Early Breast Cancer Scientific Narrative

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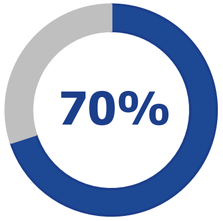
01 Early Breast Cancer Disease Overview

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Despite Treatment Advances in Breast Cancer, Recurrence Remains a Challenge in the Early Setting

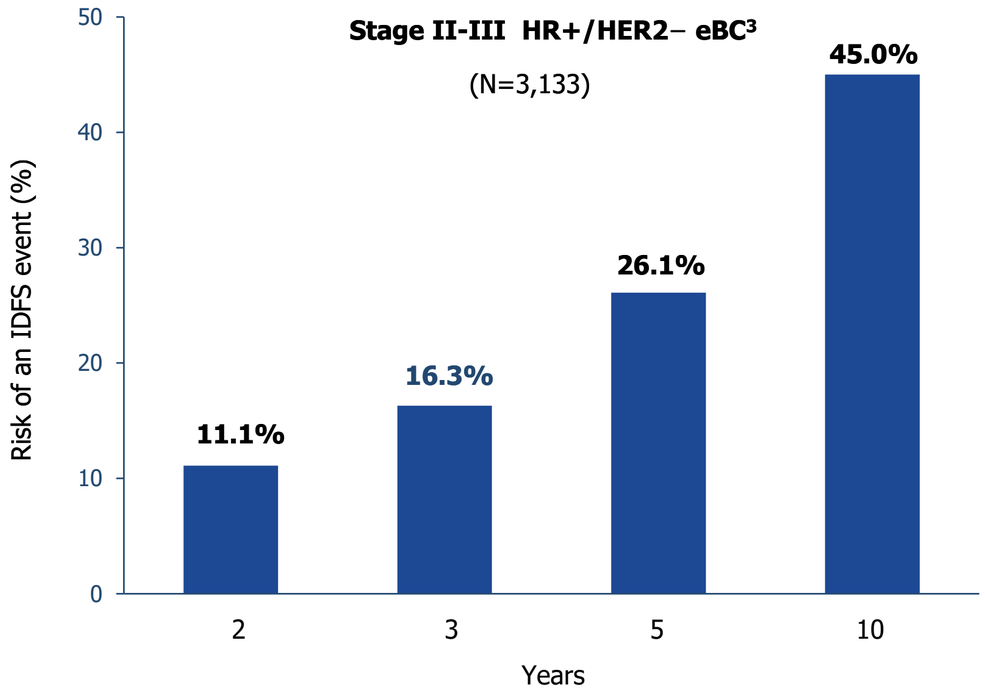
Breast cancer is one of the most diagnosed cancers globally, representing nearly **12% of all new cancer cases,** and is a **leading cause of cancer-related deaths among women**[1]

In the US, female breast cancer represents **15.5% of all new cancer cases,** and is the **fourth leading cause of cancer death**[4]



HR+/HER2− tumors are the most common type **of eBC,** accounting for **>70% of all cases worldwide**[1]

Risk of recurrence n HR+/HER2− **eBC** is **considerable** and **accumulates over time**[2]



Retrospective real-world study of patients with HR+/HER2− eBC* who received adjuvant ET[3]

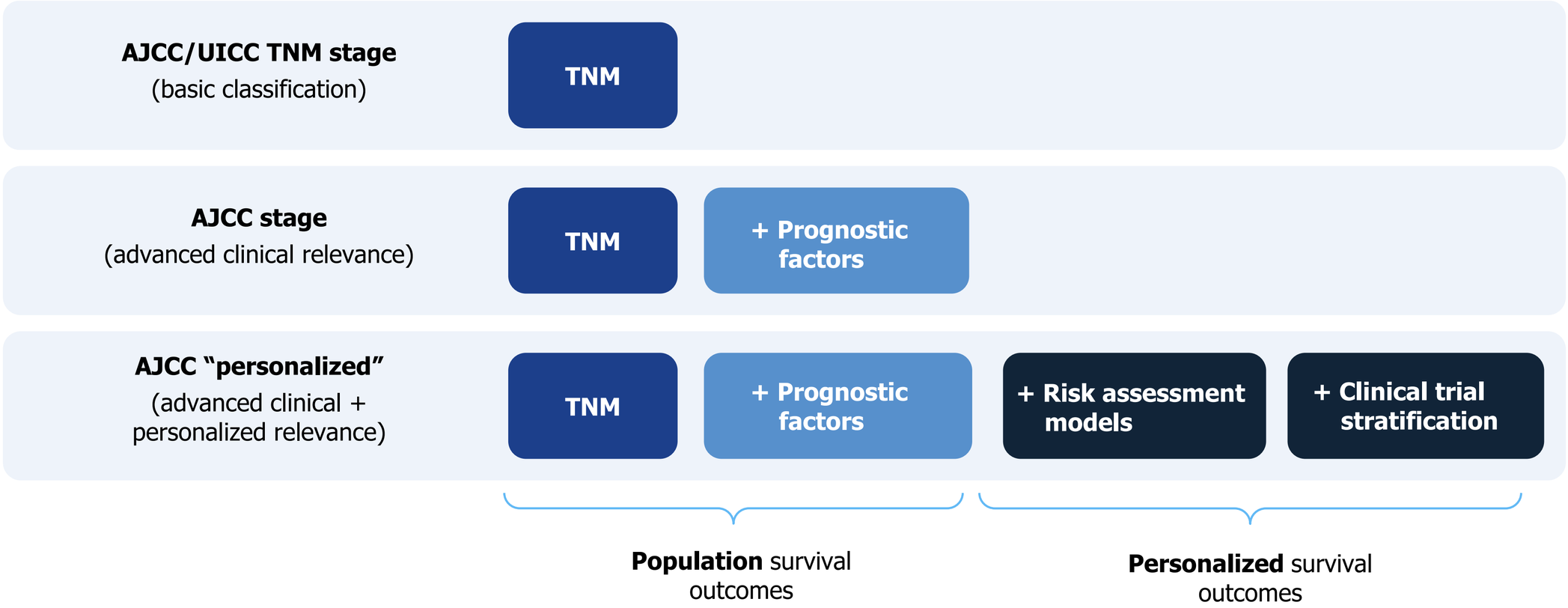
*Patients with stage II/III HR+/HER2− eBC aged ≥18 years who underwent surgery and received adjuvant ET.
eBC=early breast cancer; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; y=years.

References: 1. Loibl S, et al. *Ann Oncol.* 2024;35(2):159–182. 2. Curigliano G, et al. ASCO 2024. Abstract 541. 3. O'Shaughnessy J, et al. *The Breast.* 2025;81:104437. 4. NCI SEER. Cancer Stat Facts: Female Breast cancer https://seer.cancer.gov/statfacts/html/breast.html Accessed: Sept 9, 2025.

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Early Breast Cancer Classification Has Evolved From An Anatomical Approach To A More 'Personalized' One[1]



AJCC=American Joint Committee on Cancer; TNM=tumor, node, metastasis; UICC=Union for International Cancer Control.

Reference: 1. Amin MB, et al. *CA Cancer J Clin.* 2017;67(2):93–99.

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Understanding Risk Stratification Allows for Personalized Treatment Plans and Improved Outcomes[1]

FACTOR	High risk	Low risk
Tumor size	T3/4	T1
Nodal status	N2/N3	N0
Grade	3	1
Ki-67	>30%	<20%
ER/PgR expression level	ER <10% and/or PgR <20%	N/A
Residual cancer burden	RCB-III	RCB-0
Genomic signature (Oncotype DX, MammaPrint®, EndoPredict®, PAM50)	High-risk class	Low-risk class

Intermediate risk is defined as N0* disease with G1/2 and T2–T3 or G3 and T1c–T3, or as N1 disease with G1 and T2 or G2 and T0–T2[2]

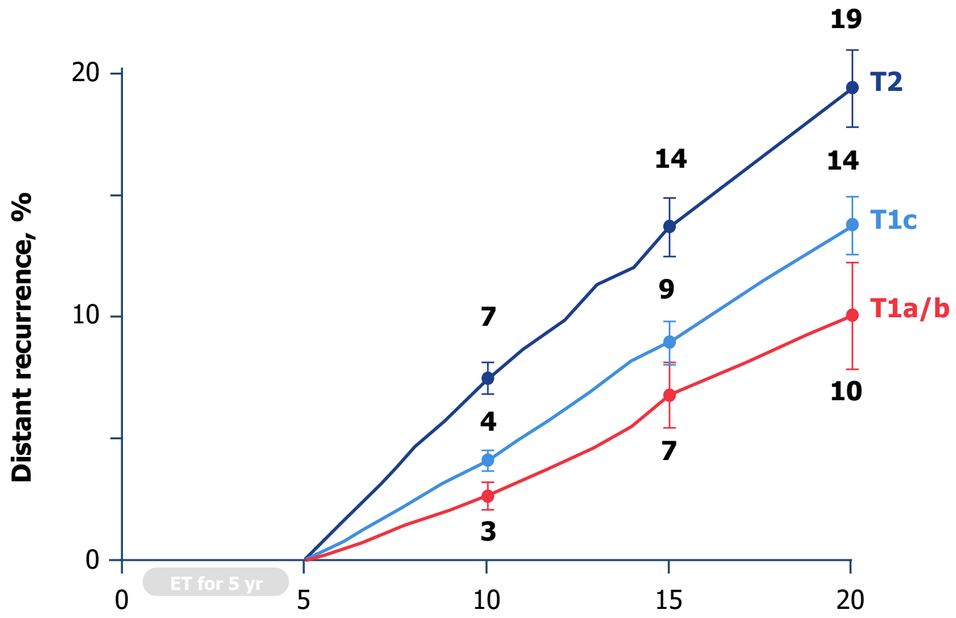
*In patients aged ≥35 years, N0 G1 tumors are intermediate risk if >3 cm, and N0 G2 if >2 cm, whereas in patients aged <35 years, N0 G1 tumors are intermediate risk if >2 cm, and N0 G2 if >1 cm.
ER=estrogen receptor; G=grade; N/A=not available; N0=nodal status 0; N2=nodal status 2; N3=nodal status 3; RCB=residual cancer burden; T=tumor size; PgR=progesterone receptor.

References: 1. Garutti M, et al. *Cancers (Basel).* 2022;14(8):1898. **2.** Lammers SWM, et al. *ESMO Open*. 2024;9(5):103008 (including supplementary data).

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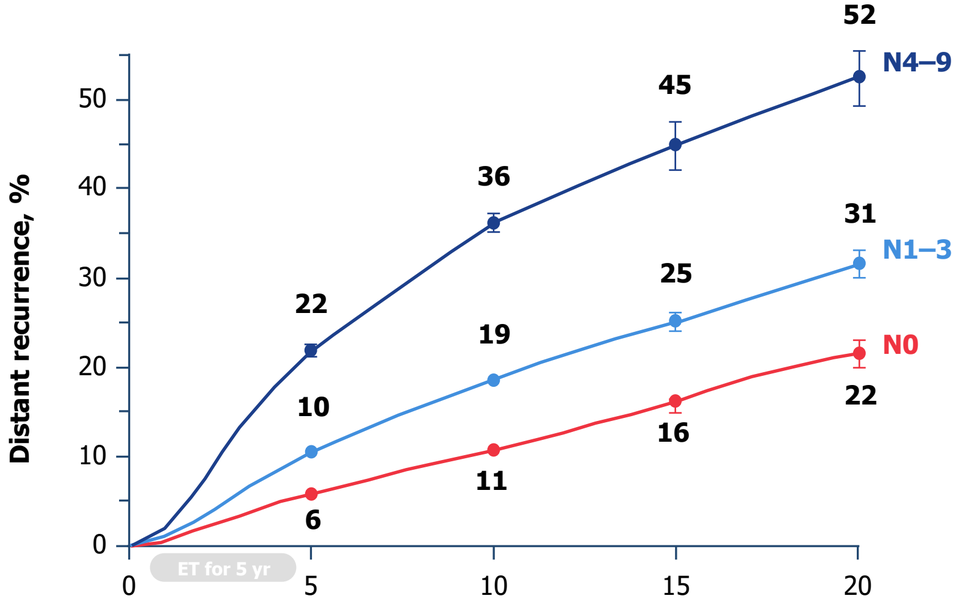
Increased Tumor Size and Nodal Involvement Are Positively Correlated With The Risk of Distant Recurrence [1]

Tumor size*



No. at risk					
T2	9,445	3,901	1,129	218	
T1c	13,875	5,967	1,641	309	
T1a/b	5,527	2,053	704	131	

Nodal status



No. at risk					
N4–9	12,333	8,116	2,165	259	52
N1–3	31,936	23,576	7,250	949	183
N0	29,925	24,081	8,571	1,982	414

*In N0 disease.

ET=endocrine therapy; N0=nodal status 0; N1–3=nodal status 1–3; N4–9=nodal status 4–9; T=tumor size; yr=years.

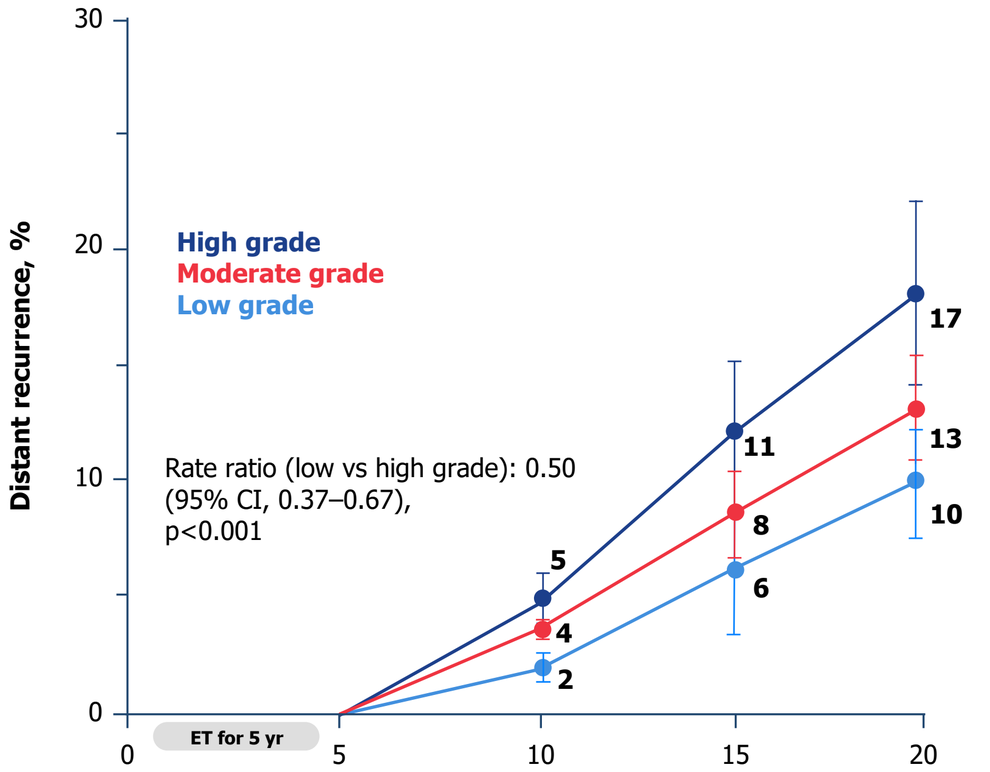
Reference: 1. Pan H, et al. *N Engl J Med*. 2017;377(19):1836–1846 (including supplementary data).

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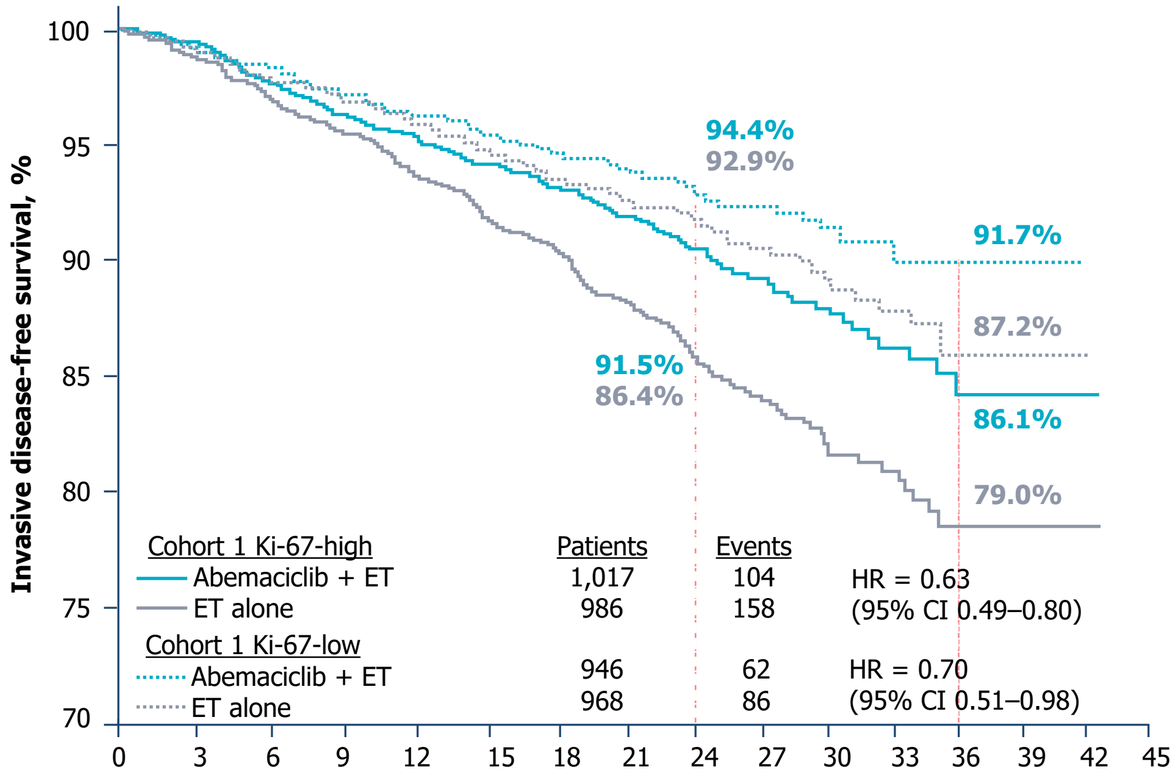
The Risk of Recurrence is Also Positively Correlated with Increased Tumor Grade and Ki-67 Status[1,2]

Tumor grade[1]



No. at risk				
High grade	3,054	1,010	188	2
Moderate grade	7,363	2,761	474	6
Low grade	3,524	1,258	239	6

Ki-67*[2]



*MonarchE Kaplan–Meier curve in Cohort 1 Ki-67 high versus Ki-67 low at additional follow-up 1.

CI=confidence interval; ET=endocrine therapy; HR=hazard ratio; yr-years.

References: 1. Pan H, et al. *N Engl J Med*. 2017;377(19):1836–1846 (including supplementary data). **2.** Harbeck N, et al. *Ann Oncol.* 2021;32(12):1571–1581.

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Multigene Panels Have Emerged as Valuable Tools to Determine the Risk of Recurrence Leading To Personalized Treatment Planning[1]

Overview of the RNA-based genomic signature assays currently used in eBC clinical practice.[2]

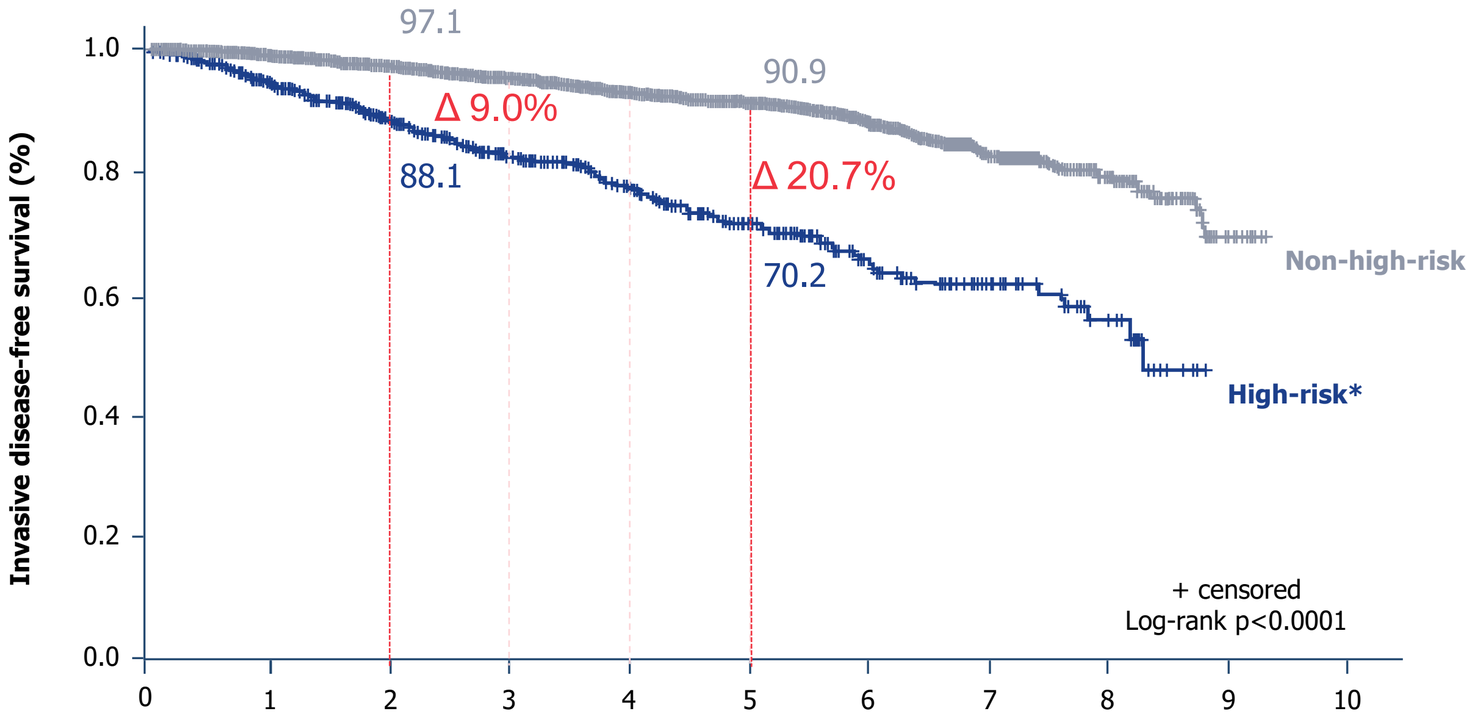
		Oncotype DX®	MammaPrint®	EndoPredict® Breast Cancer Prognostic Test	Prosigna®
Clinical indication	N0	YES	YES	YES	YES
	N+ up to 3 nodes	YES	YES	YES	YES
	Premenopausal	YES	YES	YES	NO
	Postmenopausal	YES	YES	YES	YES
	Presurgical biopsy and post-surgical samples	YES	YES	YES	NO
Prognosis		9 yrs Individual risk No risk category	5 yrs postmenopausal 10 yrs premenopausal Group risk (low/high)	10 and up to 15 yrs Individual risk Low/high	10 yrs Individual risk Low/intermediate/high
Predictive chemotherapy benefit		N0, 9 yrs group N+, 5 yrs group	NO	10 yrs individual	NO
Test includes nodal status and tumor size		NO	NO	YES	NO
Local testing center network		NO	NO	YES	YES
Recommended in ASCO, ESMO, NCCN, NICE, and AJCC		YES	NO	YES	YES

AJCC=American Joint Committee on Cancer; ASCO=American Society of Clinical Oncology; eBC=early breast cancer; ESMO=European Society for Medial Oncology; N+=nodal status +; N0=nodal status 0; NCCN=National Comprehensive Cancer Network; NICE=National Institute for Health and Care Excellence; yrs=years.

References: 1. Pescia C, et al. *Cancers.* 2023;15(22):5430. **2.** Eurobio Scientific. *Eurobio Oncology.* 2025. Accessed February 2025. https://eurobio-scientific.de/ endopredict/accurately-predict-breast-cancer-recurrence.

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Risk of Recurrence Significantly Increases in Patients After 2 Years of Treatment in the Early Setting



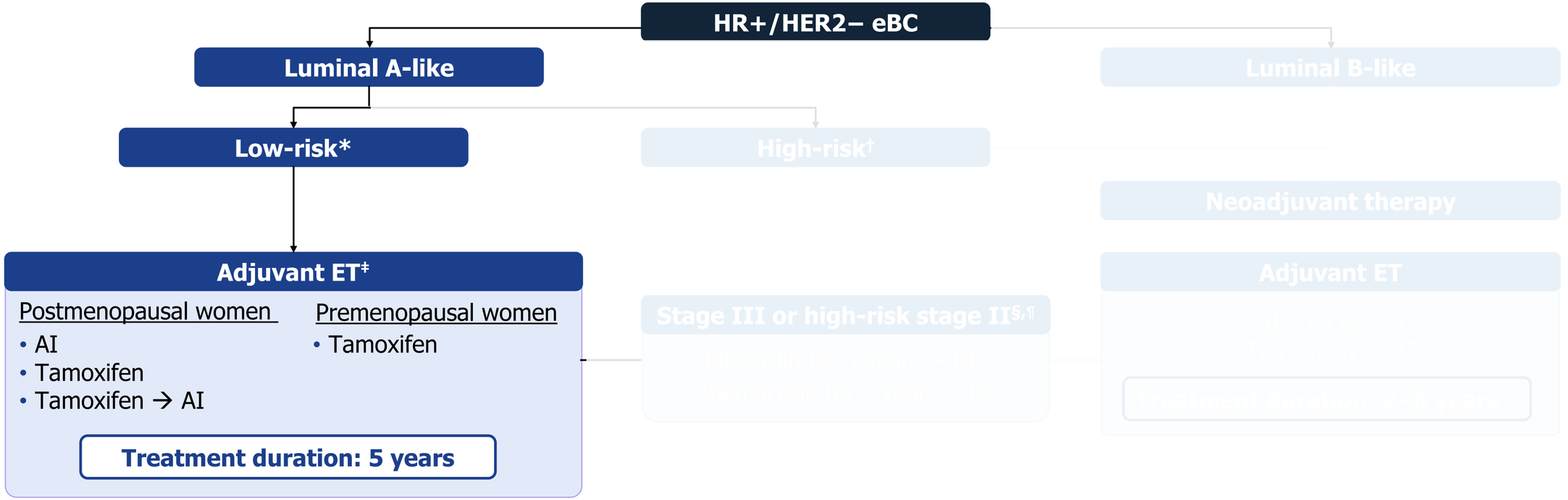
No. at risk											
High-risk group	557	466	368	274	206	148	86	47	21	0	
Non-high-risk group	3,471	2,923	2,317	1,816	1,364	897	516	278	120	18	0

High-risk tumors identified using inclusion criteria from the monarchE trial.
ET=endocrine therapy; RWE=real-world evidence.

Reference: 1. Sheffield MK, et al. *Future Oncol.* 2022;18(21):2667–2682.

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Decision-making in the Treatment of ER+/HER2− Early Breast Cancer is Based on the Risk of Recurrence[1]



*"Low risk" implies low-risk genomic score (preferred) and/or lower-risk features on traditional pathological analysis, including lower-grade histology, robust ER and PgR expression, and lower measures of proliferation. †"High risk" implies high-risk genomic score and/or higher-risk features on traditional pathological analysis, including higher-grade histology, lower ER expression, and higher measures of proliferation. ‡Premenopausal women with lower-risk tumors who are not advised/recommended to receive OFS may benefit more from adjuvant ChT (include patients with low-risk T1cN0, stage II T2–3N0, stage II T1–T2N1 tumors). §Stage N1 with primary tumor >5 cm, and/or grade 3 and/or Ki-67 ≥20%. ¶gBRCA1/2-wt or untested. #Ribociclib has been approved by regulatory agencies in this setting but has not yet been added to the official ESMO living guidelines. ‖Tamoxifen can be given if AIs are not tolerated. **If patient is premenopausal. ††7–8 years' treatment duration seems sufficient for most patients at high risk.

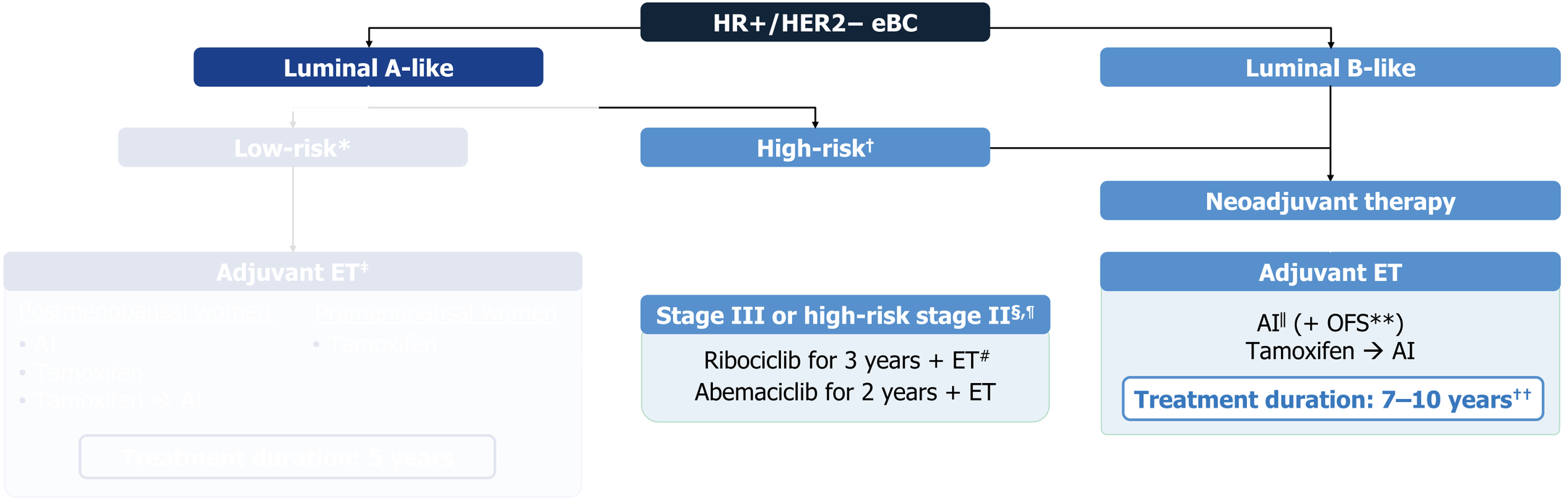
AI=aromatase inhibitors; ChT=chemotherapy; eBC=early breast cancer; ER=estrogen receptor; ET=endocrine therapy; gBRCA1/2=germline BRCA1/2; HER2=human epidermal growth factor receptor 2; OFS=ovarian function suppression; PgR=progesterone receptor; wt=wild type.

Reference: 1. Adapted from: Loibl S, et al. *Ann Oncol.* 2024;35(2):159–182.

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Treatment is Intensified in Adjuvant Settings for Tumors with High-risk Characteristics[1]



*"Low risk" implies low-risk genomic score (preferred) and/or lower-risk features on traditional pathological analysis, including lower-grade histology, robust ER and PgR expression, and lower measures of proliferation. †"High risk" implies high-risk genomic score and/or higher-risk features on traditional pathological analysis, including higher-grade histology, lower ER expression, and higher measures of proliferation. ‡Premenopausal women with lower-risk tumors who are not advised/recommended to receive OFS may benefit more from adjuvant ChT (include patients with low-risk T1cN0, stage II T2–3N0, stage II T1–T2N1 tumors). §Stage N1 with primary tumor >5 cm, and/or grade 3 and/or Ki-67 ≥20%. ¶gBRCA1/2-wt or untested. #Ribociclib has been approved by regulatory agencies in this setting but has not yet been added to the official ESMO living guidelines. ‖Tamoxifen can be given if AIs are not tolerated. **If patient is premenopausal. ††7–8 years' treatment duration seems sufficient for most patients at high risk.

AI=aromatase inhibitors; ChT=chemotherapy; eBC=early breast cancer; ER=estrogen receptor; ET=endocrine therapy; gBRCA1/2=germline BRCA1/2; HER2=human epidermal growth factor receptor 2; OFS=ovarian function suppression; PgR=progesterone receptor; wt=wild type.

Reference: 1. Adapted from: Loibl S, et al. *Ann Oncol.* 2024;35(2):159–182.

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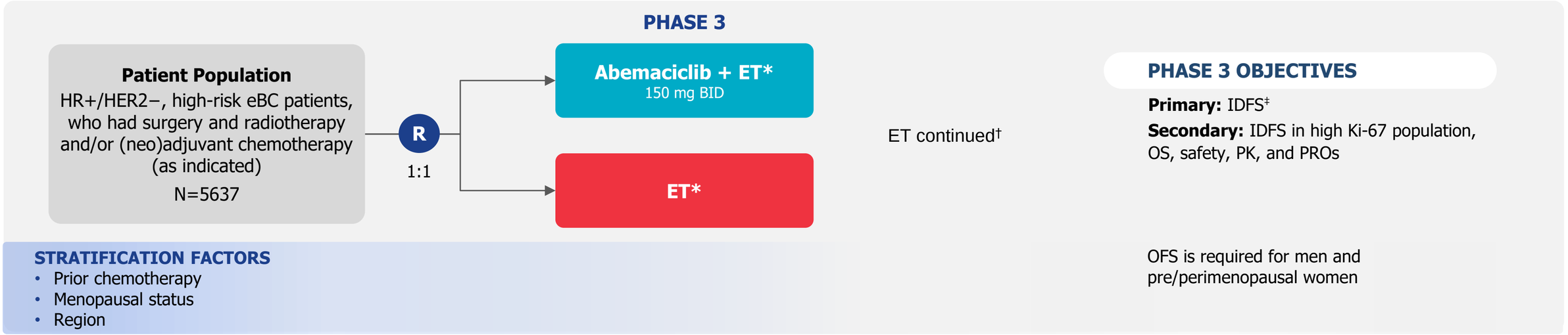
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02 Treatment Landscape in ER+/HER2– eBC with Intermediate/High Risk of Recurrence

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monarchE Study

A **Phase 3 trial that assessed the addition of abemaciclib + ET for 2 years in patients with node-positive, high-risk HR+/HER2- eBC.**[1,2]



KEY INCLUSION CRITERIA

- Women and men; ≥18 years
- HR+/HER2−, node positive, early-stage resected invasive BC with absence of any evidence of metastatic disease
- Underwent definitive surgery of the primary breast tumor(s)
- Pathological axillary lymph node involvement with at least 1 of the following: ≥4 positive ALN, tumor size ≥5 cm, Grade 3 tumor, or Ki-67 ≥20%
- Patients may have received up to 12 weeks of ET
- ECOG PS of ≤1

KEY EXCLUSION CRITERIA

- Metastatic disease (including contralateral ALNs) node-negative BC
- Inflammatory BC
- Previous treatment with any CDK4/6i
- Previously receiving ET for BC prevention
- Received an experimental treatment in a clinical trial within the past 30 days or 5 half-lives, whichever is longer
- History of venous thromboembolic events

*Endocrine therapy (physician's choice) standard-of-care was administered according to package label until discontinuation criteria were met. †ET continued for 3–8 years as clinically indicated. ‡Per STEEP criteria.

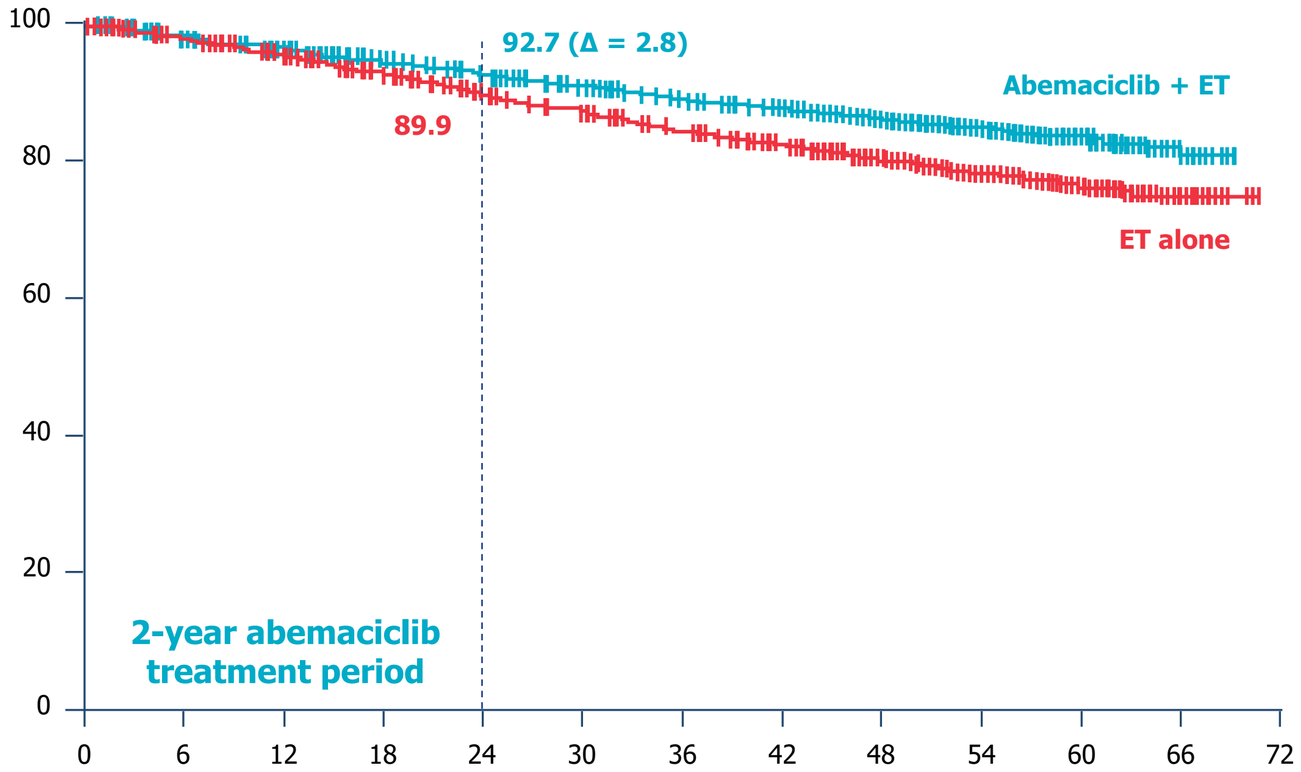
ALN=axillary lymph node; BC=breast cancer; BID=twice daily; CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; DRFS=distant relapse-free survival; eBC=early breast cancer; ECOG PS=Eastern Cooperative Oncology Group performance status; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; IDFS=invasive disease-free survival; N=number; OFS=ovarian function suppression; OS=overall survival; PK=pharmacokinetics; PROs=patient-reported outcomes; R=randomization; STEEP=Standardized Definitions for Efficacy End Points system.

References: 1. Johnston S, et al. *J Clin Oncol.* 2020;38(34):3987–3998. **2.** ClinicalTrials.gov. NCT03155997.

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monarchE: 2 Years of Adjuvant Abemaciclib + ET Demonstrated Sustained IDFS Benefit[1]



No. at risk													
Abemaciclib + ET	2,808	2,621	2,549	2,479	2,408	2,347	2,284	2,220	2,095	1,175	490	74	0
ET alone	2,829	2,653	2,573	2,474	2,374	2,281	2,195	2,125	1,974	1,124	473	67	0

	Abemaciclib + ET	ET alone	Absolute difference
2-year IDFS, %	92.7	89.9	2.8
3-year IDFS, %	89.2	84.4	4.8
4-year IDFS, %	86.0	80.0	6.0
5-year IDFS, %*	83.6	76.0	7.6
HR (95% CI)*	0.68 (0.60–0.77)		—

*Per the STEEP criteria; measured from the date of randomization to the date of first occurrence of ipsilateral invasive breast tumor recurrence, local/regional invasive breast cancer recurrence, distant recurrence, death attributable to any cause, contralateral invasive breast cancer, or second primary non-breast invasive cancer.

CI=confidence interval; ET=endocrine therapy; HR=hazard ratio; IA3=third interim analysis; IDFS=invasive disease-free survival; ITT=intention-to-treat; OS=overall survival; STEEP=Standardized Definitions for Efficacy End Points system.

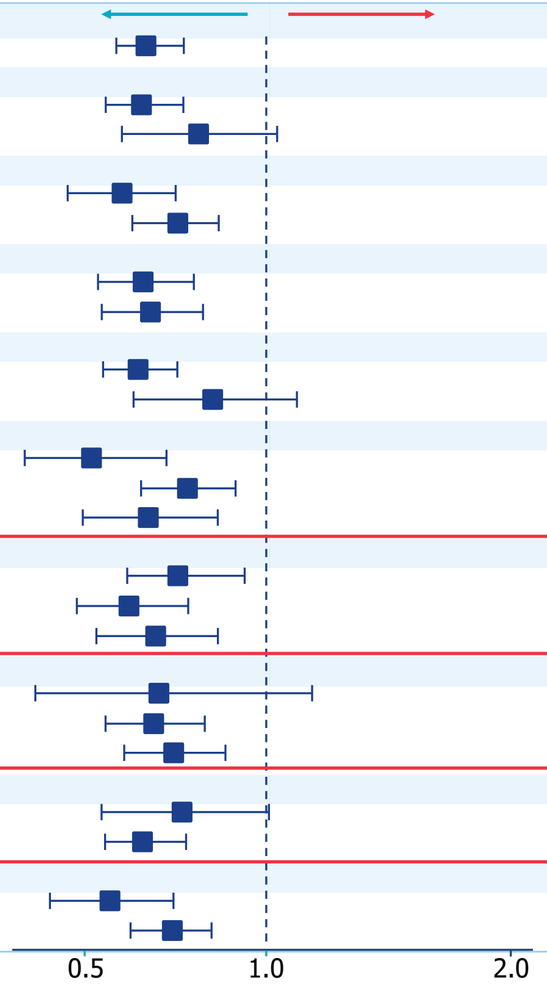
Reference: 1. Rastogi P, et al. *J Clin Oncol.* 2024;42(9):987-993.

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monarchE: Consistent IDFS Benefit Observed in Selected Subgroups with No Benefit for Stage II Patient Population[1]

	Abemaciclib + ET		ET alone			
	No.	Events	No.	Events	HR (95% CI)	Interaction p-value
Overall	2,808	407	2,829	585	0.68 (0.60–0.77)	
Pooled age group 1						0.229
<65 years	2,371	325	2,416	485	0.66 (0.57–0.76)	
≥65 years	437	82	413	100	0.80 (0.60–1.07)	
IWRS menopausal status						0.095
Premenopausal	1,221	150	1,232	237	0.60 (0.49–0.73)	
Postmenopausal	1,587	257	1,597	348	0.75 (0.64–0.88)	
IWRS prior treatment						0.596
Neoadjuvant chemotherapy	1,039	202	1,048	297	0.65 (0.54–0.78)	
Adjuvant chemotherapy	1,642	183	1,647	260	0.69 (0.57–0.84)	
Baseline ECOG PS						0.097
0	2,405	337	2,369	489	0.65 (0.57–0.75)	
1	401	70	455	95	0.87 (0.64–1.18)	
Primary tumor size						0.053
<20 mm	781	82	767	150	0.52 (0.40–0.68)	
≥20 mm but <50 mm	1,371	214	1,419	284	0.77 (0.65–0.92)	
≥50 mm	607	102	610	144	0.68 (0.53–0.87)	
Number of positive lymph nodes						0.438
1–3	1,118	136	1,142	182	0.75 (0.60–0.94)	
4–9	1,107	142	1,126	231	0.61 (0.50–0.76)	
10 or more	575	127	554	172	0.66 (0.53–0.83)	
Tumor grade						0.769
G1 – favorable	209	24	216	35	0.70 (0.42–1.17)	
G2 – moderately favorable	1,377	181	1,395	268	0.67 (0.55–0.80)	
G3 – unfavorable	1,086	185	1,064	240	0.74 (0.61-0.89)	
Tumor stage						0.382
Stage II	716	79	740	106	0.76 (0.57–1.02)	
Stage III	2,078	326	2,077	476	0.66 (0.57–0.76)	
First ET						0.054
Tamoxifen	857	111	898	196	0.56 (0.45–0.71)	
Aromatase inhibitor	1,931	293	1,887	386	0.74 (0.63–0.86)	



CI=confidence interval; ECOG PS=Eastern Cooperative Oncology Group performance status; ET=endocrine therapy; G=grade; HR=hazard ratio; IDFS=invasive disease-free survival; IWRS=interactive web response system.

Reference: 1. Rastogi P, et al. *J Clin Oncol*. 2024;42(9):987-993.

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monarchE: Safety Was Consistent with the Known Profile of Abemaciclib[1]

	Abemaciclib + ET (n=2,791)		ET alone (n=2,800)	
≥10% any grade in either arm, n (%)	**Any grade**	**Grade ≥3**	**Any grade**	**Grade ≥3**
Any adverse event	2,731 (97.9)	1,270 (45.5)	2,410 (86.1)	354 (12.6)
Diarrhea	2,294 (82.2)	212 (7.6)	199 (7.1)	3 (0.1)
Neutropenia	1,246 (44.6)	519 (18.6)	141 (5.0)	19 (0.7)
Fatigue	1,073 (38.4)	78 (2.8)	433 (15.5)	4 (0.1)
Leukopenia	1,027 (36.8)	305 (10.9)	171 (6.1)	10 (0.4)
Abdominal pain	948 (34.0)	37 (1.3)	227 (8.1)	9 (0.3)
Nausea	779 (27.9)	13 (0.5)	223 (8.0)	1 (0.0)
Anemia	638 (22.9)	48 (1.7)	90 (3.2)	10 (0.4)
Arthralgia	571 (20.5)	6 (0.2)	876 (31.3)	18 (0.6)
Vomiting	455 (16.3)	13 (0.5)	117 (4.2)	2 (0.1)
Headache	482 (17.3)	6 (0.2)	359 (12.8)	3 (0.1)

ET=endocrine therapy; n=number.

Reference: 1. Johnston et al. *J Clin Oncol.* 2020;38(34):3987–3998.

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NATALEE Study

A **Phase 3 trial that assessed the addition of ribociclib to NSAI for 3 years in patients with stage II or III HR+/HER2− eBC.**[1–4]

PHASE 3

Patient Population
HR+/HER2−, intermediate/high-risk eBC patients, who had surgery and as indicated, radiotherapy and/or (neo)adjuvant ChT
N=5101

R
1:1

Ribociclib* + NSAI†
400 mg QD

NSAI†

ET continued‡

PHASE 3 OBJECTIVES

Primary: IDFS per STEEP criteria

Secondary: RFS, DDFS, OS, safety, PK, and PROs

STRATIFICATION FACTORS
- Anatomic stage (II vs III)
- Menopausal status
- Receipt of prior chemotherapy (yes/no)
- Region

OFS is required for men and pre/perimenopausal women

KEY INCLUSION CRITERIA

- Women and men aged ≥18 years with unilateral primary invasive ER+/HER2− BC tumor and complete surgical resection with microscopic margins free of tumors with available archival tumor tissue
- Anatomical stage group II: (N1/ or N0 with G3 or G2 and/or Ki-67 ≥20%) or stage III disease
- Completion of (neo)adjuvant ChT and adjuvant radiotherapy (if indicated)
- Permitted to have received any SOC (neo)adjuvant ET but must be randomized <12 months of initial start date of ET
- ECOG PS of ≤1

KEY EXCLUSION CRITERIA

- Prior treatment with CDK4/6i
- Prior treatment with tamoxifen, raloxifene, or AIs for reduction in risk of BC and/or prior treatment for osteoporosis in the preceding 2 years
- Prior treatment with anthracyclines and cumulative doses of ≥450 mg/m2 for doxorubicin or of ≥900 mg/m2 for epirubicin
- Distant metastases of BC beyond regional lymph nodes and/or evidence of disease after curative surgery
- Clinically significant, uncontrolled heart disease and/or cardiac repolarization abnormalities
- Major surgery, ChT, or radiotherapy within 14 days prior to randomization

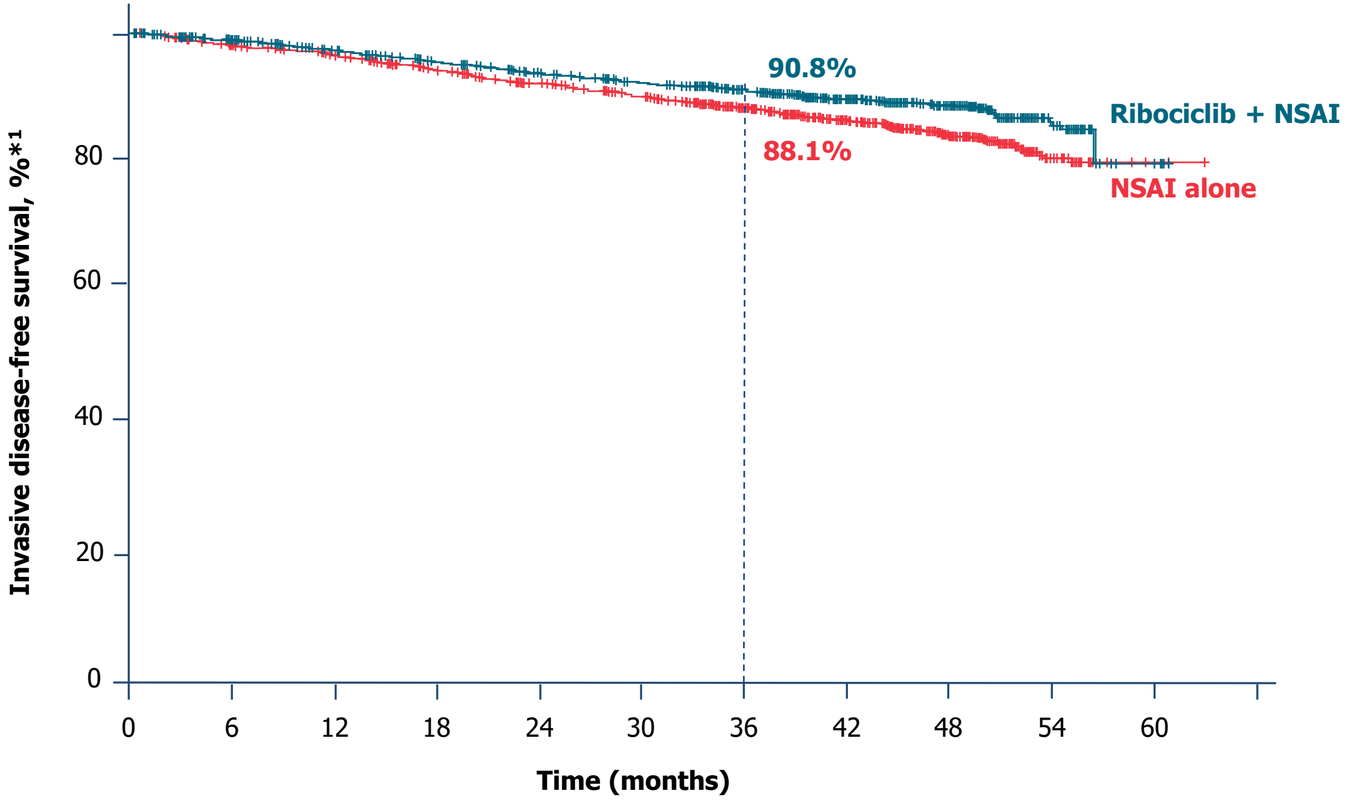
*Three weeks on, one week off. †Administered according to package label until discontinuation criteria were met. ‡Additional treatment with the NSAI beyond 60 months was at the discretion of the treating physician and was not considered to be part of the trial treatment.
AIs=aromatase inhibitors; BC=breast cancer; CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; ChT=chemotherapy; DDFS=distant disease-free survival; eBC=early breast cancer; ECOG PS=Eastern Cooperative Oncology Group performance status; ER=estrogen receptor; ET=endocrine therapy; G=grade; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; IDFS=invasive disease-free survival; N=number; N0=nodal status 0; N1=nodal status 1; NSAI=non-steroidal aromatase inhibitors; OFS=ovarian function suppression; OS=overall survival; PK=pharmacokinetics; PROs=patient reported outcomes; QD=once daily; R=randomization; RFS=recurrence-free survival; SOC=standard of care.

References: 1. Slamon D, et al. *N Engl J Med.* 2024;390(12):1080–1091. **2.** ClinicalTrials.gov. NCT03701334. **3.** Fasching PA, et al. ESMO Congress 2024. Abstract LBA13; **4.** Slamon DJ, et al. *Ther Adv Med Oncol.* 2023;15:17588359231178125.

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NATALEE: Ribociclib + NSAI Demonstrated Sustained IDFS Benefit



No. at risk												
RIB + NSAI	2,549	2,351	2,275	2,207	2,133	2,078	1,843	1,480	914	155	8	0
NSAI alone	2,552	2,240	2,168	2,082	2,006	1,935	1,687	1,366	848	150	6	0

	RIB + NSAI	NSAI alone	Absolute difference
2-year IDFS, %[1]	93.5	92.0	1.5
3-year IDFS, %[2]	90.8	88.1	2.7
4-year IDFS, %*[2]	88.5	83.6	4.9
HR (95% CI)†	0.72 (0.61–0.84)[2]		—

*Per the STEEP criteria; measured from the date of randomization to the date of first occurrence of ipsilateral invasive breast tumor recurrence, local/regional invasive breast cancer recurrence, distant recurrence, death attributable to any cause, contralateral invasive breast cancer, or second primary non-breast invasive cancer.

CI=confidence interval; HR=hazard ratio; IDFS=invasive disease-free survival; ITT=intention-to-treat; NSAI=non-steroidal aromatase inhibitors; RIB=ribociclib; STEEP=Standardized Definitions for Efficacy End Points system.

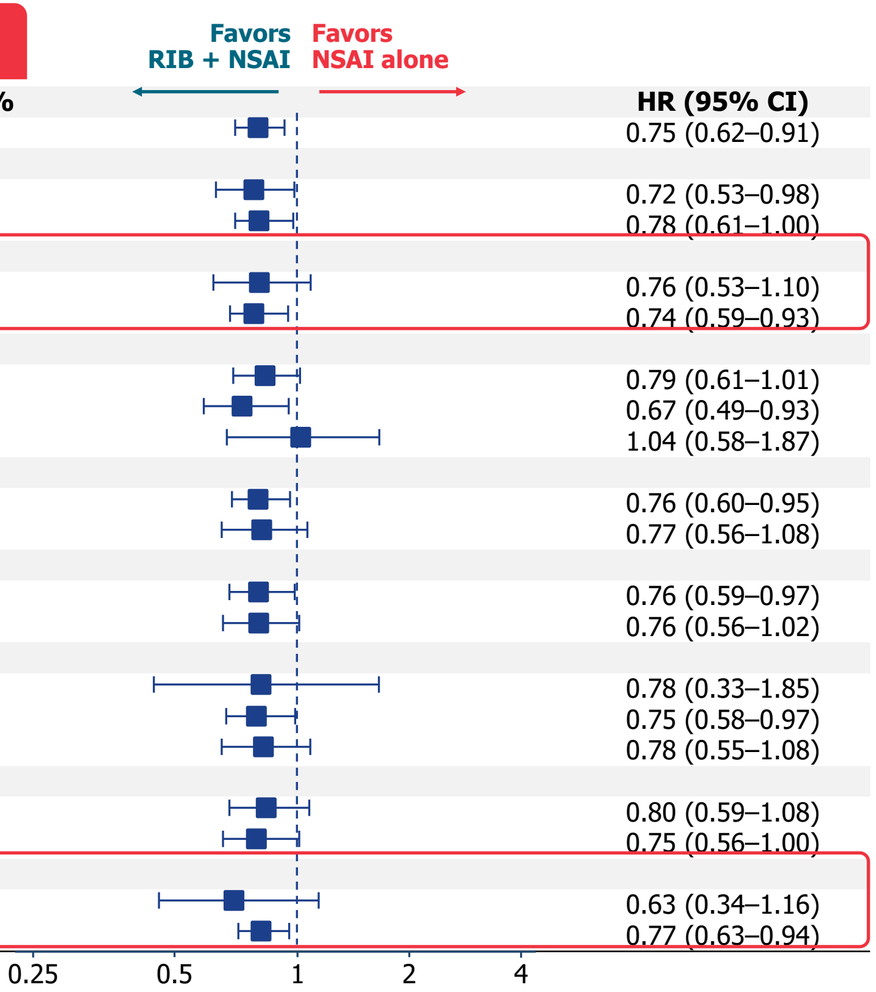
References: 1. Hortobagyi GN, et al. *Ann Oncol.* 2025;36(2):149–157. **2.** Fasching PA, et al. ESMO Congress 2024. Abstract LBA13.

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NATALEE: Consistent IDFS Benefit Observed in Selected Subgroups with No Benefit in Stage II and N0 Patient Population[1]

	RIB + NSAI n=2,549		NSAI alone n=2,552		
Subgroup	**Events/n**	**3-y IDFS rate, %**	**Events/n**	**3-y IDFS rate, %**	**HR (95% CI)**
All patients	189/2,549	90.4	237/2,552	87.1	0.75 (0.62–0.91)
Menopausal status					
Men and premenopausal women	71/1,126	90.7	93/1,132	88.6	0.72 (0.53–0.98)
Postmenopausal women	118/1,423	90.0	144/1,420	86.0	0.78 (0.61–1.00)
AJCC stage					
Stage II	49/1,011	94.2	65/1,034	91.2	0.76 (0.53–1.10)
Stage III	140/1,528	87.3	172/1,512	84.1	0.74 (0.59–0.93)
Prior ChT					
Neoadjuvant	111/1,085	87.1	132/1,095	83.2	0.79 (0.61–1.01)
Adjuvant	63/1,223	92.9	89/1,220	90.3	0.67 (0.49–0.93)
No	22/300	90.8	22/307	89.4	1.04 (0.58–1.87)
Prior ET					
Yes	127/1,824	90.9	157/1,801	88.1	0.76 (0.60–0.95)
No	62/725	89.1	80/751	85.2	0.77 (0.56–1.08)
Region					
North America/Western Europe/Oceania	111/1,563	90.6	139/1,565	86.7	0.76 (0.59–0.97)
Rest of the world	78/986	89.9	98/987	87.5	0.76 (0.56–1.02)
Histological grade at time of surgery					
Grade 1	9/213	94.2	12/217	92.7	0.78 (0.33–1.85)
Grade 2	102/1,460	90.6	125/1,432	87.7	0.75 (0.58–0.97)
Grade 3	61/684	88.6	78/702	84.5	0.78 (0.55–1.08)
Ki-67 status*					
Ki-67 ≤20%	76/1,199	91.7	95/1,236	90.0	0.80 (0.59–1.08)
Ki-67 >20%	82/920	89.3	105/938	84.2	0.75 (0.56–1.00)
Nodal status†,‡					
N0	16/285	93.7	28/328	88.6	0.63 (0.34–1.16)
N1–N3	173/2,261	89.8	208/2,219	87.0	0.77 (0.63–0.94)



*From archival tumor tissue. †Nodal status classification according to AJCC staging. ‡Nodal status is from the worst stage derived per surgical specimen or at diagnosis.

AJCC=American Joint Committee on Cancer; ChT=chemotherapy; CI=confidence interval; ET=endocrine therapy; HR=hazard ratio; IDFS=invasive disease-free survival; n=number; N0=nodal status 0; N1–N3=nodal status 1–3; NSAI=non-steroidal aromatase inhibitor; RIB=ribociclib; y=year.

Reference: 1. Slamon D, et al. *N Engl J Med.* 2024;390(12):1080–1091 (including supplementary data).

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NATALEE: Safety Was Consistent with the Known Profile of Ribociclib[1]

	Ribociclib + NSAI (n=2,524)		NSAI alone (n=2,444)	
Event	**All grade**	**Grade ≥3**	**All grade**	**Grade ≥3**
Any adverse event, n (%)	2,470 (97.9)	1,579 (62.6)	2,128 (87.1)	436 (17.8)
Adverse events that occurred in ≥15% of patients in either group, n (%)				
Neutropenia*	1,568 (62.1)	1,106 (43.8)	110 (4.5)	20 (0.8)
Arthralgia	921 (36.5)	24 (1.0)	1,038 (42.5)	31 (1.3)
Nausea	580 (23.0)	6 (0.2)	184 (7.5)	1 (<0.1)
Headache	556 (22.0)	10 (0.4)	403 (16.5)	4 (0.2)
Fatigue	554 (21.9)	18 (0.7)	311 (12.7)	4 (0.2)
SARS-CoV-2 test positive	487 (19.3)	0 (0)	310 (12.7)	0 (0)
Covid-19	477 (18.9)	21 (0.8)	314 (12.8)	12 (0.5)
Alanine aminotransferase increased	478 (18.9)	185 (7.3)	128 (5.2)	16 (0.7)
Hot flush	473 (18.7)	6 (0.2)	482 (19.7)	3 (0.1)
Asthenia	417 (16.5)	15 (0.6)	273 (11.2)	3 (0.1)
Aspartate aminotransferase increased	408 (16.2)	112 (4.4)	131 (5.4)	12 (0.5)

Neutropenia is a grouped term that combines the preferred terms neutropenia and neutrophil count decreased.
Covid-19=coronavirus disease 2019; n=number; NSAI=non-steroidal aromatase inhibitor; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

Reference: 1. Slamon D, et al. *N Eng J Med.* 2024;390(12):1080–1091.

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monarchE and NATALEE Efficacy Data Demonstrated Increasing IDFS Benefit Over Time

	monarchE[1]			NATALEE[2,3]		
	Abemaciclib + ET	**ET alone**	**Absolute difference**	**RIB + NSAI**	**NSAI alone**	**Absolute difference**
2-year IDFS, %	92.7	89.9	2.8	93.5	92.0	1.5
3-year IDFS, %	89.2	84.4	4.8	90.8	88.1	2.7
4-year IDFS, %	86.0	80.0	6.0	88.5	83.6	4.9
5-year IDFS, %*	83.6	76.0	7.6	NR	NR	NR
HR (95% CI)	0.68 (0.60–0.77)		—	0.72 (0.61–0.84)		—

Safety All grades, ≥15% of patients[4–5]

monarchE

- Diarrhea (82.2%)
- Neutropenia (44.6%)
- Fatigue (38.4%)
- Leukopenia (36.8%)
- Abdominal pain (34%)
- Nausea (27.9%)
- Anemia (22.9%)
- Arthralgia (20.5%)
- Headache (17.3%)
- Vomiting (16.3%)

NATALEE

- Neutropenia (62.1%)
- Arthralgia (36.5%)
- Nausea (23%)
- Headache (22%)
- Fatigue (21.9%)
- SARS-CoV-2 test positive (19.3%)
- Covid-19 (18.9%)
- Alanine aminotransferase increased (18.9%)
- Hot flush (18.7%)
- Asthenia (16.5%)
- Aspartate aminotransferase increased (16.2%)

*Per the STEEP criteria; measured from the date of randomization to the date of first occurrence of ipsilateral invasive breast tumor recurrence, local/regional invasive breast cancer recurrence, distant recurrence, death attributable to any cause, contralateral invasive breast cancer, or second primary non breast invasive cancer.

CI=confidence interval; Covid-19=coronavirus disease 2019; eBC=early breast cancer; ET=endocrine therapy; HR=hazard ratio; IDFS=invasive disease-free survival; ITT=intention-to-treat; NR=not reached; NSAI=non-steroidal aromatase inhibitors; RIB=ribociclib; ; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

References: 1. Rastogi P, et al. *J Clin Oncol.* 2024;42(9):987-993. **2.** Hortobagyi GN, et al. *Ann Oncol*. 2025;36(2):149–157. **3.** Fasching PA, et al. ESMO Congress 2024. Abstract LBA13. **4.** Johnston SRD et al. *J Clin Oncol.* 2020;38(34):3987–3998. **5.** Slamon D, et al. *N Eng J Med*. 2024;390(12):1080–1091.

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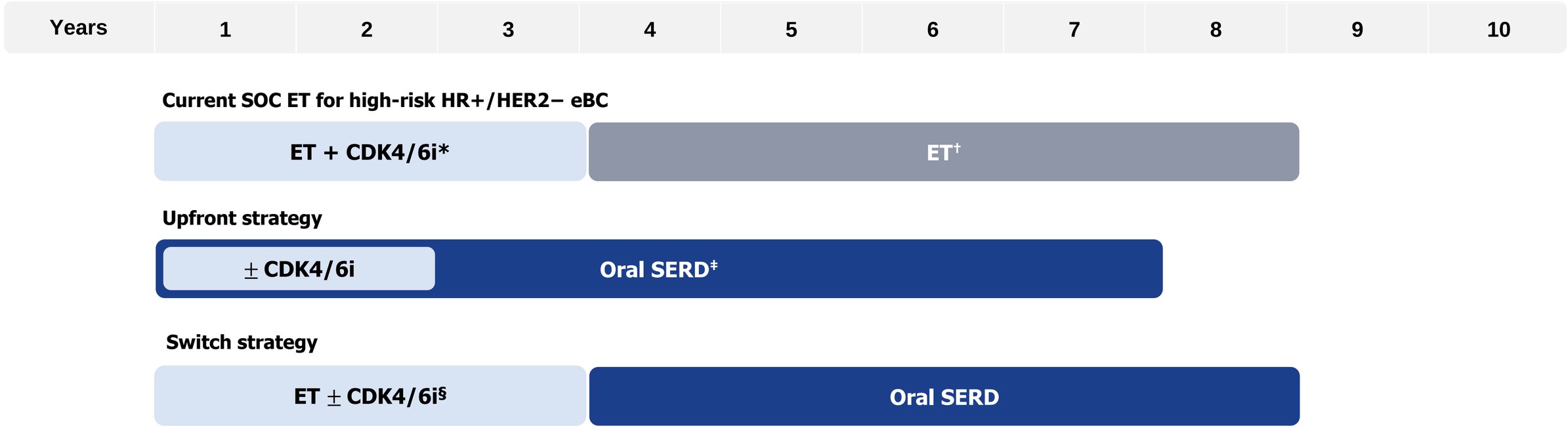
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03 Investigating Elacestrant in ER+/HER2– eBC Patients with High Risk of Recurrence

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Treatment Strategic Approach for Adjuvant Therapy in ER+/HER2− eBC

- Oral SERDs have shown evidence of superior efficacy over SOC in metastatic settings[1,2]
- Their potential is now being explored in early-stage disease to enhance treatment outcomes in adjuvant settings
- Current investigations focus on 2 strategies: upfront[3,4] or a switch approach[5–7]



The diagram is provided for illustrative purposes only. Therapy time frames may vary based on individual treatment plans.

*Patients may receive 2 or 3 years of CDK4/6i depending on whether they are treated with abemaciclib or ribociclib, respectively. †Patients may receive up to 10 years adjuvant treatment, although 7–8 years are usually sufficient per current ESMO guidelines. ‡Patients may receive 5 or 7 years of oral SERD therapy depending on whether they are treated with giredestrant or camizestrant, respectively. §Patients may receive 2–5 years of adjuvant ET (± CDK4/6i).

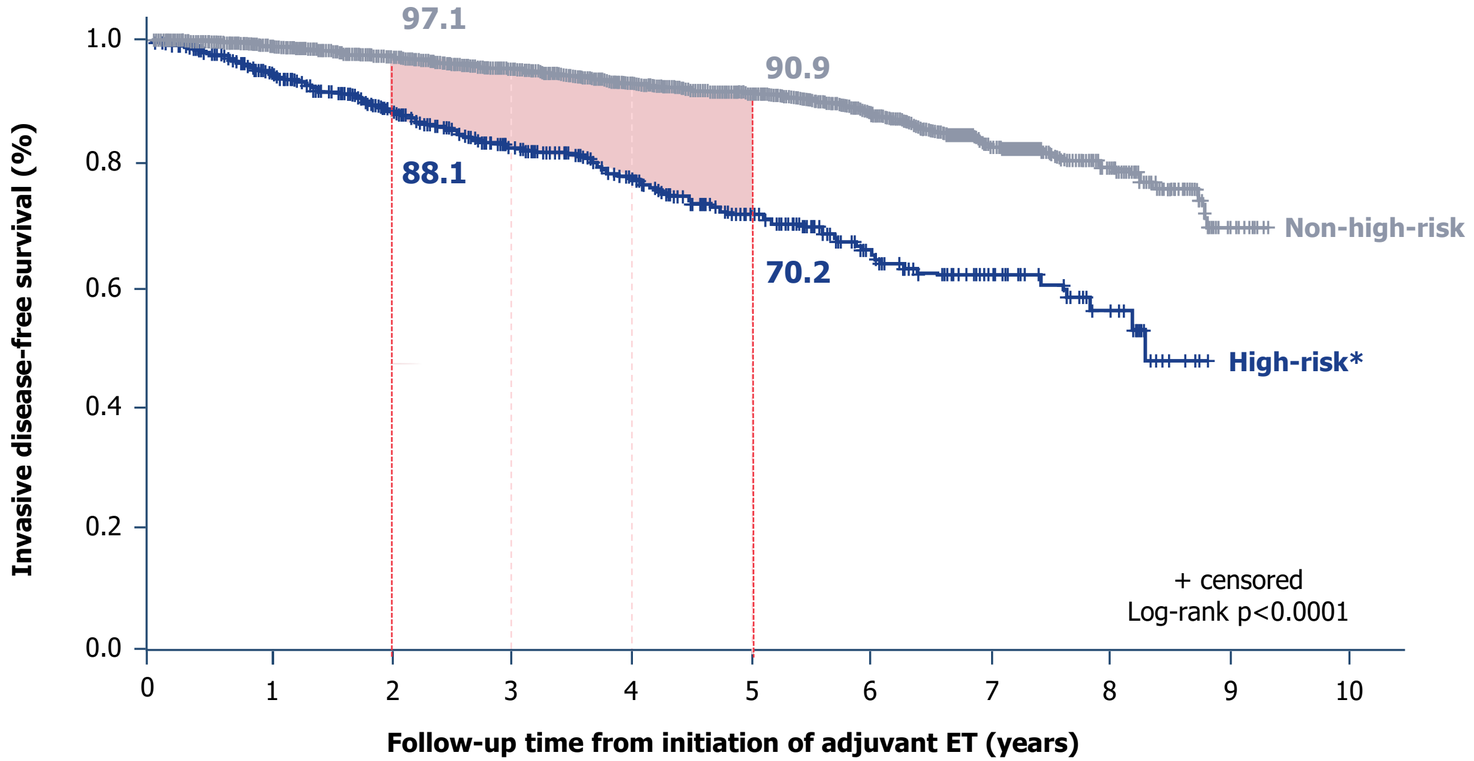
CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; eBC=early breast cancer; ER=estrogen receptor; ET=endocrine therapy; HER2=human epidermal growth factor 2; HR=hormone receptor; SERD=selective estrogen receptor degrader; SOC=standard of care.

References: 1. Bidard FC, et al. *J Clin Oncol*. 2022;40:3246–3256. **2.** Jhaveri KL, et al. *N Engl J Med*. Published online December 11, 2024. doi:10.1056/NEJMoa2410858. **3.** ClinicalTrials.gov. NCT04961996. **4.** ClinicalTrials.gov. NCT05952557. **5.** ClinicalTrials.gov. NCT05514054. **6.** ClinicalTrials.gov. NCT06492616. **7.** ClinicalTrials.gov. NCT05774951.

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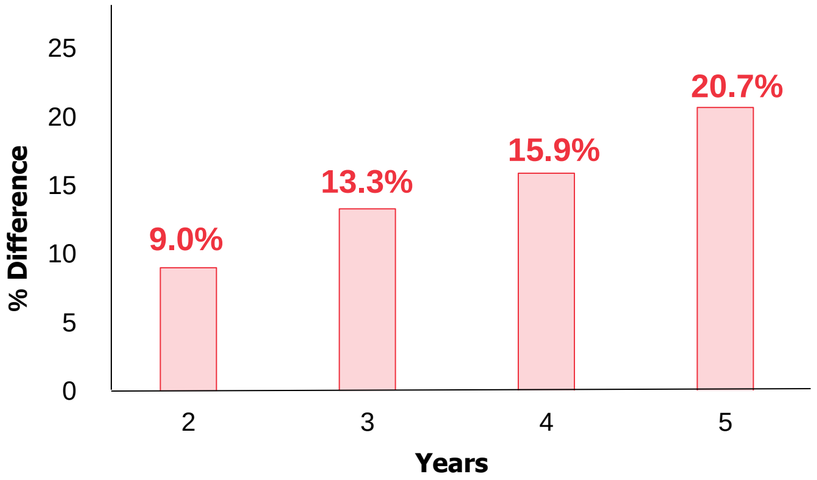
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Recurrence rate is doubled between years 2 and 5 after initiating adjuvant ET



No. at risk											
High-risk group	557	466	368	274	206	148	86	47	21	0	
Non-high-risk group	3,471	2,923	2,317	1,816	1,364	897	516	278	120	18	0

Recurrence or death rates increase in patients with high-risk vs non-high-risk of recurrence during the 2-5 yr adjuvant



*High-risk tumors identified using inclusion criteria from the monarchE trial in HR+, HER2- early breast cancer (≥4 lymph nodes, or 1–3 lymph nodes and grade 3, tumor ≥5 cm or Ki-67 ≥20%).
eBC= early breast cancer; ET=endocrine therapy; RWE=real-world evidence.

Reference: 1. Sheffield MK, et al. *Future Oncol.* 2022;18(21):2667–2682.

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Elacestrant Shows Both Degradative and Partial Agonist Properties

Elacestrant exhibits selective **degradative activity** in breast and uterine tissues and **agonist activity** in bone[1]

- **SERD activity:** Elacestrant reduced ER availability, showing reduction in tumors regardless of *ESR1* mutation status[2]
- **Agonistic properties:** Elacestrant may function as a partial agonist, which can both reduce hot flashes and protect against bone loss[1,3,4, 5]



Adapted from: McDonnell DP, et al., 2021

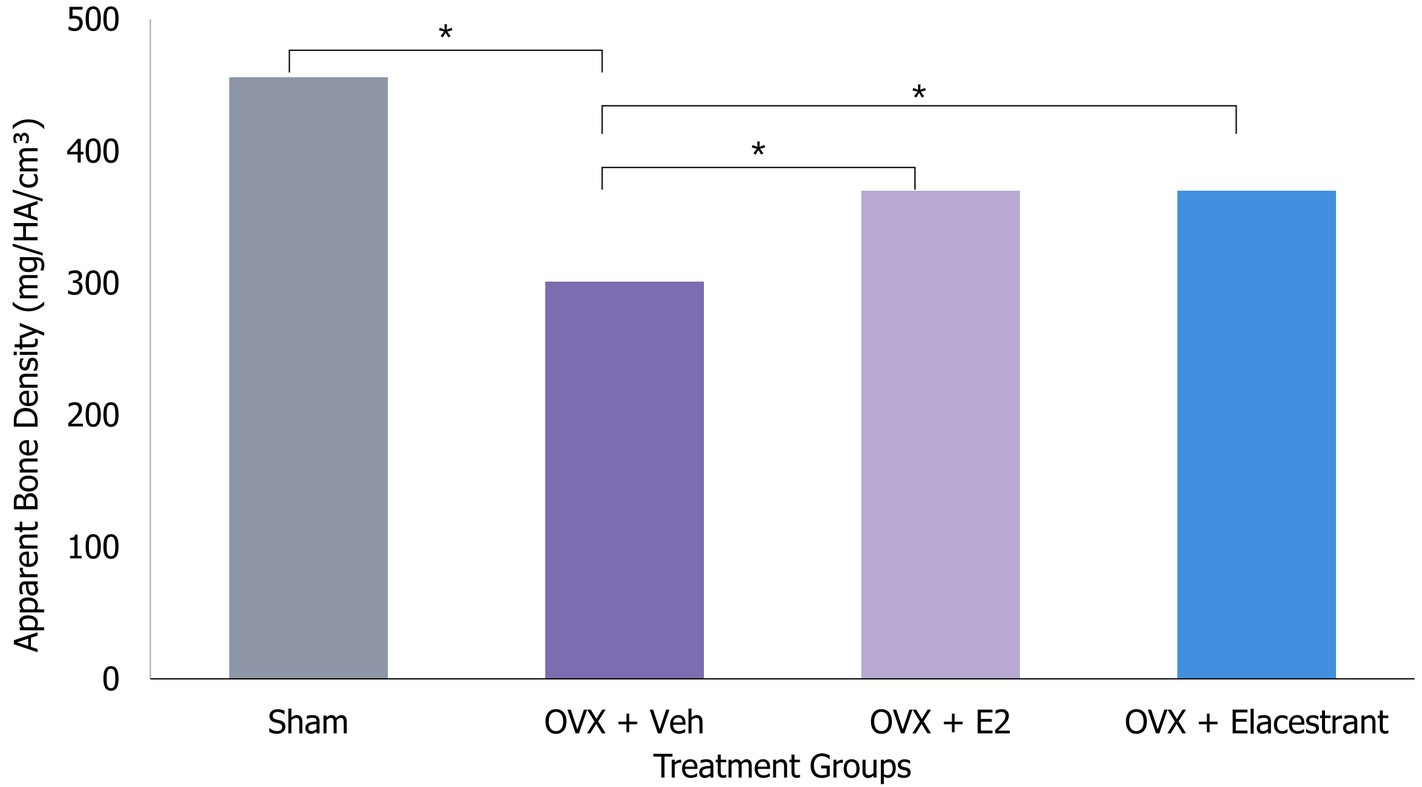
ER=estrogen receptor; SERD=selective estrogen degrader; SERM=selective estrogen receptor modulator.

References: 1. Garner F, et al. *Anticancer Drugs.* 2015;26(9):948–956. **2.** Bardia A, et al. *J Clin Oncol.* 2021;39(12):1360–1370. **3.** McDonnell DP, et al. *J Clin Oncol.* 2021;39(12):1383–1388. **4.** Wardell SE, et al. *Endocr Relat Cancer.* 2015;22:713-724. **5**. https://sites.duke.edu/mcdonnelllab/mechanism-based-discovery-of-serms-and-serds/

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Bone Density is Preserved with Elacestrant

Effect of elacestrant on apparent bone density in ovariectomized rats†



Comparable to standard treatment

- Elacestrant shows equivalent efficacy to E2 treatment in preserving bone density

Prevention of bone loss

- Elacestrant treatment showed a 23% increase in bone density compared to untreated ovariectomized controls

E2=estradiol; OVX=ovariectomized; Veh=vehicle.
†Adult female rats underwent either sham or ovariectomy surgery before treatment initiation with vehicle, E2 (0.01 mg/kg), or elacestrant (3 mg/kg) once daily (n = 20 per treatment group). After 4 weeks, bone microarchitecture was evaluated using microcomputed tomography. Data are expressed as mean ± SD.
*P <0.05 versus the corresponding OVX + Veh control.
References: Garner et, al. Anti-Cancer Drugs 2015, 26:948–956.

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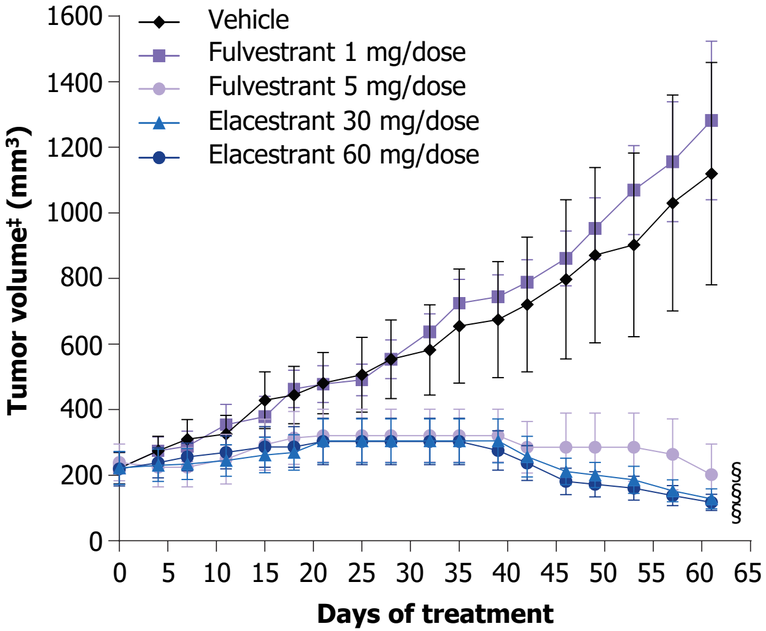
Elacestrant Demonstrated Activity in *ESR1* Wild-type Tumors

Elacestrant provides a numerical benefit* in PFS at 6–12 months[1]

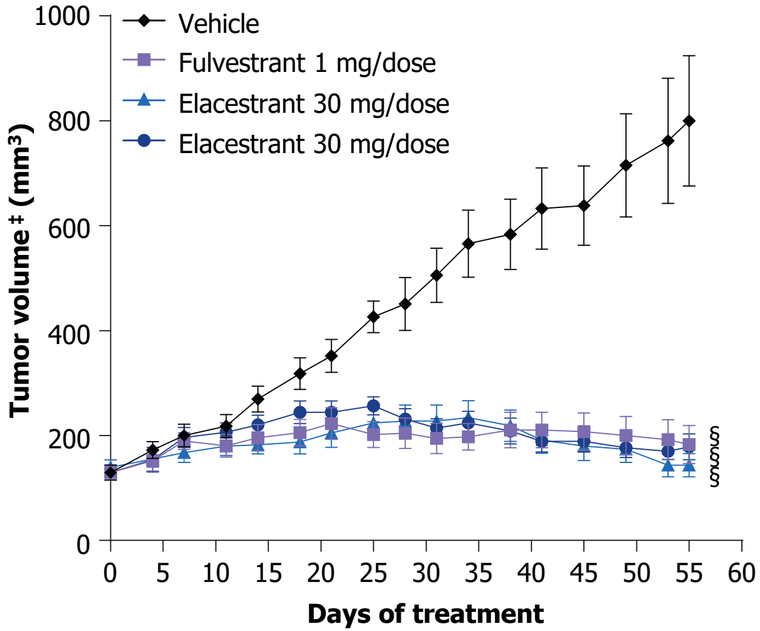
	Elacestrant (N=124)	SOC (N=125)
Event	82	78
Hazard ratio (95% CI)	0.863 (0.628–1.186)	
P value	0.308	
6-month PFS, % (95% CI)	28.58 (18.98–38.18)	21.85 (12.71–30.99)
12-month PFS, % (95% CI)	18.16 (8.60–27.73)	11.22 (2.82–19.62)

Elacestrant showed growth inhibition in cells† resistant to CDK4/6i[2]

ST986
***ESR1*wt, *PIK3CA*mut** *(E542K)*
84% ER+, 77% PR+



HBCX-21
***ESR1*wt, *PIK3CA*wt**
99% ER+, 98% PR+



*EMERALD study was not powered to demonstrate statistical significance for ESR1-wt; †PDX models ST986, MAXF.71 and HBCX-21 were selected based on relatively high expression levels of wild-type ER and PR; ‡Mean tumor volumes±SEM of indicated PDX models treated with elacestrant of fulvestrant at the indicated doses. §Significant differences of the indicated treatment groups relative to vehicle control at end of treatment.

CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; CI=confidence interval; ER=estrogen receptor; PFS=progression-free survival; PIK3CAmut=phosphatidylinositol-3-kinase, catalytic subunit alpha mutation; PIK3CAwt=phosphatidylinositol-3-kinase, catalytic subunit alpha wild-type; PR=progesterone receptor; SOC=standard of care.

References: 1. Bidard FC et al. *J Clin Oncol.* 2022;40(28):3246-3256 (supplementary data). **2.** Kaklamani VG, et al. ASCO 2023. Poster 291.

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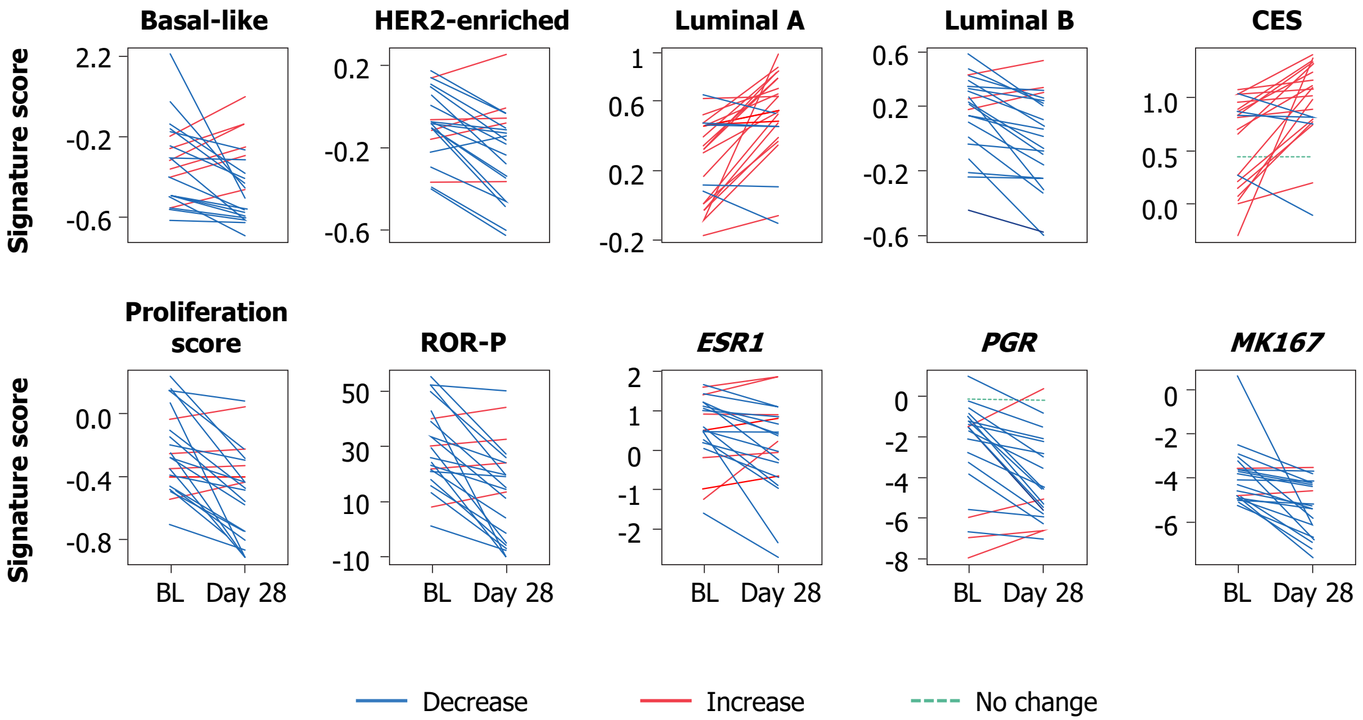
Elacestrant Demonstrated Relevant Biological and Molecular Responses in eBC[1]

Treatment with elacestrant results in a 27% CCCA rate and substantial Ki67 suppression

	Overall population
n	23
Histologic type, n (%)	
Ductal	17 (73.9)
Lobular	4 (17.4)
Other	2 (8.6)
Centralized Baseline Ki67	
Median (Range)	13 (5–70)

	Overall population	Luminal A
n	22	12
CCCA at Day 28, n (%)	6 (27.3)	5 (41.7)
Ki67 ≤10% at Day 28, n (%)*	14 (63.7)	10 (90.1%)†
Ki67 geometric mean change, % (95% CI)	-52.9 (-67.4 to -32.1)	-64.6 (-79.4 to -39.3)

Tumor biology evolved to a more endocrine sensitive and less proliferative phenotype



*Ki67 variation between paired baseline and posttreatment (Day 28) tumor samples, overall, Ki67 was available in 19 out of 22 baseline tumor samples. †There were 11 paired luminal A samples, therefore 10/11.
CCCA=complete cell cycle arrest; CI=confidence interval; eBC=early breast cancer; n=number.

Reference: 1. Vidal M, et al. *Clin Cancer Res.* 2025;31(7):1223-1232. doi:10.1158/1078-0432.CCR-24-2460.

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ELEGANT

An investigational Phase 3, global, multicenter study of elacestrant vs standard ET in patients with node-positive, ER+/HER2− eBC with high risk of recurrence.[1,2]

PHASE 3

Patient Population

Node-positive, ER+/HER2− eBC with high risk of recurrence who received between 2-5 years of SOC ET ± CDK4/6i

LHRH agonist will be administered for pre/perimenopausal women and men

N=4220

R

1:1

Elacestrant
345 mg* QD

Continue ET†
Anastrozole 1 mg QD, Letrozole 2.5 mg QD, Exemestane 25 mg QD or Tamoxifen 20 mg QD

5 years

PHASE 3 OBJECTIVES

Primary: Evaluate IBCFS

Key Secondary: Evaluate DRFS and OS

Secondary: Evaluate IDFS, safety, PROs-QoL, and PK

Exploratory: Evaluate ctDNA and bone health

STRATIFICATION FACTORS

- Menopausal status (pre-/perimenopausal vs post-menopausal)
- Prior CDK4/6i treatment in the adjuvant setting (yes or no)
- Time since curative surgery (≤48 mo vs >48 mo)

KEY INCLUSION CRITERIA

- Women or men age ≥18 years
- Confirmed ER+/HER2− early stage II-III resected invasive BC without evidence of recurrence‡ or distant metastases
- High risk of recurrence defined at initial staging with one of the following criteria:
  - ≥4 positive axillary lymph nodes, OR
  - 1–3 positive axillary lymph nodes AND
    - Histologic grade 3 disease and/or
    - Tumor size ≥5 cm
- 2–6 yrs from the date of curative surgical resection
- If indicated, completed adjuvant and/or neoadjuvant chemotherapy according to guidelines
- Currently taking ET and received ≥24 mo but not more than 60 mo of ET (AIs or tamoxifen) ± CDK4/6i§
- Pre/perimenopausal women and men will be administered a LHRH agonist
- Considered a candidate for an additional 5 yrs of ET
- ECOG PS 0-1

KEY EXCLUSION CRITERIA

- Stage IV metastatic BC
- Inflammatory BC
- History of any prior (ipsilateral and/or contralateral) invasive BC with the exception of ipsilateral DCIS treated by local regional therapy alone ≥5 years prior to randomization or contralateral DCIS treated by local regional therapy at any time. No systemic treatment is allowed for DCIS.
- History of malignancy within 3 years of the date of randomization, except for adequately treated basal or squamous cell skin cancer, superficial bladder cancer or carcinoma *in situ* of the cervix
- >6 mo of continuous interruption of prior SOC adjuvant ET or who are off current adjuvant ET >6 mo prior to randomization

*Elacestrant 345 mg is equivalent to 400 mg elacestrant hydrochloride. †Change in endocrine therapy after randomization in the control arm from an AI to another AI or to tamoxifen is allowed as per investigator's judgment. ‡Histopathologically or cytologically confirmed ER+ (≥ 10% by IHC), HER2- [IHC = 0, 1+, or 1, or (IHC = 2+ and ISH negative)] on tumor biopsy or final surgical pathology specimen; High-risk of recurrence and recurrence-free per the Investigator's assessment 2-6 years after curative surgical resection of the primary tumor. §Patients who received prior CDK4/6i or PARPi must have already completed or discontinued these treatments. AI=aromatase inhibitor; BC=breast cancer; CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; cfNA=cell-free nucleic acid; DRFS=distant relapse-free survival; eBC=early breast cancer; ER=endocrine receptor; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; IBCFS=invasive breast cancer-free survival; IHC=immunohistochemistry; ISH=*in situ* hybridization; LHRH=luteinizing hormone-releasing hormone; mo=months; OS=overall survival; PRO=patient-reported outcomes; QD=once daily; QoL=quality of life; SOC=standard of care; yrs=years.

References: 1. A Study of Elacestrant Versus Standard Endocrine Therapy in Women and Men With ER+,HER2-, Early Breast Cancer With High Risk of Recurrence (ELEGANT). ClinicalTrials.gov. July 09, 2024. Accessed August 07, 2025. https://clinicaltrials.gov/study/NCT06492616.
2. Bardia A et al Proceedings of the San Antonio Breast Cancer Symposium Dec 10-13, 2024 Clin Cancer Res 2025;31(12 Suppl):Abstract nr P2-08-21.

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Summary of Ongoing Studies Investigating Oral SERDs as Adjuvant Therapy for HR+/HER2− eBC

			ELEGANT[1]	EMBER-4[2,3]	CAMBRIA-1[3,4]	lidERA[3,5,6]	CAMBRIA-2[3,7]
N			4,220	6,000	4,300	4,200	5,500
Intervention			**Elacestrant**	**Imlunestrant**	**Camizestrant**	**Giredestrant**	**Camizestrant (± abema 2 y)**
Trial design			**TREATMENT SWITCH AFTER 2–5 YEARS OF ADJUVANT ET**			**UPFRONT ADJUVANT TREATMENT**	
Risk of recurrence			+++	++	+	+	+
Patient population			Pure high-risk	Increased risk	Intermediate/high-risk	Intermediate/high-risk	Intermediate/high-risk
Prior CDK4/6i exposure allowed			YES	YES	YES	NO	NO
ECOG PS			0–1			0–2	0–1
Disease stage	IIA	T0 N1	If Grade 3	If Grade 3	NO	YES	NO
		T1 N1	If Grade 3	If Grade 3	If ≥2 LN+, or Grade 3, or genomic high-risk, or Ki-67 ≥20%	YES	If ≥2 ILN+, or Grade 3, or genomic high-risk, or Ki-67 ≥20%
		T2 N0	NO	If tumor size 5 cm or Grade 3	If Grade 3 or genomic high-risk or Ki-67 ≥20%	If Grade 3 or genomic high-risk‡ or Ki-67 ≥20%	If Grade 3, or genomic high-risk, or Ki-67 ≥20%
	IIB	T2 N1	If tumor size 5 cm and/or Grade 3 and/or genomic high risk	If tumor size 5 cm or Grade 2/3	YES*	YES	YES*
		T2 N0	NO	If tumor size 5 cm or Grade 3	YES	If Grade 3 or genomic high-risk‡, or Ki-67 ≥20%	If Grade 3, or genomic high-risk, or Ki-67 ≥20%
	IIIA		YES	YES	YES	YES	YES
	IIIB	T4 N0	NO	If tumor size ≥5 cm, or Grade 3 and 2–5 cm	YES†	If Grade 3, or genomic high-risk, or Ki-67 ≥20%	YES
		T4 N1	If tumor size 5 cm and/or Grade 3 and/or genomic high risk	If tumor size ≥5 cm, or Grade 3 or Grade 2 and 2–5 cm	YES†	YES	YES
		T4 N2	YES	YES	YES†	YES	YES
	IIIC		YES	YES	YES	YES	YES

Comparisons of efficacy and safety should not be drawn or inferred in the absence of head-to-head studies.

*For 1 LN+ only if Grade 3, or genomic high risk, or Ki-67 >20%. †T4d excluded. ‡Oncotype DX or MammaPrint high.

Abema=abemaciclib; CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; eBC=early breast cancer; ECOG PS=Eastern Cooperative Oncology Group performance status; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; ILN=ipsilateral lymph node; incl=including; LN=lymph node; mic=microinvasion;N=number; N0=nodal status 0; N1=nodal status 1; N2=nodal status 2; SERD=selective estrogen receptor degrader; T=tumor size; y=year.

References: 1. ClinicalTrials.gov. NCT06492616. **2.** ClinicalTrials.gov. NCT05514054. **3.** Ascione L, et al. *Curr Opin Oncol.* 2024;36(6):465–473. **4.** ClinicalTrials.gov. NCT05774951. **5.** ClinicalTrials.gov. NCT04961996. **6.** ClinicalTrials Register EU. Accessed March 2026. https://www.clinicaltrialsregister.eu/ctr-search/search?query=LidERA. **7.** ClinicalTrials.gov. NCT05952557.

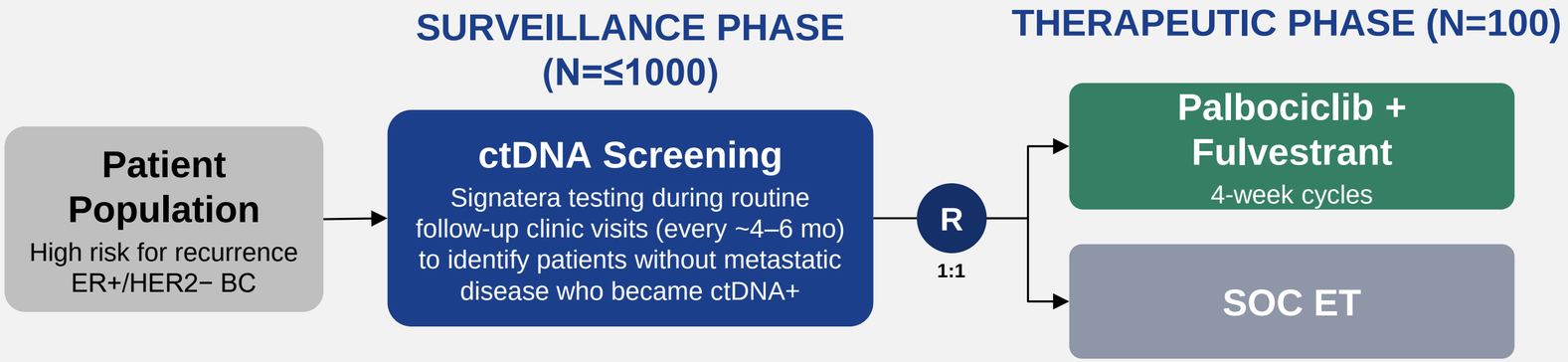
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04 Other Ongoing Studies Investigating Elacestrant in eBC

DARE Study Design

A randomized, Phase 2 trial of circulating tumor DNA-guided second line adjuvant therapy for high residual risk, ER+/HER2− breast cancer.[1]



SCREENING PHASE OBJECTIVES

Primary: Measure incidence of ctDNA positivity

Secondary: Determine correlation between metastatic or local disease and positive ctDNA results

THERAPEUTIC PHASE OBJECTIVES

Primary: Assess relapse free survival

Secondary: Evaluate efficacy, safety, and tolerability

SURVEILLANCE PHASE

KEY INCLUSION CRITERIA

- Completed adjuvant ET and ≤7 years since definitive breast surgery
- Taking an AI or tamoxifen as adjuvant ET, and completed ≥6 mo to ≤7 years of ET*
- Available FFPE tissue from primary BC for ctDNA testing

KEY EXCLUSION CRITERIA

- Prior or current fulvestrant treatment
- CDK4/6i treatment currently or in prior 12 mo
- Current or prior invasive cancer†
- Synchronous HER2+ BC or TNBC

THERAPEUTIC PHASE

KEY INCLUSION CRITERIA

- ctDNA positive‡
- No CT scan evidence of metastasis in chest, abdomen, and pelvis
- Willing to use an adequate method of contraception§

KEY EXCLUSION CRITERIA

- Known contraindications to receive fulvestrant or palbociclib, or are unable to tolerate the drugs
- Concurrent severe and uncontrolled medical conditions
- Taking any CYPC3A4 strong inducers and inhibitors that cannot be changed

*Prior CDK4/6 therapy in the adjuvant setting, including participation in the PALLAS and PENELOPE trials, is allowed if the last treatment was ≥12 months ago. Adjuvant bisphosphonate therapy is allowed. †Other than BC, except: adequately treated basal or squamous cell carcinoma of the skin and cancer survivors of previously diagnosed invasive cancer, who were treated with a curative intent, have no evidence of disease recurrence for ≥5 years, and are considered low risk for future recurrence by the treating physician. ‡Defined as 2 of 16 cancer-specific markers positive in plasma. §Pre-menopausal women and male patients. For the duration of trial treatment and for 4 additional weeks after completion of treatment in the control arm, and for 2 years after the last dose of fulvestrant, if randomized into the experimental arm.

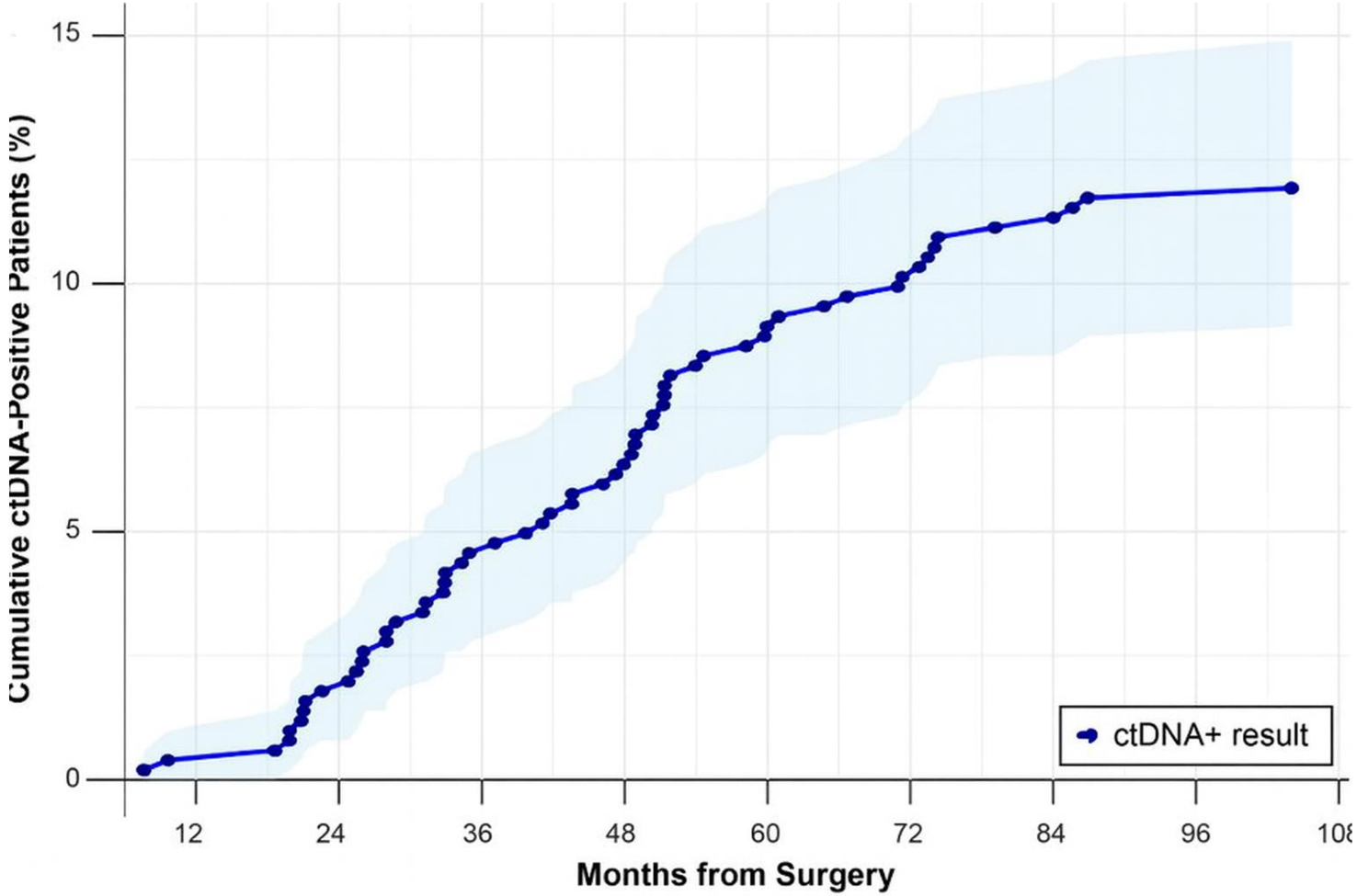
AI=aromatase inhibitor; BC=breast cancer; CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; CT=computed tomography; ctDNA=circulating tumor DNA; CYPC3A4=cytochrome P450 3A4; ER=estrogen receptor; ET=endocrine therapy; FFPE=formalin-fixed, paraffin-embedded; HER2=human epidermal growth factor receptor 2; mo=months; R=randomization; SOC=standard-of-care; TNBC=triple-negative breast cancer.

1. DNA-guided Second Line Adjuvant Therapy for High Residual Risk, Estrogen Receptor Positive, HER-2 Negative Breast Cancer (DARE). ClinicalTrials.gov. September 25, 2025. Accessed October 15, 2025. https://clinicaltrials.gov/study/NCT04567420.

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In the DARE study, an increase on molecular relapse was detected mainly between the 2–5-year period post-surgery[1]



CI=confidence interval; ctDNA=circulating tumor deoxyribonucleic acid; IDFS=invasive free survival; n=number; N=number; N/A=not available.

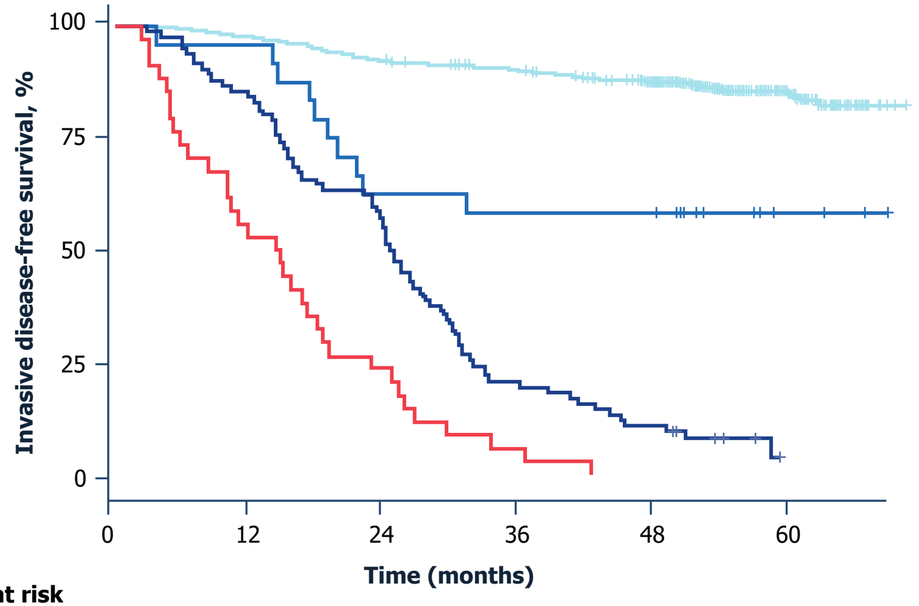
Reference: 1. Adapted from Lajos Pusztai et al. Circulating tumor (ct)DNA monitoring of ER+/HER2- high-risk breast cancer during adjuvant endocrine therapy. JCO 43, 1010-1010 (2025).

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In monarchE, Patients with Persistent ctDNA Positivity Exhibited a Higher Risk of IDFS Events Compared to Those Who Achieved ctDNA Clearance[1]

Patients who remained or became ctDNA+ on treatment were more likely to experience recurrence compared to those who became or remained undetected.



No. at risk						
Persistently –	749	731	691	664	611	162
Became –	24	23	15	14	14	3
Became +	82	70	46	17	9	0
Persistently +	34	18	8	2	0	0

	Longitudinal analysis (N=889)*			
	Baseline (−), undetected n=831		Baseline (+), detected n=58	
	Persistently –	Became +	Persistently +	Became – (undetected)
N	749 (90)	82 (10)	34 (60)	24 (40)
IDFS event, n (%)	107 (14)	76 (93)	34 (100)	10 (42)
4-year IDFS rate, % (95% CI)	87.5 (85.1–89.9)	11.0 (5.9–20.3)	N/A	58.3 (41.6–81.8)

*The ctDNA subset was enriched by patients with IDFS events within 24 months; therefore, the estimated IDFS rates in each subgroup are not reflective of that in the overall population.
Robust assessment was limited in 194 patients with <3 post-baseline timepoints and there may be differences in IDFS; total events 227.

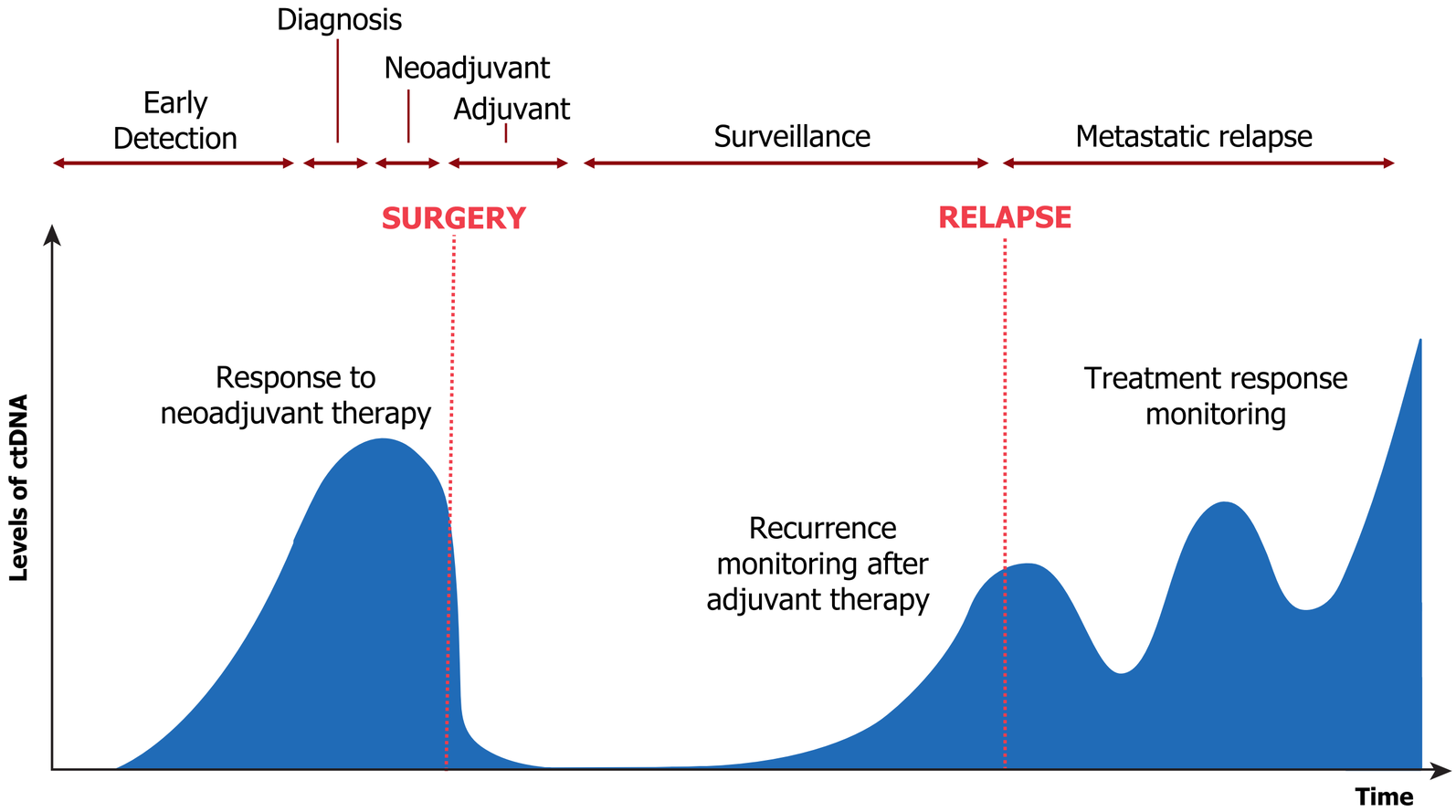
CI=confidence interval; ctDNA=circulating tumor deoxyribonucleic acid; IDFS=invasive free survival; n=number; N=number; N/A=not available.

Reference: 1. Loi S et al. ASCO 2024. Abstract LBA507.

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Monitoring of Minimal Residual Disease Through ctDNA is Likely to Prove Beneficial for Anticipating Recurrence[1]



ctDNA=circulating tumor DNA.

Reference: 1. Adapted from: Natera. Signatera. Accessed March 6, 2025. Available at: https://www.natera.com/oncology/signatera-advanced-cancer-detection.

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TREAT ctDNA EORTC-2129-BCG

An investigational Phase 3 study of elacestrant vs standard ET in patients with ctDNA+ ER+/HER2− eBC[1,2]

PHASE 3 (n=220)

Patient Population

ctDNA screening by Signatera™ assay every 6 mo from study entry until the end of accrual, while receiving adjuvant ET

N=1960

R

1:1

- **Elacestrant** 345 mg*
- **Continue SOC ET**

2–6 years†

Intense follow-up for a maximum of 3 years after randomization that includes:

- ctDNA testing
- CT/MRI
- Mammogram
- Bone scan

PHASE 3 OBJECTIVES

Primary: Evaluate DMFS with elacestrant vs SOC ET in patients with ctDNA-relapse

Secondary: Evaluate efficacy (iDFS, RFS, OS), safety, tolerability, and PROs

STRATIFICATION FACTORS

- Country
- Duration of ET at time of ctDNA detection (≤5 years vs >5 years)
- Stage II vs III
- Prior CDK4/6i treatment (yes vs no)
- Prior neoadjuvant chemotherapy (yes vs no)
- ctDNA assay (Signatera™ from Natera™ vs others)

KEY INCLUSION CRITERIA

- Women (pre- or postmenopausal) or men age ≥18 years
- ER+‡/HER2− BC
- Intermediate to high risk of recurrence after definitive treatment for eBC§
- Received 1–7.5 years of ET
- Prior CDK4/6i or PARPi allowed if completed ≥12 mo prior to enrollment
- ctDNA+ per the Signatera™ assay (Randomization phase)
- ECOG PS 0–1
- Adequate organ function

KEY EXCLUSION CRITERIA

- Suspected recurrent disease
- Prior treatment with any SERD or investigational ER antagonist
- Previous history of invasive BC or bilateral BC
- Child-Pugh score greater than Class A
- Uncontrolled significant active infections‖
- Any history of coagulopathy in the past 6 mo

*Elacestrant 345 mg is equivalent to 400 mg elacestrant hydrochloride . †For patients on ET between 1–5 years (12–60 months) at the time of randomization: 2–6 years (allowing for 7 years of ET at the end of the study treatment); For patients on ET between 5–7.5 years (60–90 months) at the time of randomization: 2 years. ‡≥10% staining. §**Patients with primary surgery:** Any patient with ≥4 positive axillary lymph nodes (stage pN2–3), 1–3 positive axillary lymph nodes (stage pN1) and either (tumor size ≥5 cm or/and, histologic Grade 3 or/and, Ki67 ≥20% or/and, high genomic risk defined as Oncotype Dx Recurrence Score ≥26, Mammaprint high risk, Prosigna score >40, or EPclin risk score ≥4.0); Negative axillary lymph nodes (stage pN0) and tumor size ≥5 cm and either (histologic Grade 3 a or/and, Ki67 ≥20% and/or, high genomic risk defined as Oncotype Dx Recurrence Score ≥26, Mammaprint high risk, Prosigna score >60, or EPclin risk score ≥4.0). **Patients with neoadjuvant systemic treatment followed by surgery:** Patient may have received neoadjuvant endocrine therapy or neoadjuvant chemotherapy provided that: the initial tumor and/or the tumor after surgery meet the criteria above defined for patients treated with primary surgery or the initial tumor was staged as cT4anyN and there is no pathological complete response, defined as no invasive disease in the breast and axilla (ypT0/is ypN0). ‖Grade 3 per CTCAE v5.0. BC=breast cancer; CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; cT=cinical tumor; CT=computed tomography; CTCAE=Common Terminology Criteria for Adverse Events; ctDNA=circulating tumor deoxyribonucleic acid; DMFS=distant metastasis-free survival; eBC=early breast cancer; ER=estrogen receptor; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; iDFS=invasive disease-free survival; Ki67=Antigen Kiel 67; mo=months; MRI=magnetic resonance imaging; N=total number; n=number; OS=overall survival; PARPi=poly-ADP ribose polymerase inhibitor; pN=pathological node; PRO=patient-reported outcome; R=randomization; RFS=relapse-free survival; SERD=selective estrogen receptor degrader; SOC=standard of care; v=version. ypT/N=post-neoadjuvant treatment tumor size/lymph node status.

References: 1. Elacestrant for Treating ER+/HER2- Breast Cancer Patients With ctDNA Relapse (TREAT ctDNA) (TREAT ctDNA). Clinicaltrials.gov. January 24, 2024. Accessed August 26, 2024. https://clinicaltrials.gov/study/NCT05512364. **2.** Elacestrant for treating ER+/HER2- breast cancer patients with ctDNA relapse (TREAT ctDNA). EORTC-2129-BCG. October 13, 2023. Accessed May 21, 2025. https://euclinicaltrials.eu/search-for-clinical-trials/?lang=en&EUCT=2022-501453-36-00.

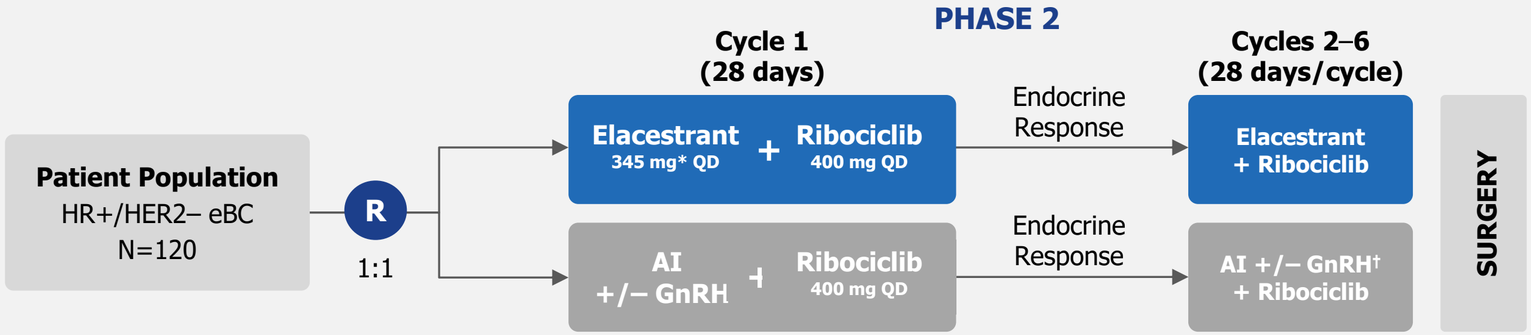
Investigator initiated clinical study sponsored by EORTC.

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ERIKA ABCSG-63

An investigational Phase 2 study of elacestrant + ribociclib vs AI (and GnRH agonist in pre-/perimenopausal women and men) + ribociclib as neoadjuvant therapy for endocrine-responsive HER2– early breast cancer.[1]



PHASE 2 OBJECTIVES

Primary: Evaluate PEPI score at time of surgery

Secondary: Evaluate Ki-67 concordance, radiological tumor size, RCB, pCR, QoL, and safety

STRATIFICATION FACTORS

- Menopausal status
- Nodal status
- Ki-67 status

KEY INCLUSION CRITERIA

- Women (pre-, peri-, or postmenopausal) or men age ≥18 years
- Histologically confirmed HR+/HER2– invasive adenocarcinoma of the breast ‡
- Adequate hematologic and end-organ function
- ECOG PS 0–1

KEY EXCLUSION CRITERIA

- Metastatic or locally advanced disease
- History of prior systemic cancer therapy for invasive BC
- History of malignancy except in specific circumstances§
- Clinically significant, uncontrolled heart disease and/or cardiac repolarization abnormalities‖
- Documented pneumonitis/ILD

*Elacestrant 345 mg is equivalent to 400 mg elacestrant dihydrochloride. †+GnRH agonist in pre-/perimenopausal women and men. ‡Invasive (unilateral or bilateral) adenocarcinoma of the breast with the following characteristics: cT1c-4a-c, cN0-3, M0 per AJCC (American Joint Committee on Cancer) Breast Cancer Staging version 8 (refer to section 23.3); - In case of a multifocal tumor (defined as the presence of two or more foci of cancer within the same breast quadrant) or multicentric tumor (defined as the presence of two or more foci of cancer within different quadrants), the overall largest lesion must be > 1 cm and designated as the "target" lesion for all subsequent tumor evaluations; - Histologically confirmed HER2-negative tumors; HER2 measurement to be assessed locally according to the ASCO/CAP guideline; - ER-positive tumors (i.e. > 10 % positive stained tumor cells); - PR-positive or negative tumors. §Includes history of malignancy other than invasive BC if disease-free for ≥5 years and deemed by the investigator to be at low risk for recurrence of that malignancy, completely resected non-metastatic, non-melanoma skin cancer, successfully treated *in situ* carcinoma, contralateral breast carcinoma *in situ*, or ipsilateral breast carcinoma *in situ* (only if not a component of the invasive BC). ‖Includes acute coronary syndromes (eg, myocardial infarction, unstable angina, coronary artery bypass grafting, coronary angioplasty, stenting), symptomatic pericarditis ≤6 mo prior to screening, documented congestive heart failure (NYHA functional classification III–IV), documented cardiomyopathy, clinically significant cardiac arrhythmias (eg, ventricular tachycardia), complete left bundle branch block, high-grade AV block (eg, bifascicular block, Mobitz type Ⅱ and third-degree AV block), long QT syndrome or family history of idiopathic sudden death or congenital long QT syndrome, or systolic blood pressure >160 mmHg or <90 mmHg at screening. AI=aromatase inhibitor; ALP=alkaline phosphatase; ALT=alanine amino transferase; ANC=absolute neutrophil count; AST=aspartate aminotransferase; AV=atrioventricular; BC=breast cancer; eBC=early breast cancer; ECOG PS= Eastern Cooperative Oncology Group Performance Status; G-CSF= granulocyte colony-stimulating factor; GnRH=gonadotropin-releasing hormone; HER2=human epidermal growth factor receptor 2; Hgb=hemoglobin; HR=hormone receptor; ILD=interstitial lung disease; mo=month; NYHA=New York Heart Association; pCR=pathologic complete response; PEPI=preoperative endocrine prognostic index; QD=once daily; QoL=quality of life; RCB=residual cancer burden; ULN=upper limit of normal.

References: 1. ABCSG 63/ERIKA: Elacestrant and RIbociclib in Ki67-tested endocrine responsive breAst cancer: An open-label, two-arm, randomized, phase II study of elacestrant plus ribociclib vs. AI (plus GnRH agonist in pre-/perimenopausal women and men) plus ribociclib as neoadjuvant therapy for endocrine-responsive HER2-negative early breast cancer. euclinicaltrials.eu. Accessed May 21, 2025. https://euclinicaltrials.eu/search-for-clinical-trials/?lang=en&EUCT=2023-505758-17-00.

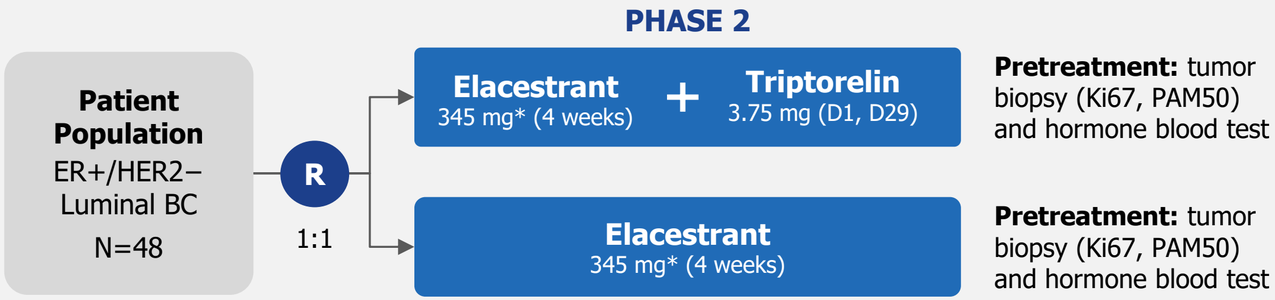
Investigator initiated clinical study sponsored by Austrian Breast and Colorectal Cancer Study Group

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PREMIERE SOLTI-2104

An investigational Phase 2 study of elacestrant ± triptorelin in premenopausal women with luminal BC.[1,2]



PHASE 2 OBJECTIVES

Primary: Evaluate the biological activity of elacestrant ± OFS by the rate of CCCA determined by Ki67 ≤2.7% after 4 weeks of treatment

Secondary: Identify changes in the research-based PAM50 subtypes, changes in estradiol and FSH, and safety

KEY INCLUSION CRITERIA

- Women (premenopausal at the time of study) age ≥35 years
- Stage I–IIB operable BC per AJCC v7 and eligible for primary surgery
- ER+/HER2− BC
- Ki67 expression 10–35% by local assessment
- ECOG PS 0 or 1

KEY EXCLUSION CRITERIA

- Inoperable locally advanced or inflammatory BC (any Stage III) or mBC (Stage IV), or synchronous invasive bilateral or multicentric BC
- Immediate neoadjuvant chemotherapy or immediate surgical intervention required
- Sentinel lymph node biopsy or tumor excisional biopsy prior to study treatment
- Any local or systemic treatment (including prior chemotherapy, ET, targeted therapy, and/or radiation therapy) for the currently diagnosed BC prior to enrollment

*Elacestrant 345 mg is equivalent to 400 mg elacestrant hydrochloride.

AJCC=American Joint Committee on Cancer; BC=breast cancer; CCCA=complete cell cycle arrest; D=day; eBC=early breast cancer; ECOG PS= Eastern Cooperative Oncology Group performance status; ER=estrogen receptor; ET=endocrine therapy; FSH=folicule stimulating hormone; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; Ki67=Ki67 proliferation index; mBC=metastatic breast cancer; N=number; OFS=ovarian function suppression; PAM50=Predication Analysis of Microarray 50; R=randomization; v=version.

References: 1. ClinicalTrials.gov. NCT05982093. **2.** Preoperative trial — PreiÈRe. SOLTI-2104. April 18, 2024.

Investigator initiated clinical study sponsored by SOLTI.

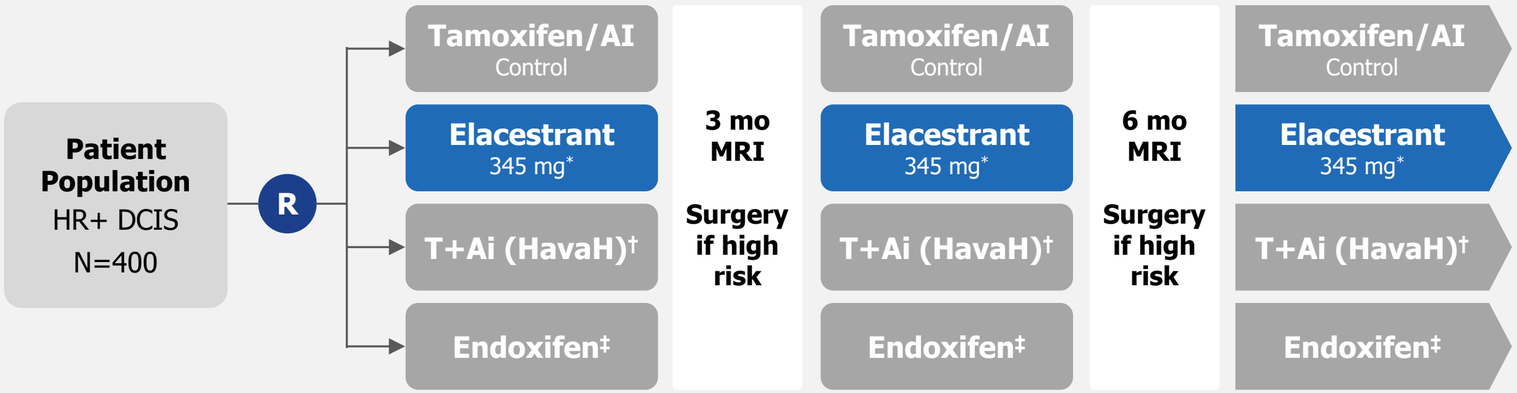
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DCIS RECAST

An investigational study re-evaluating conditions for active surveillance suitability as treatment for DCIS patients.[1]

PHASE 2



PHASE 2 OBJECTIVES

Primary: Evaluate the fraction of patients remaining on active surveillance at 7 mo vs control

Secondary: Determine whether novel ET increases the fraction of patients who will be suitable for long-term active surveillance (as measured by the fraction of patients deemed to be low-risk for invasive cancer) after 3 and 6 mo vs control

KEY INCLUSION CRITERIA

- Women age ≥18 years
- Previous diagnosis of HR+ DCIS (≥50% ER or PR and 2+; biopsy will have been performed previously at diagnosis) with or without microinvasion
- Willingness and ability to provide tumor samples

KEY EXCLUSION CRITERIA

- Invasive carcinoma or identification of a mass on MRI that is subsequently biopsied and found to be invasive cancer
- Ongoing treatment for DCIS other than what is specified in this protocol
- Uncontrolled intercurrent illness, including psychiatric conditions, that would limit compliance with study requirements
- Medical history or ongoing gastrointestinal disorders potentially affecting the absorption of investigational agent and/or tamoxifen

*Elacestrant 345 mg is equivalent to 400 mg elacestrant hydrochloride. †T+Ai™ (HavaH): Investigational subcutaneous extended-release formulation of testosterone and anastrozole manufactured by HavaH Therapeutics. ‡Endoxifen is an investigational agent that is the most active metabolite of tamoxifen.

AI=aromatase inhibitor; DCIS=ductal carcinoma *in situ;* ER=estrogen receptor; ET=endocrine therapy; HR=hormone receptor; mo=months; MRI=magnetic resonance imaging; N=number; PR=progesterone receptor; R=randomization.

Reference: 1. ClinicalTrials.gov. NCT06075953.

Investigator initiated clinical study sponsored by QuantumLeap Healthcare Collaborative, including: trial design, regulatory agencies and investigator collaborations, and study extension.

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Summary

Risk assessment enables personalized treatment approaches, which may improve therapeutic outcomes[1,2]

High-risk patients exhibit significantly lower invasive disease-free survival than do intermediate/low-risk groups, underscoring the need for enhanced treatment strategies[3]

Adjuvant ET intensification with CDK4/6 inhibitors has shown clinical benefit; however, emerging resistance remains a challenge, contributing to disease recurrence[4,5]

Oral SERDs have shown evidence of superior efficacy over SOC in metastatic settings, particularly in the presence of *ESR1*-mut and are now being explored in early-stage disease as either an upfront or switch treatment strategy[6–8]

Elacestrant is an oral SERD with partial agonistic properties being investigated as a switch strategy in a pure high-risk population in eBC. **Preoperative studies with elacestrant in eBC have demonstrated reductions in Ki67. Preclinical data have reported tumor reductions in *ESR1* wild-type BC PDX** models[6,9–12]

BC=breast cancer; CCCA=complete cell cycle arrest; CDK4/6=cyclin dependent kinase 4/6; eBC=early breast cancer; ESR1=estrogen receptor 1; ET=endocrine therapy; SERD=selective estrogen receptor degrader; SOC=standard of care.

References: 1. Amin MB, et al. *CA Cancer J Clin.* 2017;67(2):93–99. **2.** Garutti M, et al. *Cancers (Basel).* 2022;14(8):1898. **3.** Sheffield MK, et al. *Future Oncol.* 2022;18(21):2667–2682. **4.** Johnston S, et al. *J Clin Oncol.* 2020;38(34):3987–3998. **5.** Hortobagyi GN, et al. *Ann Oncol.* 2025;36(2):149–157. **6.** Bidard FC, et al. *J Clin Oncol.* 2022;40:3246–3256. **7.** Jhaveri KL, et al. *N Engl J Med.* Published online December 11, 2024. doi:10.1056/NEJMoa2410858. **8.** Ascione L, et al. *Curr Opin Oncol.* 2024;36(6):465–473. **9.** Wardell SE, et al. *Endocr Relat Cancer.* 2015;22:713-724. **10.** ClinicalTrials.gov. NCT06492616. **11.** Vidal M, et al. *Clin Cancer Res.* 2025;31(7):1223-1232. doi:10.1158/1078-0432.CCR-24-2460. **12.** Kaklamani VG, et al. ASCO 2023. Poster 291.

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