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# Optimizing Therapy for Patients with Hormone Receptor-Positive Localized Breast Cancer

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SAB Chair of the Lobular Breast Cancer Alliance

The University of Texas MD Anderson Cancer Center

Houston, Texas

# Disclosures

<b>Consulting Agreements</b>	Agendia Inc, Aptitude Health, AstraZeneca Pharmaceuticals LP, BostonGene, GE Healthcare, PreludeDX, Stemline Therapeutics Inc
<b>Contracted Research</b>	Bristol Myers Squibb, Lilly, Summit Therapeutics
<b>Nonrelevant Financial Relationships</b>	Community Health Media

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Development Service  
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Harvard Medical School  
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# Key Datasets

- Andre F et al. **Biomarkers for adjuvant endocrine and chemotherapy** in early-stage breast cancer: ASCO Guideline update. *J Clin Oncol* 2022;40:1816-37.
- Sparano JA et al. Trial Assigning Individualized Options for treatment (**TAILORx**): **An update** including 12-year event rates. San Antonio Breast Cancer Symposium 2022; Abstract GS1-05.
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- Chen N et al. **Impact of anthracyclines in genomic high-risk, node-negative, HR-positive/HER2-negative** breast cancer. *Ann Oncol* 2025;36(11):1356-65.
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- Piccart M et al. **70-gene signature** as an aid for treatment decisions in early breast cancer: **Updated results** of the phase 3 randomised **MINDACT trial** with an exploratory analysis by age. *Lancet Oncol* 2021;22(4):476-88.
- Sestak I et al. **Comparison** of the performance of 6 **prognostic signatures** for estrogen receptor-positive breast cancer: A **secondary analysis of a randomized clinical trial**. *JAMA Oncol* 2018;4(4):545-53.
- Noordhoek I et al. **Breast Cancer Index** predicts **extended endocrine benefit** to individualize selection of patients with HR+ early-stage breast cancer for **10 years of endocrine therapy**. *Clin Cancer Res* 2021;27(1):311-19.

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- Woolpert KM et al. **Biomarkers predictive** of a response to **extended endocrine therapy** in breast cancer: A systematic review and meta-analysis. *Breast Cancer Res Treat* 2024;203(3):407-17.
- Johnston S et al. **monarchE: Primary overall survival (OS)** results of adjuvant abemaciclib + endocrine therapy (ET) for HR+, HER2-, high-risk early breast cancer (EBC). ESMO 2025;Abstract LBA13.
- Johnston S et al. **Overall survival with abemaciclib** in early breast cancer. *Ann Oncol* 2026;37(2):155-65.
- Cortés 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.
- Crown JP et al. **Adjuvant ribociclib (RIB) plus nonsteroidal aromatase inhibitor (NSAI)** in patients (pts) with HR+/HER2- early breast cancer (EBC): **NATALEE 5-year outcomes**. ESMO 2025;Abstract LBA14.
- Rugo HS et al. **Adjuvant abemaciclib combined with endocrine therapy** for high-risk early breast cancer: **Safety and patient-reported outcomes** from the **monarchE** study. *Ann Oncol* 2022;33(6):616-27.
- Barrios C et al. **NATALEE update: Safety and treatment (tx) duration of ribociclib (RIB) + nonsteroidal aromatase inhibitor (NSAI)** in patients (pts) with HR+/HER2- early breast cancer (EBC). ESMO Breast 2024;Abstract 113MO.
- Mayer EL 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* 2025;31(1):117-24.
- 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.

# Management of Hormone Receptor (HR)-Positive Localized Breast Cancer

**Module 1: Risk Assessment and Genomic Assays for HR-Positive, HER2-Negative Localized Breast Cancer**

**Module 2: Clinician Survey Results**

**Module 3: Adjuvant CDK4/6 Inhibitors for High-Risk, HR-Positive, HER2-Negative Localized Breast Cancer**

**Module 4: Clinician Survey Results**

**Module 5: Tolerability and Other Practical Considerations with Adjuvant CDK4/6 Inhibitor Therapy**

**Module 6: Clinician Survey Results**

**Module 7: Adjuvant Oral SERDs for HR-Positive, HER2-Negative Localized Breast Cancer**

# Management of Hormone Receptor (HR)-Positive Localized Breast Cancer

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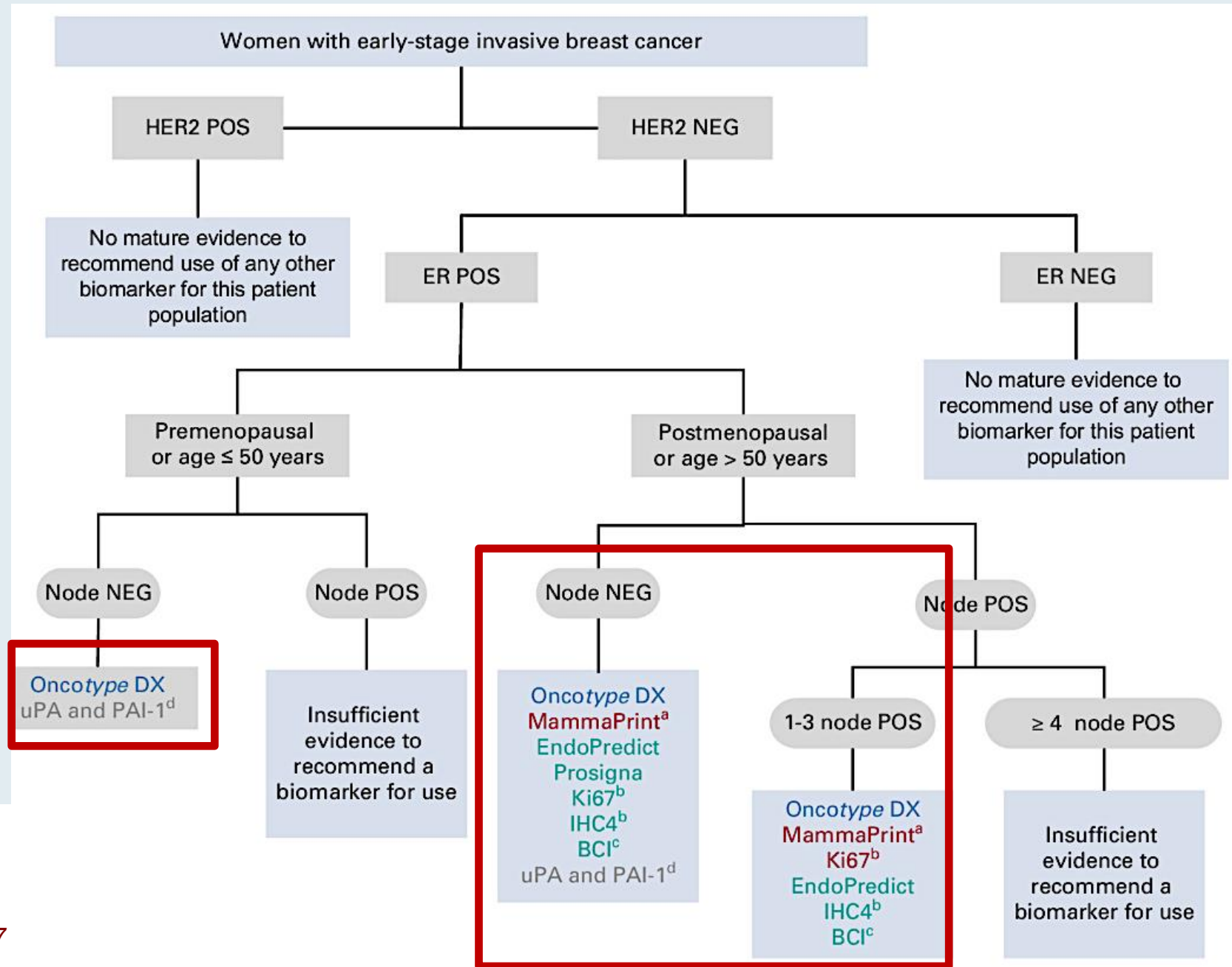
### Module 7: Adjuvant Oral SERDs for HR-Positive, HER2-Negative Localized Breast Cancer

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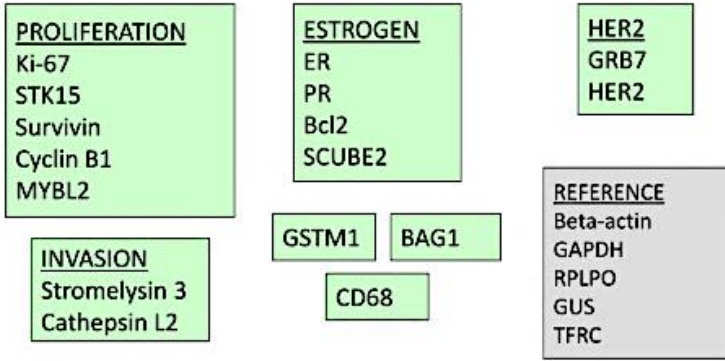
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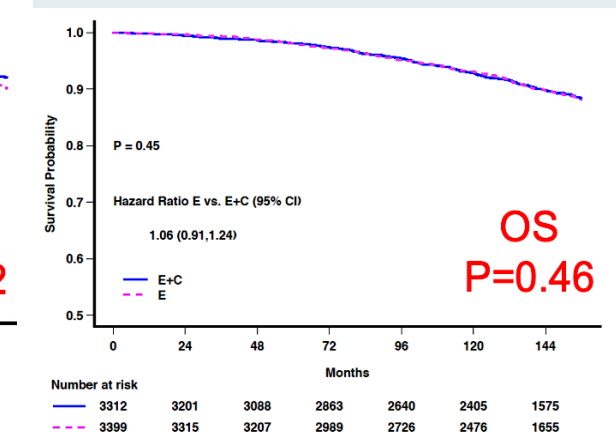
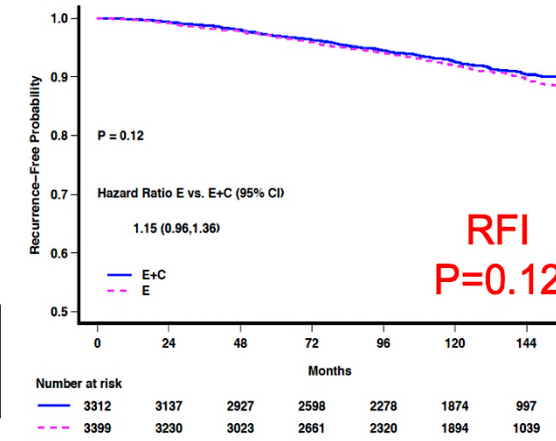
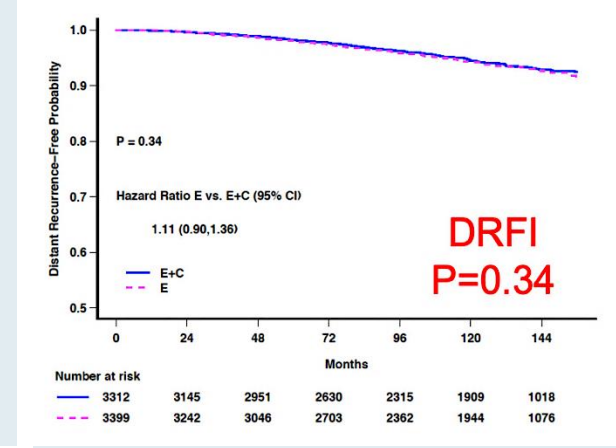
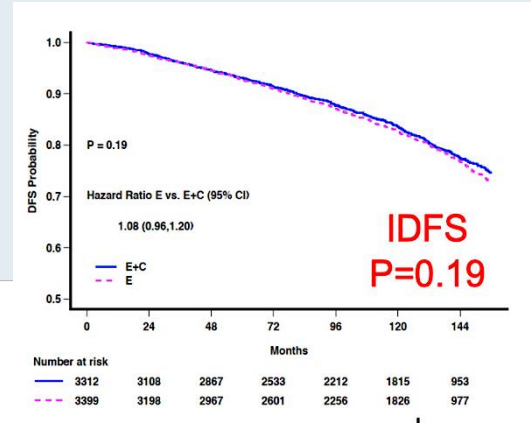
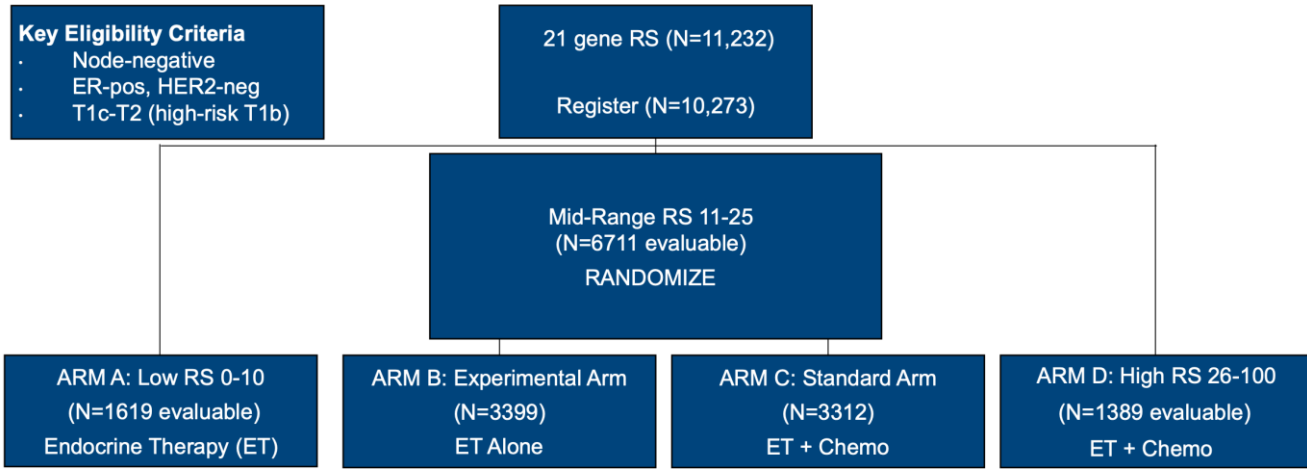
# OncotypeDX<sup>®</sup>: TAILORx Trial Key Results for Node-Negative Disease

16 Cancer and 5 Reference Genes From 3 Studies



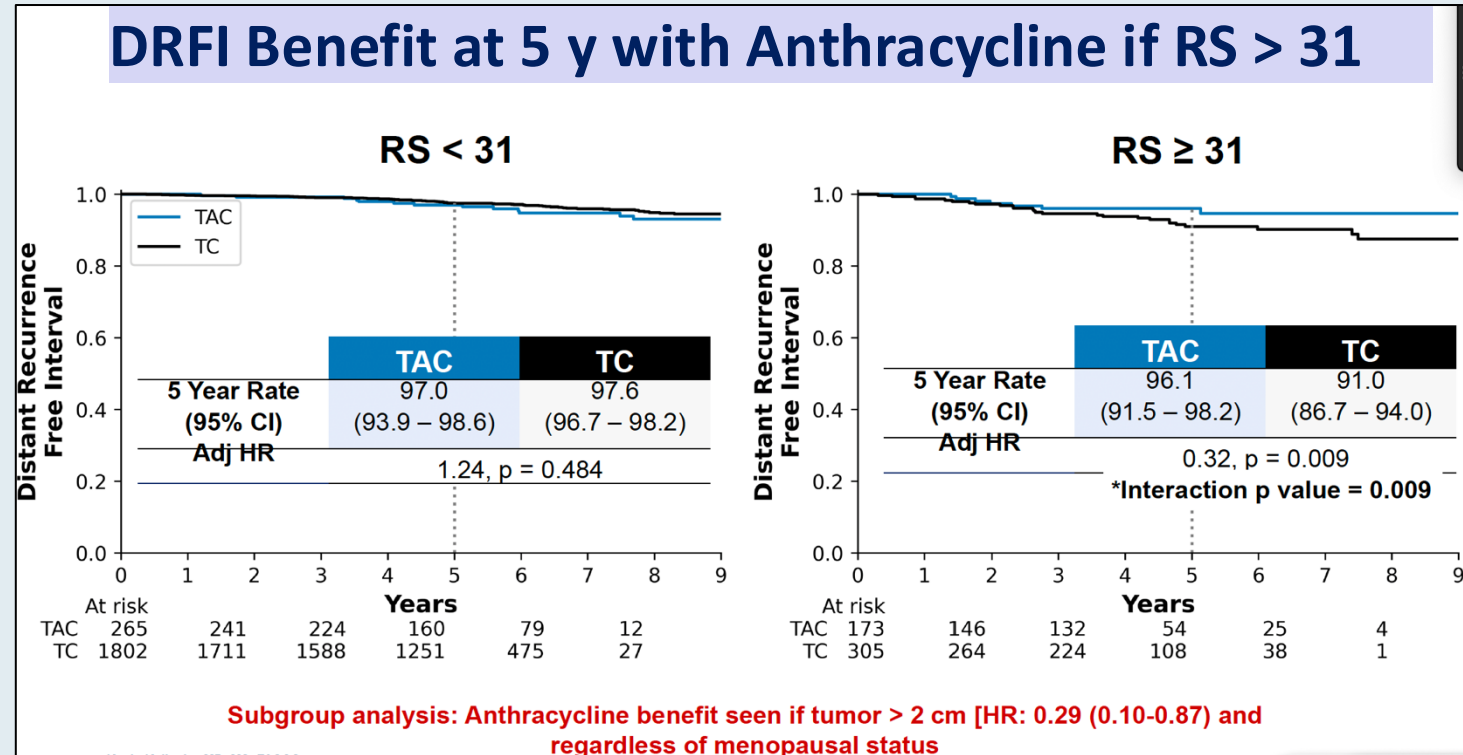
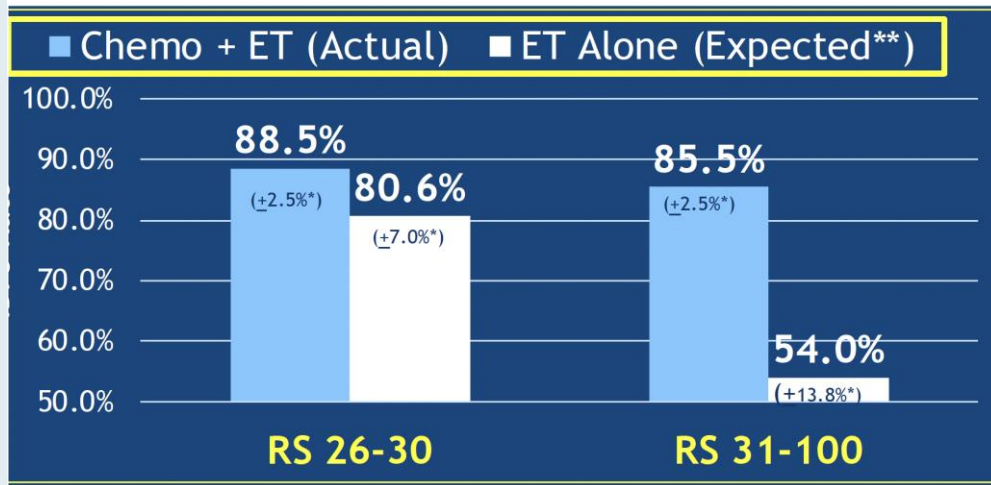
Intermediate risk (11-25):  
No overall benefit to chemotherapy (2022 update)

## TAILORx Trial Design



# Chemotherapy and Anthracycline Benefits for Patients with High Recurrence Scores® (>25)

High Risk (RS > 25): Expected benefit with chemotherapy

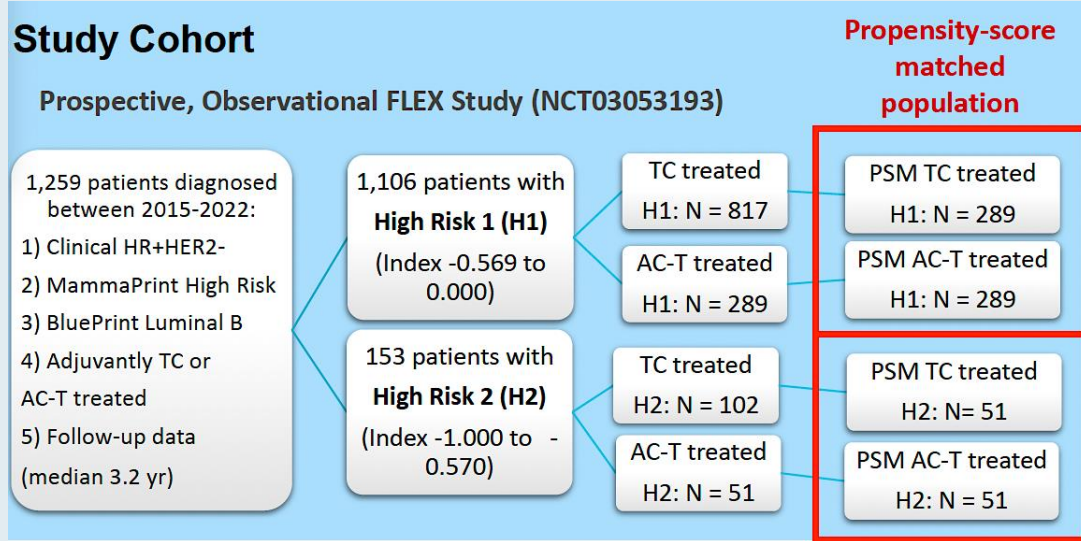


“No chemotherapy” rates estimated by combining

- patient-specific distant recurrence risk information with
- patient-specific chemotherapy benefit information
- from the ERBB2-negative cohort of NSABP B20

TAILORx N = 2,549. T-AC vs TC  
 5-y DRFI 96.1 vs 91%, HR 0.31, p = 0.006  
 5-y DRFS 95.4% vs 89.8%, aHR 0.49, p = 0.032  
 OS NS

# Propensity-Score Matched Analysis of Real-World FLEX Data: IDFS with Anthracycline-Based Therapy for Patients with MammaPrint® High 2, Luminal B, HR-Positive, HER2-Negative Localized Breast Cancer



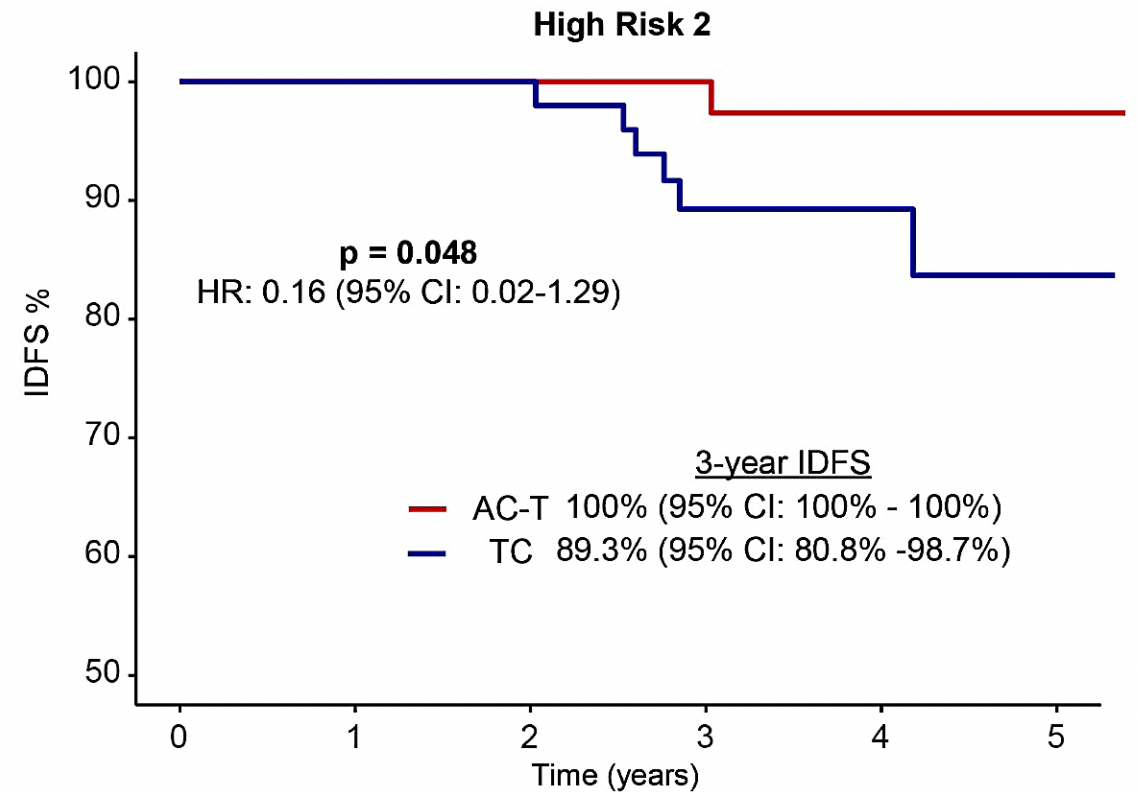
## Conclusions

- In this PSM analysis of a non-randomized, prospective, real-world FLEX Study data with 3.2 years median follow-up, patients with H2, HR+HER2-cancer had significantly improved IDFS with AC-T compared to TC
- Although adjusted analyses were limited by few events, the direction and magnitude of benefit remained consistent
- In contrast, patients with H1 cancer did not benefit more from AC-T vs. TC
- These findings further support the utility of MammaPrint in informing chemotherapy selection in patients with HR+HER2- breast cancer

IDFS = invasive disease-free survival

O'Shaughnessy J et al. SABCS 2025;Abstract PS2-07-03.

Figure 2. IDFS in patients with High Risk 2 cancer: AC-T vs TC



Numbers at Risk

H2	0	1	2	3	4	5
AC-T	51	50	49	40	17	8
TC	51	51	50	30	16	9

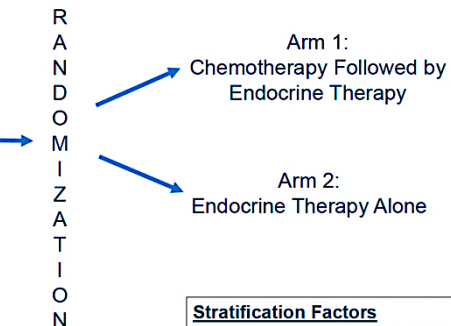
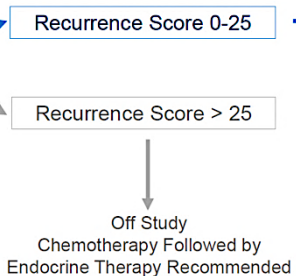
# OncotypeDX: RxPONDER Trial Results Summary One to Three Positive Lymph Nodes

## RxPONDER Trial Design

### Key Entry Criteria

- Women age  $\geq 18$  yrs
- ER and/or PR  $\geq 1\%$ , HER2- breast cancer with 1\*-3 LN+ without distant metastasis
- Able to receive adjuvant taxane and/or anthracycline-based chemotherapy\*\*
- Axillary staging by SLNB or ALND

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N = 5,000 pts

### Stratification Factors

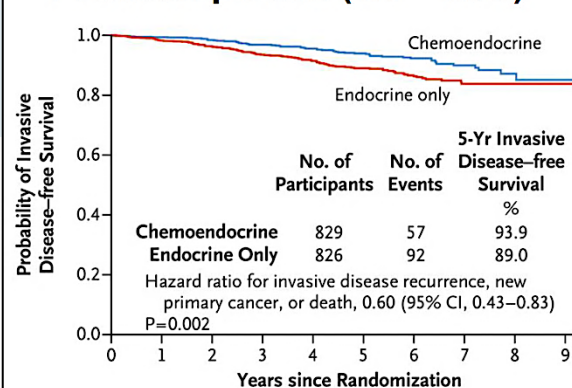
Recurrence Score: 0-13 vs. 14-25  
Menopausal Status: pre vs. post  
Axillary Surgery: ALND vs. SLNB

### RxPONDER Population

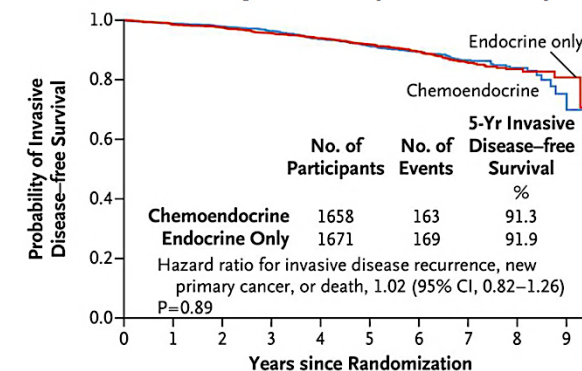
T1	58%	T3	5%
1 LN+	66%	3 LN+	9%
Grade 2	64%	Grade 3	10%
40-49 yrs	21%	< 40 yrs	3%

## RxPONDER: Chemo Benefit Different by Menopausal Status if RS 0-25

### Premenopausal (1/3<sup>rd</sup> Trial)



### Postmenopausal (2/3<sup>rd</sup> Trial)



## IDFS Benefit Modified by Score for Women Age $\leq 50$

### Women $\leq 50$ yr

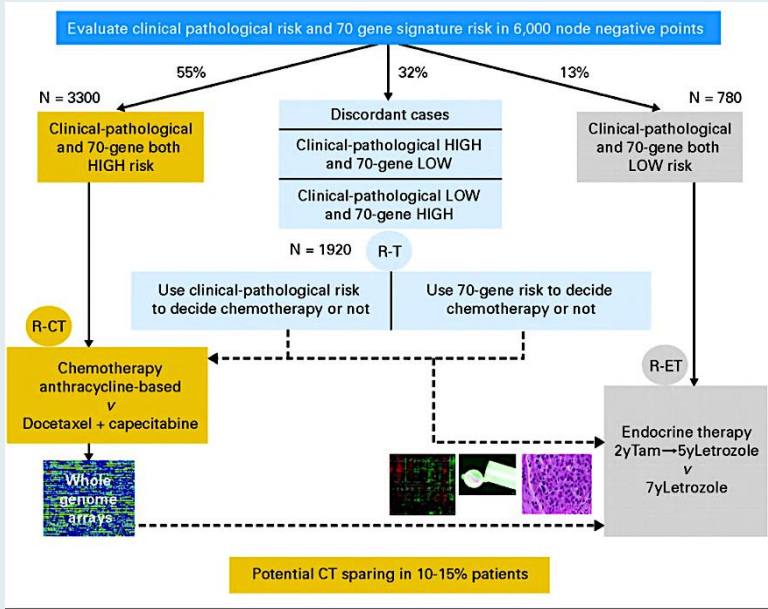
Group	No. of Participants	5-Yr Invasive Disease-free Survival %	Hazard Ratio (95% CI)
$\leq 10$ , endocrine only	145	91.0 $\pm$ 2.6	0.31 (0.10–0.94)
$\leq 10$ , chemoendocrine	135	97.9 $\pm$ 1.5	
11–15, endocrine only	247	93.1 $\pm$ 1.8	0.71 (0.33–1.51)
11–15, chemoendocrine	235	95.4 $\pm$ 1.6	
16–20, endocrine only	227	85.1 $\pm$ 2.6	0.58 (0.33–1.00)
16–20, chemoendocrine	224	92.2 $\pm$ 2.0	
21–25, endocrine only	107	80.0 $\pm$ 4.3	0.56 (0.27–1.17)
21–25, chemoendocrine	98	90.0 $\pm$ 3.6	

# MammaPrint: MindACT Trial Key Results

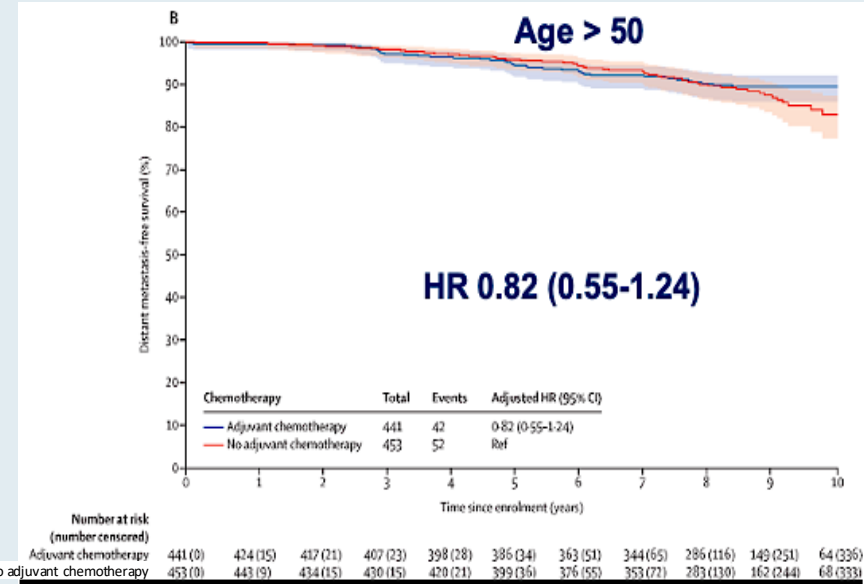
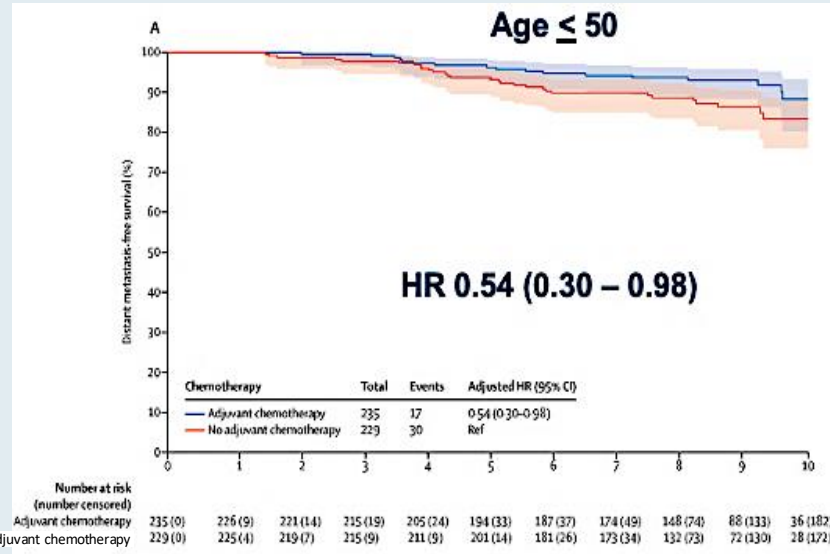
Clinical “high risk”: <88% 10-yr BCSS  
 Modified Adjuvant! Online to determine  
 Model included: T size, Node (0-3), grade, ER status, age, comorbidity

Chemo benefit increases over time overall. Lost in those age >50, maintained in those age <50

	ET	CET	Absolute diff
5-y DMFS	94.7% (92.5 – 96.2)	95.9% (94-97.2)	1.2%
8-yr DMFS	89.4% (86.8- 91,5)	92% (896-93.8)	2.6%



Met primary outcome: Lower bound of 95% CI >92% 5-y DMFS in the High Clinical/Low Genomic risk group



BCSS = breast cancer-specific survival; DMFS = distant metastasis-free survival  
 Cardoso F et al. *N Engl J Med* 2016; Piccart M et al. *Lancet Oncol* 2021.

# Prosigna<sup>®</sup> ROR, EndoPredict<sup>®</sup> EPclin and Breast Cancer Index<sup>®</sup>

## ROR (risk of recurrence, Prosigna)

- 50-gene RNA-based molecular subtyping assay
- ROR available in US; PAM50 not available

## EPclin (EndoPredict)

- 12 genes – Proliferation and hormone receptor

## Breast Cancer Index (BCI)

- 7 genes – Proliferation and hormone receptor (HoxB13/IL17BR)

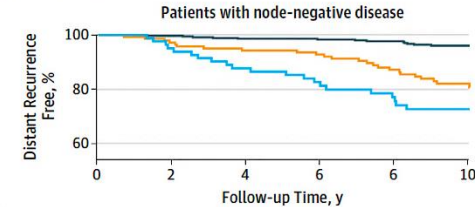
JAMA Oncology | Original Investigation

Comparison of the Performance of 6 Prognostic Signatures for Estrogen Receptor-Positive Breast Cancer  
A Secondary Analysis of a Randomized Clinical Trial

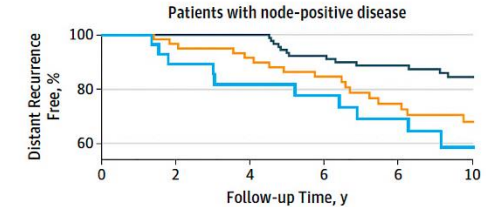
- Largest retrospective prognostic validation in TransATAC Trial (included *Oncotype DX* and BCI as well)
- N = 535 node-negative, 154 node-positive
- Examined risk years 0 to 10
- ROR, EPclin and BCI provided most prognostic information
- ROR HR 2.56 (1.96-3.35)
- EPclin HR 2.14 (1.71-2.68)
- BCI HR 2.46 (1.88-3.23)

## BCI

A Breast cancer index



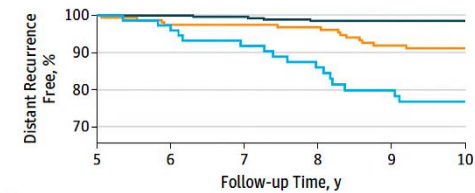
No. at risk	0	2	4	6	8	10
Low risk	365	356	346	331	309	173
Intermediate risk	143	137	128	122	105	59
High risk	83	78	71	60	52	30



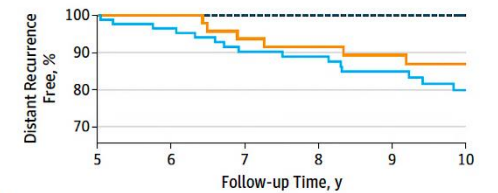
No. at risk	0	2	4	6	8	10
Low risk	95	95	92	80	69	35
Intermediate risk	60	58	53	45	37	21
High risk	28	25	21	18	15	7

## ROR

C Risk of recurrence score



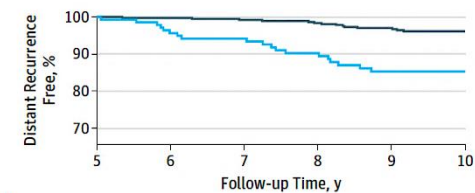
No. at risk	5	6	7	8	9	10
Low risk	292	288	279	270	257	157
Intermediate risk	165	155	149	138	125	72
High risk	78	70	64	58	50	33



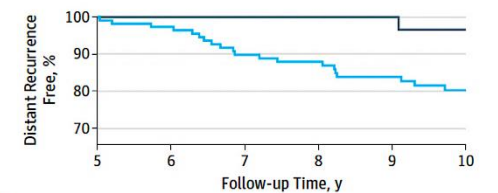
No. at risk	5	6	7	8	9	10
Low risk	15	15	15	13	13	6
Intermediate risk	51	48	44	42	38	23
High risk	88	80	70	66	56	34

## EPclin

D EPclin



No. at risk	5	6	7	8	9	10
Low risk	393	384	369	356	335	202
Intermediate risk	142	129	123	110	97	60

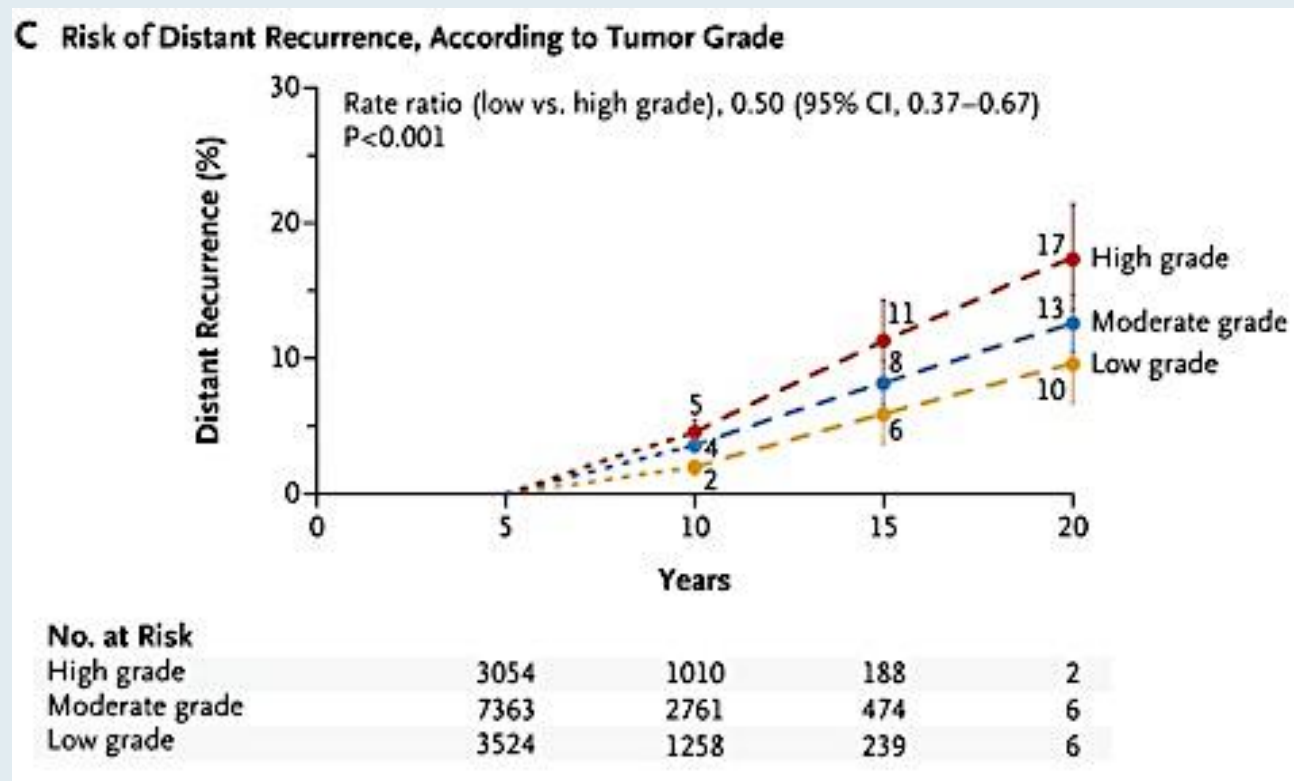
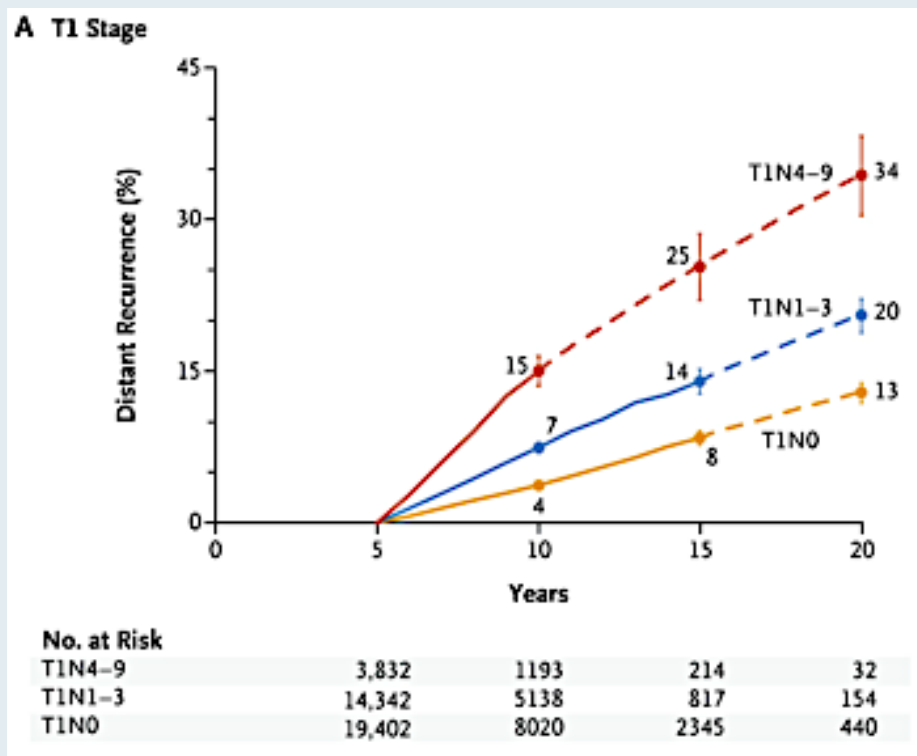


No. at risk	5	6	7	8	9	10
Low risk	40	37	34	32	30	15
Intermediate risk	114	106	95	89	77	48

— Low risk — Intermediate risk — High risk

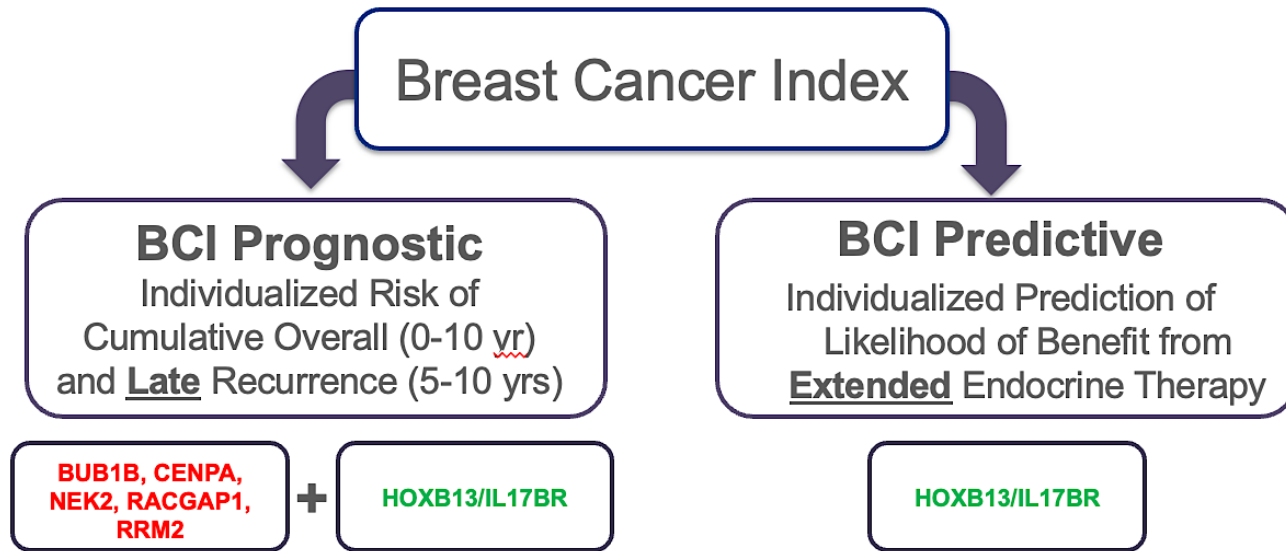
# Persistent Long-Term Risk of Distant Recurrence

Risk of late distant recurrence after 5 years of adjuvant endocrine therapy persists across all clinical stages



# Breast Cancer Index

## BCI Components



- Algorithmic combination of **proliferation**-related gene signature (Molecular Grade Index, MGI) and an **estrogen** signaling pathway signature (HoxB13/IL17BR, a.k.a. H/I)

- A separate algorithm based exclusively on H/I to provide a quantitative molecular assessment of estrogen signaling pathways

## Distribution of BCI scores

Low Risk (<4.8%) / Low Likelihood of Benefit

~45%

High Risk (>4.8%) / High Likelihood of Benefit

~30%

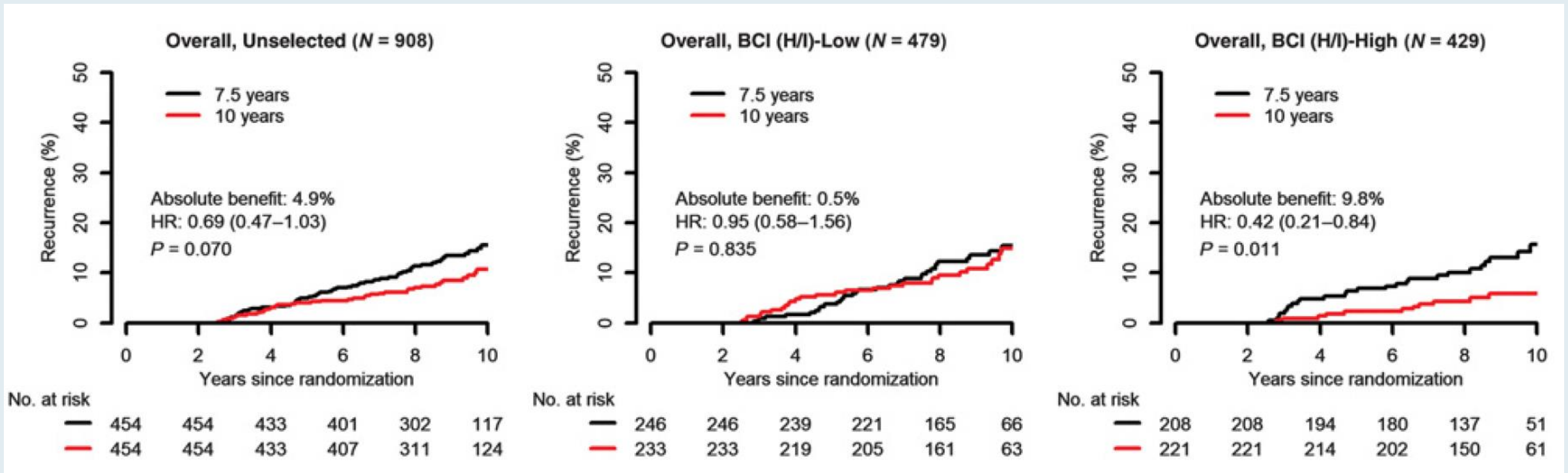
High Risk (>4.8%) / Low Likelihood of Benefit

~15%

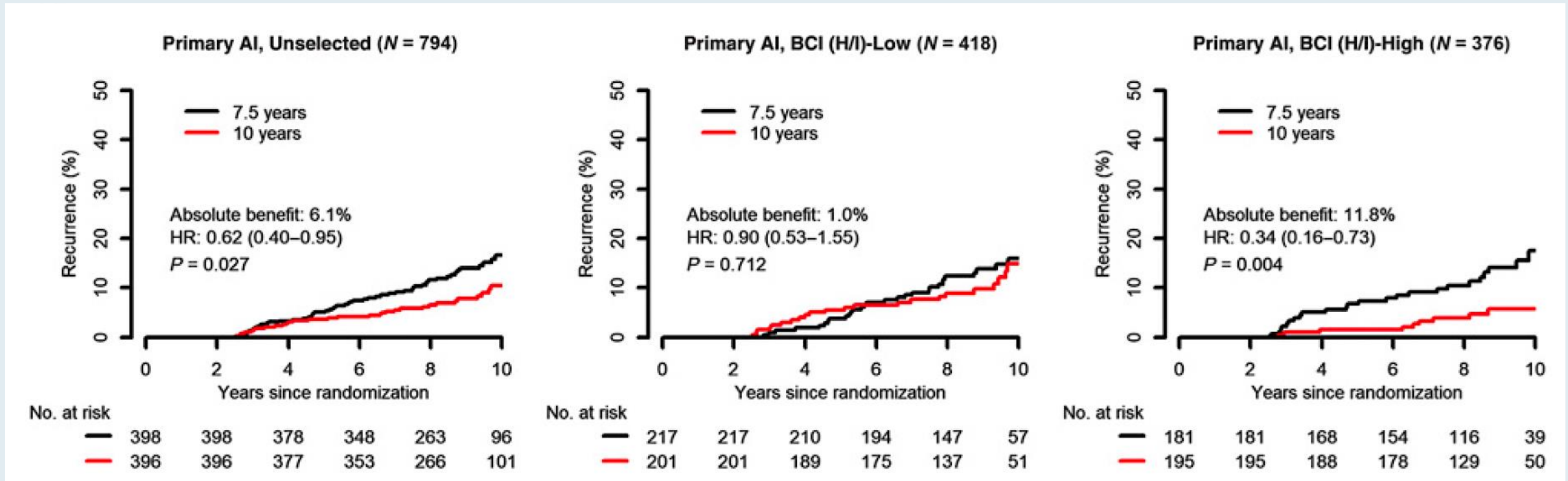
Low Risk (<4.8%) / High Likelihood of Benefit

~10%

# Predictive Performance by Breast Cancer Index® (BCI) H/I Groups Based on Recurrence-Free Interval in the Overall Cohort of the Phase III IDEAL Trial



# Predictive Performance by BCI H/I Groups Based on Recurrence-Free Interval in the Subset of Patients in the Phase III IDEAL Trial Who Received a Primary Aromatase Inhibitor (AI)

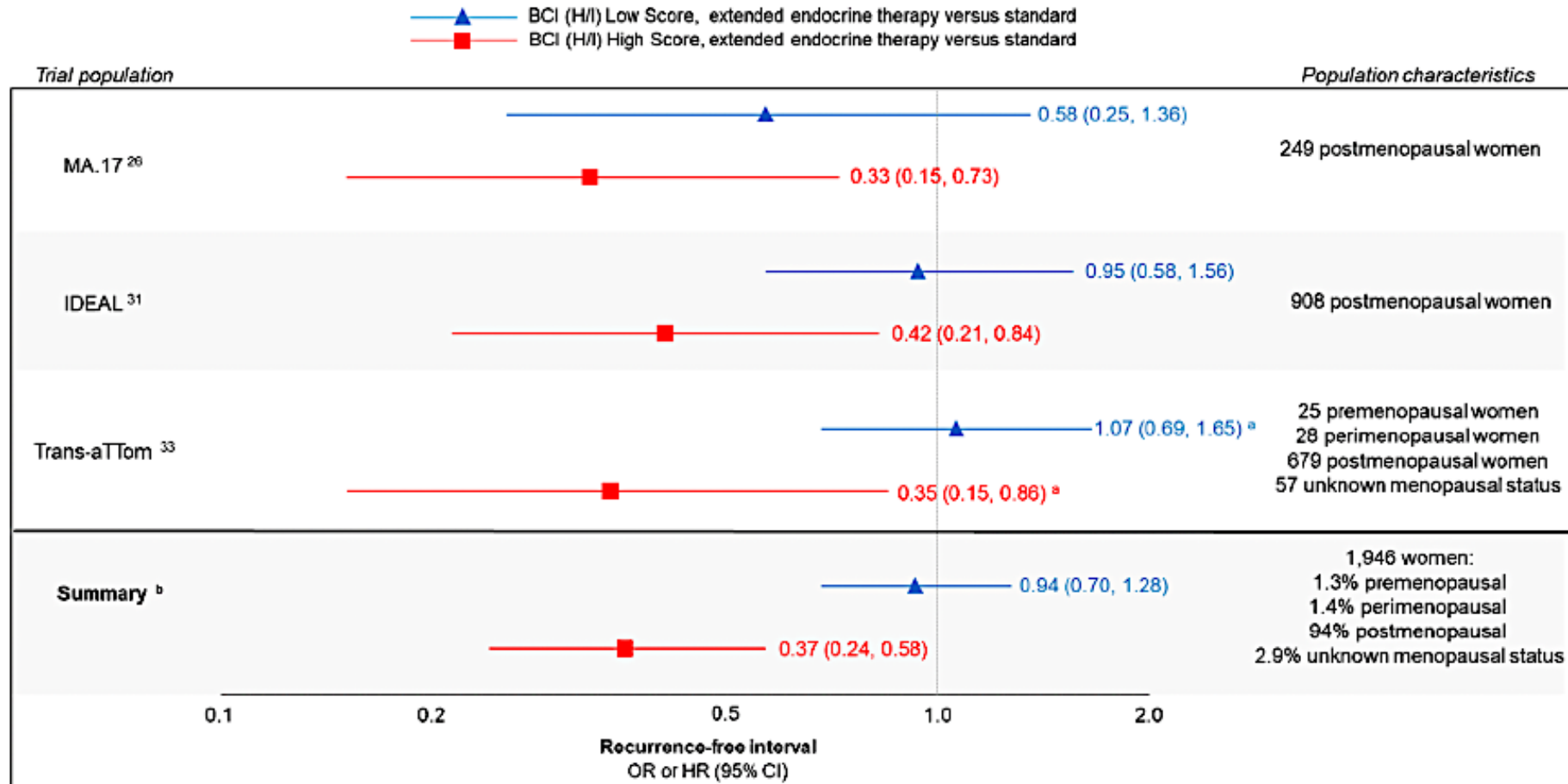


# Risk of Recurrence at Year 10 Since Randomization for Patients Who Received 5 Years versus 2.5 Years of Additional Letrozole in the Overall Cohort and in the Primary AI Subset of the Phase III IDEAL Trial

Groups	5-year letrozole		2.5-year letrozole		HR (95% CI)*
	Number of Patients	10-year risk (95% CI)	Number of Patients	10-year risk (95% CI)	
<b>Overall (N=908)</b>					
Unselected	454 (100%)	10.6% (7.1-14.0)	454 (100%)	15.5% (11.5-19.3)	0.69 (0.47-1.03)
BCI (H/I)-High	221 (49%)	5.9% (2.3-9.3)	208 (46%)	15.7% (9.5-21.5)	0.42 (0.21-0.84)
BCI (H/I)-Low	233 (51%)	14.9% (9.1-20.3)	246 (54%)	15.4% (10.1-20.4)	0.95 (0.58-1.56)
<b>Primary AI (N=794)</b>					
Unselected	396 (100%)	10.5% (6.6-14.2)	398 (100%)	16.6% (12.1-20.8)	0.62 (0.40-0.95)
BCI (H/I)-High	195 (49%)	5.7% (1.9-9.4)	181 (45%)	17.5% (10.1-24.4)	0.34 (0.16-0.73)
BCI (H/I)-Low	201 (51%)	14.9% (8.2-21.1)	217 (55%)	15.9% (10.2-21.3)	0.90 (0.53-1.55)

\*HR was calculated to compare 5-year letrozole vs. 2.5-year letrozole. HR=hazard ratio. CI=confidence interval.

# BCI validation in extended adjuvant therapy trials



a. Estimates reported are from most recent update on results from this population.

b. Summary statistic calculated using a random effects model incorporating each study's OR or HR and its associated 95% confidence interval.

# ASCO Guideline: Extended Adjuvant Therapy

## Extended Endocrine Therapy for ER-Positive HER2-Negative Breast Cancer

### ***Oncotype DX, EndoPredict, Prosigna, Ki67, or IHC4.***

**Recommendation 1.23.** If a patient has node-negative breast cancer and has had 5 years of endocrine therapy without evidence of recurrence, there is insufficient evidence to use Oncotype DX, EndoPredict, Prosigna, Ki67, or IHC4 scores to guide decisions about extended endocrine therapy (Type: evidence-based; Evidence quality: intermediate; Strength of recommendation: moderate).

### ***Breast Cancer Index.***

**Recommendation 1.24.** If a patient has node-negative or node-positive breast cancer with 1-3 positive nodes and has been treated with 5 years of primary endocrine therapy without evidence of recurrence, the clinician may offer the BCI test to guide decisions about extended endocrine therapy with either tamoxifen, an AI, or a sequence of tamoxifen followed by AI (Type: evidence-based; Evidence quality: intermediate; Strength of recommendation: moderate).

**Recommendation 1.25.** If a patient has node-positive breast cancer with  $\geq 4$  positive nodes and has been treated with 5 years of primary endocrine therapy without evidence of recurrence, there is insufficient evidence to use the BCI test to guide decisions about extended endocrine therapy with either tamoxifen, an AI, or a sequence of tamoxifen followed by AI (Type: evidence-based; Evidence quality: intermediate; Strength of recommendation: strong).

### ***Clinical treatment score post-5 years.***

**Recommendation 1.26.** If a patient is postmenopausal and had invasive breast cancer and is recurrence-free after 5 years of adjuvant endocrine therapy, the clinical treatment score post-5 years (CTS5) web tool may be used to calculate the estimated risk of late recurrence (recurrence between years 5-10), which could assist in decisions about extended endocrine therapy (Type: evidence-based; Evidence quality: intermediate; Strength of recommendation: moderate).

# Summary: ASCO Guideline 2022

ER+ and HER2–	Premenopausal or Age ≤ 50 Years (evidence quality/strength of recommendation)	Postmenopausal or Age > 50 Years (evidence quality/strength of recommendation)
Node-negative	Oncotype DX ( <i>high/strong</i> )	Oncotype DX ( <i>high/strong</i> ) MammaPrint <sup>a</sup> ( <i>intermediate/strong</i> ) EndoPredict ( <i>intermediate/moderate</i> ) Prosigna ( <i>intermediate/moderate</i> ) Ki67 <sup>b</sup> ( <i>intermediate/moderate</i> ) IHC4 <sup>b</sup> ( <i>intermediate/moderate</i> ) BCI <sup>c</sup> ( <i>intermediate/moderate</i> )
1-3 positive nodes	Insufficient evidence to recommend a biomarker for use	Oncotype DX ( <i>high/strong</i> ) MammaPrint <sup>a</sup> ( <i>intermediate/strong</i> ) EndoPredict ( <i>intermediate/moderate</i> ) Ki67 <sup>b</sup> ( <i>intermediate/strong</i> ) IHC4 <sup>b</sup> ( <i>intermediate/moderate</i> ) BCI <sup>c</sup> ( <i>intermediate/moderate</i> )
≥ 4 positive nodes	Insufficient evidence to recommend a biomarker for use	
HER2+ (ER+ or ER–)	No mature evidence to recommend use of any other biomarker for this patient population	
ER–/HER2–	No mature evidence to recommend use of any other biomarker for this patient population	

# Management of Hormone Receptor (HR)-Positive Localized Breast Cancer

**Module 1: Risk Assessment and Genomic Assays for HR-Positive, HER2-Negative Localized Breast Cancer**

**Module 2: Clinician Survey Results**

**Module 3: Adjuvant CDK4/6 Inhibitors for High-Risk, HR-Positive, HER2-Negative Localized Breast Cancer**






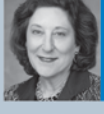


**Module 4: Clinician Survey Results**

**Module 5: Tolerability and Other Practical Considerations with Adjuvant CDK4/6 Inhibitor Therapy**








**Module 6: Clinician Survey Results**

**Module 7: Adjuvant Oral SERDs for HR-Positive, HER2-Negative Localized Breast Cancer**

# Outside of a clinical trial, which genomic assay(s) do you routinely order to assist with decision-making regarding adjuvant systemic therapy for your patients with HR-positive, HER2-negative localized breast cancer (BC)?









 <b>Dr Brufsky</b>	<b><i>Oncotype DX</i><sup>®</sup>, <i>MammaPrint</i><sup>®</sup>, <i>EndoPredict</i><sup>®</sup>, <i>Breast Cancer Index</i><sup>®</sup></b>
 <b>Dr Jhaveri</b>	<b><i>Oncotype DX</i></b>
 <b>Dr Kalinsky</b>	<b><i>Oncotype DX</i></b>
 <b>Dr Mahtani</b>	<b><i>Oncotype DX</i>, <i>MammaPrint</i>, <i>Breast Cancer Index</i></b>
 <b>Dr Mouabbi</b>	<b><i>Oncotype DX</i>, <i>MammaPrint</i>, <i>Breast Cancer Index</i></b>
 <b>Dr Rugo</b>	<b><i>Oncotype DX</i> and <i>MammaPrint</i></b>
 <b>Dr Sharma</b>	<b><i>Oncotype DX</i> and <i>MammaPrint</i></b>
 <b>Dr Shatsky</b>	<b><i>Oncotype DX</i>, <i>MammaPrint</i>, <i>Breast Cancer Index</i></b>

Would you recommend adjuvant chemotherapy for a 40-year-old premenopausal patient with node-negative, HR-positive, HER2-negative localized BC and the 21-gene Recurrence Score® (RS) listed below?

		RS = 8	RS = 17	RS = 20
	Dr Brufsky	No	No	Yes, but offer OFS/OA as alternative
	Dr Jhaveri	No	Yes, but offer OFS/OA as alternative	Yes, but offer OFS/OA as alternative
	Dr Kalinsky	No	No	Yes
	Dr Mahtani	No	Yes, but offer OFS/OA as alternative	Yes, but offer OFS/OA as alternative
	Dr Mouabbi	No	No	No
	Dr Rugo	No	No*	No*
	Dr Sharma	No	No	Yes, but offer OFS/OA as alternative
	Dr Shatsky	No	No*	No*

OFS/OA = ovarian function suppression/ovarian ablation; \* Would offer OFS/OA

Would you recommend adjuvant chemotherapy for a 40-year-old premenopausal patient with HR-positive, HER2-negative localized BC with 3 positive nodes and the 21-gene RS listed below?

		RS = 8	RS = 17	RS = 20
	Dr Brufsky	Yes, but offer OFS/OA as alternative	Yes, but offer OFS/OA as alternative	Yes, but offer OFS/OA as alternative
	Dr Jhaveri	Yes	Yes	Yes
	Dr Kalinsky	Yes	Yes	Yes
	Dr Mahtani	Yes	Yes	Yes
	Dr Mouabbi	Yes, but offer OFS/OA as alternative	Yes, but offer OFS/OA as alternative	Yes, but offer OFS/OA as alternative
	Dr Rugo	Yes	Yes	Yes
	Dr Sharma	Yes	Yes	Yes
	Dr Shatsky	Yes	Yes	Yes

OFS/OA = ovarian function suppression/ovarian ablation

Would you recommend adjuvant chemotherapy for a 65-year-old postmenopausal patient with HR-positive, HER2-negative localized BC with 3 positive nodes and the 21-gene RS listed below?

	RS = 8	RS = 17	RS = 20
 Dr Brufsky	No	No	No
 Dr Jhaveri	No	No	No
 Dr Kalinsky	No	No	Yes
 Dr Mahtani	No	No	Yes
 Dr Mouabbi	No	No	No
 Dr Rugo	No	No	No
 Dr Sharma	No	No	No
 Dr Shatsky	No	No	No

Have you ordered or would you order a genomic assay to assist with treatment decision-making in the localized setting for any patients with HR-positive, HER2-negative localized BC and 4 or more positive nodes?



**Dr Brufsky**

**I have**



**Dr Jhaveri**

**I have not but would for the right patient**



**Dr Kalinsky**

**I have not but would for the right patient**



**Dr Mahtani**

**I have not and would not**



**Dr Mouabbi**

**I have not and would not**



**Dr Rugo**

**I have**



**Dr Sharma**









**I have not and would not**



**Dr Shatsky**






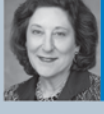


**I have**

# Outside of a clinical trial, which genomic assay(s) do you routinely order to assist with decision-making in the neoadjuvant setting for your patients with HR-positive, HER2-negative localized BC?

 Dr Brufsky	MammaPrint
 Dr Jhaveri	<i>Oncotype DX</i>
 Dr Kalinsky	MammaPrint
 Dr Mahtani	MammaPrint
 Dr Mouabbi	MammaPrint
 Dr Rugo	MammaPrint and <i>Oncotype DX</i> *
 Dr Sharma	<i>Oncotype DX</i> and MammaPrint
 Dr Shatsky	MammaPrint and <i>Oncotype DX</i> *









\* All my patients with HR+ disease screen for I-SPY with rare exceptions and we order Mammaprint and BluePrint. I will occasionally order *Oncotype DX*

**Outside of a clinical trial, do you routinely employ Breast Cancer Index (BCI) to determine whether to continue adjuvant endocrine therapy beyond 5 years for patients with HR-positive, HER2-negative localized BC? If so, in which clinical situations?**

 <b>Dr Brufsky</b>	<b>Yes, for node-positive disease when MammaPrint not available</b>
 <b>Dr Jhaveri</b>	<b>Yes, per patient preference and for N0 and N1, especially if patients are struggling with toxicities</b>
 <b>Dr Kalinsky</b>	<b>Yes, in situations where I'm on the fence about extending ET</b>
 <b>Dr Mahtani</b>	<b>Yes, for patients with N0 disease or up to 3 pos nodes</b>
 <b>Dr Mouabbi</b>	<b>Yes, for patients for whom we are considering extended ET</b>
 <b>Dr Rugo</b>	<b>No*</b>
 <b>Dr Sharma</b>	<b>Yes, for patients with high-risk, node-negative disease</b>
 <b>Dr Shatsky</b>	<b>Yes, N0/N1 tumors with decent risk for late relapse</b>









ET = endocrine therapy; \* No due to reimbursement issues, but I would for patients with poor tolerance to ET and high-risk disease

# Approximately what proportion of the time would you estimate that having the results from BCI cause you to change your recommendation regarding extended-adjuvant endocrine therapy (ET)?









		Recommending ET to not recommending	Not recommending ET to recommending
	Dr Brufsky	25%	25%
	Dr Jhaveri	5% to 10%	<5%
	Dr Kalinsky	10%	10%
	Dr Mahtani	20%	20%
	Dr Mouabbi	80%	20%
	Dr Rugo	NA	NA
	Dr Sharma	10%	10%
	Dr Shatsky	25%	5%

NA = not applicable

# Outside of a clinical trial, do you routinely employ any genomic assays other than Breast Cancer Index to determine whether to continue adjuvant endocrine therapy beyond 5 years for patients with HR-positive, HER2-negative localized BC?

 Dr Brufsky	Yes, MammaPrint
 Dr Jhaveri	No
 Dr Kalinsky	No
 Dr Mahtani	No
 Dr Mouabbi	Yes, MammaPrint
 Dr Rugo	No
 Dr Sharma	No
 Dr Shatsky	No

Have you ordered or would you order a circulating tumor DNA (ctDNA)-based molecular residual disease (MRD) assay to assist with clinical decision-making for a patient with localized BC? If you were to order a ctDNA-based MRD assay for a patient with localized BC, which specific assay(s) would you use?

		Order a ctDNA-based MRD assay?	Assay
	<b>Dr Brufsky</b>	I have	Signatera™
	<b>Dr Jhaveri</b>	I have not and would not	NA
	<b>Dr Kalinsky</b>	I have not but would for the right patient	Signatera
	<b>Dr Mahtani</b>	I have not and would not	NA
	<b>Dr Mouabbi</b>	I have	Signatera
	<b>Dr Rugo</b>	I have	Signatera
	<b>Dr Sharma</b>	I have not and would not	NA
	<b>Dr Shatsky</b>	I have	Signatera first, then Guardant Reveal™ if not enough tissue

NA = not applicable

# Management of Hormone Receptor (HR)-Positive Localized Breast Cancer

**Module 1: Risk Assessment and Genomic Assays for HR-Positive, HER2-Negative Localized Breast Cancer**

**Module 2: Clinician Survey Results**

**Module 3: Adjuvant CDK4/6 Inhibitors for High-Risk, HR-Positive, HER2-Negative Localized Breast Cancer**

**Module 4: Clinician Survey Results**

**Module 5: Tolerability and Other Practical Considerations with Adjuvant CDK4/6 Inhibitor Therapy**

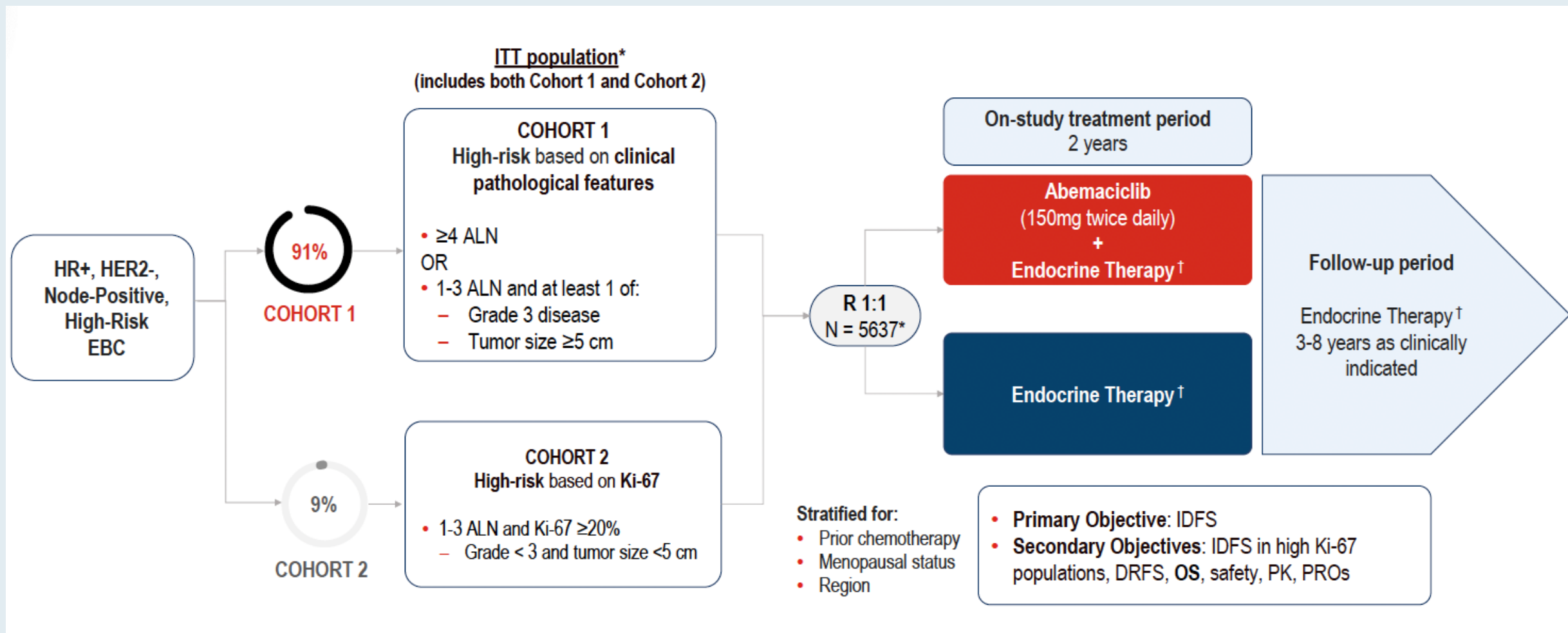
**Module 6: Clinician Survey Results**

**Module 7: Adjuvant Oral SERDs for HR-Positive, HER2-Negative Localized Breast Cancer**

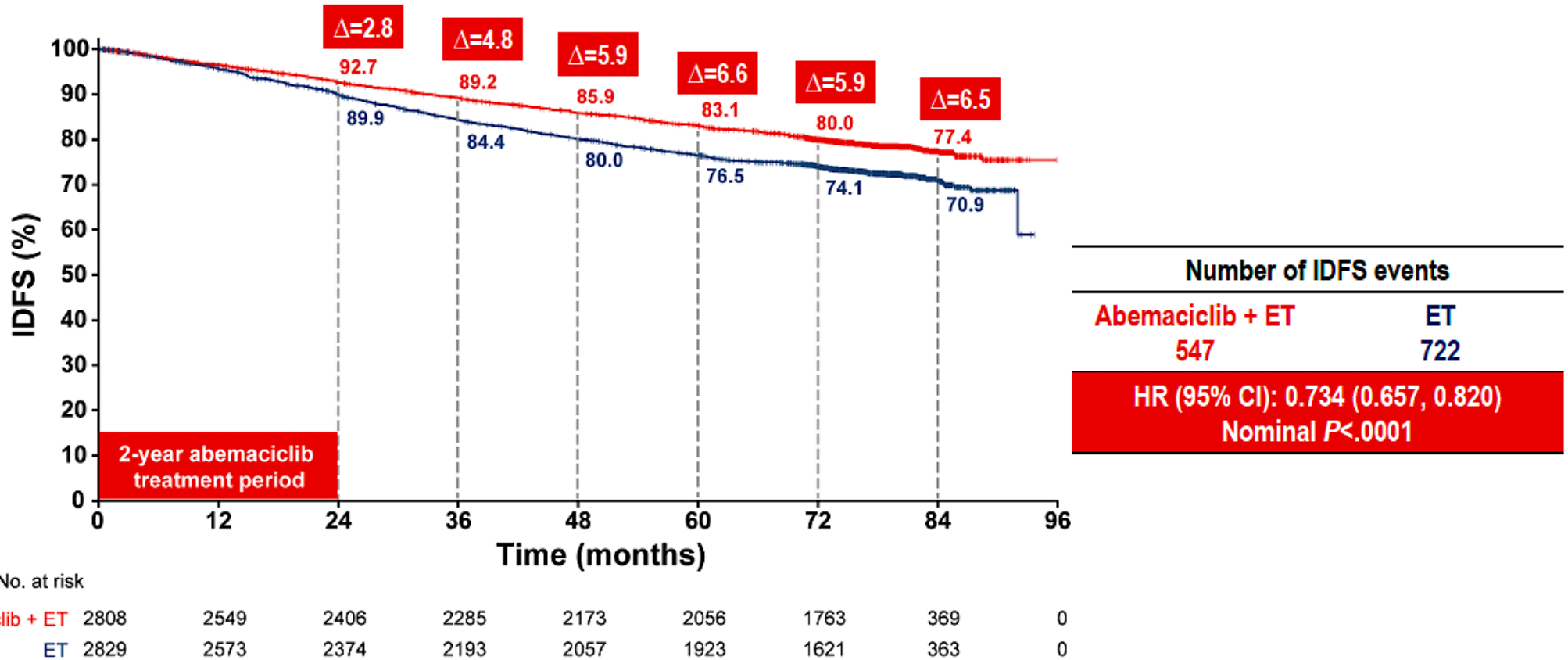
# Key Datasets

- Johnston S et al. **monarchE: Primary overall survival (OS)** results of adjuvant abemaciclib + endocrine therapy (ET) for HR+, HER2-, high-risk early breast cancer (EBC). ESMO 2025;Abstract LBA13.
- Johnston S et al. **Overall survival with abemaciclib** in early breast cancer. *Ann Oncol* 2026;37(2):155-65.
- Cortés 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.
- Crown JP et al. **Adjuvant ribociclib (RIB) plus nonsteroidal aromatase inhibitor (NSAI)** in patients (pts) with HR+/HER2- early breast cancer (EBC): **NATALEE 5-year outcomes**. ESMO 2025;Abstract LBA14.

# monarchE Study Design



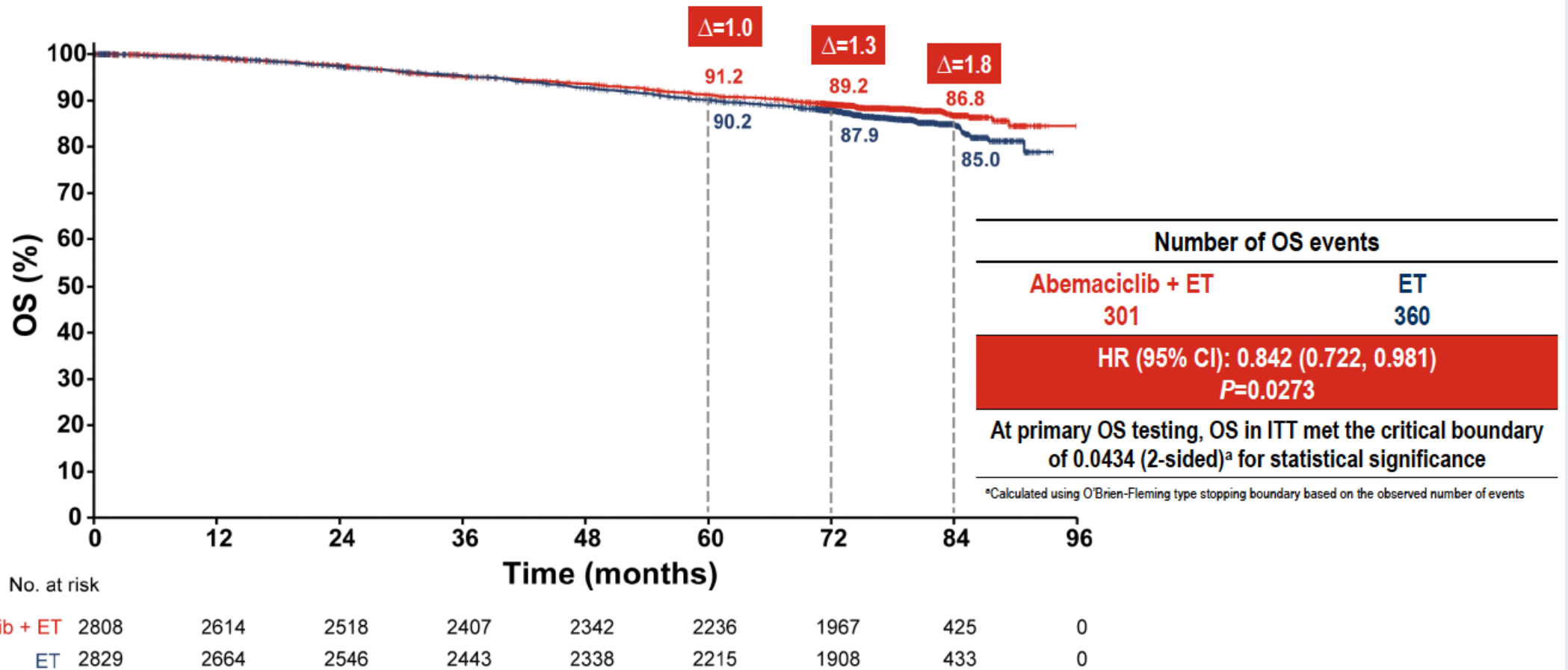
# monarchE: Invasive Disease-Free Survival (IDFS) Outcomes



**Abemaciclib + ET reduced the risk of IDFS events by 26.6% compared to ET alone**

ET = endocrine therapy

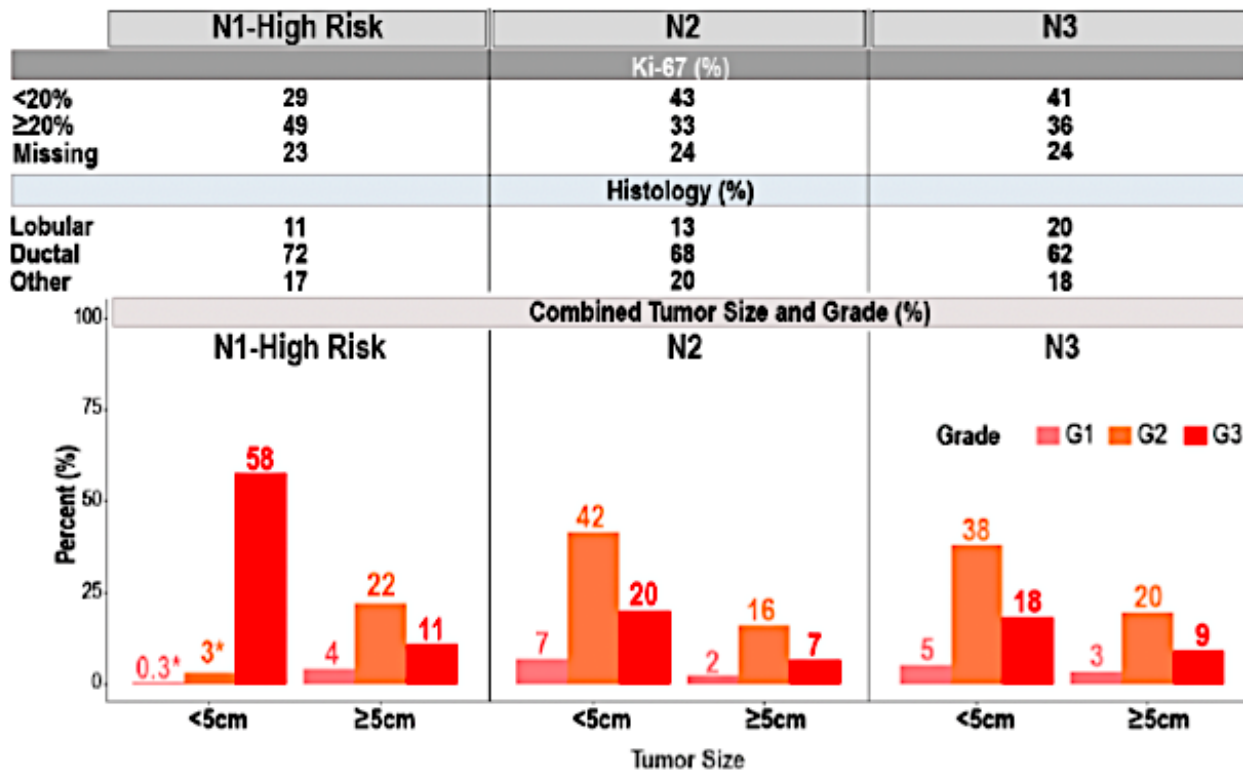
# monarchE: Overall Survival (OS) Outcomes



**At a median follow-up of 6.3 years, abemaciclib + ET reduced the risk of death by 15.8% compared to ET alone**

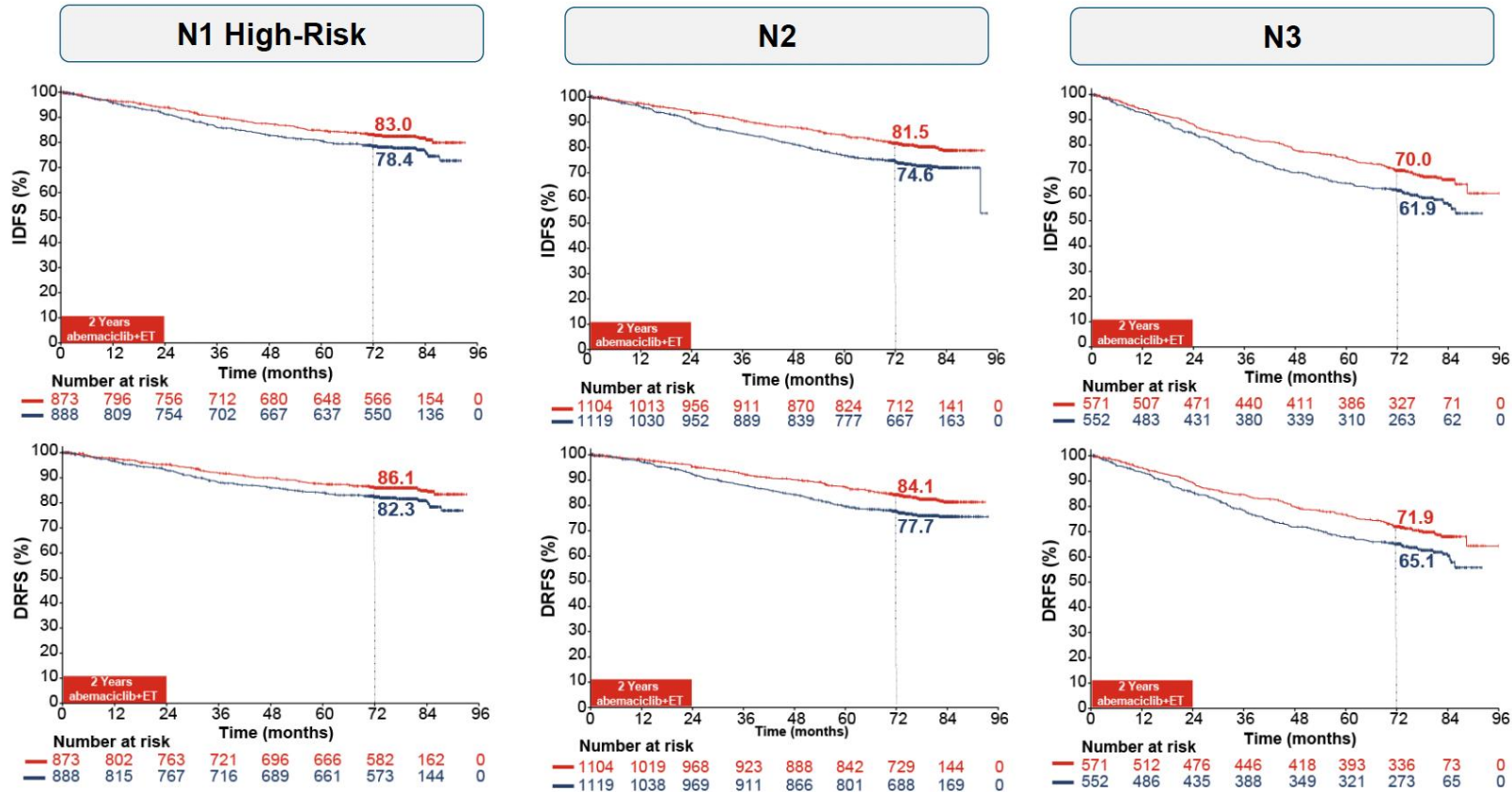
# monarchE: Subgroup Analysis by Nodal Status

## Tumor Characteristics in Cohort 1



- monarchE eligible patients with N1 high risk disease presented more Grade 3 tumors and Ki-67 ≥20% compared to N2 and N3
- Distribution of ductal/lobular histology was similar in N1-high risk and N2 while N3 had more lobular tumors
- Over 40% of patients with N1-High risk disease received neoadjuvant chemotherapy compared to less than 30% of those with N3 disease
- Conversely, the use of adjuvant chemotherapy and radiation therapy was higher among patients with N2 and N3 disease

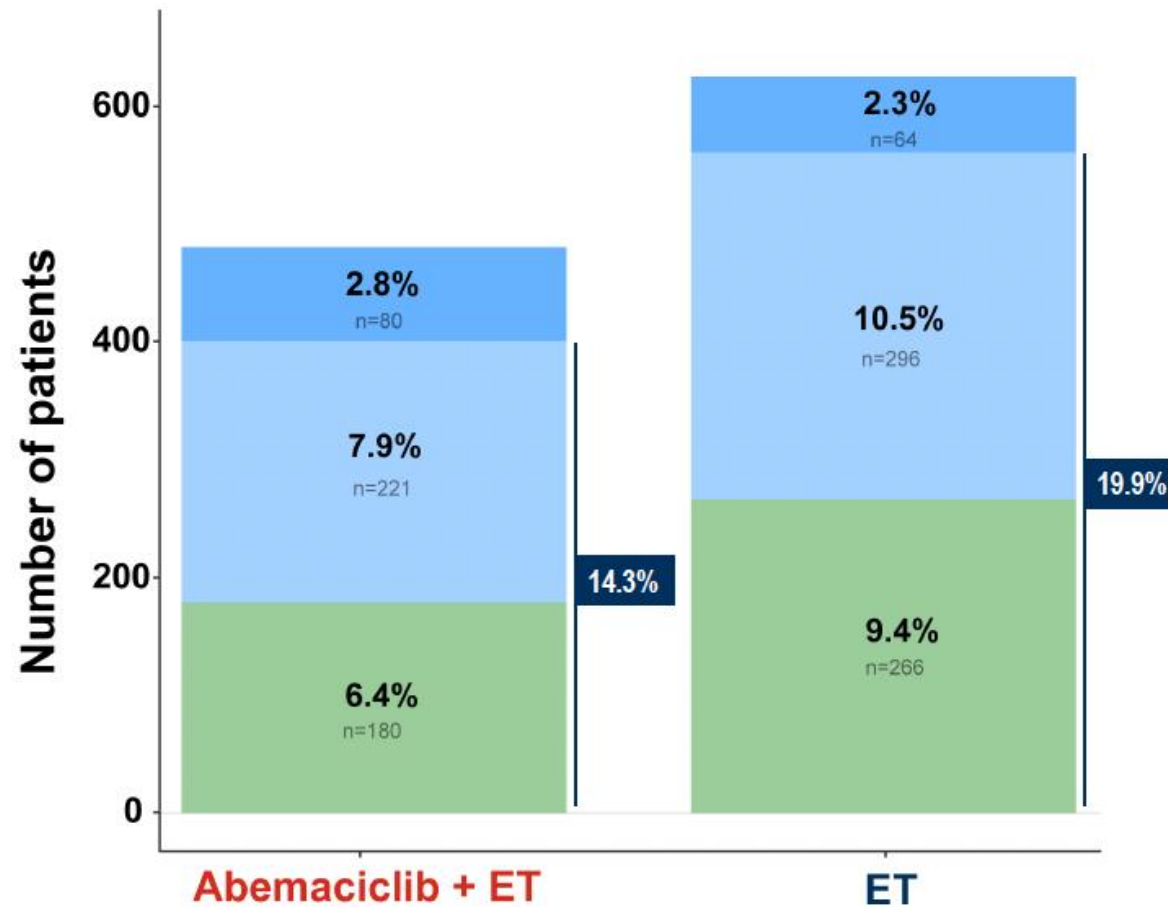
# monarchE: IDFS and DRFS by Nodal Status



- In the ET alone arm, patients with N1-High risk and N2 disease had comparable risk of recurrence and death, while higher risk was observed in N3 subgroup
- Abemaciclib plus ET reduced the risk of IDFS events by 24.8% (N1), 31.5% (N2) and 27.4% (N3), compared to ET

DRFS = distant relapse-free survival

# monarchE: Survival Status



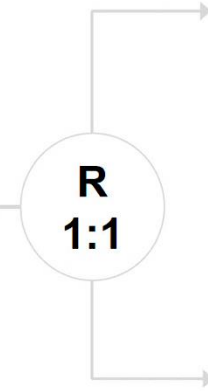
**Status** ■ Deaths not related to breast cancer<sup>a</sup> ■ Deaths due to breast cancer ■ Alive with metastatic disease

**~30% Fewer Patients in Abemaciclib Arm Living with Metastatic Disease**

# NATALEE Study Design

## Adult patients with stage II and III HR+/HER2- EBC

- Prior ET allowed up to 12 months
- **Anatomical stage IIA<sup>a</sup>**
  - N0 with:
    - Grade 2 and evidence of high risk:
      - Ki-67  $\geq$  20%
      - Oncotype DX Breast Recurrence Score  $\geq$  26 or
      - High risk via genomic risk profiling
    - Grade 3
  - N1
- **Anatomical stage IIB<sup>a</sup>**
  - N0 or N1
- **Anatomical stage III**
  - N0, N1, N2, or N3



**RIB**  
400 mg/day  
3 weeks on/1 week off for 3 y  
**+**  
**NSAI**  
Letrozole or anastrozole<sup>b</sup> for  $\geq$ 5 y  
+ goserelin in men and premenopausal women

**NSAI**  
Letrozole or anastrozole<sup>b</sup> for  $\geq$ 5 y  
+ goserelin in men and premenopausal women

**Primary End Point**  
iDFS using STEEP criteria

**Secondary End Points**

- RFS, DDFS, OS
- PROs
- Safety and tolerability
- PK

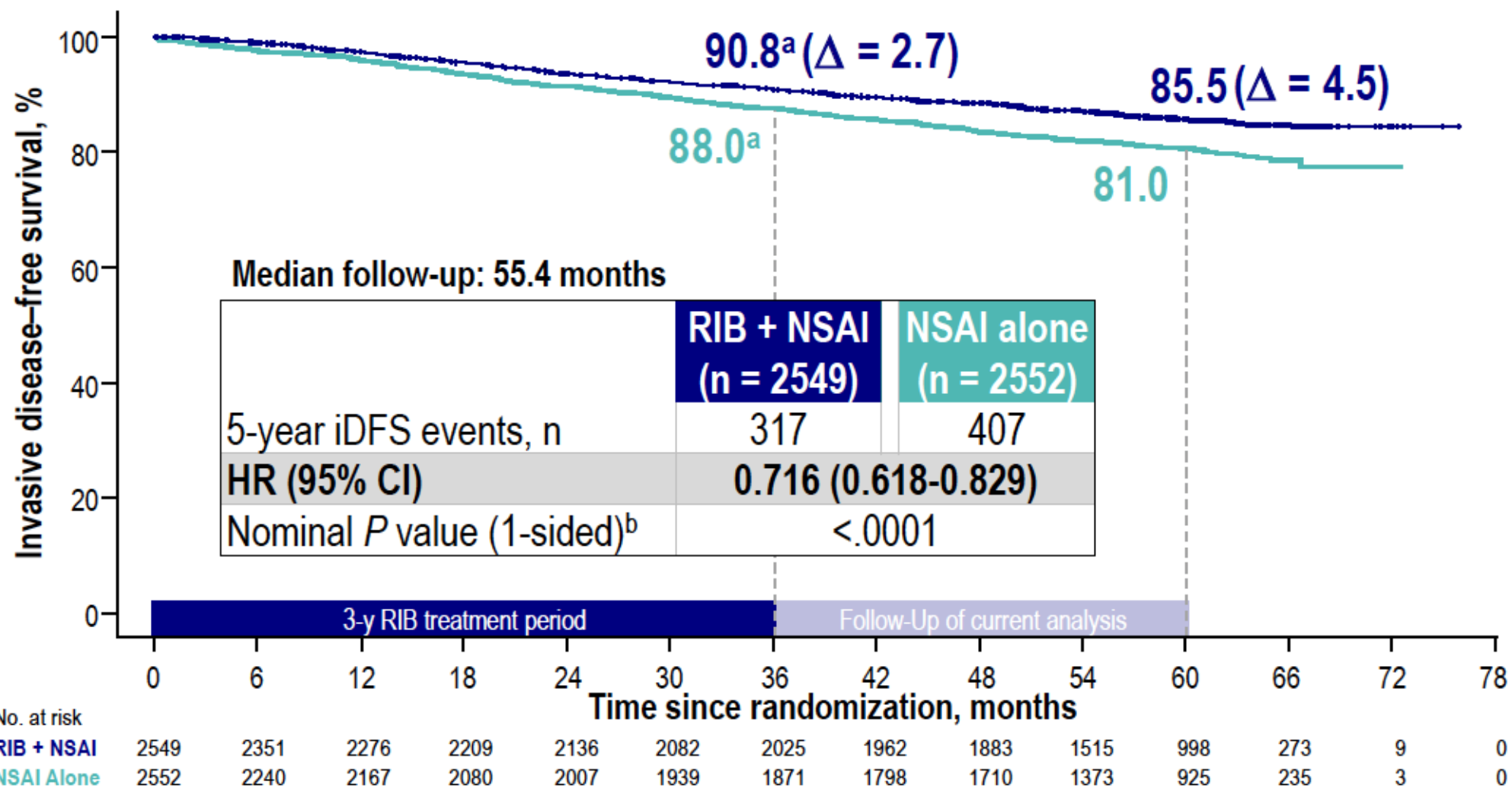
**Exploratory End Points**

- DRFS
- Gene expression and alterations in tumor ctDNA/ctRNA samples

Efficacy outcomes for the 5-year analysis were estimated by the Kaplan-Meier method, and results are descriptive. The Cox proportional hazards model was used to estimate the HRs and 95% CIs.

RIB = ribociclib; NSAI = nonsteroidal aromatase inhibitor

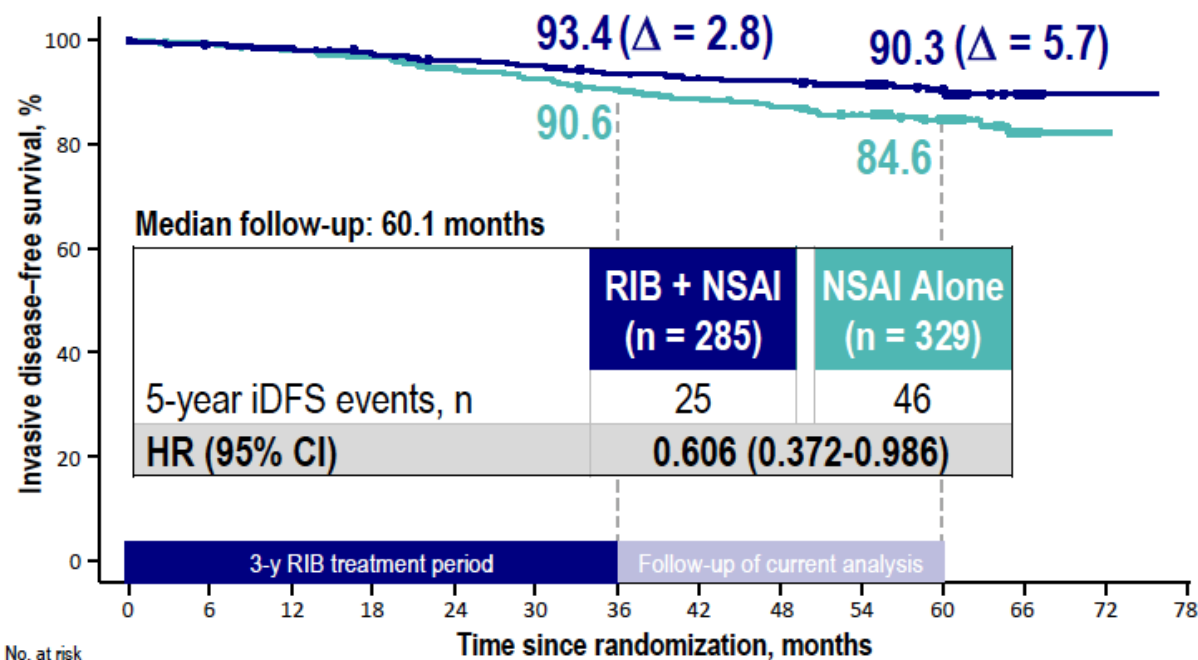
# NATALEE: IDFS Outcomes



NSAI = nonsteroidal aromatase inhibitor

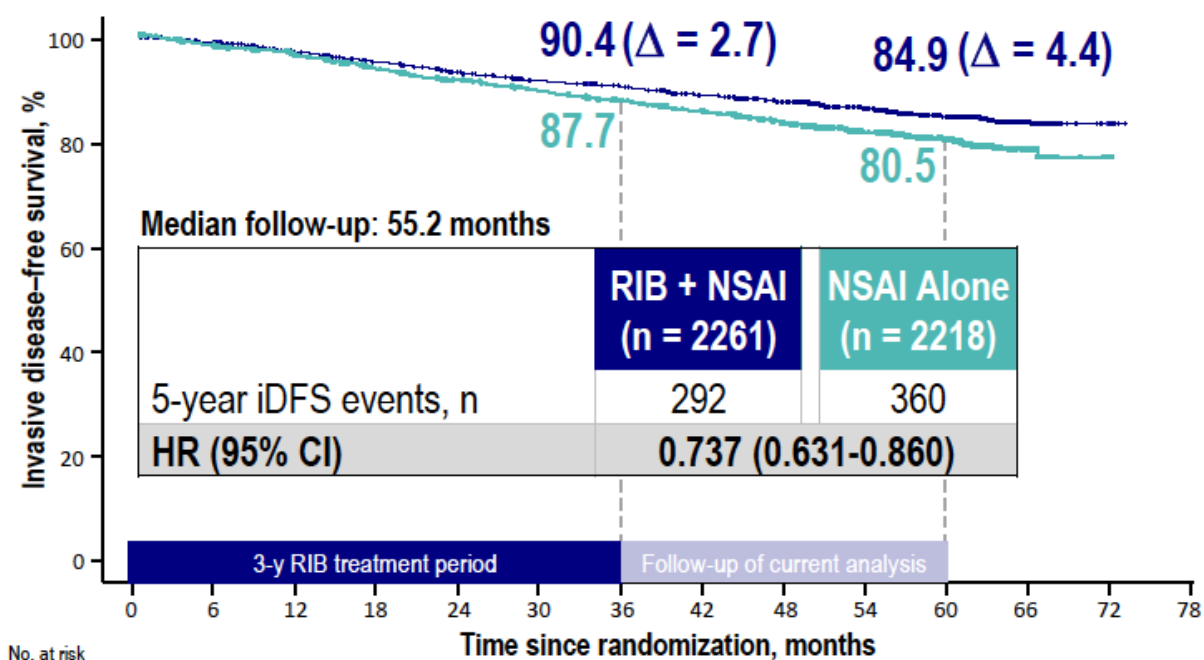
# NATALEE: IDFS by Nodal Status

**N0**



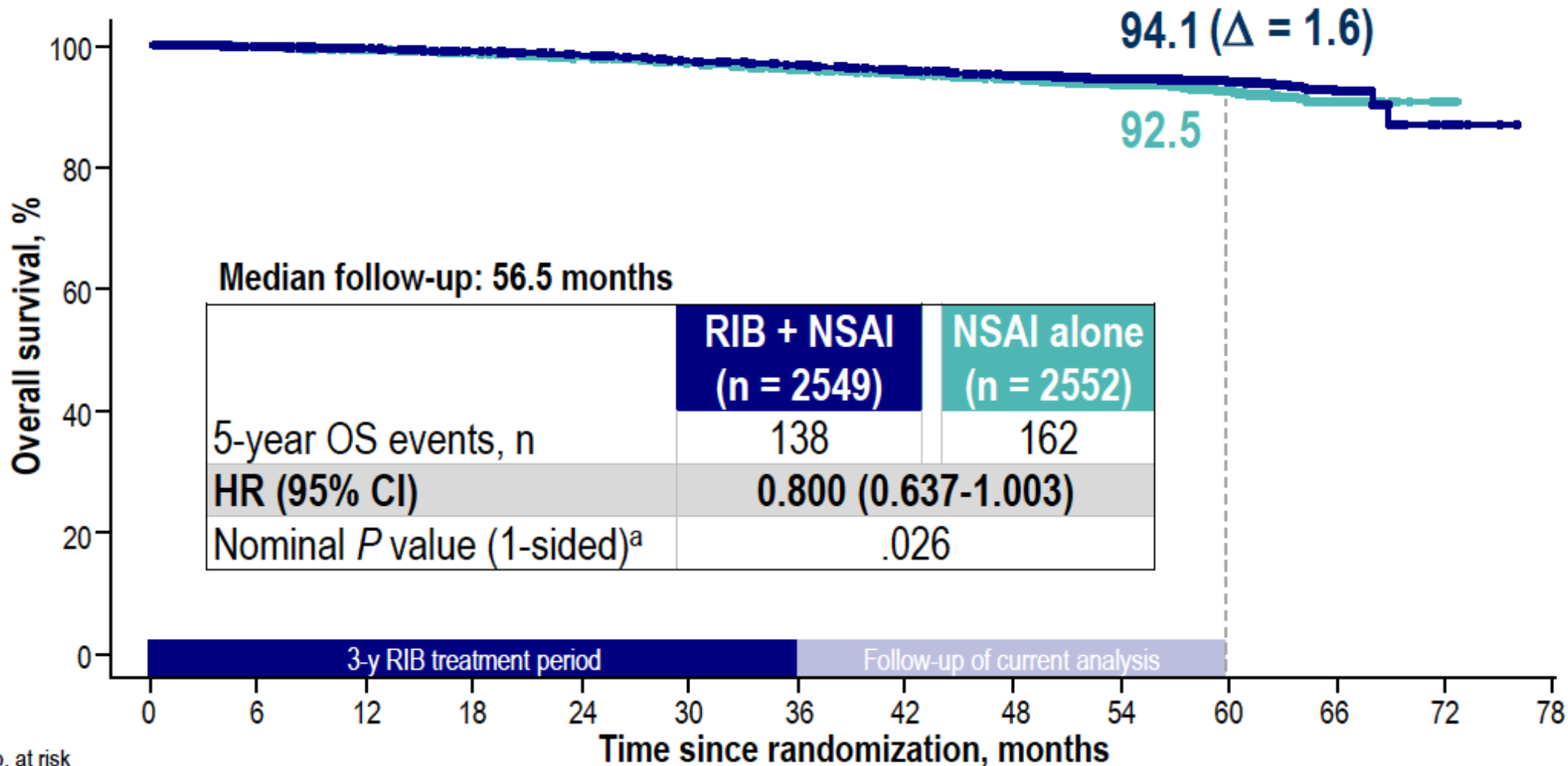
No. at risk	0	6	12	18	24	30	36	42	48	54	60	66	72	78
<b>RIB + NSAI</b>	285	262	258	250	244	240	233	229	227	214	164	52	3	0
<b>NSAI Alone</b>	329	301	295	289	279	271	259	253	245	225	164	56	1	0

**N+**



No. at risk	0	6	12	18	24	30	36	42	48	54	60	66	72	78
<b>RIB + NSAI</b>	2261	2086	2015	1956	1889	1839	1789	1730	1653	1300	834	221	6	0
<b>NSAI Alone</b>	2218	1936	1870	1789	1726	1666	1610	1543	1463	1146	759	179	2	0

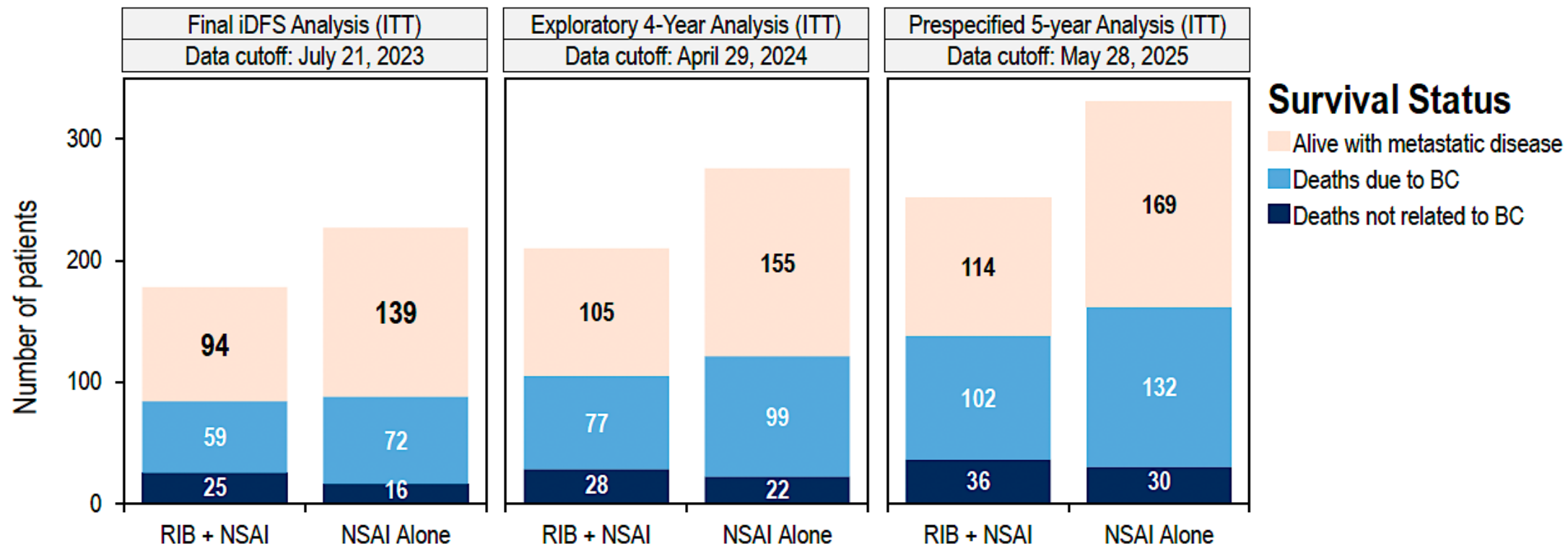
# NATALEE: OS Outcomes



No. at risk

	0	6	12	18	24	30	36	42	48	54	60	66	72	78
RIB + NSAID	2549	2404	2236	2299	2259	2219	2185	2132	2072	1684	1128	325	10	0
NSAID Alone	2552	2301	2255	2208	2160	2116	2063	2009	1956	1591	1076	309	7	0

# NATALEE: Survival Status over Time



Approximate median follow-up (months)	36	44	57
<b>OS HR (95% CI)</b>	<b>0.89 (0.66-1.20)</b>	<b>0.83 (0.64-1.07)</b>	<b>0.800 (0.637-1.003)</b>

# Management of Hormone Receptor (HR)-Positive Localized Breast Cancer

**Module 1: Risk Assessment and Genomic Assays for HR-Positive, HER2-Negative Localized Breast Cancer**

**Module 2: Clinician Survey Results**

**Module 3: Adjuvant CDK4/6 Inhibitors for High-Risk, HR-Positive, HER2-Negative Localized Breast Cancer**









**Module 4: Clinician Survey Results**

**Module 5: Tolerability and Other Practical Considerations with Adjuvant CDK4/6 Inhibitor Therapy**









**Module 6: Clinician Survey Results**

**Module 7: Adjuvant Oral SERDs for HR-Positive, HER2-Negative Localized Breast Cancer**

Regulatory and reimbursement issues aside, would you generally recommend an adjuvant CDK4/6 inhibitor in addition to adjuvant endocrine therapy to a patient with 5.5-cm, Grade 2, HR-positive, HER2-negative localized breast cancer (BC) and the following nodal status?

		Node-negative	2 positive nodes	4 positive nodes
	Dr Brufsky	Yes, ribociclib	Yes, abemaciclib	Yes, abemaciclib
	Dr Jhaveri	Yes, ribociclib	Yes, abemaciclib	Yes, abemaciclib
	Dr Kalinsky	Yes, ribociclib	Yes, abemaciclib	Yes, abemaciclib
	Dr Mahtani	Yes, ribociclib	Yes, either	Yes, either
	Dr Mouabbi	Yes, ribociclib	Yes, either	Yes, either
	Dr Rugo	Yes, ribociclib	Yes, either	Yes, abemaciclib
	Dr Sharma	Yes, ribociclib	Yes, either	Yes, either
	Dr Shatsky	Yes, ribociclib	Yes, ribociclib	Yes, abemaciclib

**Regulatory and reimbursement issues aside, would you generally recommend an adjuvant CDK4/6 inhibitor in addition to adjuvant endocrine therapy to a patient with 2.5-cm Grade 2, HR-positive, HER2-negative localized BC and the following nodal status?**

		<b>Node-negative</b>	<b>2 positive nodes</b>	<b>4 positive nodes</b>
	<b>Dr Brufsky</b>	No	No	Yes, abemaciclib
	<b>Dr Jhaveri</b>	Yes, ribociclib	Yes, abemaciclib	Yes, abemaciclib
	<b>Dr Kalinsky</b>	Yes, ribociclib	Yes, abemaciclib	Yes, abemaciclib
	<b>Dr Mahtani</b>	No	Yes, ribociclib	Yes, either
	<b>Dr Mouabbi</b>	No	Yes, either	Yes, either
	<b>Dr Rugo</b>	Yes, ribociclib	Yes, either	Yes, abemaciclib
	<b>Dr Sharma</b>	No	Yes, either	Yes, either
	<b>Dr Shatsky</b>	Yes, ribociclib	Yes, ribociclib	Yes, abemaciclib

# Management of Hormone Receptor (HR)-Positive Localized Breast Cancer

**Module 1: Risk Assessment and Genomic Assays for HR-Positive, HER2-Negative Localized Breast Cancer**

**Module 2: Clinician Survey Results**

**Module 3: Adjuvant CDK4/6 Inhibitors for High-Risk, HR-Positive, HER2-Negative Localized Breast Cancer**

**Module 4: Clinician Survey Results**

**Module 5: Tolerability and Other Practical Considerations with Adjuvant CDK4/6 Inhibitor Therapy**

**Module 6: Clinician Survey Results**

**Module 7: Adjuvant Oral SERDs for HR-Positive, HER2-Negative Localized Breast Cancer**

# Key Datasets

- Rugo HS et al. **Adjuvant abemaciclib** combined **with endocrine therapy** for high-risk early breast cancer: **Safety and patient-reported outcomes** from the **monarchE** study. *Ann Oncol* 2022;33(6):616-27.
- Barrios C et al. **NATALEE update: Safety and treatment (tx) duration of ribociclib (RIB) + nonsteroidal aromatase inhibitor (NSAI)** in patients (pts) with HR+/HER2– early breast cancer (EBC). ESMO Breast 2024;Abstract 113MO.
- Mayer EL 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* 2025;31(1):117-24.

# monarchE: Overall Safety Profile

**Table 1. Clinically relevant adverse events observed in the abemaciclib + ET arm regardless of causality**

	Abemaciclib + ET (N = 2791)				ET alone (N = 2800)			
	Any grade	G1	G2	G ≥ 3	Any grade	G1	G2	G ≥ 3
≥10% in the abemaciclib + ET arm								
Patients with ≥1 AE, <sup>a</sup> n (%)	2745 (98.4)	165 (5.9)	1192 (42.7)	1388 (49.7)	2486 (88.8)	634 (22.6)	1396 (49.9)	456 (16.3)
Diarrhea	2331 (83.5)	1255 (45.0)	857 (30.7)	219 (7.8) <sup>b</sup>	242 (8.6)	184 (6.6)	52 (1.9)	6 (0.2)
Infections <sup>c</sup>	1429 (51.2)	245 (8.8)	1029 (36.9)	155 (5.6)	1102 (39.4)	229 (8.2)	790 (28.2)	83 (3.0) <sup>d</sup>
Neutropenia	1278 (45.8)	178 (6.4)	554 (19.8)	546 (19.6)	157 (5.6)	66 (2.4)	68 (2.4)	23 (0.8)
Fatigue	1133 (40.6)	632 (22.6)	421 (15.1)	80 (2.9)	499 (17.8)	378 (13.5)	117 (4.2)	4 (0.1)
Nausea	824 (29.5)	623 (22.3)	187 (6.7)	14 (0.5)	252 (9.0)	198 (7.1)	52 (1.9)	2 (0.1)
Anemia	681 (24.4)	383 (13.7)	241 (8.6)	57 (2.0)	104 (3.7)	75 (2.7)	19 (0.7)	10 (0.4)
Headache	546 (19.6)	415 (14.9)	123 (4.4)	8 (0.3)	421 (15.0)	321 (11.5)	95 (3.4)	5 (0.2)
Vomiting	491 (17.6)	375 (13.4)	101 (3.6)	15 (0.5)	130 (4.6)	98 (3.5)	29 (1.0)	3 (0.1)
Stomatitis <sup>e</sup>	385 (13.8)	309 (11.1)	72 (2.6)	4 (0.1)	151 (5.4)	133 (4.8)	18 (0.6)	0 (0.0)
Thrombocytopenia	373 (13.4)	276 (9.9)	61 (2.2)	36 (1.3)	52 (1.9)	40 (1.4)	8 (0.3)	4 (0.1)
Decreased appetite	329 (11.8)	243 (8.7)	70 (2.5)	16 (0.6)	68 (2.4)	53 (1.9)	13 (0.5)	2 (0.1)
Alopecia	313 (11.2)	283 (10.1)	30 (1.1)	N/A	75 (2.7)	68 (2.4)	7 (0.3)	0 (0.0)
Alanine aminotransferase increase (ALT)	343 (12.3)	184 (6.6)	82 (2.9)	77 (2.8)	157 (5.6)	113 (4.0)	25 (0.9)	19 (0.7)
Aspartate aminotransferase increase (AST)	330 (11.8)	220 (7.9)	58 (2.1)	52 (1.9)	137 (4.9)	103 (3.7)	19 (0.7)	15 (0.5)
Rash	312 (11.2)	239 (8.6)	61 (2.2)	11 (0.4)	127 (4.5)	104 (3.7)	23 (0.8)	0 (0.0)
Other AEs of interest—composite terms								
VTE <sup>f</sup>	71 (2.5)	2 (0.1)	31 (1.1)	38 (1.4) <sup>h</sup>	17 (0.6)	0 (0.0)	9 (0.3)	8 (0.3)
PE <sup>g</sup>	28 (1.0)	N/A	N/A	28 (1.0) <sup>i</sup>	4 (0.1)	N/A	N/A	4 (0.1)
ILD <sup>j</sup>	89 (3.2)	44 (1.6)	34 (1.2)	11 (0.4)	37 (1.3)	26 (0.9)	10 (0.4)	1 (0.0)
Pneumonitis	49 (1.8)	21 (0.8)	21 (0.8)	7 (0.3)	10 (0.4)	7 (0.3)	3 (0.1)	0 (0.0)
Radiation pneumonitis	25 (0.9)	13 (0.5)	10 (0.4)	2 (0.1)	15 (0.5)	9 (0.3)	5 (0.2)	1 (0.0)
Increased transaminases <sup>k</sup>	433 (15.5)	241 (8.6)	94 (3.4)	98 (3.5)	209 (7.5)	143 (5.1)	38 (1.4)	28 (1.0)

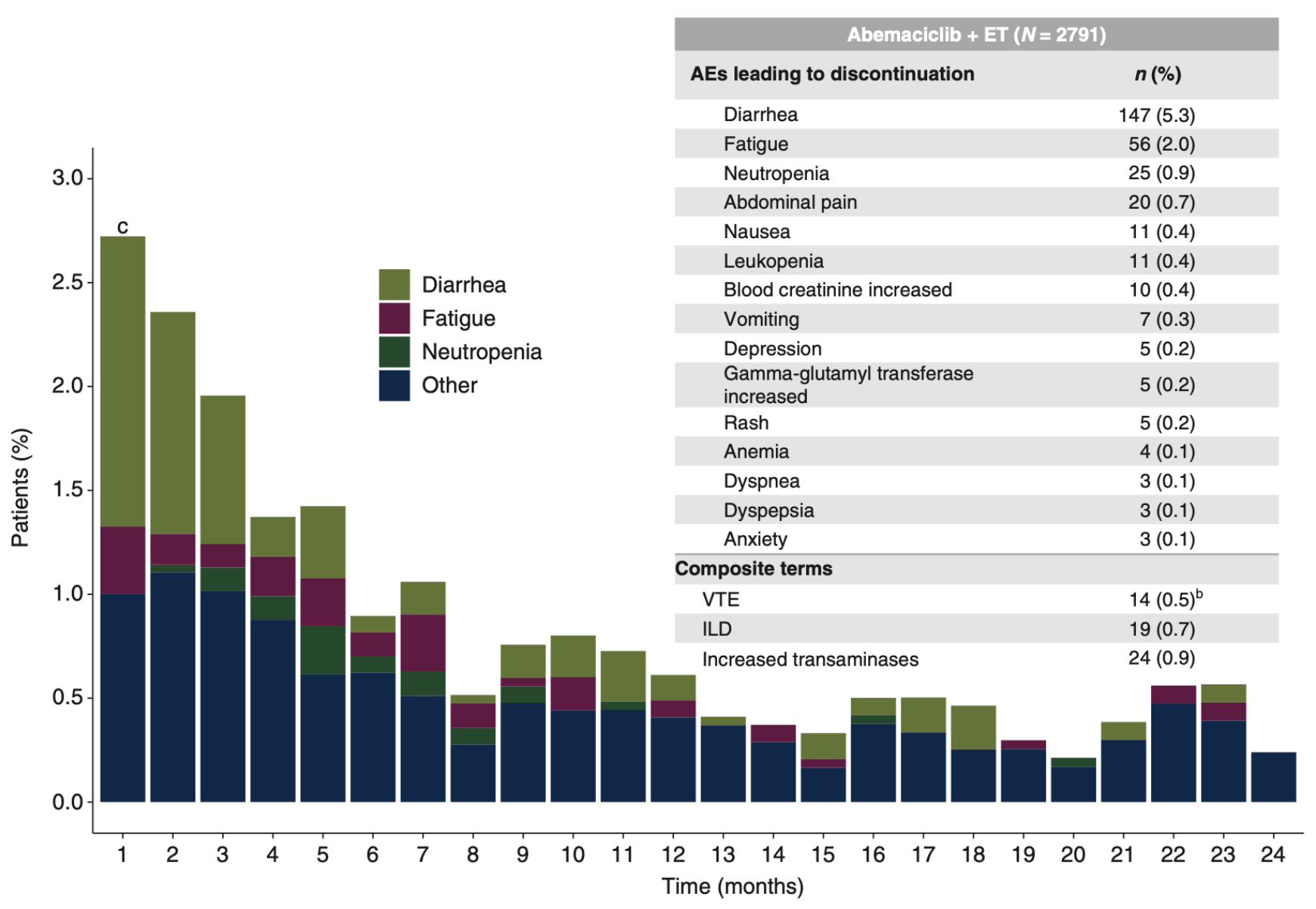
# monarchE: Serious and Fatal Adverse Events (AEs) in Long-Term Follow-Up

	Abemaciclib + ET N=2791, n (%)		ET N=2800, n (%)	
	On Therapy <sup>a</sup>	Post-Discontinuation <sup>b</sup>	On Therapy <sup>a</sup>	Post-Discontinuation <sup>b</sup>
<b>≥1 SAE* LTFU, regardless of causality</b>	<b>NA</b>	<b>197 (7.5)</b>	<b>NA</b>	<b>213 (8.1)</b>
<b>Deaths due to AE by SOC and PT<sup>c</sup></b>	<b>15 (0.5)</b>	<b>44 (1.6)</b>	<b>11 (0.4)</b>	<b>30 (1.1)</b>
Infections and infestations	3 (0.1)	13 (0.5)	5 (0.2)	5 (0.2)
COVID-19	3 (0.1)	6 (0.2)	1 (<0.1)	2 (0.1)
Second primary neoplasm	0 (0)	13 (0.5)	1 (<0.1)	7 (0.3)
Cardiac disorders	5 (0.2)	6 (0.2)	0 (0)	9 (0.3)

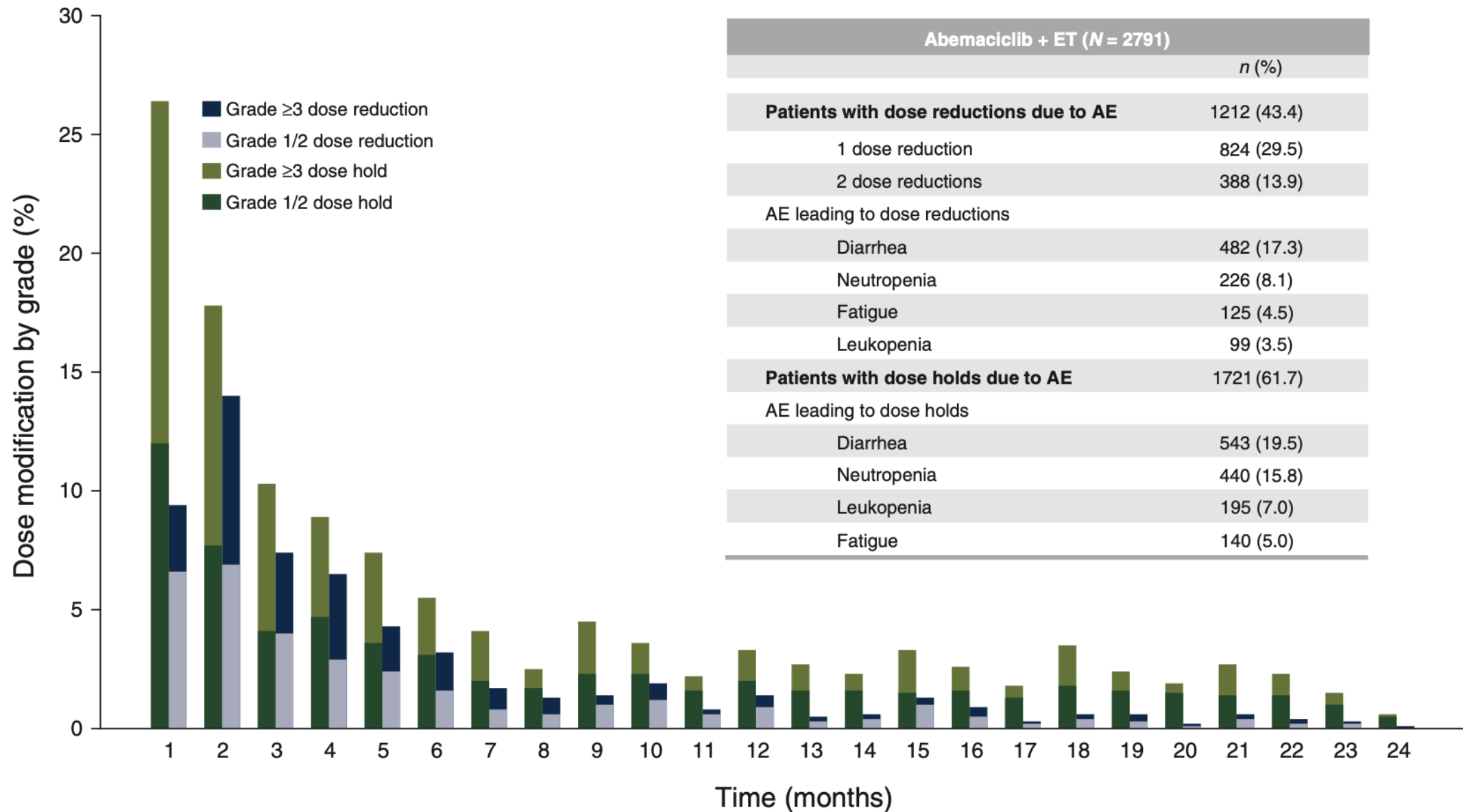
**Consistent safety results from prior analyses, as all treated patients completed treatment ≥ 4 years ago**  
**No relevant differences between treatment arms in causes of deaths due AEs**

SAE = serious adverse event; LTFU = long-term follow-up; SOC = standard of care

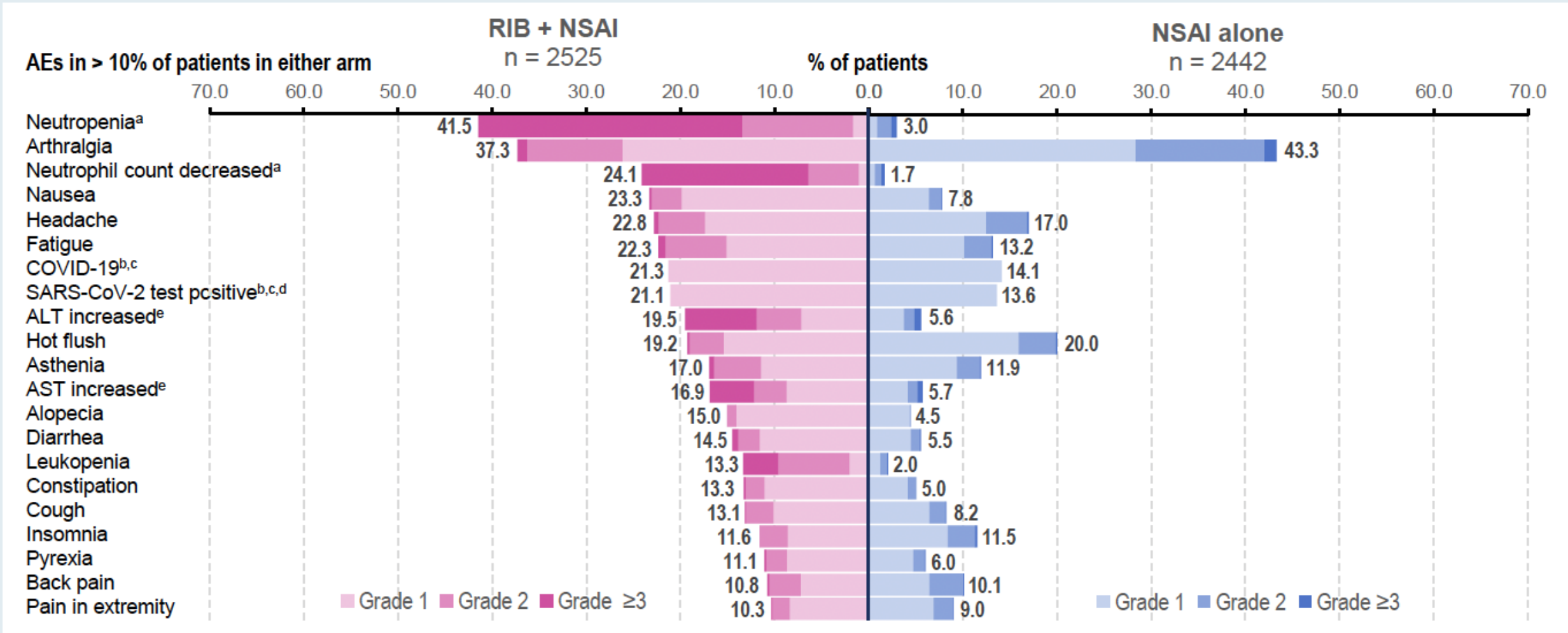
# monarchE: AEs Leading to Discontinuation



# monarchE: AEs Leading to Dose Modifications



# NATALEE: Overall Safety Profile

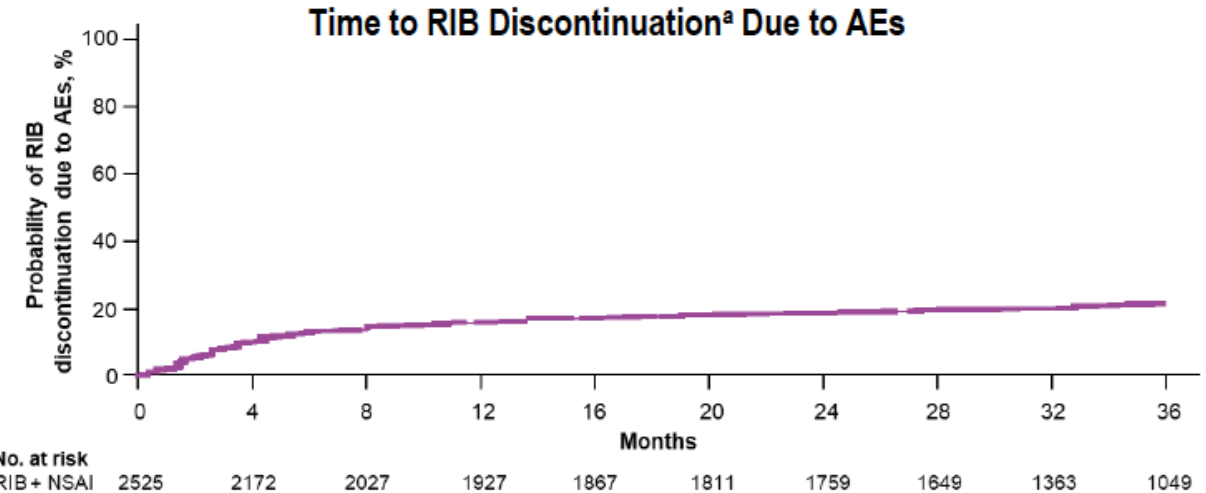
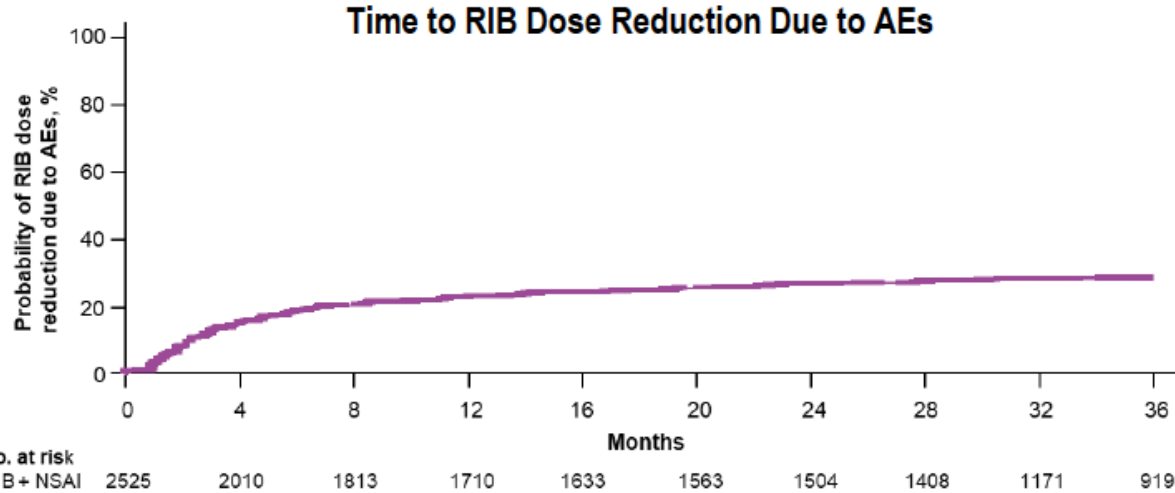


ALT = alanine aminotransferase; AST = aspartate aminotransferase

## NATALEE: AEs of Special Interest (AESIs)

AESIs (grouped terms)	Neutropenia <sup>a</sup>		Liver-related AEs <sup>c</sup>		QT interval prolongation <sup>d</sup>	
	RIB + NSAI	NSAI alone	RIB + NSAI	NSAI alone	RIB + NSAI	NSAI alone
All grade	1579 (62.5)	113 (4.6)	667 (26.4)	273 (11.2)	134 (5.3)	34 (1.4)
Grade ≥3	1118 (44.3)	22 (0.9)	217 (8.6)	42 (1.7)	26 (1.0)	15 (0.6)
Time to first grade ≥2 based on laboratory values, median mo. (range)	1.0 (0.9-1.0) <sup>b</sup>	NE	2.8 (0.5-36.7)	9.1 (0.5-33.3)	0.5 (0.5-1.5)	1.4 (0.9-2.8)
Time to resolution of grade ≥2 to ≤1 based on laboratory values, median mo. (95% CI)	1.0 (NE)	1.0 (1.0-1.0)	0.9 (0.7-1.0)	1.4 (1.0-2.5)	0.2 (0.0-0.5)	1.1 (0.5-NE)
Dose reductions, RIB, %	14.2	0	2.6	0	0.1	0
Discontinuations, any component, %	1.1	0	8.9	0.1	0.4	0

# NATALEE: AE-Related Dose Reduction and Discontinuation



- AE-related RIB dose reductions occurred in 22.8% of patients
  - Most commonly due to neutropenia (8.5%) and neutrophil count decreased (5.6%)
- Median time to AE-related RIB dose reduction: 3.15 months (range, 0.26-34.17 months)
- Median RDI during RIB treatment: 94%

- Most common AEs leading to discontinuation: ALT increased (7.1%) and AST increased (2.8%)
- Of 19.7% who discontinued due to AEs, 14.0% discontinued without prior dose reduction and 5.7% had their dose reduced before discontinuing
- Median time to AE-related RIB discontinuation: 4.17 months (range, 0.10-35.75 months)

# AEs and Dosing Must Be Considered: Distinct AE Profiles and Dosing Schedules of CDK4/6 Inhibitors in EBC

**Abemaciclib**

**Adverse Events**

- Neutropenia (41%-46%)
- Diarrhea (81%-86%)
- Increased ALT (13%-16%)
- Increased AST (12%-15%)
- Thromboembolic events (5%)

**Schedule**

Continuous daily dosing

**Dosing**

Starting dose in EBC: 150 mg BID  
 1st dose reduction: 100 mg BID  
 2nd dose reduction: 50 mg BID

**Ribociclib**

**Adverse Events**

- Neutropenia (69%-78%)
- Diarrhea (29%-35%)
- Increased ALT (15%-46%)
- Increased AST (13%-44%)
- QTc prolongation (6%)

**Schedule**

3 wk on/1 wk off

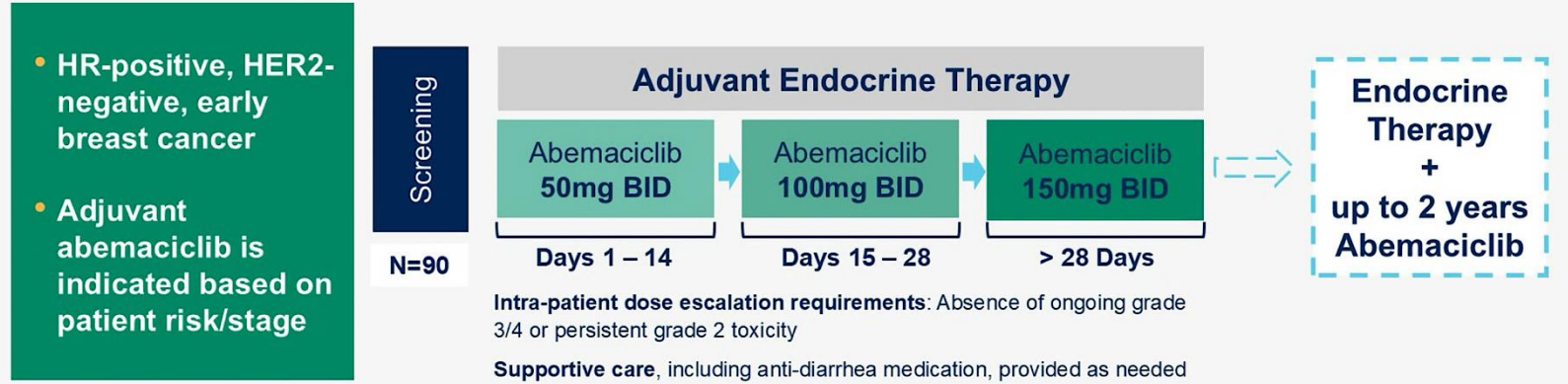
**Dosing**

Starting dose in EBC: 400 mg/day  
 1 (and only) dose reduction option available in EBC: 200 mg/day

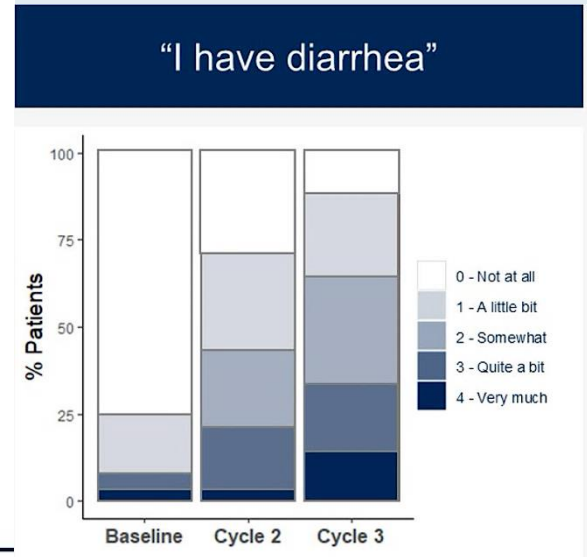
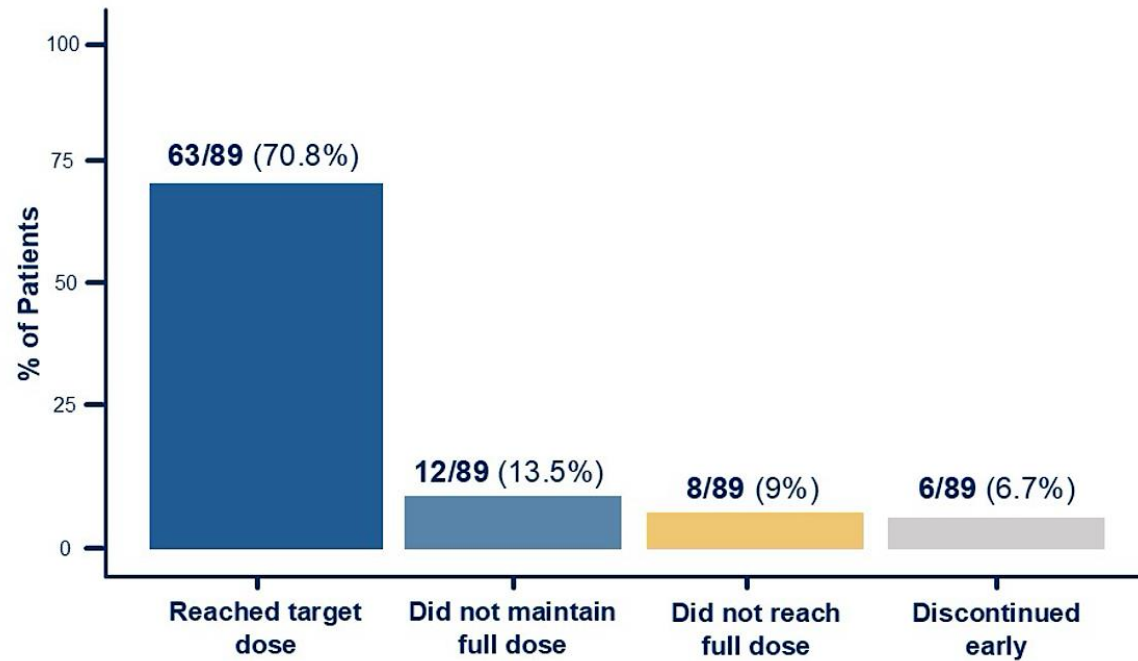
Breast Cancer Status	CDK4/6i	Trial(s)	Discontinuation Rate Due to AE
HR+/HER2- EBC	Abemaciclib	monarchE <sup>1,a</sup>	19%
	Ribociclib	NATALEE <sup>2,3</sup>	19%

# TRADE: Abemaciclib dose escalation

Patient disposition in monarchE		
Outcome in monarchE	By 12 weeks	Overall at 2 years
Discontinued abemaciclib for any reason	10%	30.6%
<ul style="list-style-type: none"> <li>Discontinued for adverse events</li> </ul>	7%	18.5%
Required abemaciclib dose reduction	27%	43.4%



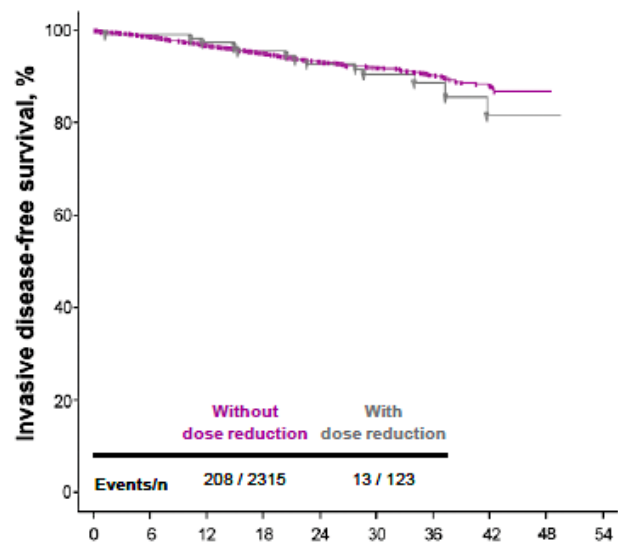
**Primary endpoint:** composite AE rate (discontinuation of adjuvant abemaciclib for any reason and/or need to dose reduce by 12 weeks of therapy)



# NATALEE: IDFS by Dose Reductions

Landmark analysis revealed that RIB dose reduction due to AEs did not impact efficacy

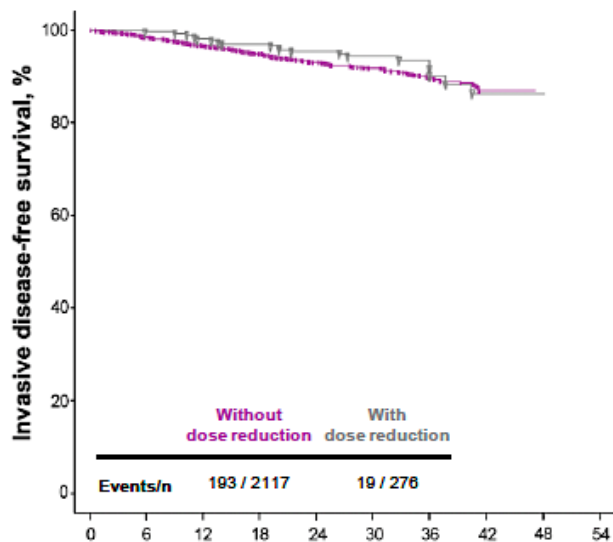
**iDFS by Dose Reduction at 25th Percentile<sup>a</sup>**  
(1.87 mo.)



Events/n    208 / 2315    13 / 123

	Months									
No. at risk	0	6	12	18	24	30	36	42	48	54
Without dose reduction	2315	2219	2142	2076	1979	1803	1039	328	8	0
With dose reduction	123	115	110	105	100	80	46	21	1	0

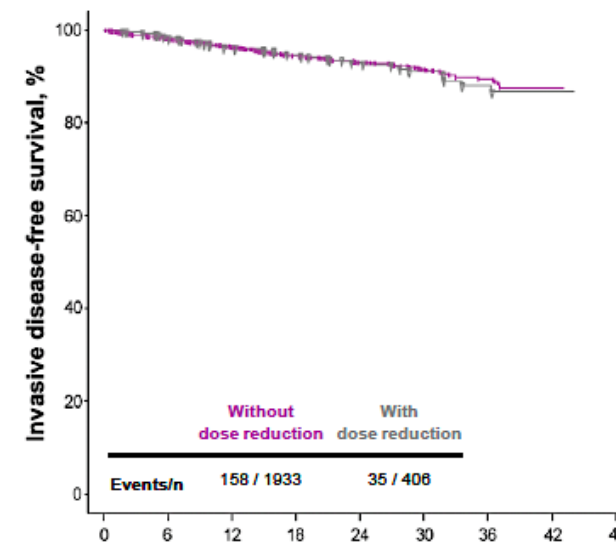
**iDFS by Dose Reduction at 50th Percentile<sup>a</sup>**  
(3.17 mo.)



Events/n    193 / 2117    19 / 276

	Months									
No. at risk	0	6	12	18	24	30	36	42	48	54
Without dose reduction	2117	2042	1981	1923	1835	1290	420	36	0	0
With dose reduction	276	266	256	245	232	157	55	5	1	0

**iDFS by Dose Reduction at 75th Percentile<sup>a</sup>**  
(7.28 mo.)



Events/n    158 / 1933    35 / 406

	Months									
No. at risk	0	6	12	18	24	30	36	42	48	
Without dose reduction	1933	1870	1820	1725	1394	914	288	14	0	
With dose reduction	406	393	376	361	291	176	69	5	0	

# Management of Hormone Receptor (HR)-Positive Localized Breast Cancer

**Module 1: Risk Assessment and Genomic Assays for HR-Positive, HER2-Negative Localized Breast Cancer**

**Module 2: Clinician Survey Results**

**Module 3: Adjuvant CDK4/6 Inhibitors for High-Risk, HR-Positive, HER2-Negative Localized Breast Cancer**

**Module 4: Clinician Survey Results**

**Module 5: Tolerability and Other Practical Considerations with Adjuvant CDK4/6 Inhibitor Therapy**

**Module 6: Clinician Survey Results**

**Module 7: Adjuvant Oral SERDs for HR-Positive, HER2-Negative Localized Breast Cancer**

# Have you employed or would you employ an initial dose-escalation strategy rather than initiating therapy at the recommended starting dose for any of your patients with HR-positive localized BC receiving an adjuvant CDK4/6 inhibitor?



**Dr Brufsky**

**I have not but would for the right patient**



**Dr Jhaveri**

**I have**



**Dr Kalinsky**

**I have**



**Dr Mahtani**

**I have**



**Dr Mouabbi**

**I have**



**Dr Rugo**

**I have**



**Dr Sharma**









**I have**











**Dr Shatsky**

**I have**

Assuming eligibility to receive abemaciclib or ribociclib, which CDK4/6 inhibitor would you prefer in the adjuvant setting for a patient with HR-positive localized BC and a history of ...?

		Colitis	Chronic liver disease	Chronic renal disease
 Dr Brufsky		Ribociclib	Abemaciclib	Ribociclib
 Dr Jhaveri		Ribociclib	Abemaciclib	Ribociclib
 Dr Kalinsky		Ribociclib	Abemaciclib	No preference
 Dr Mahtani		Ribociclib	Abemaciclib	No preference
 Dr Mouabbi		Ribociclib	Abemaciclib	Ribociclib
 Dr Rugo		Ribociclib	Abemaciclib	No preference
 Dr Sharma		Ribociclib	Abemaciclib	Ribociclib
 Dr Shatsky		Ribociclib	Abemaciclib	No preference

Assuming eligibility to receive abemaciclib or ribociclib, which CDK4/6 inhibitor would you prefer in the adjuvant setting for a patient with HR-positive localized BC and a history of ...?

		COPD	NYHA Class I congestive heart failure
 Dr Brufsky		No preference	Abemaciclib
 Dr Jhaveri		No preference	Abemaciclib
 Dr Kalinsky		No preference	Abemaciclib
 Dr Mahtani		No preference	Abemaciclib
 Dr Mouabbi		Ribociclib	Abemaciclib
 Dr Rugo		No preference	Abemaciclib
 Dr Sharma		No preference	No preference
 Dr Shatsky		No preference	Abemaciclib

COPD = chronic obstructive pulmonary disease

# Management of Hormone Receptor (HR)-Positive Localized Breast Cancer

**Module 1: Risk Assessment and Genomic Assays for HR-Positive, HER2-Negative Localized Breast Cancer**

**Module 2: Clinician Survey Results**

**Module 3: Adjuvant CDK4/6 Inhibitors for High-Risk, HR-Positive, HER2-Negative Localized Breast Cancer**

**Module 4: Clinician Survey Results**

**Module 5: Tolerability and Other Practical Considerations with Adjuvant CDK4/6 Inhibitor Therapy**

**Module 6: Clinician Survey Results**

**Module 7: Adjuvant Oral SERDs for HR-Positive, HER2-Negative Localized Breast Cancer**

# Key Datasets

- 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.



**DECEMBER 9–12, 2025**

HENRY B. GONZALEZ CONVENTION CENTER • SAN ANTONIO, TX

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

**Presenting author: Aditya L. Bardia, MD**

University of California, Los Angeles, Los Angeles, CA, USA

Abstract GS1-10

# IdERA Breast Cancer Study Design

## 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

N = 4170

R  
1:1

At least 5-year treatment duration

Giredestrant (30 mg PO QD)

SOC ET

Tamoxifen/anastrozole/letrozole/exemestane

5-year follow-up

Long-term  
follow-up

## Primary endpoint

- IDFS (excluding second primary non-breast cancer)

## Key secondary endpoints

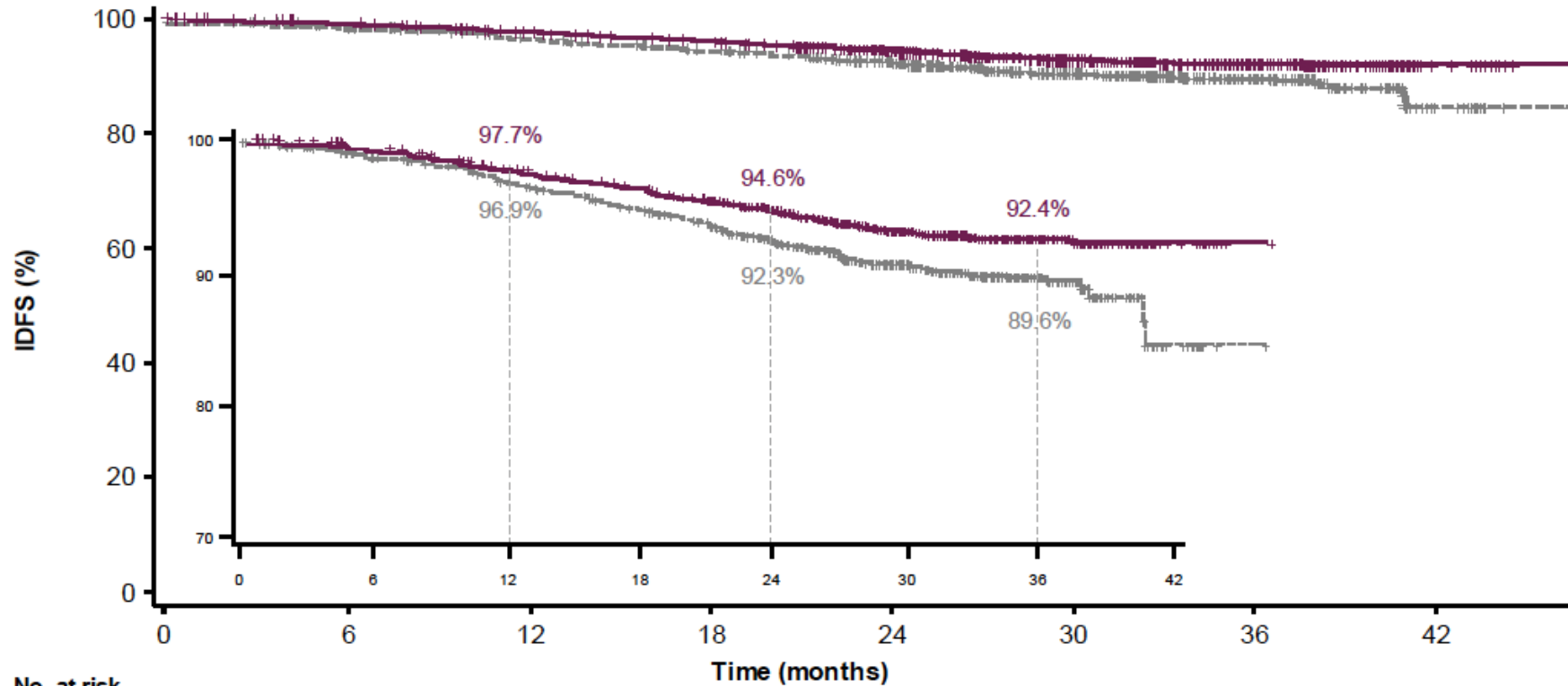
- DFS, DRFI, IDFS (including second primary non-breast invasive cancer with exception of non-melanoma skin cancers and *in situ* carcinomas of any site), LRRFI, OS, safety

DRFI = distant recurrence-free interval; LRRFI = locoregional recurrence-free interval

## IdERA Breast Cancer: Patient Demographics

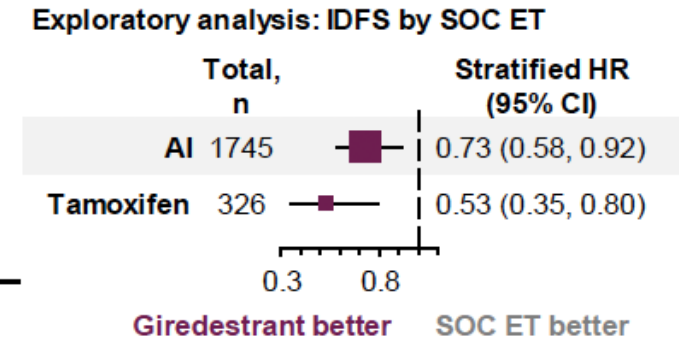
	Giredestrant n = 2084	SOC ET n = 2086		Giredestrant n = 2084	SOC ET n = 2086
<b>Median age, years (range)</b>	54.0 (22–91)	54.0 (25–89)	<b>ER status, n (%)<sup>†</sup></b>		
<b>Female sex, n (%)</b>	2073 (99.5)	2075 (99.5)	Low-positive (1–10% of cells positive)	45 (2.2)	52 (2.5)
<b>Race, n (%)</b>			Positive (> 10% of cells positive)	2030 (97.8)	2031 (97.5)
American Indian or Alaska Native	77 (3.7)	62 (3.0)	<b>AJCC stage at surgery, n (%)<sup>§</sup></b>		
Asian	461 (22.1)	467 (22.4)	I	254 (12.3)	283 (13.6)
Black or African American	50 (2.4)	50 (2.4)	II	1013 (49.0)	950 (45.7)
Other*	263 (12.6)	232 (11.1)	III	799 (38.7)	844 (40.6)
White	1233 (59.2)	1275 (61.1)	<b>Nodal status, n (%) on surgical specimen<sup>  </sup></b>		
<b>Region, n (%)</b>			pN0	449 (21.6)	441 (21.2)
Asia–Pacific	544 (26.1)	544 (26.1)	pN1	968 (46.6)	953 (45.7)
USA/Canada/Western Europe	860 (41.3)	905 (43.4)	pN2–3	662 (31.8)	691 (33.1)
Latin America/Africa/Eastern Europe	680 (32.6)	637 (30.5)	<b>Risk, n (%)</b>		
<b>Menopausal status, n (%)<sup>†</sup></b>			High	1448 (69.5)	1447 (69.4)
Pre-menopausal	849 (41.0)	838 (40.4)	Medium	636 (30.5)	639 (30.6)
Post-menopausal	1220 (59.0)	1236 (59.6)	<b>Previous chemotherapy, n (%)</b>		
			No	396 (19.0)	450 (21.6)
			Yes	1688 (81.0)	1636 (78.4)

# IdERA Breast Cancer: IDFS Outcomes



No. at risk	0	6	12	18	24	30	36	42
Giredestrant	2084	2021	1969	1932	1716	1088	345	26
SOC ET	2086	2016	1958	1898	1683	1048	325	25

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

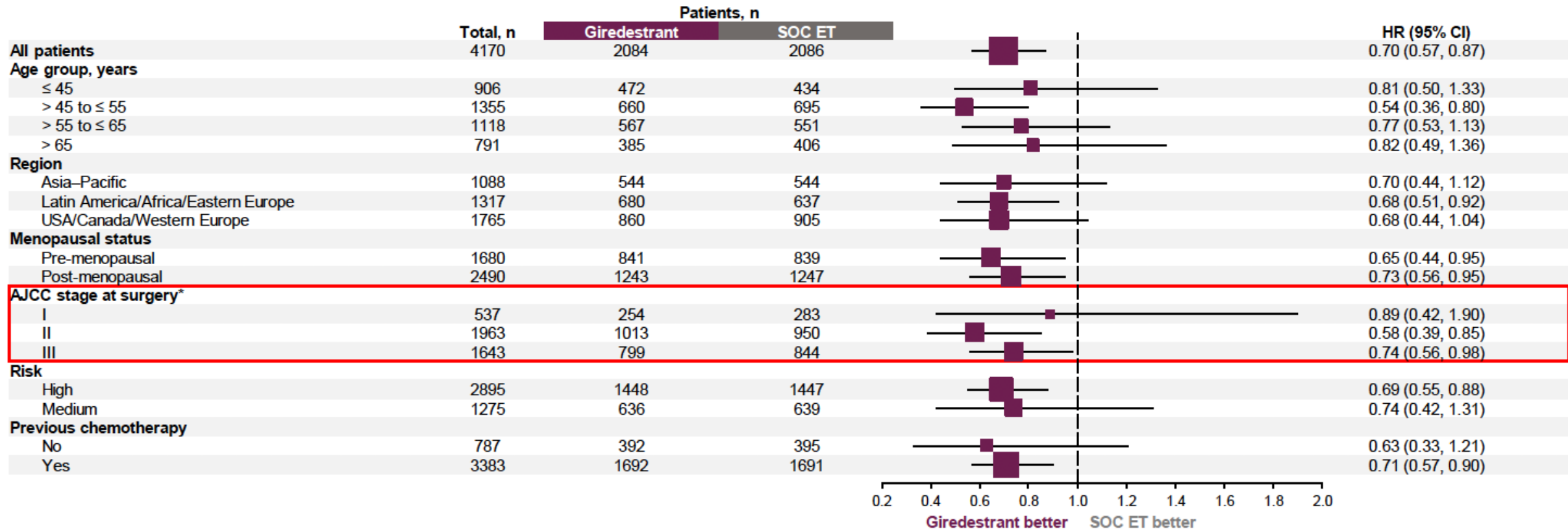


Median follow-up: 32.3 months

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

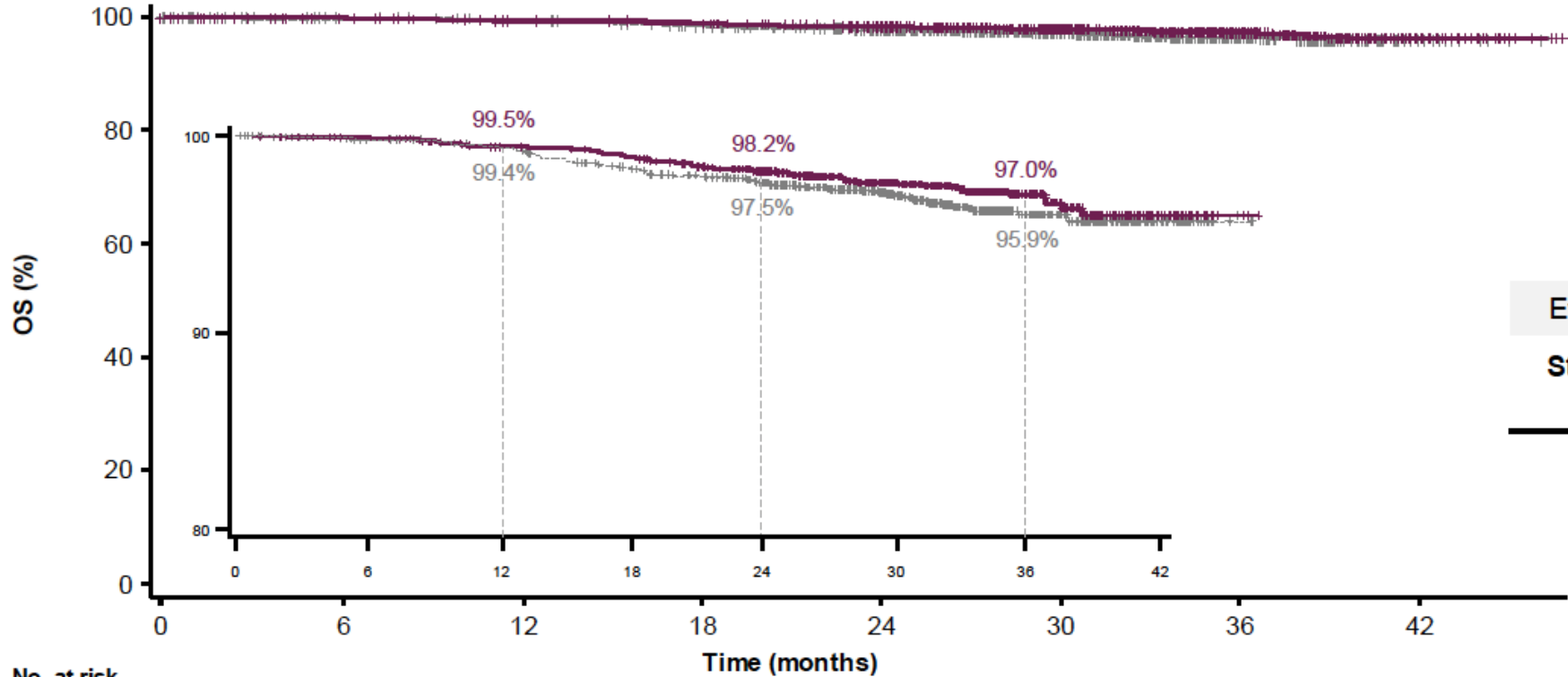


# IdERA Breast Cancer: IDFS in Key Subgroups



**IDFS benefit was consistent across key prespecified subgroups**

# lidERA Breast Cancer: OS Outcomes



	Giredestrant n = 2084	SOC ET n = 2086
Events, n (%)	57 (2.7)	71 (3.4)
<b>Stratified HR</b> (95% CI)	<b>0.79</b> (0.56, 1.12); p = 0.1863*	

No. at risk	0	6	12	18	24	30	36	42
Giredestrant	2084	2043	2013	1997	1887	1300	530	52
SOC ET	2086	2040	2018	1971	1852	1270	504	49

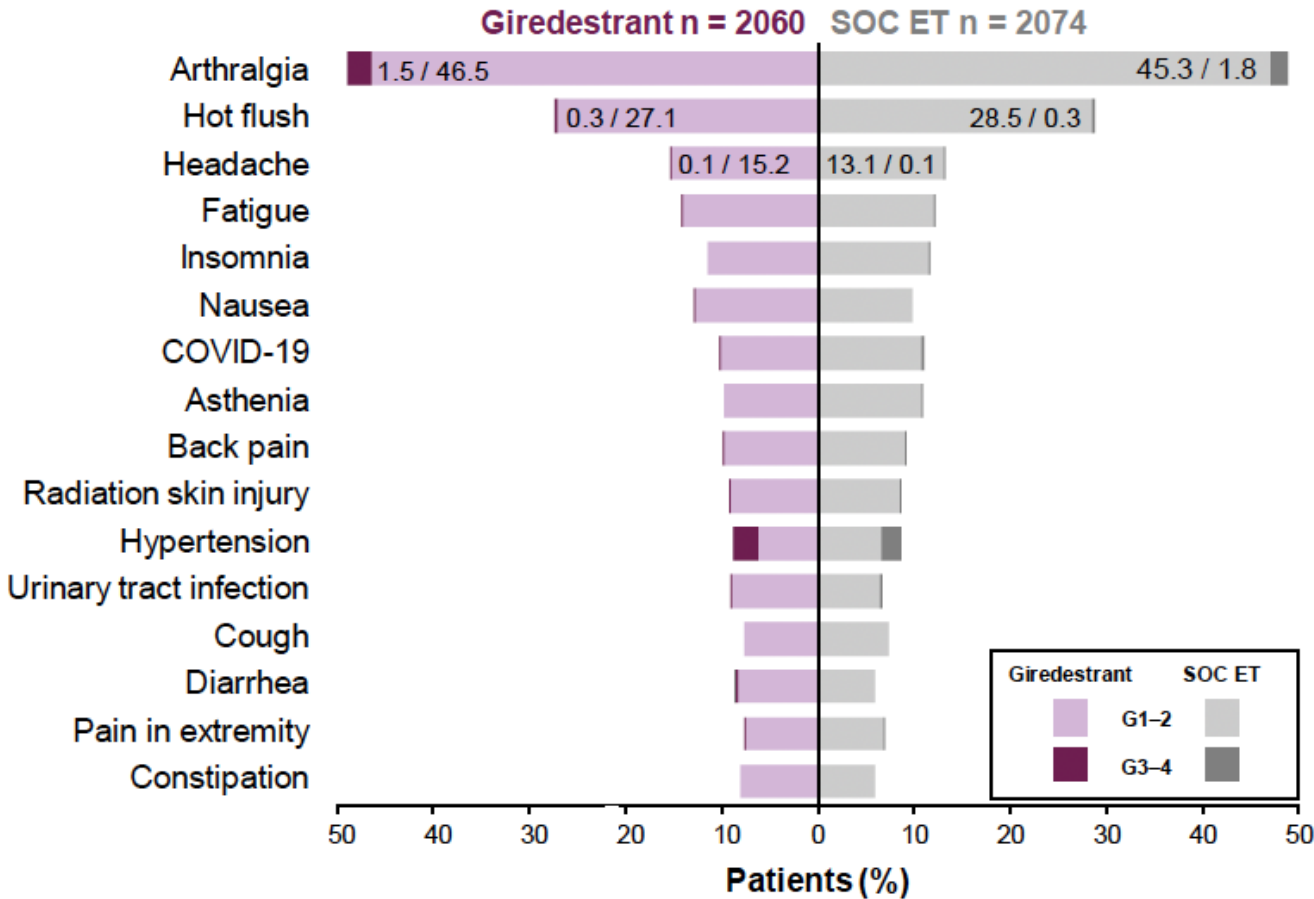
Median follow-up: 32.3 months

**While OS data were immature, a clear positive trend was observed. OS testing will continue at future analyses**



# lidERA Breast Cancer: Safety Profile

## Common TEAEs ( $\geq 7.5\%$ of patients in either arm at any grade)



## Selected AEs

	Giredestrant n = 2060	SOC ET n = 2074
<b>Patients, n (%) with treatment discontinuations due to AEs</b>		
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		
	G1	G2	G3-4	G1	G2	G3-4
<b>Patients, n (%) with selected AEs by medical concept*</b>						
Bradycardia <sup>†</sup>	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) <sup>‡</sup>	3 (0.1)	7 (0.3)	7 (0.3)

# Based on recently presented findings from the Phase III lidERA trial, would you like to have access to adjuvant giredestrant today for your patients with HR-positive, HER2-negative localized BC?



**Dr Brufsky**

**Yes, for patients with higher-risk disease**



**Dr Jhaveri**

**Yes, for those who can't tolerate a CDK4/6i and those who are reluctant to take a CDK4/6i due to toxicity**



**Dr Kalinsky**

**Yes, for patients with higher-risk disease after CDK4/6i or if cannot tolerate standard ET**



**Dr Mahtani**

**Yes, for patients with high-risk disease**



**Dr Mouabbi**

**Yes, for patients who are receiving AI monotherapy**



**Dr Rugo**

**Yes, for high-risk disease as defined in the trial**



**Dr Sharma**

**Yes, for patients that match eligibility of the lidERA trial**



**Dr Shatsky**

**Yes, for all patients, if possible; in the post CDK4/6i space if not available to all patients**

ET = endocrine therapy; CDK4/6i = CDK4/6 inhibitor

# If giredestrant were available, regulatory and reimbursement issues aside, what would you generally recommend for patients who met the criteria for both an adjuvant CDK4/6 inhibitor and adjuvant giredestrant?



**Dr Brufsky**

CDK4/6i with standard adjuvant ET for the initial 2 to 3 years of tx, then switch to giredestrant after discontinuation of the CDK4/6i



**Dr Jhaveri**

CDK4/6i with standard adjuvant ET for the initial 2 to 3 years of tx, then switch to giredestrant after discontinuation of the CDK4/6i



**Dr Kalinsky**

CDK4/6i with standard adjuvant ET for the initial 2 to 3 years of tx, then switch to giredestrant after discontinuation of the CDK4/6i



**Dr Mahtani**

CDK4/6i with standard adjuvant ET for the initial 2 to 3 years of tx, then switch to giredestrant after discontinuation of the CDK4/6i



**Dr Mouabbi**

CDK4/6i with standard adjuvant ET for the initial 2 to 3 years of tx, then switch to giredestrant after discontinuation of the CDK4/6i



**Dr Rugo**

CDK4/6i with standard adjuvant ET for the initial 2 to 3 years of tx, then switch to giredestrant after discontinuation of the CDK4/6i



**Dr Sharma**

CDK4/6i with standard adjuvant ET for the initial 2 to 3 years of tx, then switch to giredestrant after discontinuation of the CDK4/6i



**Dr Shatsky**

**CDK4/6 inhibitor combined with giredestrant**

ET = endocrine therapy; CDK4/6i = CDK4/6 inhibitor

**Questions?**