit noted
- Benefits are seen largely irrespective of clinical subsets
  - Remember that trials were designed for a high risk cohort of patients defined by stage and/or tumor biology
- There are persistent challenges in patient adherence given the side effects of CDK46i and the duration of therapy

Courtesy of Harold J Burstein, MD, PhD

Year in Review:
Localized HR-Positive Breast Cancer

INTRODUCTION: ODAC – April 30, 2026

MODULE 1: Adjuvant CDK4/6 Inhibitors

MODULE 2: Adjuvant Oral Selective Estrogen Receptor Degraders

MODULE 3: Premenopausal Patients

MODULE 4: Duration of Adjuvant Endocrine Treatment

MODULE 5: Genomic Predictors of Chemotherapy Benefit

MODULE 6: Neoadjuvant Treatment

RTP Year in Review 2026

Select Key Datasets

Adjuvant Oral Selective Estrogen Receptor Degraders

- Bardia A et al. Giredestrant vs standard-of-care endocrine therapy as adjuvant treatment for patients with estrogen receptor-positive, HER2-negative early breast cancer: Results from the global phase III lidERA Breast Cancer trial. San Antonio Breast Cancer Symposium 2025;Abstract GS1-10.

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

Abstract GS1-10

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

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

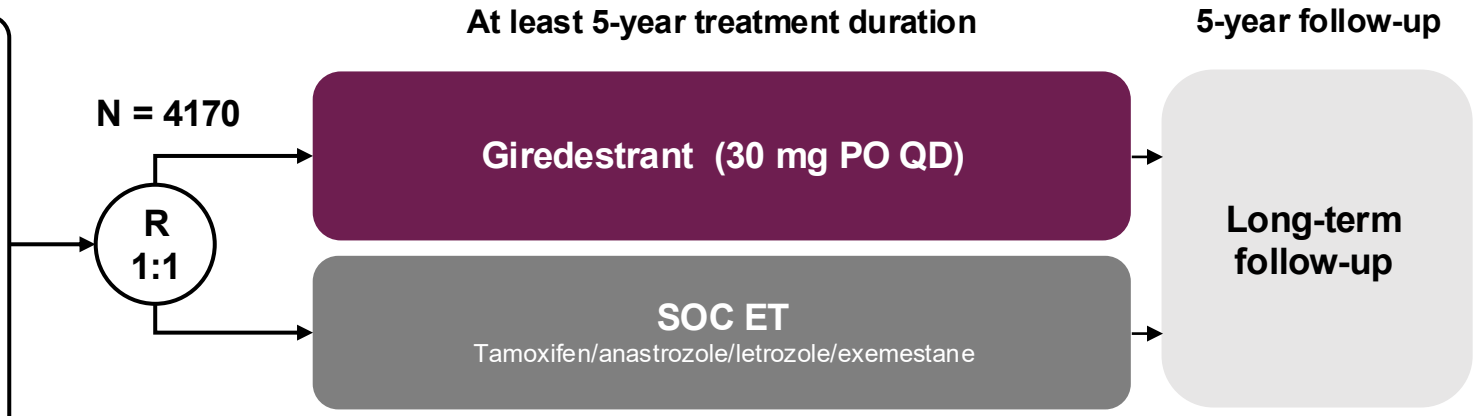
* Equal contributions

lidERA Breast Cancer study design

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

Key eligibility criteria

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



Stratification factors

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

Primary endpoint

- IDFS (excluding second primary non-breast cancer)

Key secondary endpoints

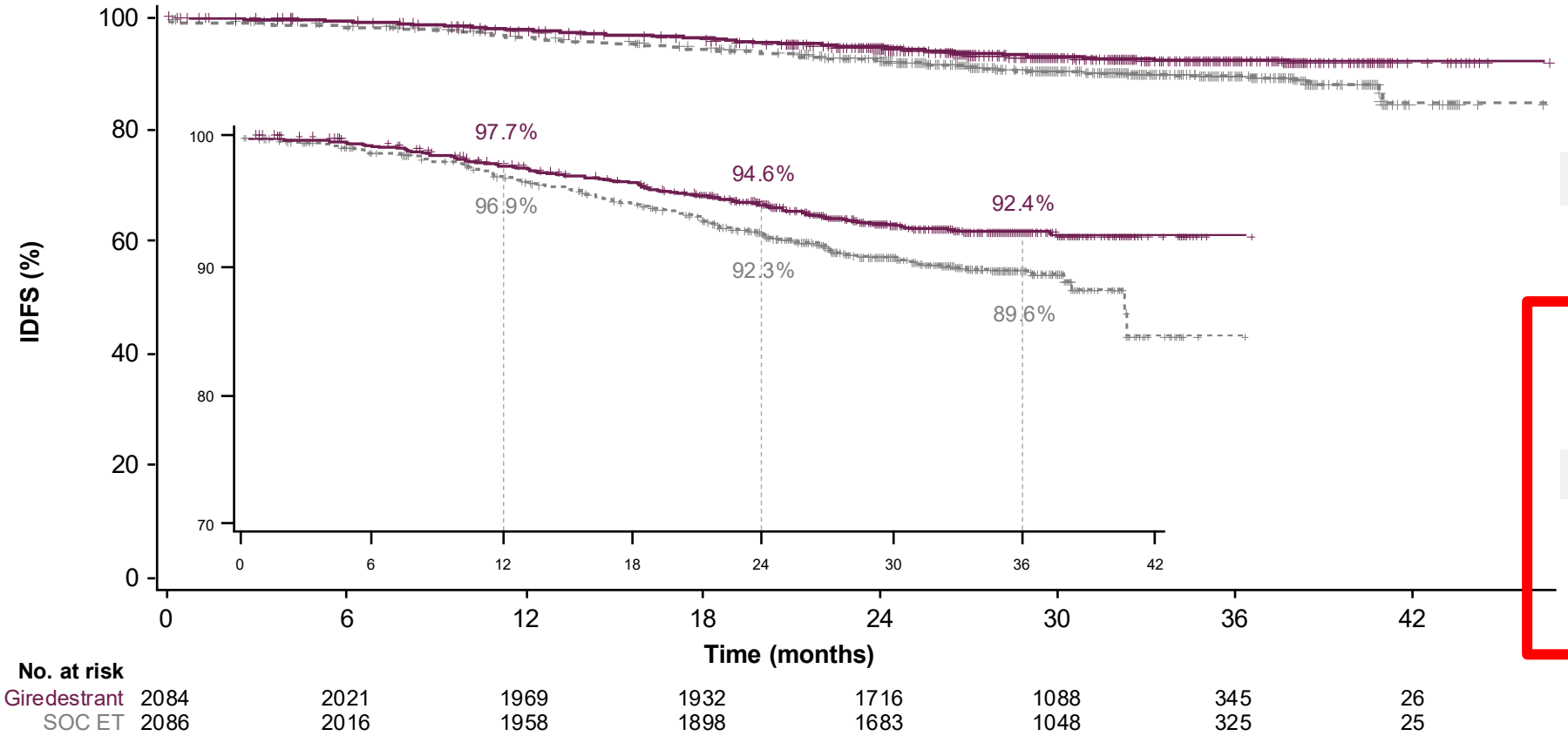
- DFS, DRFI, IDFS (including second primary non-breast invasive cancer with exception of non-melanoma skin cancers and *in situ* carcinomas of any site), LRRFI, OS, safety

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

Enrollment: August 2021 to September 2023. Up to 12 weeks of ET ± CDK4/6i were allowed. ER+ was defined as ≥ 1% positive cells by immunohistochemistry. * OncotypeDx ≥ 26 or high-risk Mammaprint.
† Pre-menopausal patients on aromatase inhibitors or giredestrant had to receive ovarian function suppression with an approved luteinizing hormone-releasing hormone agonist. ‡ Medium risk: pN0 and primary tumor > 1 cm with high-risk biologic features (Grade 3, or Ki67 ≥ 20%, or high score on genomic assay [if available]) and pN1 with low-risk biologic features (Grade 1/2 and Ki67 < 20% and tumor ≤ 5 cm and low score on genomic assay [if available]). § High risk: pT4, or pN2, or pN3 and pN1 with high-risk biologic features (Grade 3, or Ki67 ≥ 20%, or tumor > 5 cm, or high score on genomic assay [if available]).
CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; DFS, disease-free survival; DRFI, distant recurrence-free interval; ER+, estrogen receptor-positive; ET, endocrine therapy; IDFS, invasive disease-free survival; LRRFI, locoregional recurrence-free interval; OS, overall survival; PO, orally; QD, once daily; R, randomization; RoW, rest of the world; SOC, standard-of-care.
ClinicalTrials.gov number, NCT04961996. Adapted from Geyer CE, *et al*. ASCO 2023 (TPS616), with permission.
Presented by: Aditya L. Bardia, MD.

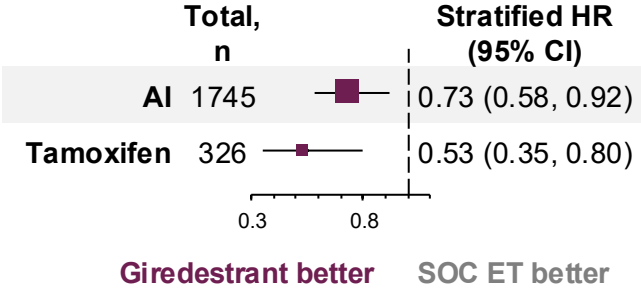
Bardia Proc SABCS 2025;Abstract GS1-10

Primary endpoint: IDFS



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

Exploratory analysis: IDFS by SOC ET



Median follow-up: 32.3 months

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

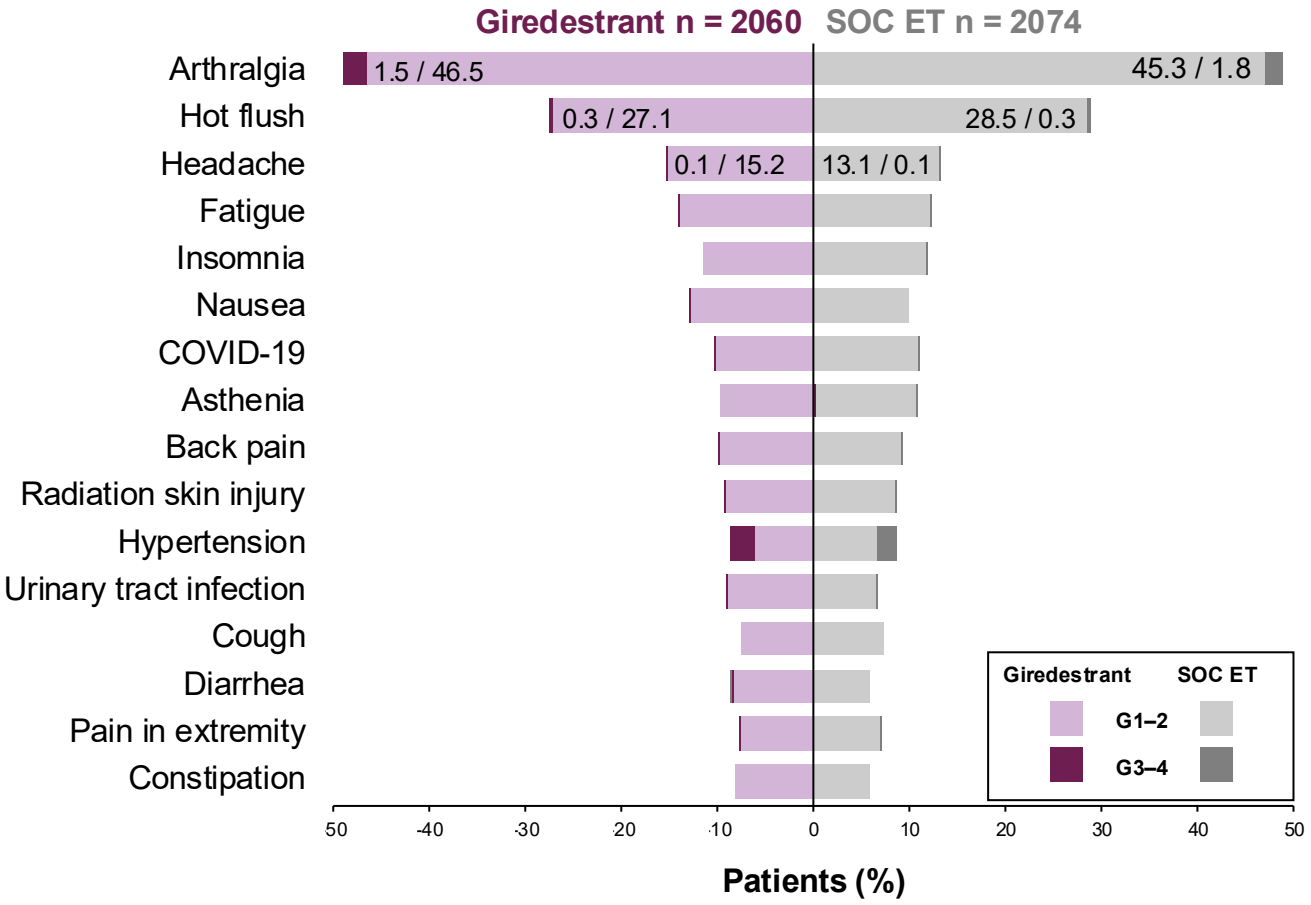
Data cutoff: August 8, 2025. Median follow-up, 32.4 months in the giredestrant arm and 32.3 months in the SOC ET arm; maximum follow-up, 46.6 months and 46.3 months, respectively. * Log-rank (2-sided). p-value boundary for IDFS interim analysis was 0.0217 (2-sided). AI, aromatase inhibitor; CI, confidence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

Presented by: Aditya L. Bardia, MD.

Bardia Proc SABCS 2025;Abstract GS1-10

AE overview *(safety-evaluable population)*

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



Selected AEs

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

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

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

Presented by: Aditya L. Bardia, MD.

Oral SERD Adjuvant Trials

Trial Name	N	Arms	Patient Population	Adjuvant CDK4/6i allowed	Trial Identifier
CAMBRIA-2	5500	Camizestrant vs ET	High-risk ER+/HER2-, **initial adjuvant therapy**	Yes	NCT05952557
lidERA	4200	Giredestrant vs ET	Medium to high-risk ER+/HER2-, **initial adjuvant therapy**	No	NCT04961996
ELEGANT	4220	Elacestrant vs SoC	ER+/HER2-, Early Breast Cancer With High Risk of Recurrence; **2-5y of prior ET**	Prior to trial entry	NCT06492616
EMBER-4	6000	Imlunestrant vs ET	High-risk ER+/HER2-, **2-5 yr of adjuvant ET**	Prior to trial entry	NCT05514054
CAMBRIA-1	4300	Camizestrant vs ET	Intermediate to high-risk ER+/HER2-, **2-5 yr of adjuvant ET**	Prior to trial entry	NCT05774951
TREAT ctDNA	220	Elacestrant vs ET	↑ risk ER+/HER2-, ctDNA relapse, **2-7 yr adjuvant ET**	≥12 mo prior to trial entry	NCT05512364

Carey SABCS 2025;Abstract GS1-10 Discussant

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RTP Year in Review 2026

Select Key Datasets
Premenopausal Patients

- Francis P et al. 15-year outcomes for women with premenopausal hormone receptor-positive early breast cancer (BC) in the SOFT and TEXT trials assessing benefits from adjuvant exemestane (E) + ovarian function suppression (OFS) or tamoxifen (T)+OFS. ASCO 2025;Abstract 505.
- O'Regan R et al. Assessment of adjuvant endocrine therapy with ovarian function suppression by breast cancer index. *JAMA Netw Open* 2025;8(11).
- O'Regan R et al. Identifying premenopausal patients with early-stage hormone receptor-positive breast cancer at minimal risk of distant recurrence by breast cancer index. *Breast* 2026;86:104714.
- Mamounas E et al. A phase III trial evaluating addition of adjuvant chemotherapy to ovarian function suppression + endocrine therapy in premenopausal women with pN0-1, HR+/HER2- breast cancer (BC) and Onco*type* Recurrence Score (RS) ≤25 (OFSET): NRG-BR009. ASCO 2025;Abstract TPS615.

2025 ASCO ANNUAL MEETING

Abstract 505

15-year Outcomes for Women with Premenopausal Hormone Receptor-positive Early Breast Cancer in the SOFT and TEXT Trials Assessing the Benefits from Adjuvant Exemestane (E)+ Ovarian Function Suppression (OFS) or Tamoxifen (T)+OFS

Prudence A Francis MD

On behalf of the SOFT and TEXT Investigators and
and the International Breast Cancer Study Group

PA Francis, O Pagani, GF Fleming, BA Walley, M Colleoni, G Rubovszky, C Tondini, EM Ciruelos, HL Gomez, HR Bonnefoi, HJ Burstein, C Chini, F Puglisi, S Spazzapan, A Bernardo, M Climent, M Bellet, T Ruhstaller, B Bermejo, SK Chia, S Martino, CE Geyer Jr, MP Goetz, JN Ingle, V Stearns, NE Davidson, F Le Du, B Müller, RE Coleman, S Loibl, EP Winer, B Ruepp, S Loi, I Láng, AS Coates, RD Gelber, A Goldhirsch, MM Regan

International Breast Cancer Study Group
IBCSG

RTP Year in Review 2026

Role of OFS in ER+ EBC

- OFS is an effective treatment in premenopausal breast cancer
  - Reduces risk in combination with tamoxifen
  - Facilitates use of AI, which further lowers recurrence risk
  - Enables adjuvant CDK46 inhibitor therapy

- Longer durations beyond 5 years are of additional benefit

- Studies need to optimize OFS

Courtesy of Harold J Burstein, MD, PhD

JAMA Network Open

Original Investigation | Oncology

Assessment of Adjuvant Endocrine Therapy With Ovarian Function Suppression by Breast Cancer Index

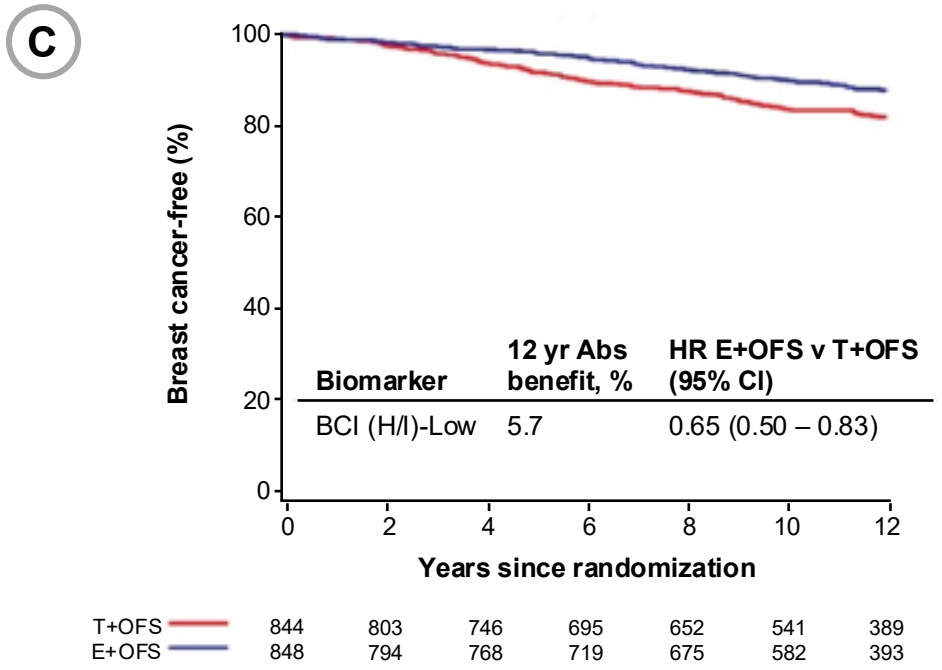
Ruth M. O'Regan, MD; Yue Ren, MS; Yi Zhang, PhD; Natalia Siuliukina, PhD; Catherine A. Schnabel, PhD; Roswitha Kammler, BA; Giuseppe Viale, MD; Patrizia Dell'Orto, DSc; Elisabetta Munzone, MD; István Láng, MD, PhD; Carlo Tondini, MD; Henry L. Gomez, MD; Claudio Chini, MD; Stefania Vittoria Luisa Nicoletti, MD; Fabio Puglisi, MD, PhD; Khalil Zaman, MD, PhD; Matthew P. Goetz, MD; Vered Stearns, MD; Silvana Martino, DO; Muhammad Salim, MD; Sibylle Loibl, MD, PhD; Charles E. Geyer, MD; Hervé R. Bonnefoi, MD; Eva M. Ciruelos, MD, PhD; Sherene Loi, MD, PhD; Marco Colleoni, MD; Gini F. Fleming, MD; Prudence A. Francis, MD; Barbara A. Walley, MD; Olivia Pagani, MD; Kai Treuner, PhD; Meredith M. Regan, ScD

2025;8(11)

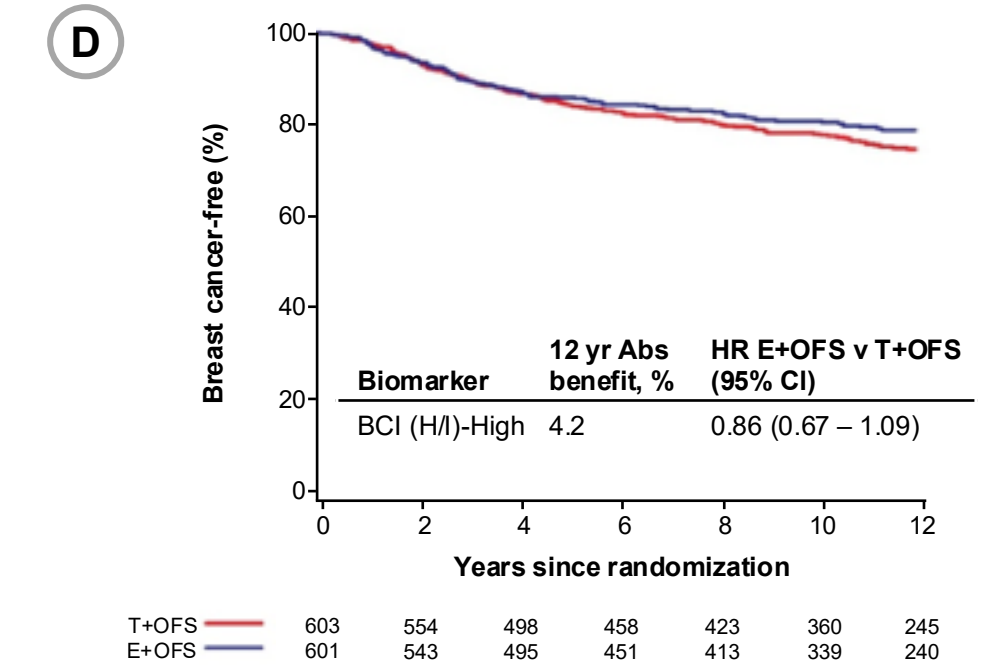
Results – Prediction

- Predictive performance of BCI (H/I) for benefit of E-OFS vs T-OFS in SOFT+TEXT

BCI (H/I) – Low



BCI (H/I) – High



O'Regan RM, et al. Presented at: ASCO 2025. Abstract 557 and *JAMA Network OPEN*, 2025.
Abs, absolute; BCI, breast cancer index; E, exemestane; H/I, HOXB13/IL17BR ratio; OFS, ovarian function suppression; T, tamoxifen.

Conclusions

- BCI was confirmed as prognostic in premenopausal patients
- BCI (H/I) did not clearly demonstrate differential benefit between exemestane-OFS and tamoxifen-OFS in this population, especially those with BCI (H/I)-high tumors
- For patients with BCI (H/I)-low tumors, may benefit more from more intensive ET with exemestane
- Different findings by age
  - The authors hypothesized this was possibly because of changing benefit from those older patients with BCI (H/I)-high tumors as they become postmenopausal over time

O'Regan RM, et al. Presented at: ASCO 2025. Abstract 557 and ***JAMA Network OPEN*, 2025**.
BCI, breast cancer index; ET, endocrine therapy; H/I, HOXB13/IL17BR ratio; OFS, ovarian function suppression.

The Breast 86 (2026) 104714

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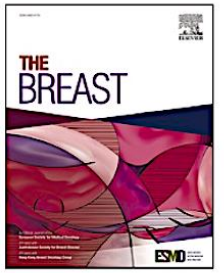


Identifying premenopausal patients with early-stage hormone receptor–positive breast cancer at minimal risk of distant recurrence by breast cancer index

Ruth M. O'Regan [a], Yue Ren [b], Yi Zhang [c], Gini F. Fleming [d], Prudence A. Francis [e,f,g,h], Olivia Pagani [i,j,k], Barbara A. Walley [l,m], Roswitha Kammler [n], Patrizia Dell'Orto [o,p], Giuseppe Viale [o,p], Sherene Loi [e,q], Marco Colleoni [r], Kai Treuner [c], Meredith M. Regan [b,s,*]

Conclusions: This study confirmed prognostic ability of the minimal-risk BCI cutpoint to classify patients estimated to have minimal-risk of distant recurrence within 10 years among premenopausal patients treated for hormone-receptor-positive node-negative breast cancer, providing relevant information for personalizing adjuvant endocrine therapy.

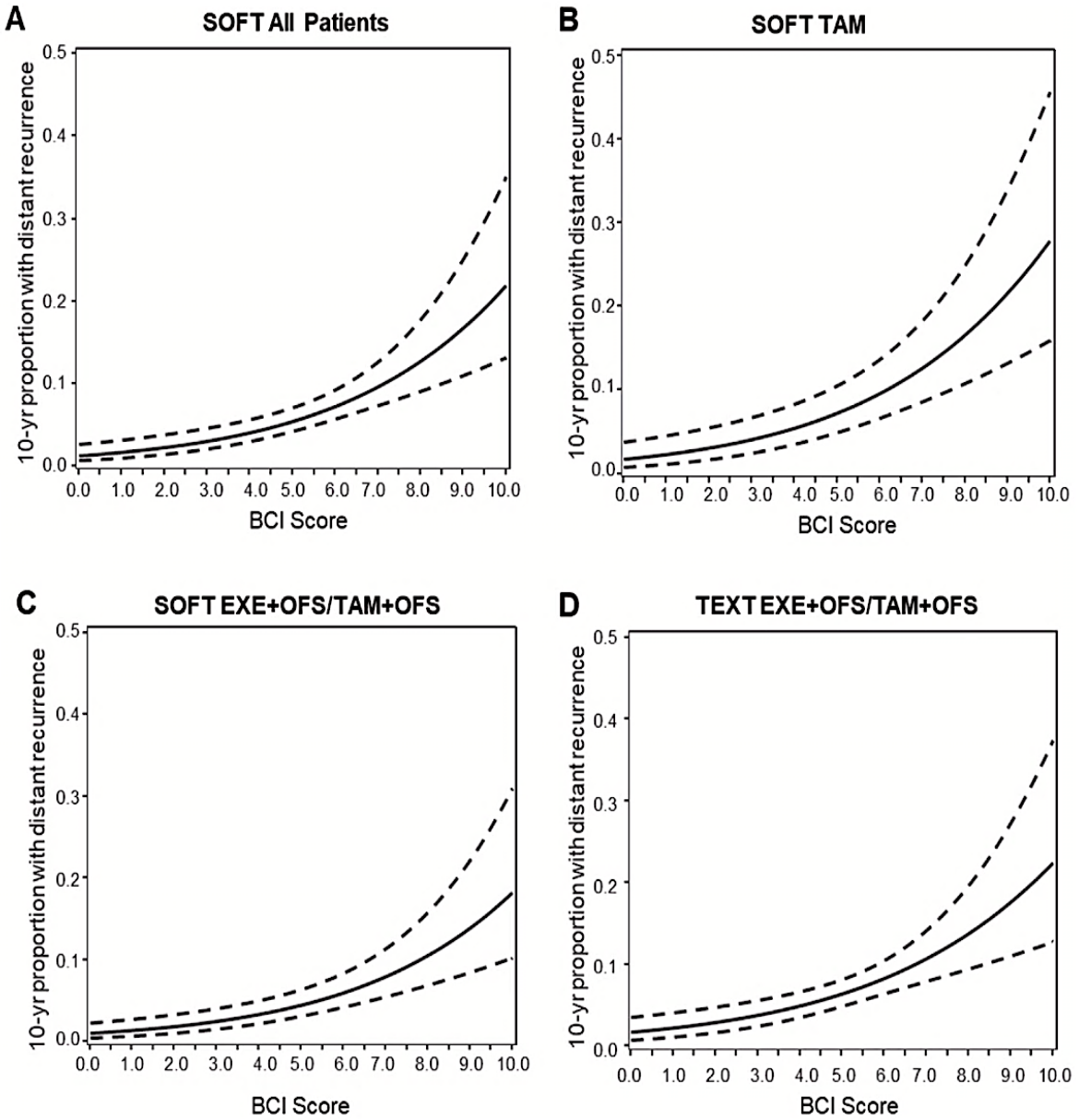


Fig. 2. Relation of the continuous BCI score with estimated probability of distant recurrence within 10 years of randomization in the SOFT and TEXT N0 cohorts. **(A)** SOFT all patients; **(B)** SOFT assigned tamoxifen (TAM); **(C)** SOFT assigned exemestane (exemestane (EXE) + OFS or tamoxifen + OFS; (D) TEXT all patients. Values are one minus survivorship probabilities for distant recurrence-free interval (DRFI) at 10 years since randomization estimated from a Cox model, with pointwise 95 % CI. For the adjusted BCI model, the new cutpoint to differentiate minimal-from low-risk is 3.0; the current cutpoints for intermediate- and high-risk are 5.1 and 6.5.

O'Regan R et al. The Breast, 2026

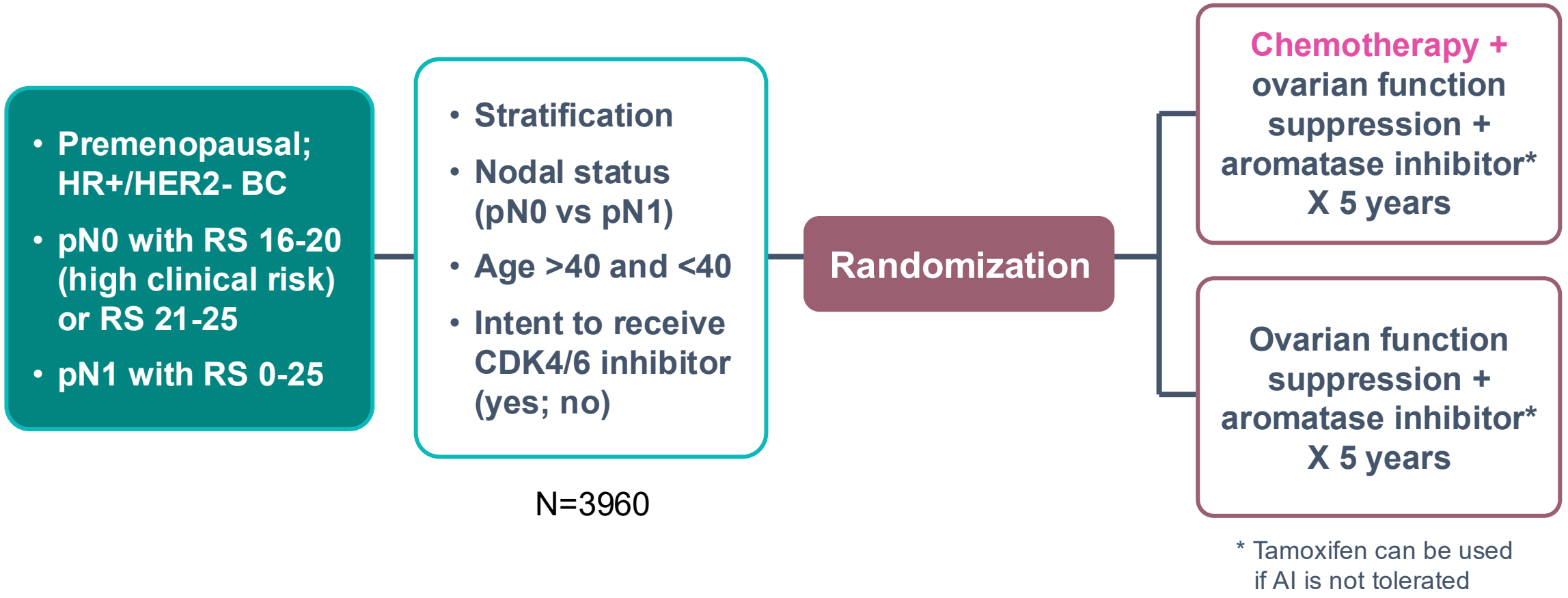
NRG-BR009:
A Phase III Trial Evaluating Addition of Adjuvant Chemotherapy to Ovarian Function Suppression Plus Endocrine Therapy in Premenopausal Women with pN0-1, HR+/HER2- Breast Cancer and Oncotype Recurrence Score ≤ 25 (OFSET): NRG BR009

TPS615 ASCO 2025

Eleftherios P. Mamounas,[1] Gong Tang,[2] Shannon L. Puhalla,[3] Sandra M. Swain,[4] Patricia A. Ganz,[5] N. Lynn Henry,[6] Reena S. Cecchini,[2] Sonya A. Reid,[7] Priya Rastogi,[3] Charles E. Geyer, Jr,[3] Julia R. White,[8] Amy S. Clark,[9] Tufia C. Haddad,[10] Gregory A. Vidal,[11] Norman Wolmark[3,12]

[1]AdventHealth Cancer Institute, Orlando, FL; [2]NRG Oncology SDMC, Department of Biostatistics and Health Data Science, University of Pittsburgh, Pittsburgh, PA; [3]UPMC Hillman Cancer Center, University of Pittsburgh School of Medicine, Pittsburgh, PA; [4]Georgetown Lombardi CCC, Georgetown University Medical Center, MedStar Health, Washington, DC; [5]David Geffen School of Medicine at UCLA, UCLA Fielding School of Public Health, UCLA Jonsson CCC, Los Angeles, CA; [6]University of Michigan Medical School, Ann Arbor, MI; [7]Vanderbilt University Medical Center, Nashville, TN; [8]University of Kansas Medical Center CCC, Kansas City, KS; [9]Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA; [10]Mayo Clinic CCC, Rochester, MN; [11]West Cancer Center and Research Institute, Germantown, TN; [12]NSABP Foundation, Inc., Pittsburgh, PA

NRG-BR009 (OFSET): Schema



ClinicalTrials.gov. NCT05879926. Accessed September 2, 2025. https://www.clinicaltrials.gov/study/NCT05879926
AI, aromatase inhibitor; BC, breast cancer; CDK, cyclin-dependent kinase; HR, hormone receptor; N, node; RS, recurrence score.

Mamounas ASCO 2025;Abstract TPS615

Additional Treatment Considerations

- Abemaciclib, ribociclib OK:
  - » Patients who meet criteria for adjuvant CDK 4/6 inhibitors may take this as per package label
  - » The intent to use CDK 4/6 inhibitors will have to be declared prior to randomization; need to be captured on the case report form
- Bisphosphonates OK

CONCLUSIONS: <u>Neo/Adjuvant Chemotherapy is SOC for HR+ N+ premenopausal pts</u>

ClinicalTrials.gov. NCT05879926. Accessed September 2, 2025. https://www.clinicaltrials.gov/study/NCT05879926

Mamounas ASCO 2025;Abstract TPS615

Year in Review:
Localized HR-Positive Breast Cancer

INTRODUCTION: ODAC – April 30, 2026

MODULE 1: Adjuvant CDK4/6 Inhibitors

MODULE 2: Adjuvant Oral Selective Estrogen Receptor Degraders

MODULE 3: Premenopausal Patients

MODULE 4: Duration of Adjuvant Endocrine Treatment

MODULE 5: Genomic Predictors of Chemotherapy Benefit

MODULE 6: Neoadjuvant Treatment

RTP Year in Review 2026

Select Key Datasets
Duration of Adjuvant Endocrine Treatment

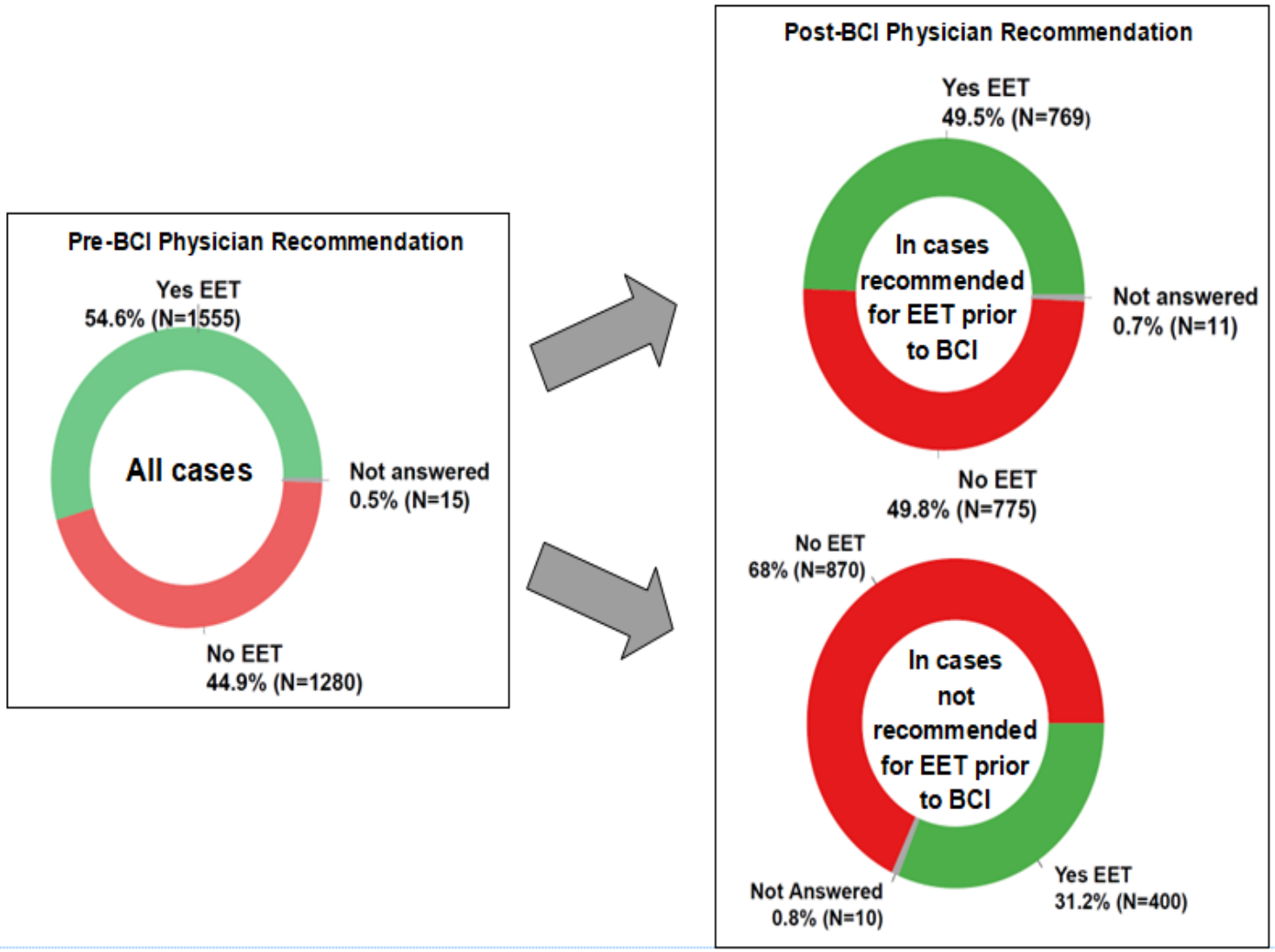
- Sanft T et al. Prospective decision impact study of the Breast Cancer Index: Results from the BCI Registry study. ASCO 2025;Abstract 531.
- Mamounas E et al. Evaluation of the Sensitivity to Endocrine Therapy (SET ER/PR) assay to predict benefit from extended endocrine therapy in the NRG/NSABP B-42 trial. San Antonio Breast Cancer Symposium 2025;Abstract GS3-05.

Prospective Decision Impact Study of the Breast Cancer Index: Results from the BCI Registry Study

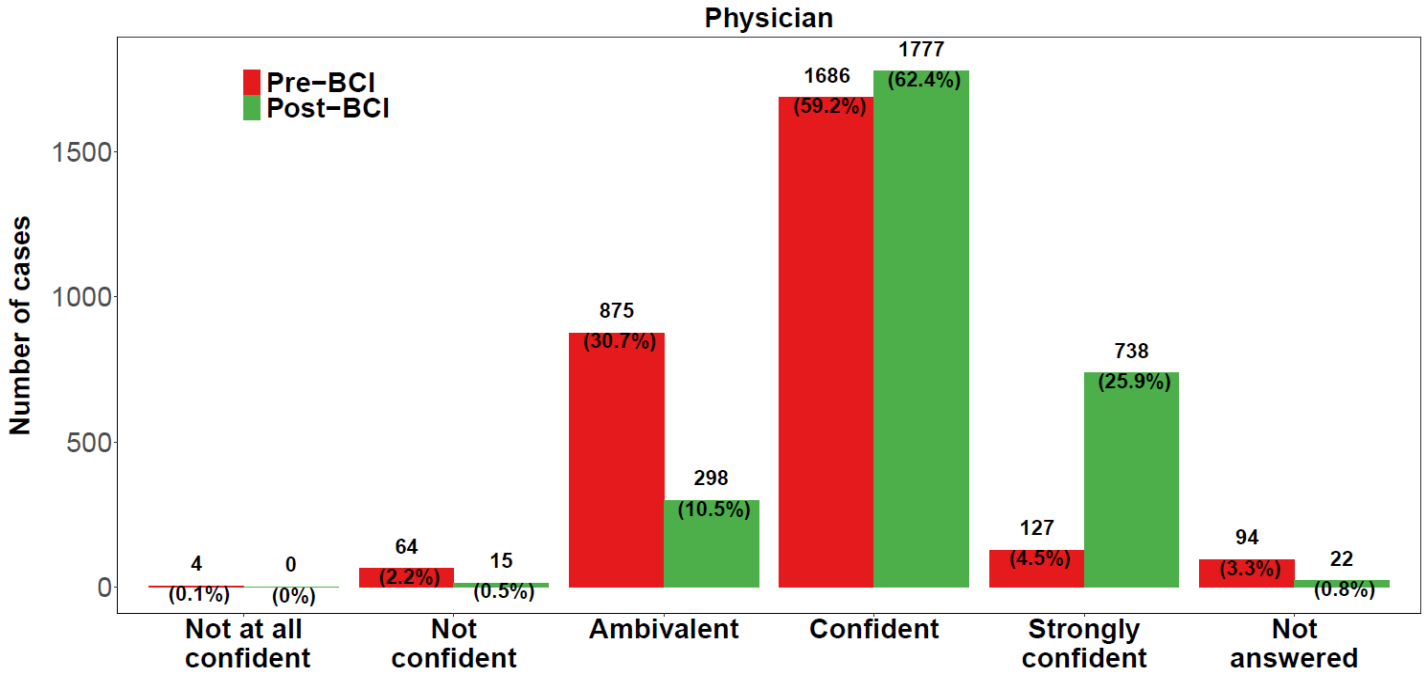
ASCO 2025 Abst 531

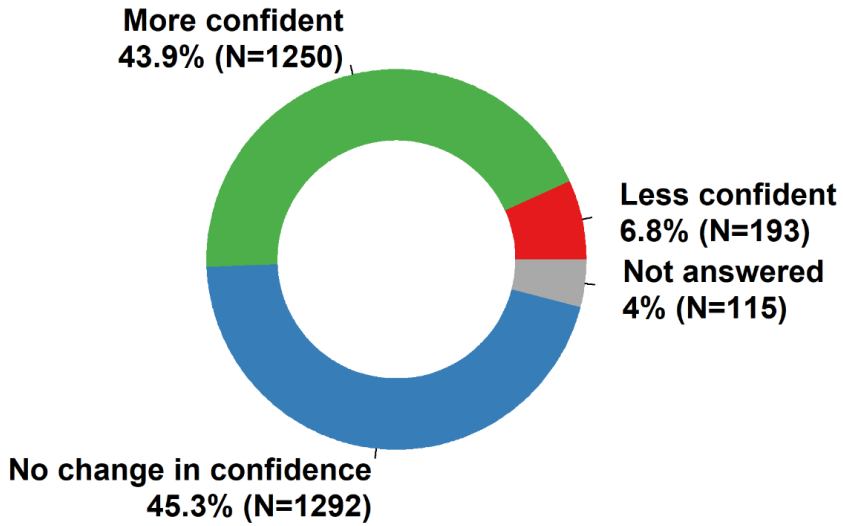
Tara B. Sanft[1], Natalia Siuliukina[2], Brandon O'Neal[2], Amanda K. L. Anderson[2], Rachel C. Jankowitz[3], Mark D. Pegram[4], Sami Diab[5], Yi Zhang[2], Kai Treuner[2], Joyce A. O'Shaughnessy[6]

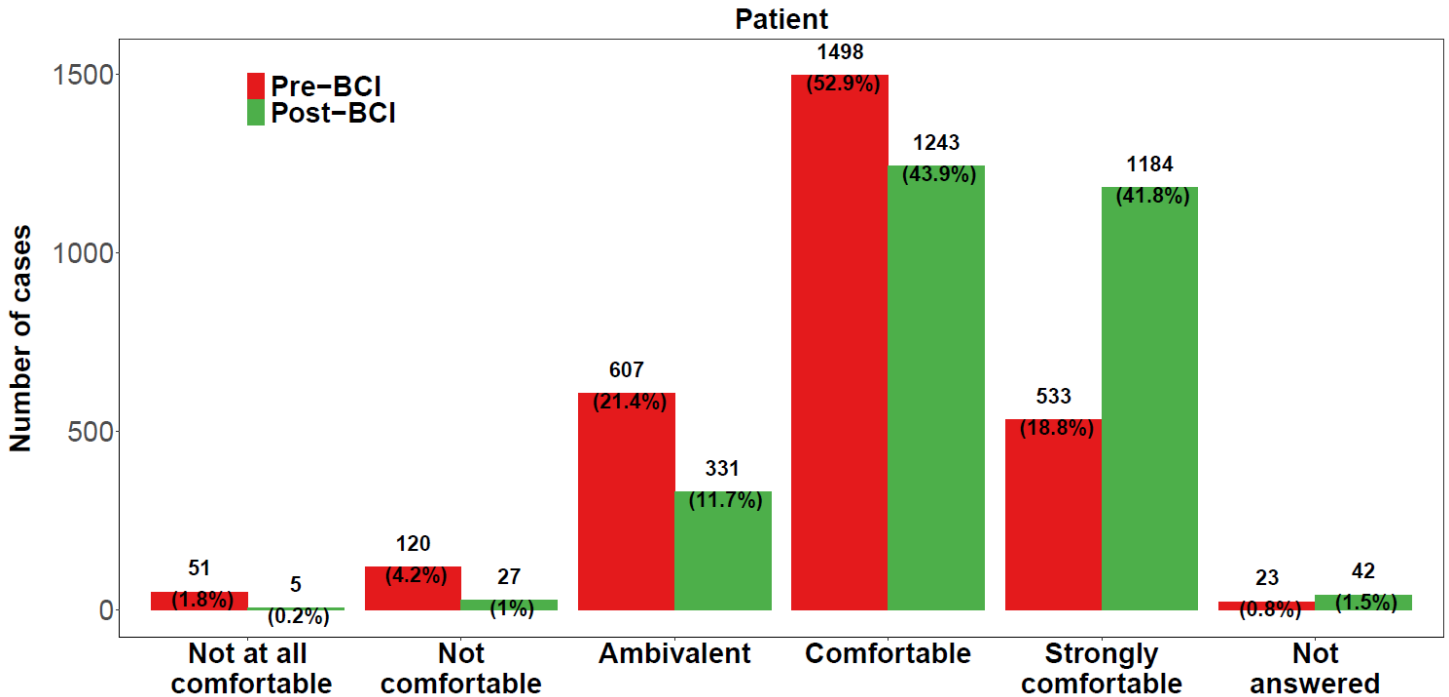
	Total cohort (N = 3,005)
Age	
<40	25 (0.8%)
40-49	205 (6.8%)
50-59	658 (21.9%)
60-74	1,546 (51.4%)
T stage	
T1	2,194 (73.0%)
T2	749 (24.9%)
T3	62 (2.1%)
Grade	
1	846 (28.2%)
2	1,609 (53.5%)
3	548 (18.2%)
Unknown	2 (0.1%)
Nodal status	
N0	2,299 (76.5%)
N1	697 (23.2%)
Unknown	9 (0.3%)
Ki-67	
<20	1,213 (40.4%)
≥20	978 (32.5%)
Unknown	814 (27.1%)

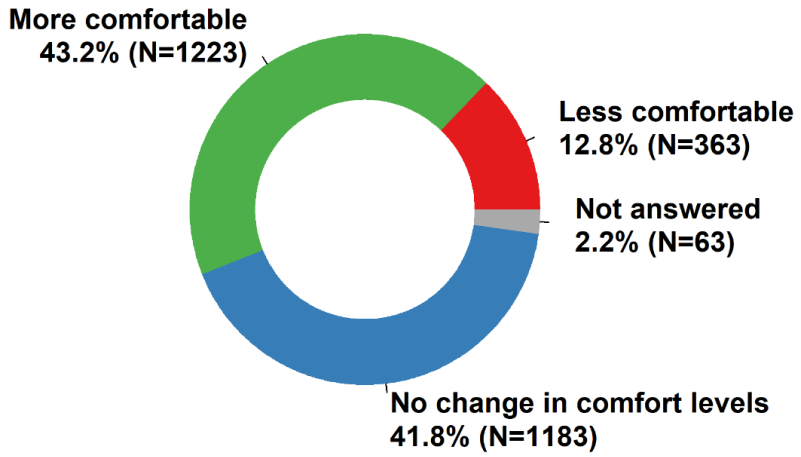


Sanft ASCO 2025; Abstract 531









Sanft ASCO 2025; Abstract 531

CONCLUSIONS BCI Registry

- Incorporating BCI into clinical practice resulted in changes in physician recommendations for EET in 41.2% cases
- Following BCI testing, 43.9% of physicians felt more confident in their recommendation for EET.
- BCI significantly increased physician confidence in their recommendation for EET
- Changes in both physician recommendations and patient preferences for EET correlated with BCI test results
- Following BCI testing, 43.2% of patients felt more comfortable with their EET decision
- Compared with baseline, patient concerns regarding cost, drug safety and benefit of EET significantly decreased

Sanft ASCO 2025; Abstract 531

Evaluation of the Sensitivity to Endocrine Therapy ($SET_{ER/PR}$) Assay to Predict Benefit from Extended Endocrine Therapy in NRG Oncology/NSABP B-42 Trial

Eleftherios P. Mamounas,[1] Hanna Bandos,[2] Keith J. Sweeney,[3] Kevin M. Tran,[3] Eveline Chen,[3] Priya Rastogi,[4] Vicente Valero,[3] Tanner J. Freeman,[4] Charles E. Geyer, Jr,[4] Louis Fehrenbacher,[5] Stephen KL Chia,[6] Adam M. Brufsky,[4] Janice M. Walshe,[7] Gamini S. Soori,[8] Shaker R. Dakhil,[9] Soonmyung Paik,[10] Sanda M. Swain,[11] Norman Wolmark,[4] and W. Fraser Symmans[3]

[1]AdventHealth Cancer Institute, Orlando, FL; [2]NRG Oncology Statistical and Data Management Center, University of Pittsburgh, Pittsburgh, PA; [3]University of Texas MD Anderson Cancer Center, Houston, TX; [4]University of Pittsburgh School of Medicine, Pittsburgh, PA; [5]Kaiser Permanente Northern CA, Vallejo, CA; [6]British Columbia Cancer Agency, Vancouver Cancer Centre, Vancouver, BC, Canada; [7]St. Vincent's University Hospital and Cancer Trials Ireland, Dublin, Ireland; [8]Florida Cancer Specialists, Ft. Meyers, FL; [9]Wichita NCORP, Via Christi Regional Medical Center, Cancer Center of Kansas, Wichita, KS; [10]Theragenbio, Inc, Pankyo, South Korea; [11]Georgetown University Medical Center and MedStar Health, Washington, DC

NRG ONCOLOGY
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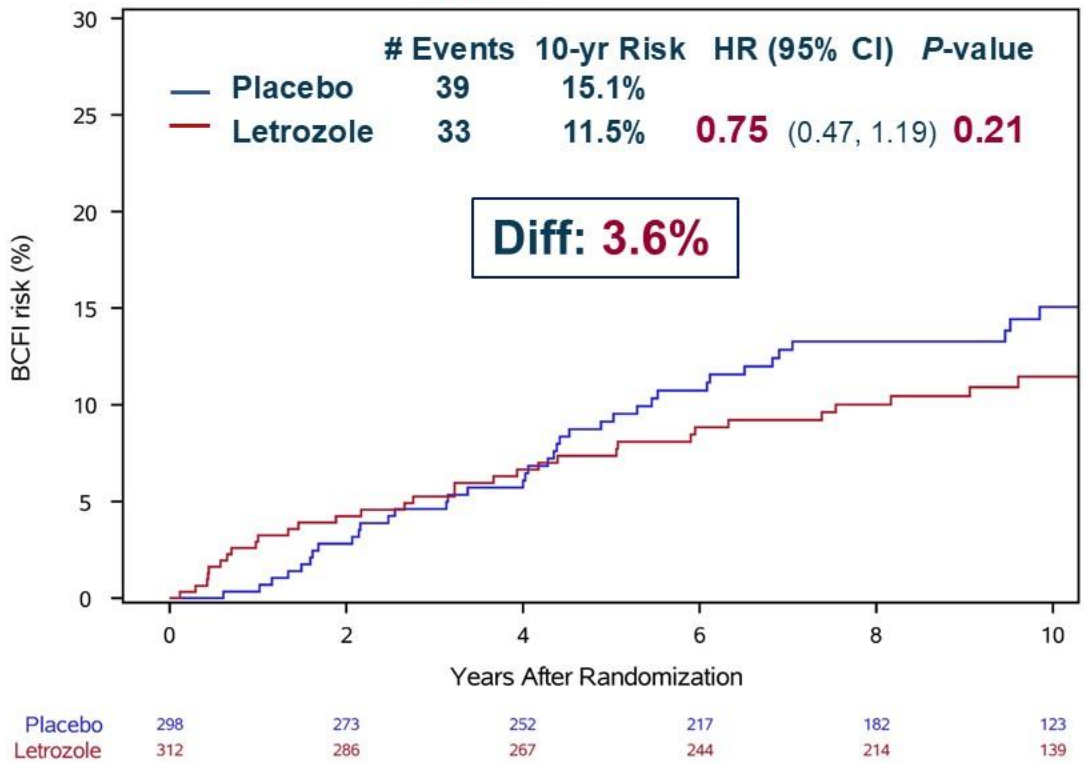
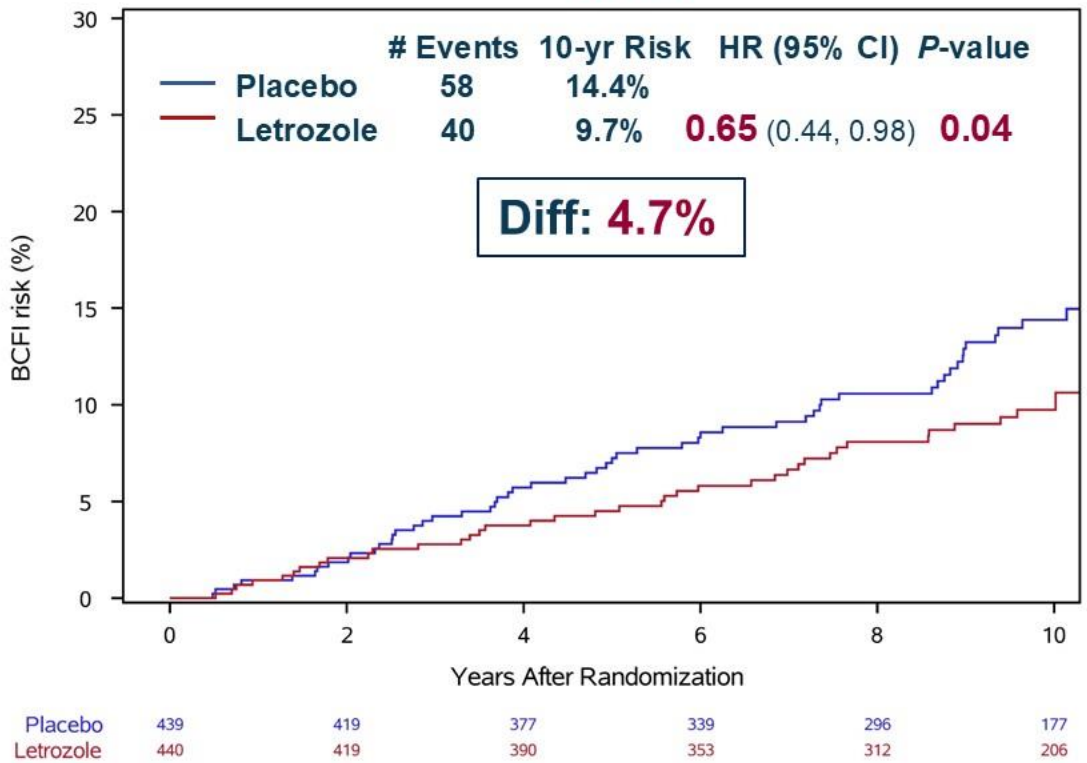
Abstract GS3-05

ELT BCFI Benefit by $SET_{ER/PR}$: Primary Analysis

$SET_{ER/PR}$ < 1.10, > 2.10



$1.10 \leq SET_{ER/PR} \leq 2.10$



Treatment by $SET_{ER/PR}$ Category Interaction: p=0.71

Mamounas SABCS 2025; Abstract GS3-05

Year in Review:
Localized HR-Positive Breast Cancer

INTRODUCTION: ODAC – April 30, 2026

MODULE 1: Adjuvant CDK4/6 Inhibitors

MODULE 2: Adjuvant Oral Selective Estrogen Receptor Degraders

MODULE 3: Premenopausal Patients

MODULE 4: Duration of Adjuvant Endocrine Treatment

MODULE 5: Genomic Predictors of Chemotherapy Benefit

MODULE 6: Neoadjuvant Treatment

RTP Year in Review 2026

Select Key Datasets

Genomic Predictors of Chemotherapy Benefit

- Hwang RF et al. Sentinel lymph node biopsy and clinical outcome of patients with node-positive breast cancer in the RxPONDER trial (S1007). San Antonio Breast Cancer Symposium 2025;Abstract PD12-05.
- Pusztai L et al. Development and validation of the RSClinN+ tool to predict prognosis and chemotherapy benefit for hormone receptor-positive, node-positive breast cancer. *J Clin Oncol* 2025;43(8):919-28.
- Sparano JA et al. Multimodal artificial intelligence (AI) models integrating image, clinical, and molecular data for predicting early and late breast cancer recurrence in TAILORx. San Antonio Breast Cancer Symposium 2025;Abstract GS1-08.

Select Key Datasets

Genomic Predictors of Chemotherapy Benefit

- Samiian L et al. Molecular insights into HR+/HER2+ early-stage breast cancer: Neoadjuvant therapy responses by MammaPrint® and BluePrint® genomic subtypes. ASCO 2025;Abstract 605.
- Brufsky AM et al. MammaPrint predicts chemotherapy benefit in HR+HER2- early breast cancer: FLEX Registry real-world data. *JNCI Cancer Spectr* 2025;9(5).
- O'Shaughnessy J et al. Improved 3-year IDFS with anthracycline-based therapy for patients with 70-gene signature High 2, Luminal B, HR+HER2- early-stage breast cancer. San Antonio Breast Cancer Symposium 2025;Abstract PS2-07-03.

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Sentinel Lymph Node Biopsy and Clinical Outcome of Patients with Node-Positive Breast Cancer in the RxPONDER Trial (S1007)

R. F. Hwang, MD[1]; W.E. Barlow PhD[2]; K. Kalinsky MD MS[3]; R. Jagsi MD DPhil[4]; L. Pusztai MD, DPhil[5]; A. Thompson MBChB MD[6]; G.N. Hortobagyi MD[7]; P. Sharma MD[8]; F. Meric-Bernstam MD[1,9]
[1]UT-MD Anderson Cancer Center, Breast Surgical Oncology; [2]Cancer Research and Biostatistics, SWOG; [3]Emory University, Medical Oncology; [4]Emory University, Radiation Oncology; [5]Yale University, Medical Oncology; [6]Baylor College of Medicine, Surgical Oncology; [7]UT-MD Anderson Cancer Center, Breast Medical Oncology; [8]University of Kansas, Medical Oncology; [9]UT-MD Anderson Cancer Center, Investigational Cancer Therapeutics

SAN ANTONIO BREAST CANCER SYMPOSIUM®
UT Health San Antonio Mays Cancer Center
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Abstract PD12-05

RTP Year in Review 2026

Conclusions

- In RxPONDER, over one-third of patients underwent SLNB alone for axillary staging.
- SLNB-only patients were older, more likely postmenopausal and had more favorable tumors.
- Outcomes including IDFS, DRFS, and LRR were similar in the SLNB-only group compared to the SLNB+ALND group.
- For premenopausal patients who underwent SLNB only, chemotherapy did not have statistically significant improvements in outcome which may be related to relatively small group size.
- These findings support the safety of SLNB alone for axillary staging in selected patients with node-positive disease.

Development and Validation of the RSClinN+ Tool to Predict Prognosis and Chemotherapy Benefit for Hormone Receptor–Positive, Node-Positive Breast Cancer

Authors: Lajos Pusztai, MD, DPhil , Jess R. Hoag, PhD, Kathy S. Albain, MD , William E. Barlow, PhD , Salomon M. Stemmer, MD, Allison Meisner, PhD, Gabriel N. Hortobagyi, MD , Steven Shak, MD, James M. Rae, PhD , Rick Baehner, MD , Priyanka Sharma, MD , and Kevin M. Kalinsky, MD | AUTHORS INFO & AFFILIATIONS

J Clin Oncol **43**, 919-928(2025) • Volume 43, Number 8 • DOI: 10.1200/JCO-24-01507

Key Takeaways

- Clinical-pathological factors and the 21-gene OncotypeDX Recurrence Score (RS)® independently influence prognostic risk.

- Our goal was to develop a new tool, RSClinN+, that integrates the RS® with clinical-pathological factors to provide individualized prognostic risk and chemotherapy benefit predictions for pre- and postmenopausal patients with **HR+/HER2-, 1-3 lymph node-positive** breast cancer.

- RSClinN+ provides more accurate personalized prognostic information and better estimates of absolute chemotherapy benefit than either RS® alone or clinical-pathological factors alone.
  - In external validation, RSClinN+ risk estimates were highly concordant with observed risk.

® Registered Trade Mark

Pusztai L et al. J Clin Oncol 2025

SAN ANTONIO BREAST CANCER SYMPOSIUM®
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Abstract GS1-08

DECEMBER 9–12, 2025
HENRY B. GONZALEZ CONVENTION CENTER • SAN ANTONIO, TX

Multimodal Artificial Intelligence (AI) Models Integrating Image, Clinical, and Molecular Data for Predicting Early and Late Breast Cancer Recurrence in TAILORx

Joseph A. Sparano[1], Norsang Lama[2], Robert J. Gray[3], Md Ashequr Rahman[2], Victoria Wang[3], Della F. Makower[4], Yating Cheng[2], Kathy S. Albain[5], Ming Chen[2], Daniel F. Hayes[6], Anthony Helmstetter[2], Charles E. Geyer, Jr.[7], Casey Bales[2], Elizabeth C. Dees[8], Matthew P. Goetz[9], John A. Olson, Jr.[10], Sunil S. Badve[11], Thomas J. Saphner[12], Timothy J. Whelan[13], Virginia G. Kaklamani[14], Matthew Oberley[2], Milan Radovich[2], David Spetzler[2], Eleftherios P. Mamounas[15,16], Norman Wolmark[16], George W. Sledge[2].

Icahn School of Medicine at Mount Sinai, Tisch Cancer Institute, NY, NY[1], Caris Life Sciences, Irving, TX[2], ECOG-ACRIN Biostatistical Center, Dana-Farber Cancer Institute, Boston, MA[3], Montefiore Einstein Comprehensive Cancer Center, Bronx, NY[4], Loyola University Medical Center, Maywood, IL[5], University of Michigan, Ann Arbor, MI[6], University of Pittsburgh, Pittsburgh, PA[7], University of North Carolina, Chapel Hill, NC[8], Mayo Clinic, Rochester, MN[9], Washington University School of Medicine, St. Louis, MO[10], Winship Cancer Institute, Emory University, Atlanta, GA[11], Aurora Medical Center, Two Rivers, WI[12], McMaster University, Hamilton, CAN[13], University of Texas Health, San Antonio, TX14, AdventHealth Cancer Institute, Orlando, FL[15], National Surgical Adjuvant Breast and Bowel Project, Pittsburgh, PA[16]

Mount Sinai Tisch Cancer Center

Canadian Cancer Trials Group · Alliance for Clinical Trials in Oncology · ECOG-ACRIN cancer research group · Reshaping the future of patient care · National Cancer Institute · SWOG · NRG Oncology

CARIS LIFE SCIENCES

Conclusions

- **Training/5-fold cross validation set:**
  - **C Model:** Clinical features provided some prognostic information
  - **M+ Model**: 42-gene molecular model including the 21-gene RS, BCI, and EndoPredict primarily drove prognostic stratification for early DR within 5 years
  - **I Model:** Pathomic features strengthened prognostic stratification for late DR > 5 years
  - **Multimodal ICM+ Model**:
    - ❑ Strongest prognostic performance for overall and late DR that were superior to the actual ODX RS
    - ❑ Provided statistically significant and clinically relevant prognostic stratification in the low (RS 0-25) and high (RS 26-100) genomic risk groups
    - ❑ Exhibited stronger performance than **CM+** for late recurrence
- **Holdout validation set:**
  - Superior prognostic performance of both the **ICM+** & **CM+** models were validated for overall and late DR
  - Both **ICM+** & **CM+** models outperformed the actual Oncotype DX RS used to guide therapy

2025 ASCO ANNUAL MEETING

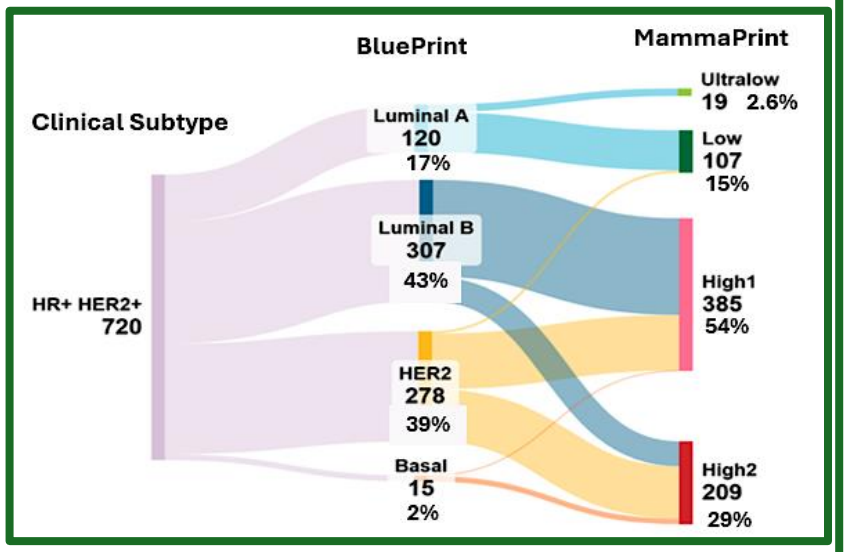
Molecular Insights into HR+/HER2+ Early-Stage Breast Cancer: Neoadjuvant Therapy Responses by MammaPrint® and BluePrint® genomic subtypes

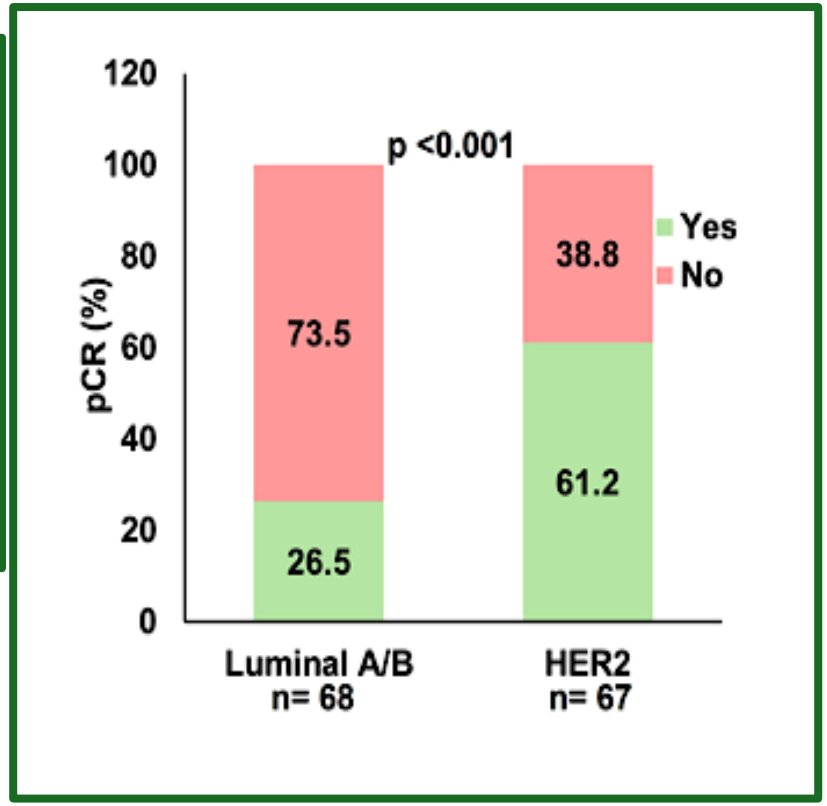
Authors: Laila Samiian, Adam Brufsky, Sahra Uygun, Isha Kapoor, Victoria Poillucci, William Audeh, Joyce O'Shaughnessy

Presenter: Laila Samiian, MD

Abstract 605, June 2, 2025, 9am-12pm
Poster Session – Breast Cancer—Local/Regional/Adjuvant

Molecular Insights into HR+/HER2+ Early-Stage Breast Cancer: Neoadjuvant Therapy Responses by MammaPrint and BluePrint genomic subtypes *(Samiian et al., ASCO 2025)*





BP HER2 cancers showed significantly higher pCR rates with NHT compared to Luminal A/B

Conclusions:

- **BP identified heterogeneity within HR+/HER2+ early stage cancers, with ~60% classified genomically as non-HER2-type**
- Consistent with I-SPY2, BP HER2 tumors showed higher pCR rates than Luminal A/B, underscoring the need for improved therapies for patients with Luminal A/B subtypes, and the potential value of BP subtyping in predicting HER2-targeted therapy response
- WTA revealed differential gene expression between pCR and non-pCR in BP HER2 cancers, but findings were not statistically significant
- Future WTA in larger cohorts of HR+/HER2+ EBC patients enrolled in FLEX, further classified by BP may elucidate the biology of these cancers from patients with pCR vs non-pCR

Samiian ASCO 2025;Abstract 605

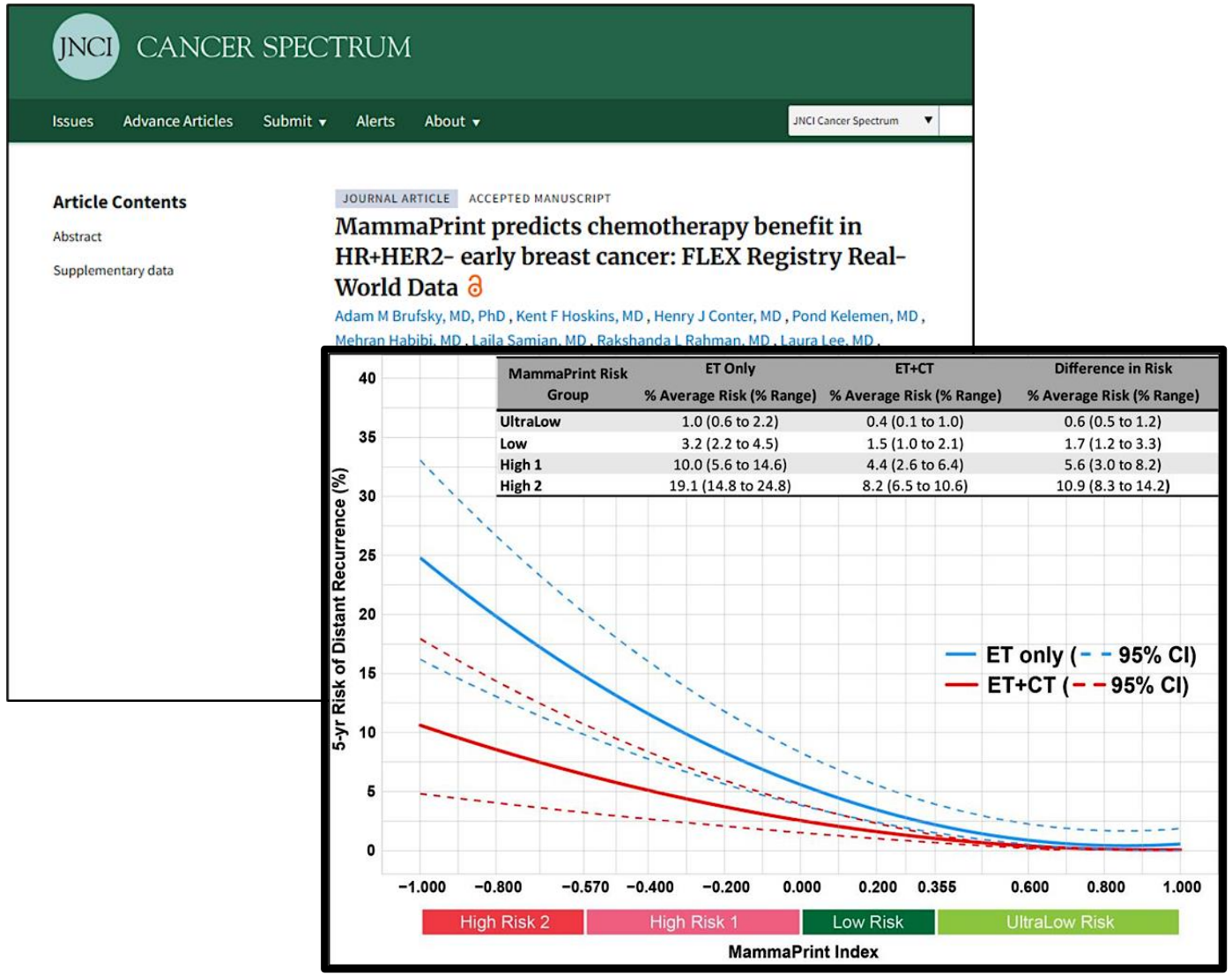
Prediction of Chemotherapy Benefit by MammaPrint® in HR+HER2- Early-Stage Breast Cancer Revealed by the FLEX Registry of Real World Data

Adam Brufsky[1], Kent Hoskins[2], Henry Conter[3], Pond Kelemen[4], Mehran Habibi[5], Laila Samian[6], Robert Maganini[7], Rakshanda Rahman[8], Laura Lee[9], Eduardo Dias[10], Regina Hampton[11], Beth Seiling[12], Cynthia Osborne[13], Eric Brown[14], Jailan Elayoubi[15], Priyanka Sharma[16], Jayanthi Ramadurai[17], Laurie Matt-Amaral[18], Alfredo Santillan[19], Sasha Strain[20], Philip Albaneze[21], Harshini Ramaswamy[22], Nicole Stivers[22], Andrea Menicucci[22], William Audeh[22], Pat Whitworth[23], Nathalie Johnson[24], Joyce O'Shaughnessy[25], FLEX Investigators' Group

[1]University of Pittsburgh Medical Center, Pittsburg, PA; [2]University of Illinois Cancer Center, Chicago, IL; [3]William Osler Cancer Centre and Department of Oncology, Brampton, Canada; [4]Northwell Health, Sleepy Hollow, NY; [5]Northwell Health, Staten Island, NY; [6]Baptist MD Anderson Cancer Center, Jacksonville, FL; [7]Ascension Medical Group, Bartlett, IL; [8]Texas Tech University Health Sciences Center School of Medicine, Lubbock, TX; [9]Comprehensive Cancer Center, Palm Springs, CA; [10]Nashville Breast Center, Nashville, TN; [11]Luminis Health, Lanham, MD; [12]Trinity Health of New England, Southbury, CT; [13]Texas Oncology, Dallas, TX; [14]Comprehensive Breast Care, Troy, MI; [15]Karmanos Cancer Institute, Detroit, MI; [16]University of Kansas Medical Center; [17]Affiliated Oncologists, LLC, Chicago Ridge, IL; [18]Cleveland Clinic, Akron, OH; [19]Texas Oncology, San Antonio, TX; [20]Texas Oncology, Tyler, TX; [21]Roper St. Francis Healthcare, Charleston, SC; [22]Medical Affairs, Agendia Inc., Irvine, CA; [23]Nashville Breast Center, Nashville, TN; [24]Legacy Health System, Portland, OR; [25]Baylor University Medical Center, Texas Oncology, Sarah Cannin Research Institute, Dallas, TX

San Antonio Breast Cancer Symposium
and
Brufsky et al., JNCI Cancer Spectrum, 2025.

MammaPrint PREDICTS chemotherapy benefit in HR+HER2- early breast cancer: FLEX Registry Real-World Data *(Brufsky et al., JNCI Cancer Spectrum)*



MammaPrint Risk Group	ET Only % Average Risk (% Range)	ET+CT % Average Risk (% Range)	Difference in Risk % Average Risk (% Range)
UltraLow	1.0 (0.6 to 2.2)	0.4 (0.1 to 1.0)	0.6 (0.5 to 1.2)
Low	3.2 (2.2 to 4.5)	1.5 (1.0 to 2.1)	1.7 (1.2 to 3.3)
High 1	10.0 (5.6 to 14.6)	4.4 (2.6 to 6.4)	5.6 (3.0 to 8.2)
High 2	19.1 (14.8 to 24.8)	8.2 (6.5 to 10.6)	10.9 (8.3 to 14.2)

ET pts propensity score matched with ET+CT patients based on menopausal status, tumor stage, and nodal status

Conclusions:

- **Patients with increasing MPI risk (High Risk) had significantly lower risk of DRFI events when treated with ET+CT compared to ET alone**
- Consistent with findings from MINDACT, patients with MammaPrint indices within Low and UltraLow Risk ranges did not derive significant CT benefit
- CT benefit is not predicted by higher tumor grade after adjusting for MPI and clinical factors
- **These RWD confirm MammaPrint's comprehensive utility, as prognostic of recurrence risk and predictive of CT benefit for patients with HR+HER2- early-stage breast cancer**

Brufsky et al., JNCI Cancer Spectrum, 2025.

Improved 3-year IDFS with anthracycline-based therapy for patients with 70-gene signature High 2, Luminal B, HR+HER2- early-stage breast cancer

Joyce O'Shaughnessy[1], Adam Brufsky[2], Cathy Lynne Graham[3], Cynthia R. C. Osborne[4], Rakhshanda Layeequr Rahman[5], Ahmed Elkhanany[6], Eric Allen Brown[7], Linsey P. Gold[7], Nathalie M. Johnson[8], Danilo Giffoni[9], J. Jaime Alberty-Oller[10], Reshma L. Mahtani[11], Harshini Ramaswamy[12], Nicole Stivers[12], Andrea R. Menicucci[12], William Audeh[12], FLEX Investigators' Group

[1]Baylor University Medical Center, Texas Oncology, Sarah Cannon Research Institute, Dallas, TX; [2]University of Pittsburgh, Pittsburgh, PA; [3]Piedmont Cartersville Breast, Carterville, GA; [4]Texas Oncology, Dallas, TX; [5]Texas Tech University Health Sciences Center School of Medicine, Lubbock, TX; [6]Baylor College of Medicine, Houston, Texas; [7]Comprehensive Breast Care, Troy, MI; [8]Legacy Health System, Portland, OR; [9]London Regional Cancer Program, London, Ontario, CA; [10]Kings County Hospital Center, Brooklyn, NY; [11]Miami Cancer Institute, Baptist Health South Florida, Miami, FL;[12]Medical Affairs, Agendia, Inc., Irvine, CA

San Antonio Breast Cancer Symposium®
Presentation ID: PS2-07-03, Date: Dec 10, 2025

Abstract PS2-07-03

Conclusions

- **When matched for clinical risk features:**
- **Patients with MammaPrint H2, Luminal B, HR+HER2- cancer had significantly improved IDFS with AC-T compared to TC, even with clinical low-risk features**
- **Patients with MammaPrint H1 cancer did not benefit more from AC-T vs. TC, even with clinical high-risk features**

Year in Review:
Localized HR-Positive Breast Cancer

INTRODUCTION: ODAC – April 30, 2026

MODULE 1: Adjuvant CDK4/6 Inhibitors

MODULE 2: Adjuvant Oral Selective Estrogen Receptor Degraders

MODULE 3: Premenopausal Patients

MODULE 4: Duration of Adjuvant Endocrine Treatment

MODULE 5: Genomic Predictors of Chemotherapy Benefit

MODULE 6: Neoadjuvant Treatment

RTP Year in Review 2026

Select Key Datasets
Neoadjuvant Treatment

- Cottu PH et al. Risk of recurrence (ROR) after neoadjuvant ribociclib plus ET in clinically high-risk ER+/HER2– BC: Preliminary analysis of the SOLTI-RIBOLARIS trial. ESMO 2025;Abstract 296O.
- Martín M et al. Neoadjuvant abemaciclib plus letrozole versus chemotherapy in patients with HR+/HER2- highly proliferative breast cancer. *Clin Cancer Res* 2026 March 2;32(5):850-8.
- Cussac AL et al. Preoperative window-of-opportunity study with giredestrant or tamoxifen (tam) in premenopausal women with estrogen receptor-positive (ER+)/human epidermal growth factor receptor 2-negative (HER2-) and Ki67≥10% early breast cancer (EBC): The EMPRESS study. ESMO 2025;Abstract 294MO.

Abstract 296O

BERLIN 2025 ESMO congress

Risk of Recurrence (ROR) After Neoadjuvant Ribociclib Plus Endocrine Therapy in Clinically High-Risk ER+/HER2− Breast Cancer: First Interim Analysis of the SOLTI-UNICANCER RIBOLARIS Trial

Paul H. Cottu

Department of Medical Oncology & Institute of Women Cancers, Institut Curie, Paris
Université Paris Cité, Paris
UNICANCER UCBG, Paris

On behalf of

Aleix Prat, Tomás Pascual, Huilin Hu, Estelle Roux, Francisco Javier Salvador Bofill, Joana Mourato Ribeiro, Isabel Blancas, Thomas Bachelot, Jerôme Lemonnier, Juan Manuel Ferrero-Cafiero, Pablo Tolosa-Ortega, Antonio Mulero-Sánchez, Thayane Antoniolli Crestani, Roisin M. Connolly, Cynthia X Ma, Antonio C. Wolff, Guillermo Villacampa, Thibault de La Motte Rouge and Joaquin Gavilá Gregori

October 17th 2025

CLINICAL CANCER RESEARCH | CLINICAL TRIALS: MOLECULARLY TARGETED THERAPY

Neoadjuvant Abemaciclib plus Letrozole Versus Chemotherapy in Patients with HR+/HER2– Highly Proliferative Breast Cancer

Miguel Martín[1,2,3], Ángel L. Guerrero-Zotano[3,4], María E. Pérez-López[3,5], Manuel Ruiz-Borrego[3,6], Noelia Martínez Jáñez[3,7], José I. Chacón[3,8], Miguel Gil-Gil[3,9], Raquel Andrés[3,10], Begoña Bermejo[2,3,11], Pedro Sánchez-Rovira[3,12], Sonia del Barco[3,13], José J. Ponce[3,14], Isaura Fernández[3,15], Eduardo Martínez de Dueñas[3,16], Carmen Hinojo-González[3,17], Marta González[3,18], Elisa García-Garre[3,19,20], Blanca Hernando[3,21], Juan de la Haba-Rodriguez[3,22], Isabel M. Álvarez[3,23], Santiago González-Santiago[3,24], José Á. García-Sáenz[3,25], Ana Santaballa[3,26], Maribel Casas[3], Susana Bezares[3], Rosalía Caballero[3], Federico Rojo[2,3,27], and Emilio Alba[2,3,28,29]

2026 March 2;32(5):850-8.

- It is unclear that CDK46 inhibitor therapy can substitute for chemotherapy
- In preoperative treatment, chemotherapy was better for group meeting the NATALEE eligibility criteria
- RS was better predictor of chemo response than Ki-67
- Lower rates of pCR observed with either approach in lower risk patients

Courtesy of Harold J Burstein, MD, PhD

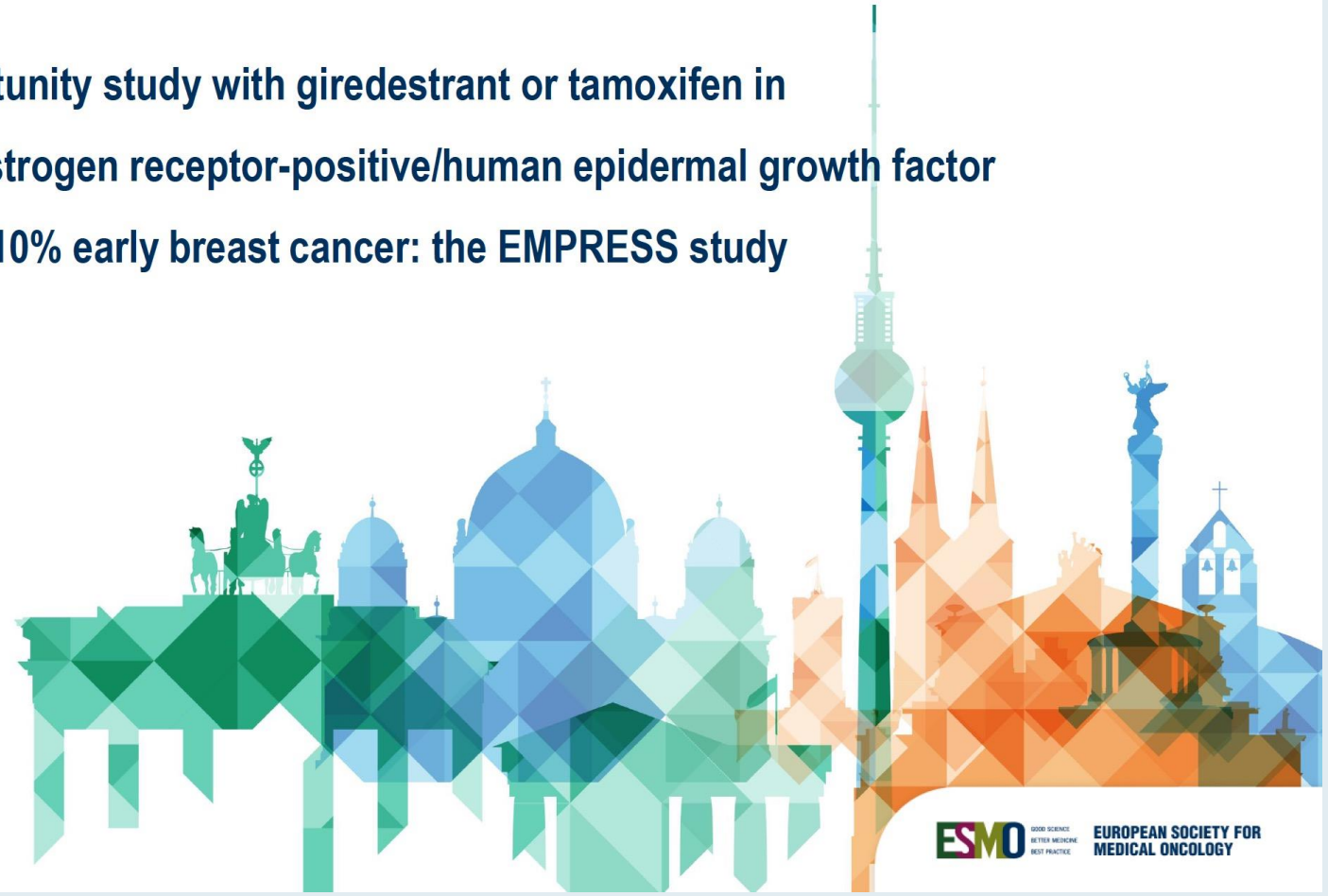
Abstract 294O

BERLIN 2025 ESMO congress

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

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

October, 2025



Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse

A Complimentary NCPD Symposium Series Held During the 51st Annual ONS Congress May 13-16

San Antonio Marriott Rivercenter | San Antonio, Texas

Antibody-Drug Conjugates

Wednesday, May 13, 2026 | 11:15 AM – 12:45 PM CT

Prostate Cancer

Thursday, May 14, 2026 | 12:15 PM – 1:45 PM CT

Ovarian Cancer

Wednesday, May 13, 2026 | 6:00 PM – 7:30 PM CT

Non-Muscle-Invasive and Muscle-Invasive Bladder Cancer

Thursday, May 14, 2026 | 6:00 PM – 7:30 PM CT

Endometrial Cancer

Thursday, May 14, 2026 | 6:00 AM – 7:30 AM CT

Pancreatic Cancer

Friday, May 15, 2026 | 6:00 AM – 7:30 AM CT

Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse

A Complimentary NCPD Symposium Series Held During the 51st Annual ONS Congress May 13-16

San Antonio Marriott Rivercenter | San Antonio, Texas

Targeting the PI3K/AKT/mTOR Pathway in HR-Positive Metastatic Breast Cancer

Friday, May 15, 2026 | 12:15 PM – 1:45 PM CT

Relapsed/Refractory Multiple Myeloma

Saturday, May 16, 2026 | 12:15 PM – 1:45 PM CT

Non-Hodgkin Lymphoma and Chronic Lymphocytic Leukemia

Friday, May 15, 2026 | 6:00 PM – 8:00 PM CT

Oral SERDs for Breast Cancer

Saturday, May 16, 2026 | 6:00 PM – 7:30 PM CT

CDK4/6 Inhibitors for HR-Positive Breast Cancer

Saturday, May 16, 2026 | 6:00 AM – 7:30 AM CT

Thank you for joining us!

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

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

RTP Year in Review 2026