St. Gallen International Breast Cancer Conference 2025
Industry Satellite Symposium

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# Current and future treatment strategies for patients with ER+/HER2− early breast cancer

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# Faculty

## Professor Michael Gnant

Medical University of Vienna, Austria

Full Professor of Surgery at the Medical University of Vienna, Austria, where he also serves as President of the Austrian Breast and Colorectal Cancer Study Group. He has been co-chairing and hosting St. Gallen International Consensus Panel for Early Breast Cancer since 2015 and is involved in many scientific societies including ASCO, AACR, ACS, BIG, EORTC, ESSO, EUSOMA, and UICC.

## Professor Giuseppe Curigliano

University of Milan, Italy

Director of the Early Drug Development Division and Co-Chair for the Experimental Therapeutics Program at the European Institute of Oncology, a comprehensive cancer center in Milan, Italy. He is a steering committee member of the Department of Oncology and Hemato-Oncology at the University of Milan. Moreover, he is a member of the Italian National Health Council, serving as an adviser to the Ministry of Health for cancer policy issues.

# Acknowledgement and disclosures

This symposium has been sponsored by Menarini Stemline and is intended for healthcare professionals only

**Expert disclosures**

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# Current and future treatment strategies for patients with ER+/HER2− early breast cancer

| Time | Title | Presenter |
|---|---|---|
| 08:00–08:10 | Definition of risk of recurrence in ER+/HER2− early breast cancer | Prof. Michael Gnant |
| 08:10–08:35 | Treatment landscape and future strategies for ER+/HER2− early breast cancer | Prof. Giuseppe Curigliano |
| 08:35–08:45 | Discussion and Q&A | Prof. Michael Gnant |

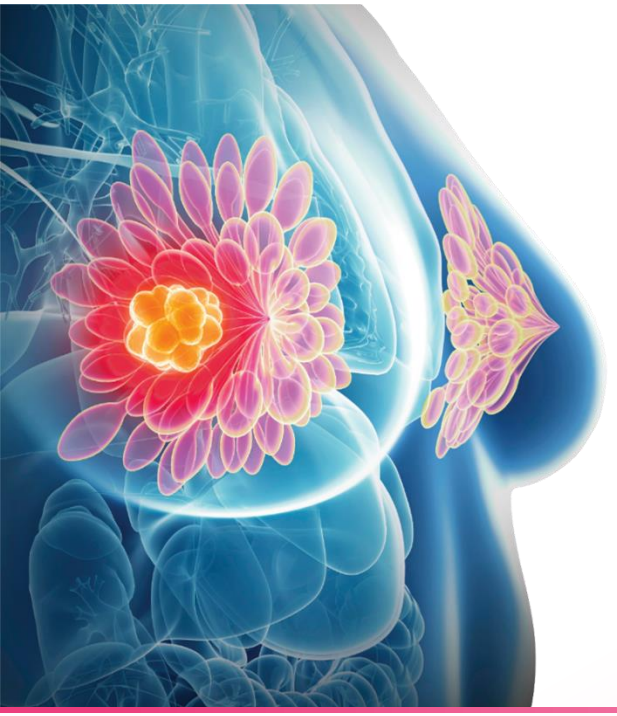


ER, estrogen receptor; HER2, human epidermal growth factor receptor 2.

# Housekeeping

Please keep your cell phone on silent mode

There will be an opportunity to ask the faculty questions during the discussion at the end of the symposium



# Definition of risk of recurrence in ER+/HER2− early breast cancer

**Prof. Michael Gnant**
Medical University of Vienna, Austria

ER, estrogen receptor; HER2, human epidermal growth factor receptor 2.

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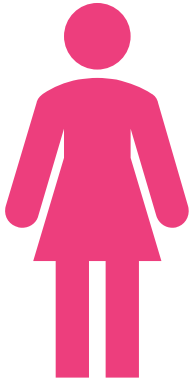
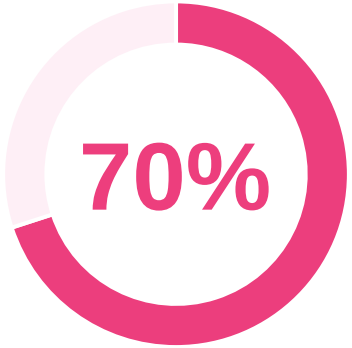
# Despite treatment advances in breast cancer, recurrence remains a challenge in the early setting

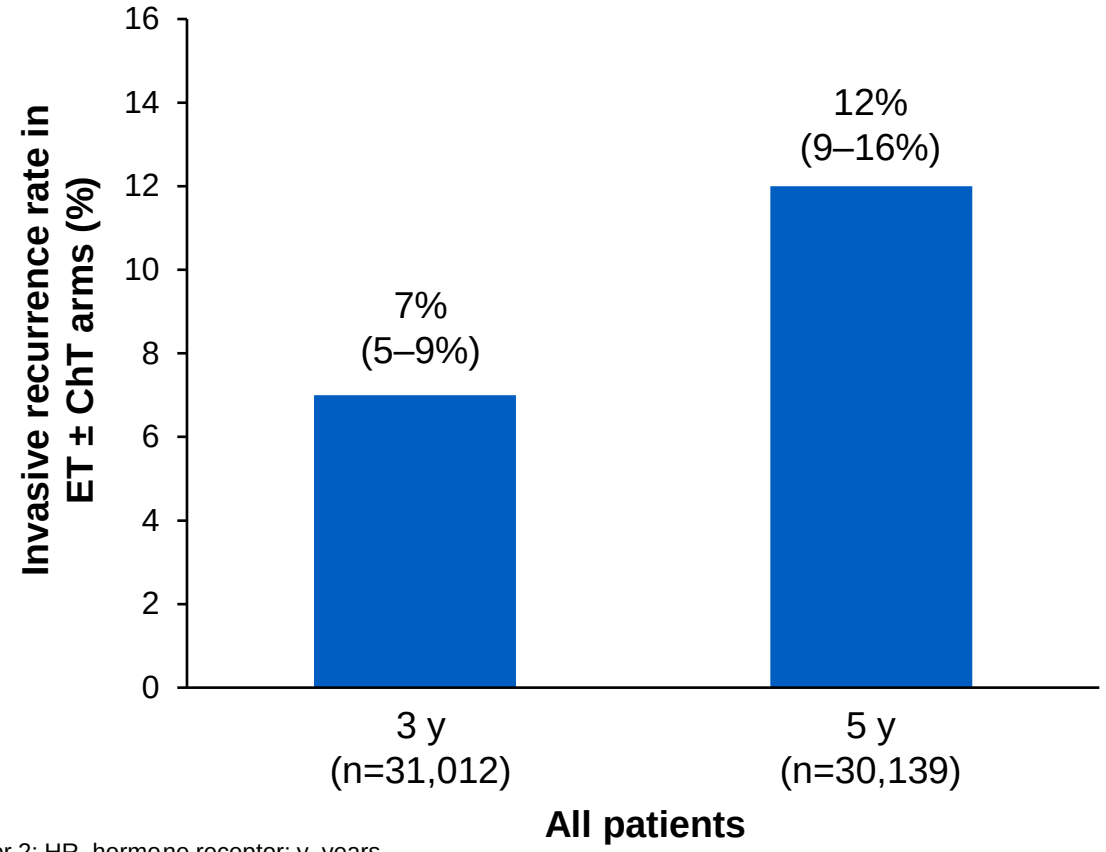


Breast cancer is one of the most diagnosed cancers globally, representing nearly **12% of all new cancer cases**, and is a **leading cause of cancer-related deaths among women**[1]




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

A meta-analysis of published adjuvant ET ± ChT trials in HR+/HER2− eBC demonstrated that early **risk of recurrence**[a] **is considerable and accumulates over time**[2]



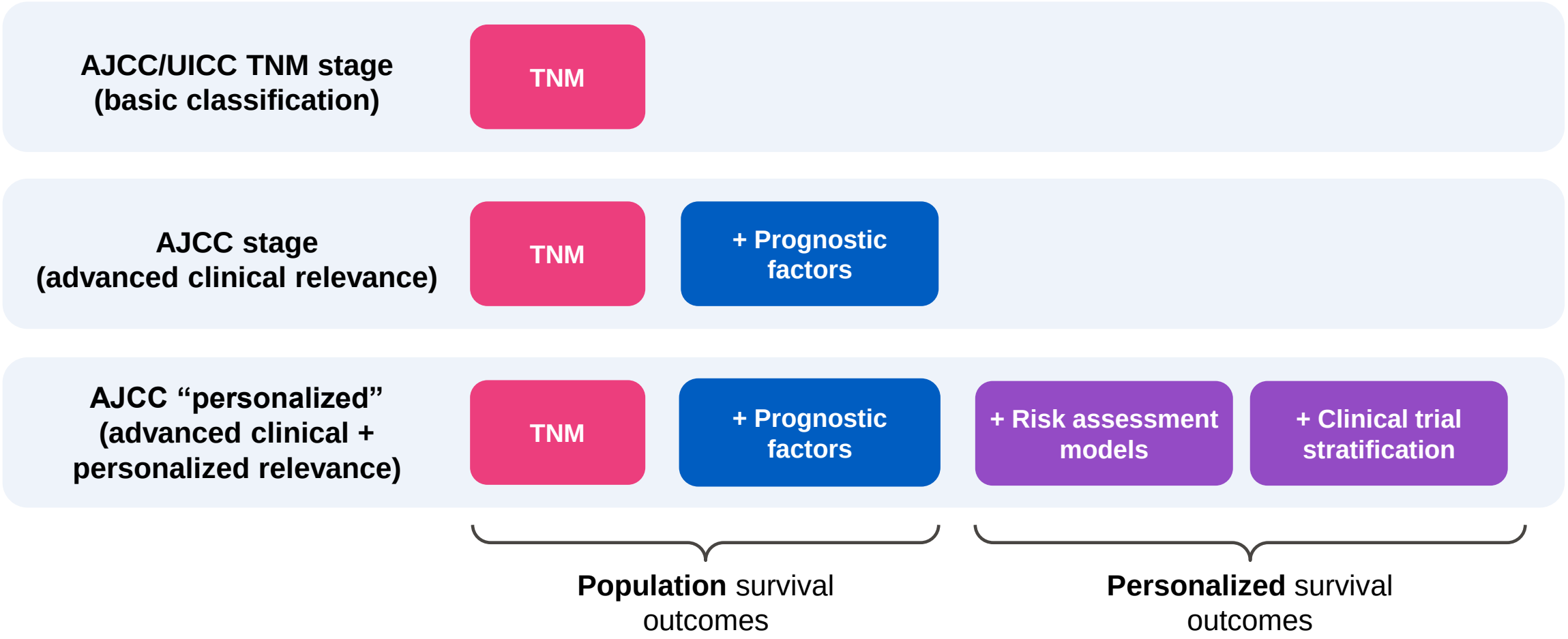

[a]ET ± ChT control arms (study arms excluded).

ChT, chemotherapy; eBC, early breast cancer; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; y, years.



1. Loibl S, et al. *Ann Oncol.* 2024;35(2):159–182. 2. Curigliano G, et al. ASCO 2024. Abstract 541.

# Early breast cancer classification has evolved from a “population” approach to a more “personalized” approach[1]




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

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

# IRIDE working group consensus: 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 |

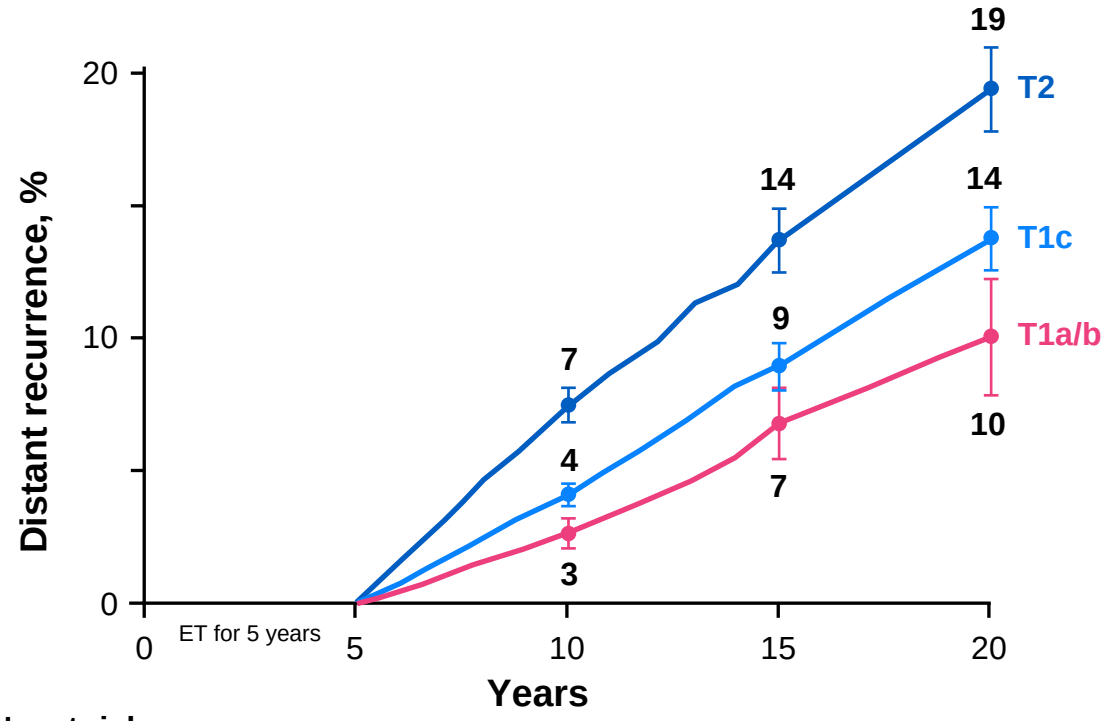
Intermediate risk is defined as N0[a] disease with G1/2 and T2–T3 or G3 and T1c–T3, or as N1 disease with G1 and T2 or G2 and T0–T2[2]

[a]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; n/a not available; PgR, progesterone receptor; RCB, residual cancer burden.


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).

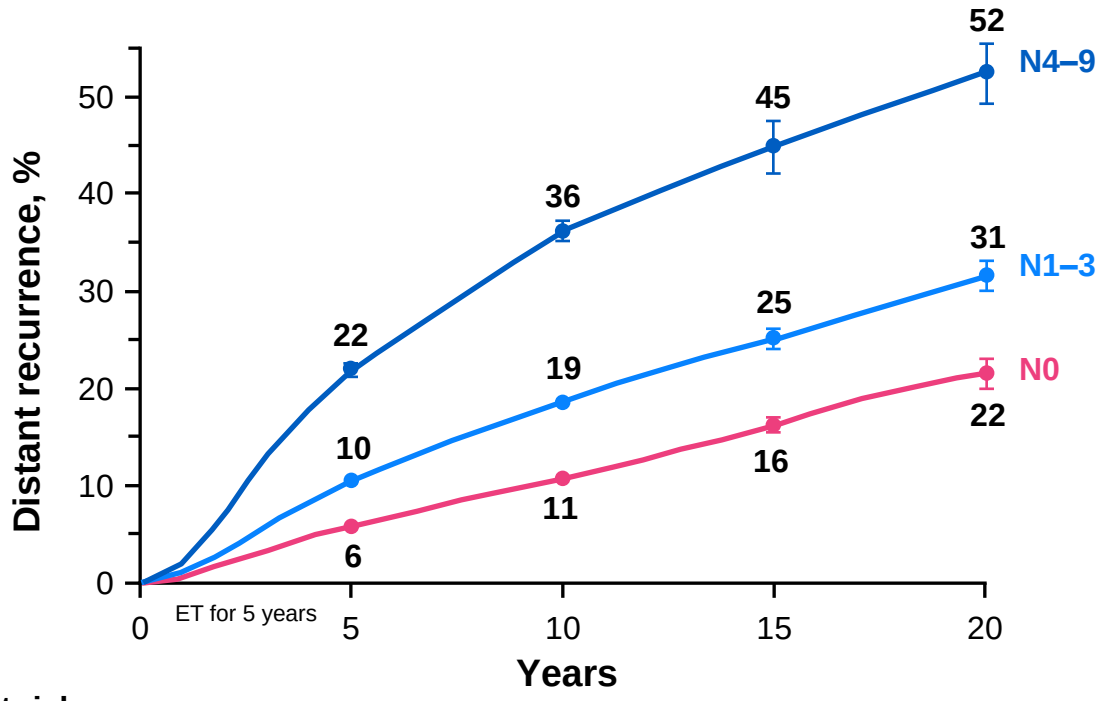
# The risk of distant recurrence is positively correlated with increased tumor size and nodal involvement[1]

## Tumor size[a]




| 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 |

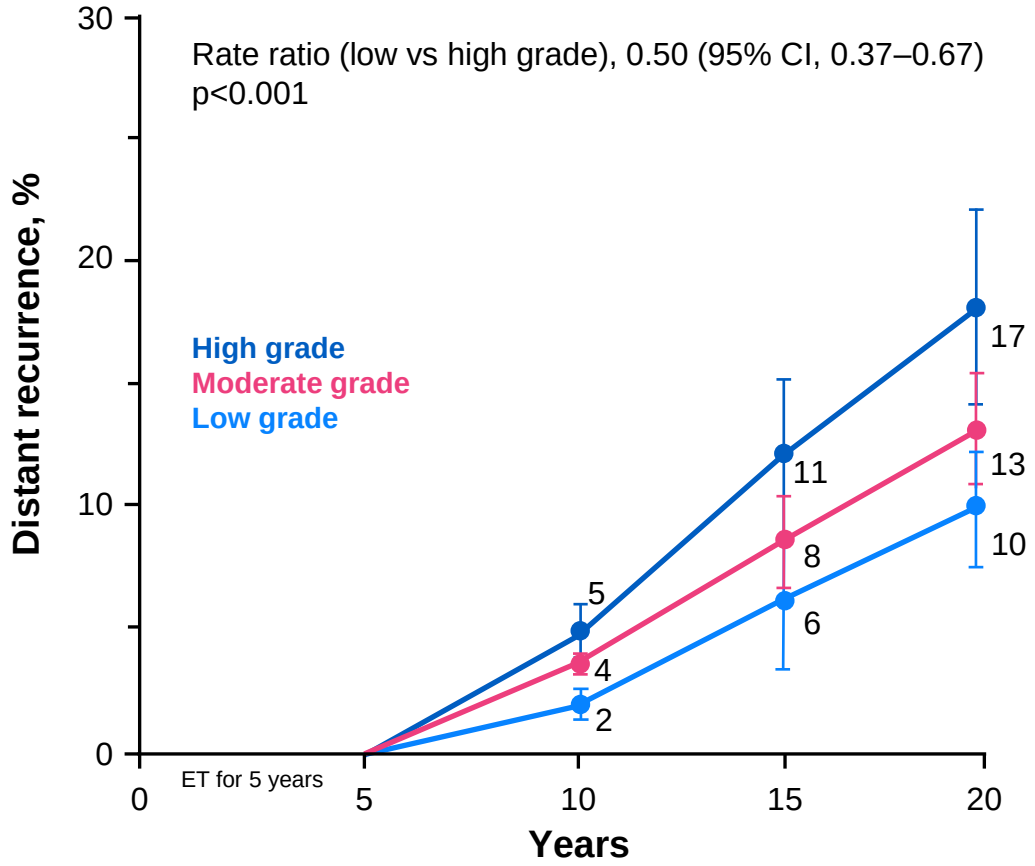
[a]In N0 disease.

ET, endocrine therapy; N, number of nodes involved; T, tumor size.

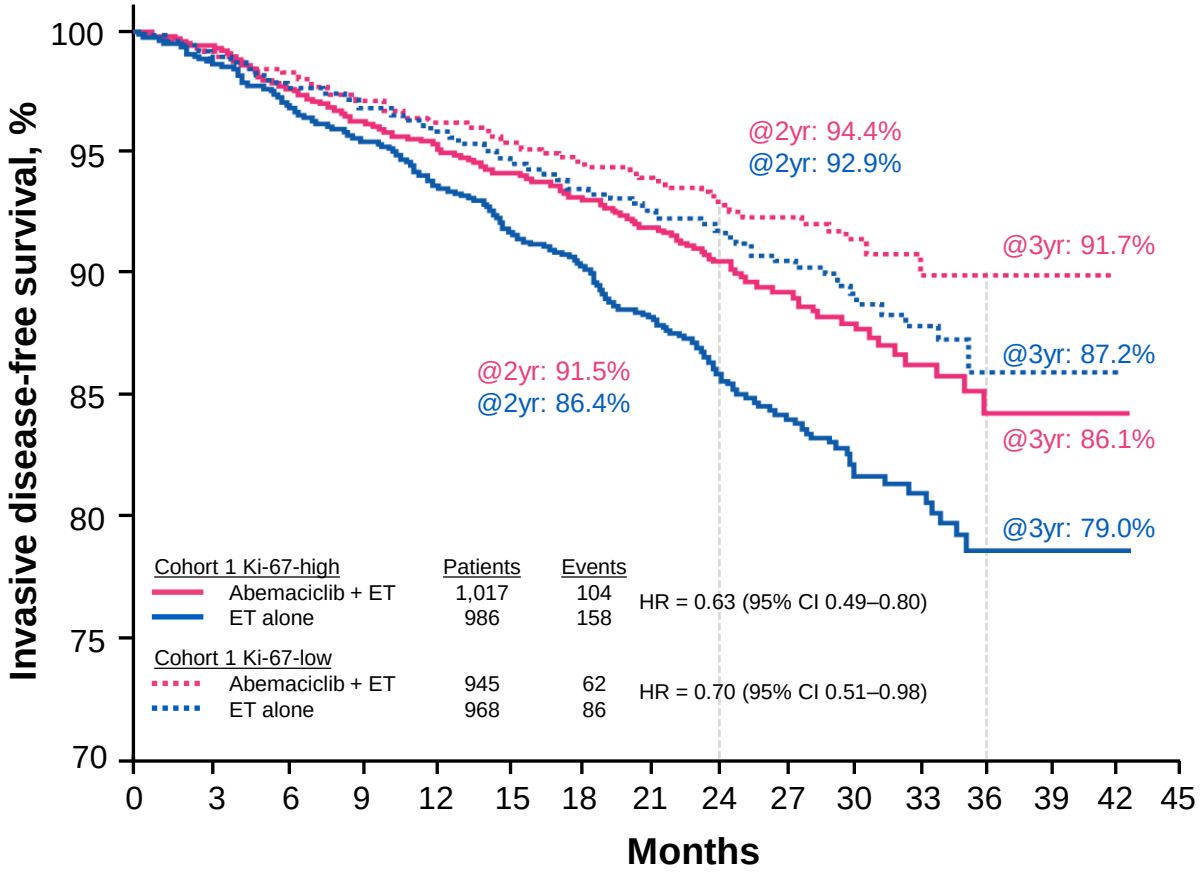
1. Adapted from: Pan H, et al. *N Engl J Med*. 2017;377(19):1836–1846 (including supplementary data).

# The risk of recurrence is positively correlated with increased tumor grade and Ki-67 status[1,2]

## Tumor grade[1]




## Ki-67[2,a]

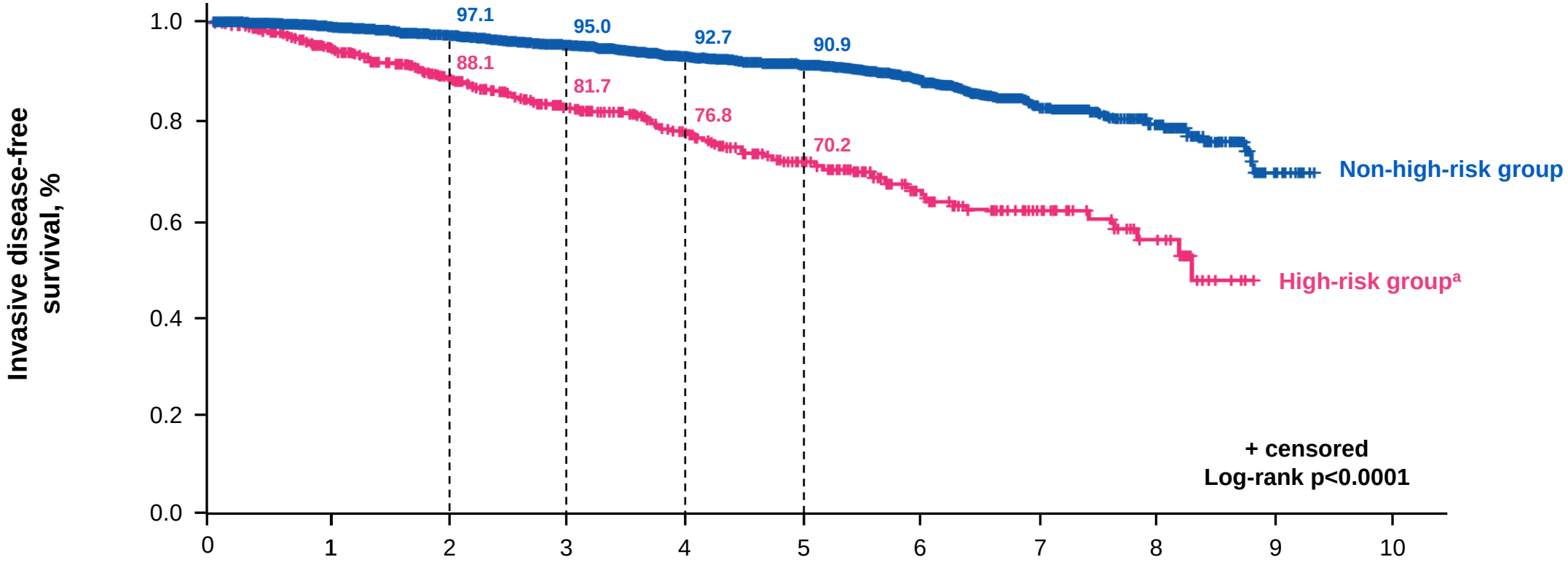



[a]MonarchE Kaplan–Meier curve in Cohort 1 Ki-67 high versus Ki-67 low at additional follow-up 1.
CI, confidence interval; ET, endocrine therapy; HR, hazard ratio; yr, year rate

1. Pan H, et al. *N Engl J Med.* 2017;377:1835–1846. 2. Harbeck N, et al. *Ann Oncol.* 2021;32(12):1571–1581.

# RWE: risk of recurrence was significantly greater in the high-risk vs non-high-risk group, highlighting the need for better therapies

**Invasive disease-free survival for the high-risk vs non-high-risk[a] groups[1]**



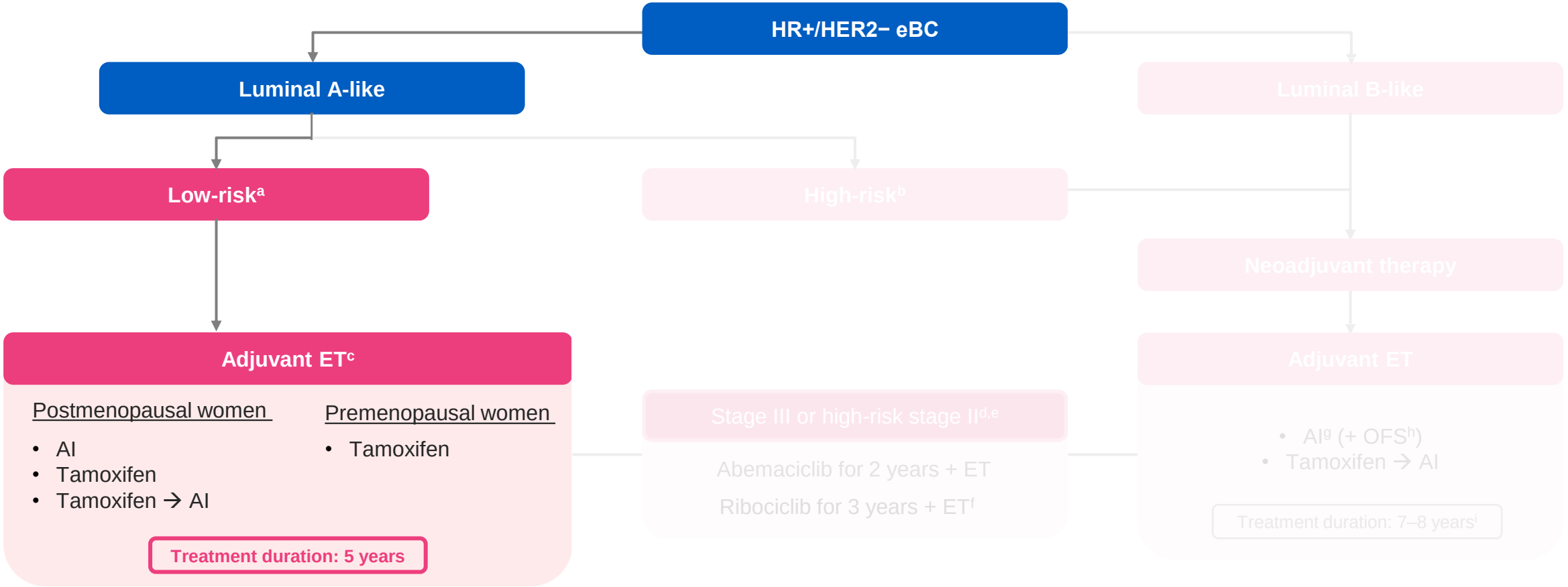

| No. at risk | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| High-risk group | 557 | 466 | 368 | 274 | 206 | 148 | 86 | 47 | 21 | 0 |
| Non-high-risk group | 3,471 | 2,923 | 2,317 | 1,816 | 1,364 | 897 | 516 | 278 | 120 | 18 | 0 |

[a]High-risk tumors identified using inclusion criteria from the monarchE trial.
RWE, real-world evidence.



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

# Decision-making in the treatment of ER+/HER2− early breast cancer is based on the risk of recurrence[1]

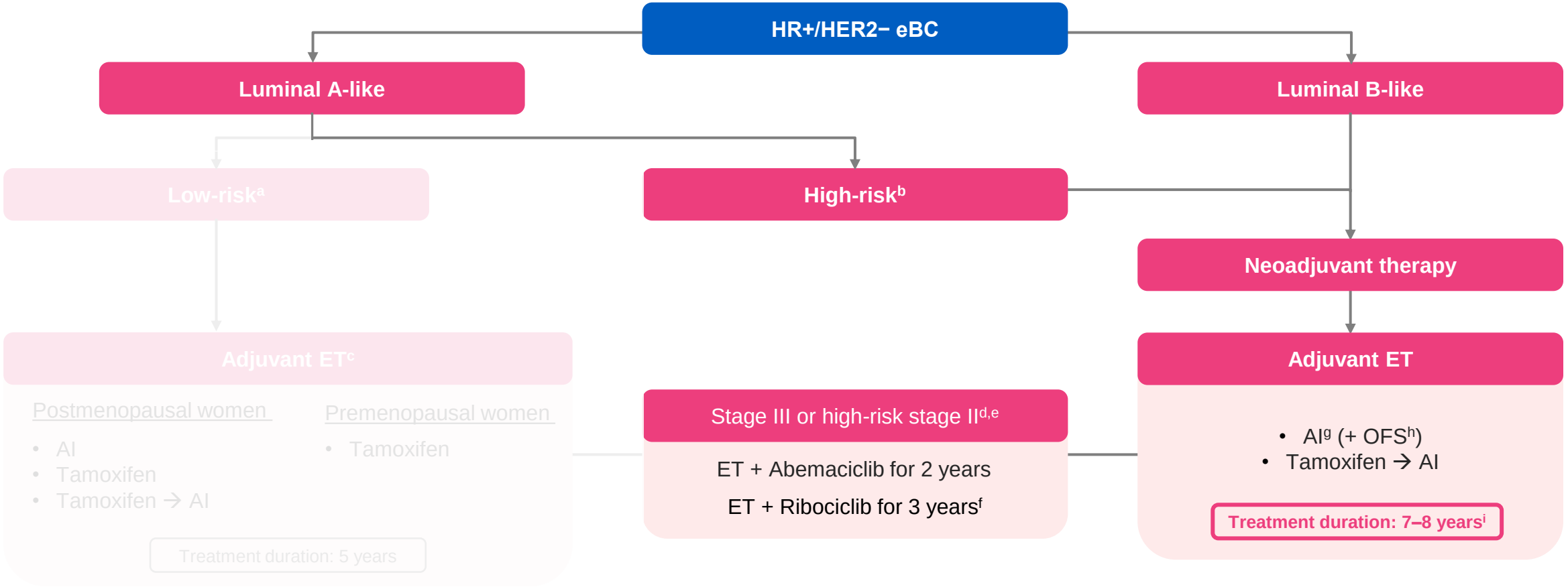



[a]"Low risk" implies low-risk genomic score (preferred) and/or lower-risk features on traditional pathological analysis, including lower-grade histology, robust ER and PgR expression, and lower measures of proliferation. [b]"High risk" implies high-risk genomic score and/or higher-risk features on traditional pathological analysis, including higher-grade histology, lower ER expression, and higher measures of proliferation. [c]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). [d]Stage N1 with primary tumor >5 cm, and/or grade 3 and/or Ki-67 ≥20%. [e]g*BRCA1/2*-wt or untested. [f]Ribociclib has been approved by regulatory agencies in this setting but has not yet been added to the official ESMO living guidelines. [g]Tamoxifen can be given if AIs are not tolerated. [h]If patient is premenopausal. [i]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; g*BRCA1/2*, germline *BRCA1/2*; HER2, human epidermal growth factor receptor 2; OFS, ovarian function suppression; PgR, progesterone receptor; wt, wild type.

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

# Treatment is intensified in adjuvant settings for tumors with high-risk characteristics[1]




[a]"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. [b]"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. [c]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). [d]Stage N1 with primary tumor >5 cm, and/or grade 3 and/or Ki-67 ≥20%. [e]g*BRCA1/2*-wt or untested. [f]Ribociclib has been approved by regulatory agencies in this setting but has not yet been added to the official ESMO living guidelines. [g]Tamoxifen can be given if AIs are not tolerated. [h]If patient is premenopausal. [i]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; g*BRCA1/2*, germline *BRCA1/2*; HER2, human epidermal growth factor receptor 2; OFS, ovarian function suppression; PgR, progesterone receptor; wt, wild type.

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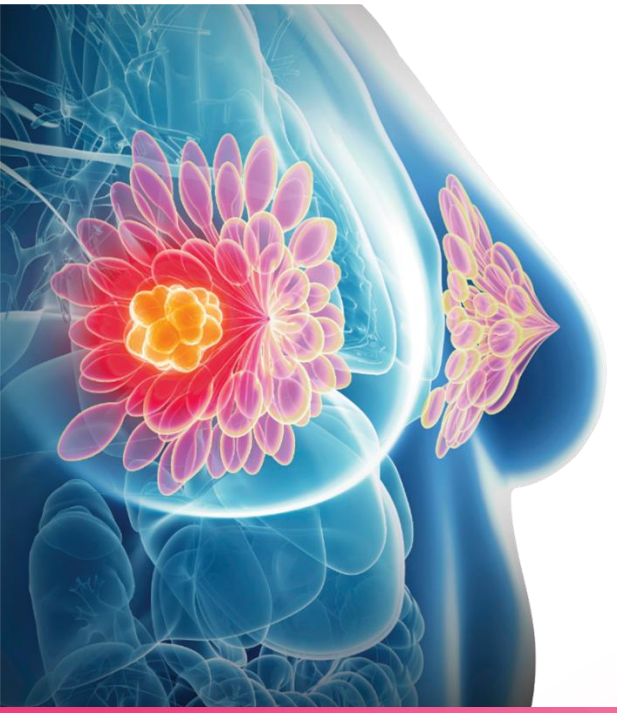

# Treatment landscape and future strategies for ER+/HER2− early breast cancer

**Prof. Giuseppe Curigliano**
University of Milan, Italy

ER, estrogen receptor; HER2, human epidermal growth factor receptor 2

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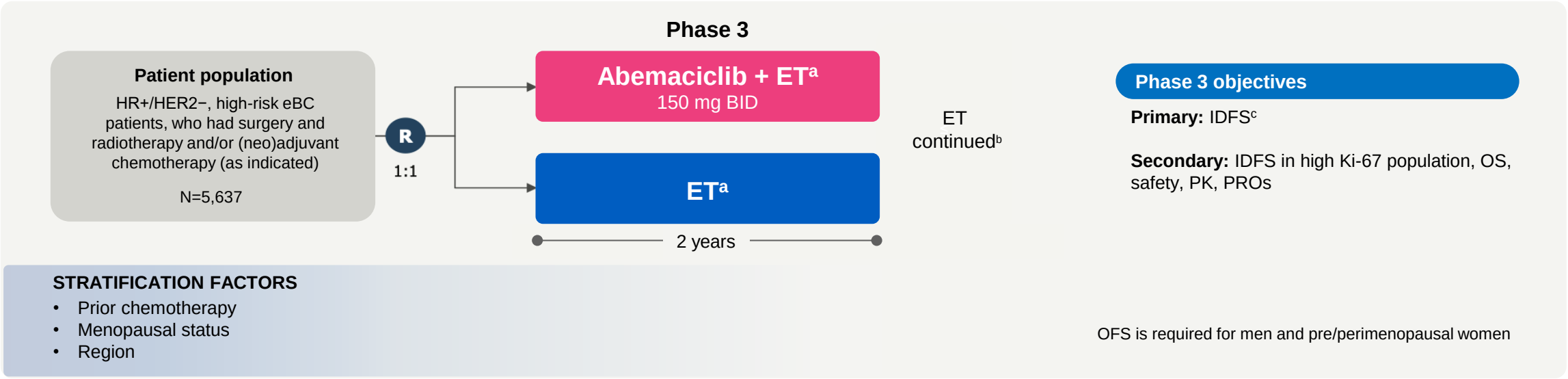
# The monarchE trial assessed the addition of abemaciclib to ET for 2 years in patients with node-positive high-risk HR+/HER2− eBC[1,2]




## 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 one of the following: ≥4 positive ALN; tumor size ≥5 cm; grade 3 tumor; Ki-67 ≥20%
- Patients may have received up to 12 weeks of ET
- ECOG PS of ≤1

## KEY EXCLUSION CRITERIA

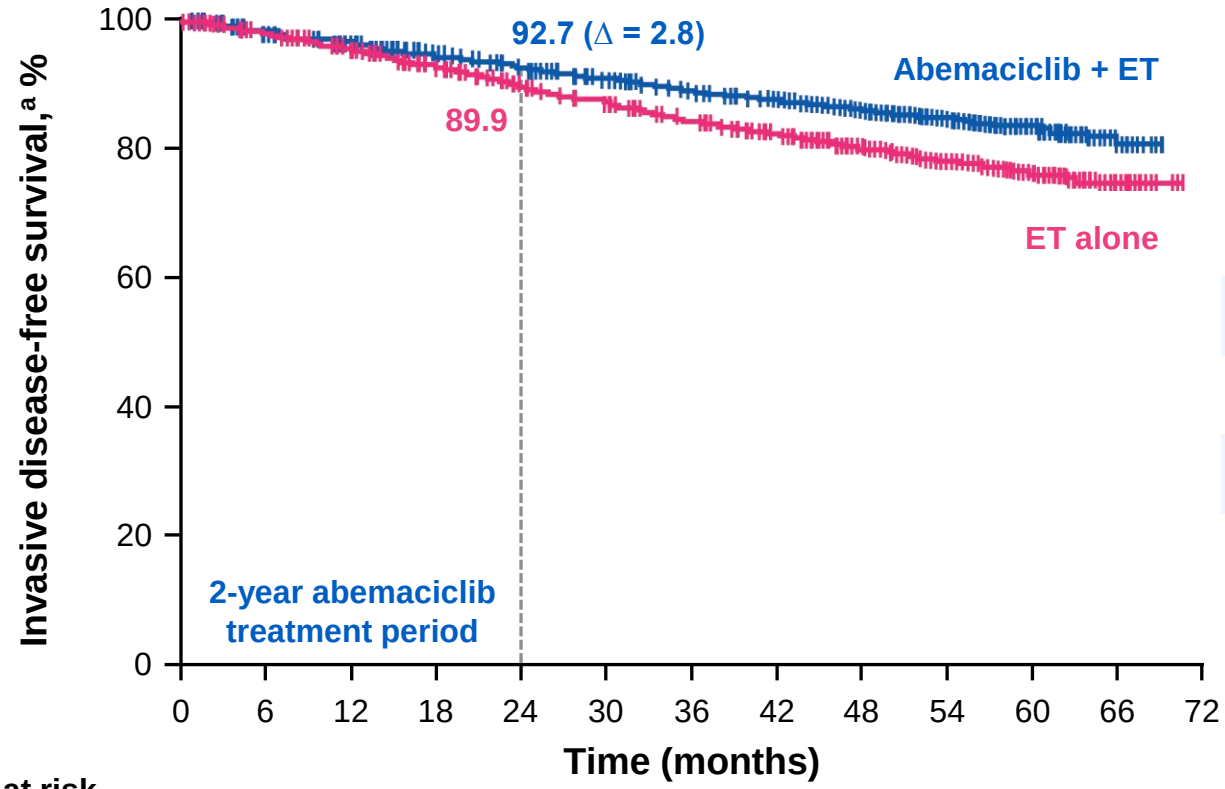
- Metastatic disease (incl contralateral ALNs) node-negative BC
- Inflammatory BC
- Previous treatment with any CDK4/6i
- Previously receiving ET for BC prevention
- Received an experimental treatment in a clinical trial within the past 30 days or five half-lives, whichever is longer
- History of venous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

[a]Endocrine therapy (physician's choice) standard-of-care was administered according to package label until discontinuation criteria were met. [b]ET continued for 3–8 years as clinically indicated. [c]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; OFS, ovarian function suppression; OS, overall survival; PK, pharmacokinetics; PROs, patient-reported outcomes; STEEP, Standardized Definitions for Efficacy End Points system.



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

# monarchE: 2 years of adjuvant abemaciclib + ET demonstrated sustained IDFS benefit in ITT[1]




| | 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, %[b]** | 83.6 | 76.0 | 7.6 |

**[b]HR (95% CI): 0.68 (0.60–0.77)**

At OS, IA3 statistical significance was not reached for OS

[a]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.

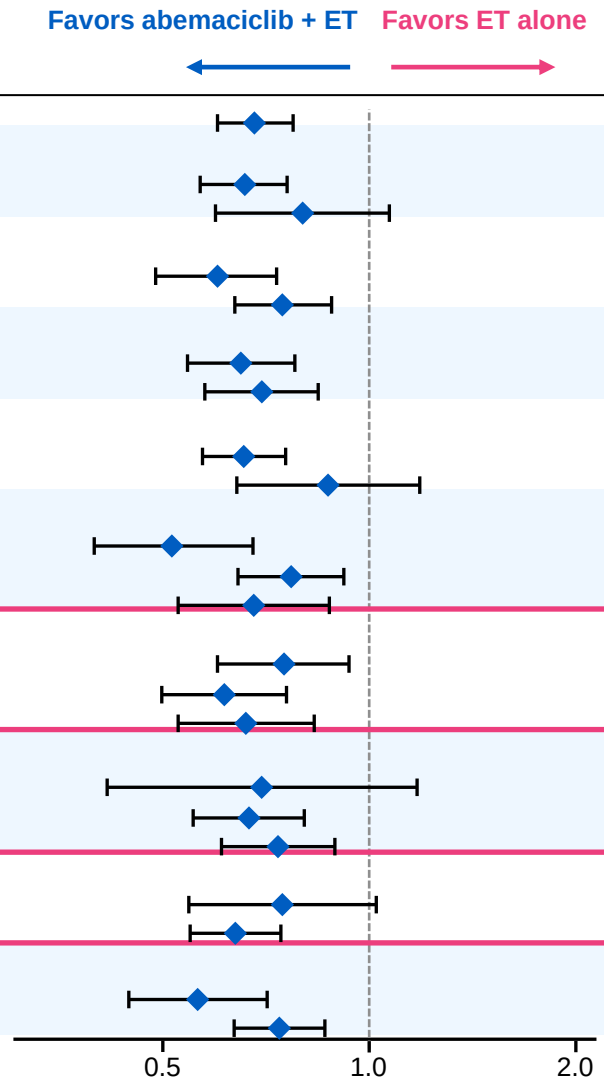
CI; confidence interval; ET, endocrine therapy; HR, hazard ratio; IA3, third interim analysis; IDFS, invasive disease-free survival; ITT, intention-to-treat; OS, overall survival; STEEP, Standardized Definitions for Efficacy End Points system.



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

# monarchE: consistent IDFS benefit observed in selected subgroups with no benefit for stage II patient population[1]

| | Abemaciclib + ET No. | Abemaciclib + ET Events | ET alone No. | ET alone 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 – mod 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; HR, hazard ratio; IDFS, invasive disease-free survival; IWRS, interactive web response system.

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

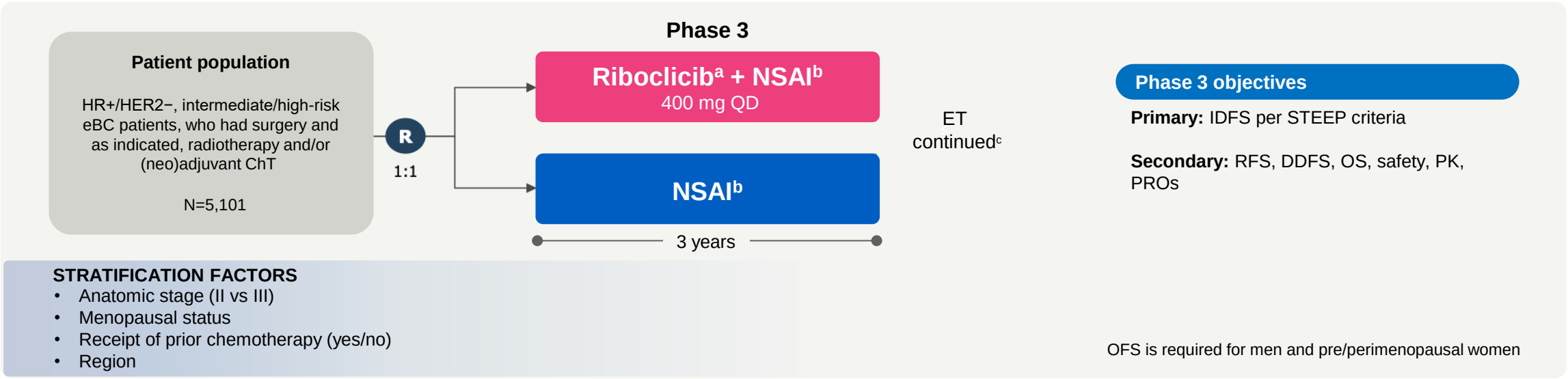
# monarchE: safety was consistent with the known profile of abemaciclib[1]

| | Abemaciclib + ET (n=2,791) | | | ET alone (n=2,800) | | |
|---|---|---|---|---|---|---|
| **≥15% any grade in either arm** | **Any grade** | **Grade 3** | **Grade 4** | **Any grade** | **Grade 3** | **Grade 4** |
| **Any adverse event** | 2,731 (97.9) | 1,200 (43.0) | 70 (2.5) | 2,410 (86.1) | 335 (12.0) | 19 (0.7) |
| **Diarrhea** | 2,294 (82.2) | 212 (7.6) | 0 | 199 (7.1) | 3 (0.1) | 0 |
| **Neutropenia** | 1,246 (44.6) | 501 (18.0) | 18 (0.6) | 141 (5.0) | 16 (0.6) | 3 (0.1) |
| **Fatigue** | 1,073 (38.4) | 78 (2.8) | 0 | 433 (15.5) | 4 (0.1) | 0 |
| **Leukopenia** | 1,027 (36.8) | 301 (10.8) | 4 (0.1) | 171 (6.1) | 10 (0.4) | 0 |
| **Abdominal pain** | 948 (34.0) | 37 (1.3) | 0 | 227 (8.1) | 9 (0.3) | 0 |
| **Nausea** | 779 (27.9) | 13 (0.5) | 0 | 223 (8.0) | 1 (0.0) | 0 |
| **Anemia** | 638 (22.9) | 47 (1.7) | 1 (0.0) | 90 (3.2) | 9 (0.3) | 1 (0.0) |
| **Arthralgia** | 571 (20.5) | 6 (0.2) | 0 | 876 (31.3) | 18 (0.6) | 0 |
| **Vomiting** | 455 (16.3) | 13 (0.5) | 0 | 117 (4.2) | 2 (0.1) | 0 |
| **Headache** | 482 (17.3) | 6 (0.2) | 0 | 359 (12.8) | 3 (0.1) | 0 |

ET, endocrine therapy.

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

# The NATALEE trial assessed the addition of ribociclib to NSAI for 3 years in patients with stage II or III HR+/HER2− eBC[1-4]




## 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/m$^2$ for doxorubicin or of ≥900 mg/m$^2$ 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

[a]Three weeks on, one week off. [b]Administered according to package label until discontinuation criteria were met. [c]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; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IDFS, invasive disease-free survival; NSAI, non-steroidal aromatase inhibitors; OFS, ovarian function suppression; OS, overall survival; PK, pharmacokinetics; PRO, patient reported outcomes; QD, once daily; RFS, recurrence-free survival; SOC, standard of care.

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

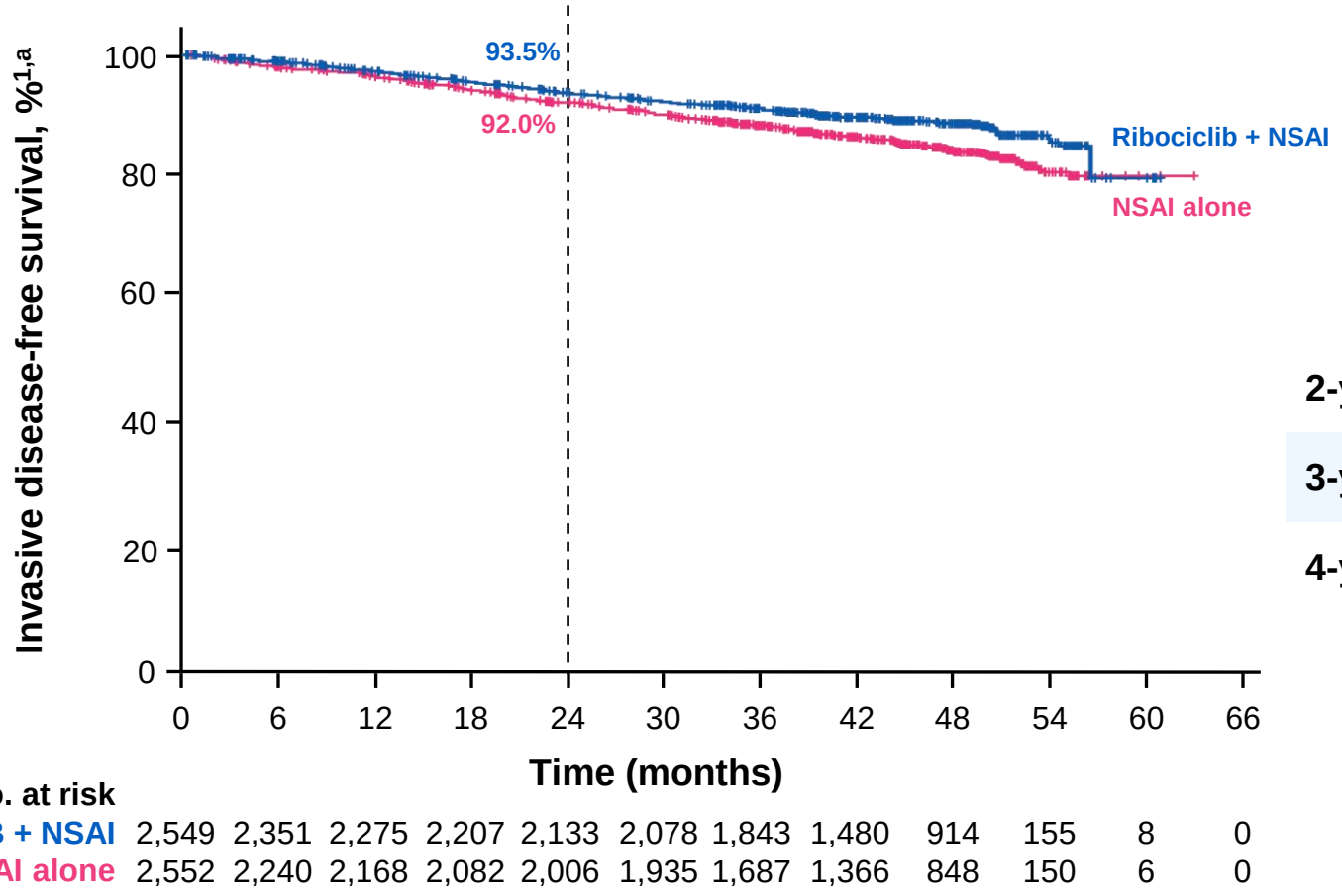
# NATALEE includes node-negative patients and a broader population of patients with stage II and III disease compared with monarchE[1,a]

| AJCC anatomical staging | TN (M0) | NATALEE | monarchE |
|---|---|---|---|
| **Stage IIA** | T0 N1 | Y | Grade 3 or Ki-67 ≥ 20% |
| | T1 N1 | Y | Grade 3 or Ki-67 ≥ 20% |
| | T2 N0 | G3 or G2 with Ki-67 ≥20% or high genomic risk[b] | N |
| **Stage IIB** | T2 N1 | Y | Grade 3 or Ki-67 ≥ 20% |
| | T3 N0 | Y | N |
| **Stage IIIA** | T0 N2 | Y | Y |
| | T1 N2 | Y | Y |
| | T2 N2 | Y | Y |
| | T3 N1 | Y | Y |
| | T3 N2 | Y | Y |
| **Stage IIIB** | T4 N0 | Y | N |
| | T4 N1 | Y | Tumor size ≥5 cm or grade 3 or Ki-67 ≥20% |
| | T4 N2 | Y | Y |
| **Stage IIIC** | Any TN3 | Y | Y |

[a]Choice of therapy will depend on approval, access, risk, long-term efficacy, safety profile, and patient preference. [b]High risk as determined by Oncotype DX, Prosigna PAM50, MammaPrint, or EndoPredict EPclin Risk Score.
AJCC, American Joint Committee on Cancer; G, grade; M, metastasis; N, node status; T, tumor size.

1. Slamon DJ, et al. *Ther Adv Med Oncol.* 2023;15:17588359231178125.

# NATALEE: ribociclib + NSAI demonstrated sustained IDFS benefit in ITT




| | 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,b]** | 88.5 | 83.6 | 4.9 |

**[b]HR (95% CI): 0.72 (0.61–0.84)[2]**

Adapted from references 1 and 2.

[a]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.

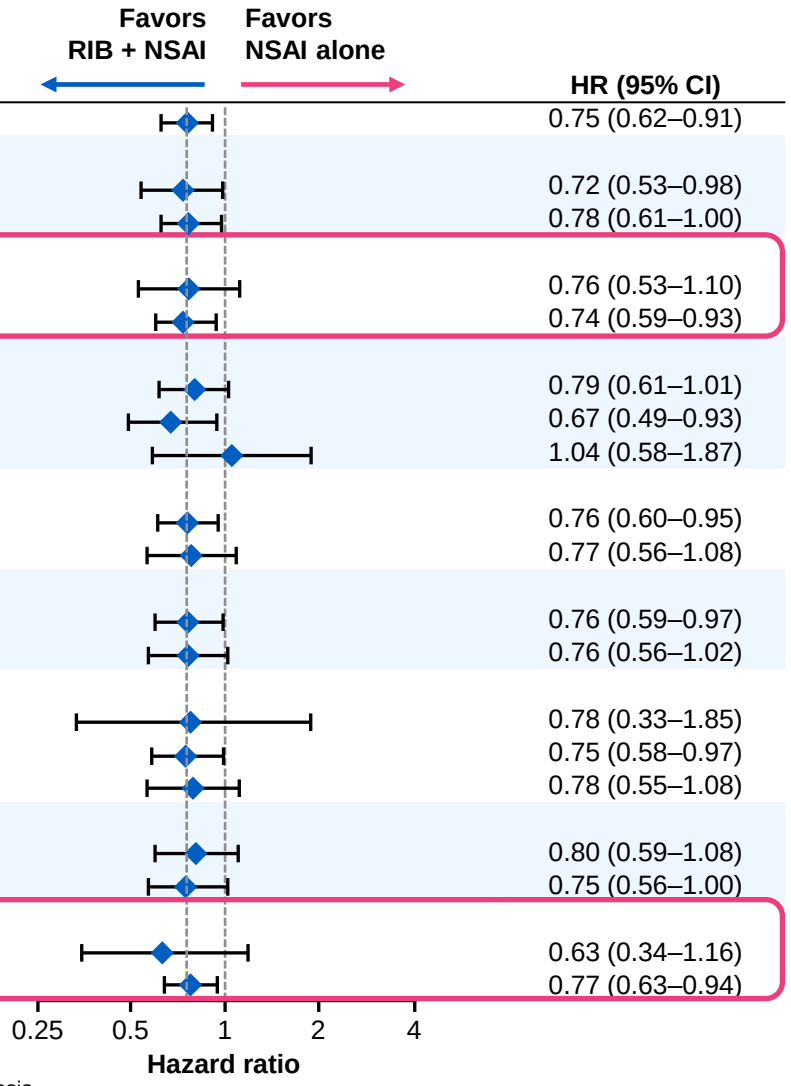
CI, confidence interval; HR, hazard ratio; IDFS, invasive disease-free survival; ITT, intention-to-treat; NSAI, non-steroidal aromatase inhibitors; RIB, ribociclib; STEEP, Standardized Definitions for Efficacy End Points system.



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

# NATALEE: consistent IDFS benefit observed in selected subgroups with no benefit in stage II and N0 patient population[1]

| Subgroup | RIB + NSAI n=2,549 Events/n | RIB + NSAI n=2,549 3-y IDFS rate, % | NSAI alone n=2,552 Events/n | NSAI alone n=2,552 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[a]** | | | | | |
| 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[b,c]** | | | | | |
| 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) |




[a]From archival tumor tissue. [b]Nodal status classification according to AJCC staging. [c]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, node; NSAI, non-steroidal aromatase inhibitor; RIB, ribociclib.

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

# NATALEE: the 3-year regimen of ribociclib at a 400 mg starting dose plus an NSAI was not associated with new safety signals[1]

| | Ribociclib + NSAI (N=2,524) | | | | NSAI alone (N=2,444) | | | |
|---|---|---|---|---|---|---|---|---|
| **Event** | **All grades** | **Grade 3** | **Grade 4** | **Grade 5** | **All grades** | **Grade 3** | **Grade 4** | **Grade 5** |
| **Any adverse event, n (%)** | 2,470 (97.9) | 1,437 (56.9) | 130 (5.2) | 12 (0.5) | 2,128 (87.1) | 394 (16.1) | 38 (1.6) | 4 (0.2) |
| **Adverse events that occurred in ≥15% of patients in either group, n (%)** | | | | | | | | |
| Neutropenia[a] | 1,568 (62.1) | 1,054 (41.8) | 52 (2.1) | 0 | 110 (4.5) | 17 (0.7) | 3 (0.1) | 0 |
| Arthralgia | 921 (36.5) | 24 (1.0) | 0 | 0 | 1,038 (42.5) | 31 (1.3) | 0 | 0 |
| Nausea | 580 (23.0) | 6 (0.2) | 0 | 0 | 184 (7.5) | 1 (<0.1) | 0 | 0 |
| Headache | 556 (22.0) | 10 (0.4) | 0 | 0 | 403 (16.5) | 4 (0.2) | 0 | 0 |
| Fatigue | 554 (21.9) | 18 (0.7) | 0 | 0 | 311 (12.7) | 4 (0.2) | 0 | 0 |
| SARS-CoV-2 test positive | 487 (19.3) | 0 | 0 | 0 | 310 (12.7) | 0 | 0 | 0 |
| Covid-19 | 477 (18.9) | 18 (0.7) | 0 | 3 (0.1) | 314 (12.8) | 11 (0.5) | 0 | 1 (<0.1) |
| Alanine aminotransferase increased | 478 (18.9) | 154 (6.1) | 31 (1.2) | 0 | 128 (5.2) | 15 (0.6) | 1 (<0.1) | 0 |
| Hot flush | 473 (18.7) | 6 (0.2) | 0 | 0 | 482 (19.7) | 3 (0.1) | 0 | 0 |
| Asthenia | 417 (16.5) | 15 (0.6) | 0 | 0 | 273 (11.2) | 3 (0.1) | 0 | 0 |
| Aspartate aminotransferase increased | 408 (16.2) | 96 (3.8) | 16 (0.6) | 0 | 131 (5.4) | 12 (0.5) | 0 | 0 |

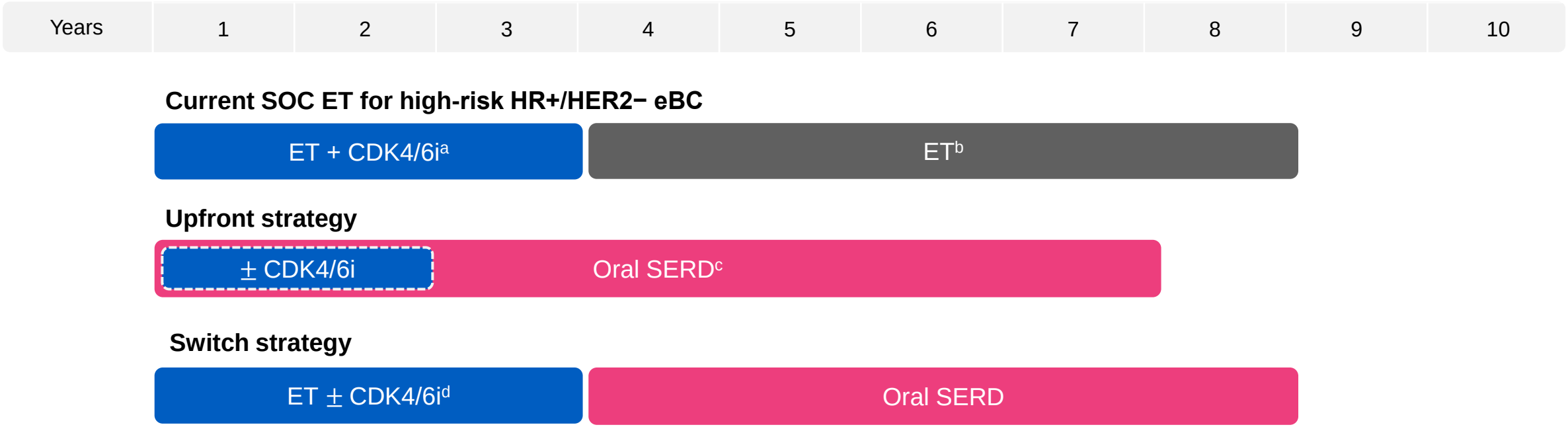
[a]Neutropenia is a grouped term that combines the preferred terms neutropenia and neutrophil count decreased.

Covid-19, coronavirus disease 2019; NSAI, non-steroidal aromatase inhibitor; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

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

# A new 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 two 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.**

[a]Patients may receive 2 or 3 years of CDK4/6i depending on whether they are treated with abemaciclib or ribociclib, respectively. [b]Patients may receive up to 10 years adjuvant treatment, although 7–8 years are usually sufficient per current ESMO guidelines. [c]Patients may receive 5 or 7 years of oral SERD therapy depending on whether they are treated with giredestrant or camizestrant, respectively. [d]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.

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.

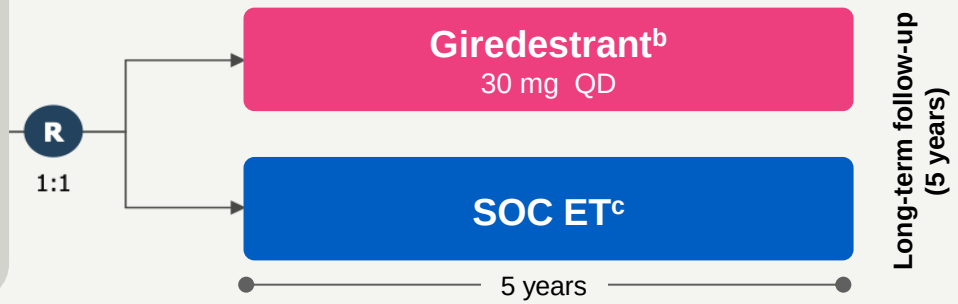
# The lidERA trial is evaluating upfront giredestrant as single-agent adjuvant therapy in intermediate/high-risk ER+/HER2− eBC[1-3]

Upfront strategy | Intermediate/high risk

**Patient population**

Intermediate/high-risk stage I–III ER+/HER2− eBC who had prior surgery with curative intent and completed (neo)adjuvant ChT (if administered) and/or surgery <12 months prior to enrollment; ≤12 weeks of prior ET allowed

N=4,200




**Phase 3 objectives**

**Primary:** IDFS (excluding second primary non-BC), time from randomization to occurrence of IDFS event

**Secondary:** OS, IDFS[d] (including second primary non-BC), DFS, DRFI, LFRRI, safety, PK, and PROs

**STRATIFICATION FACTORS**

- Risk (intermediate vs high)[e]
- Prior chemotherapy (yes or no)
- Menopausal status
- Geographic region

OFS is required for men and pre/perimenopausal women

## KEY INCLUSION CRITERIA

- Patients with intermediate- or high-risk HR+/HER2− eBC (N0 and >T1c with G3 or Ki-67 ≥20% or Oncotype DX/MammaPrint high; N+)
- Participants who received adjuvant ChT must have completed a ≥21-day washout prior to randomization
- Undergone definitive surgery of primary breast tumor(s) with tumor-free margins
- ECOG PS 0–2

## KEY EXCLUSION CRITERIA

- Prior ET with a SERM, SERD, or AI (short course of ≤12 weeks of (neo)adjuvant ET is allowed)
- Receiving or planning to receive a CDK4/6i (short course of ≤12 weeks of neoadjuvant CDK4/6i prior to randomization is allowed)
- Stage IV (metastatic) BC
- Active cardiac disease or history of cardiac dysfunction
- Prior treatment with investigational therapy within 28 days prior to initiation of study treatment
- Prior history of invasive BC or DCIS

[a]This clinical trial is being conducted globally. [b]Administered orally. [c]Endocrine therapy (investigator's choice of tamoxifen, anastrozole, letrozole, or exemestane) is administered per local label. [d]Per STEEP criteria. [e]Patients are categorized as intermediate- or high-risk based on anatomical (tumor size, nodal status) and biological (grade, Ki-67, gene signatures [Oncotype DX or MammaPrint, if available]) features.

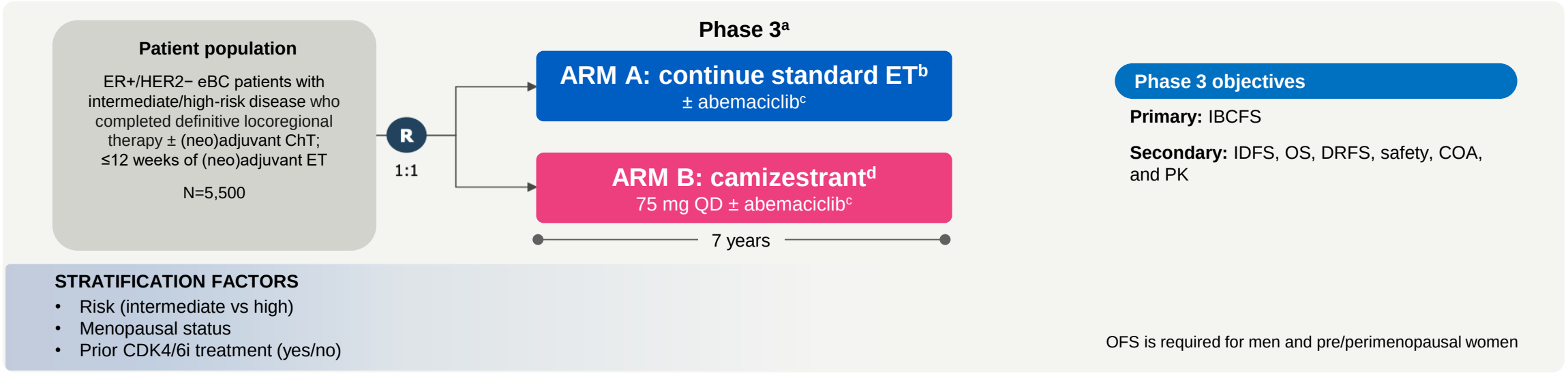
AI, aromatase inhibitor; BC, breast cancer; CDK4/6, cyclin-dependent kinase 4/6; ChT, chemotherapy; DCIS, ductal carcinoma *in situ*; DFS, disease-free survival; DRFI, distant recurrence-free interval; eBC, early breast cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; ER, estrogen receptor; ET, endocrine therapy; G, grade; HER2, human epidermal growth factor receptor 2; IDFS, invasive disease-free survival; LFRRI, locoregional-free recurrence rate at interval; N, node status; OFS, ovarian function suppression; OS, overall survival; PK, pharmacokinetics; PRO, patient-reported outcomes; QD, once daily; SERD, selective estrogen receptor degrader; SERM, selective estrogen receptor modulator; SOC, standard of care; STEEP, Standardized Definitions for Efficacy End Points system; T, tumor size.



1. ClinicalTrials.gov. NCT04961996. 2. Ascione L, et al. *Curr Opin Oncol*. 2024;36(6):465–473. 3. Geyer CE, et al. SABCS 2021. Abstract TPS616.

# The CAMBRIA-2 trial is evaluating upfront camizestrant (± abemaciclib) as adjuvant therapy in intermediate/high risk ER+/HER2− eBC[1-3]

Upfront strategy | Intermediate/high risk




## KEY INCLUSION CRITERIA

- Women and men; aged ≥18 years
- ER+/HER2− early-stage resected invasive BC with absence of any evidence of metastatic disease
- Intermediate or high risk of recurrence (T4; ≥2 ILN; T1c–T3 N0 [mic], or 1 LN and G3, or poor genomic risk, or Ki-67 ≥ 20%)
- Completed locoregional therapy ± (neo)adjuvant ChT
- Patients may have received up to 12 weeks of ET
- ECOG PS 0–1

## KEY EXCLUSION CRITERIA

- Inoperable locally advanced or metastatic BC
- Pathological complete response following neoadjuvant therapy
- Prior camizestrant, investigational SERD/ investigational ER targeting agents, or fulvestrant
- History of any other cancer (except non-melanoma skin cancer or carcinoma *in situ* of the cervix) unless in complete remission with no therapy for ≥5 years
- Any evidence of severe/uncontrolled systemic diseases

[a]The clinical trial study design presented aligns with clinical study protocol global amendment 2 v3 (July 20, 2023). [b]Endocrine therapy (investigator's choice of tamoxifen, anastrozole, letrozole, or exemestane) is administered per local label once daily. [c]Standard dose per approved local guidelines or per institutional SOC. [d]Administered orally.

BC, breast cancer; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; ChT, chemotherapy; COA, clinical outcome assessment; DRFS, distant relapse-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 2; IBCFS, invasive breast-cancer-free survival; IDFS, invasive disease-free survival; (I)LN, (ipsilateral) ymph node; mic, microinvasion; N, node; OFS, ovarian function suppression; OS, overall survival; PK, pharmacokinetics; QD, once daily; SERD, selective estrogen receptor degrader; SOC, standard of care; T, tumor.

1. ClinicalTrials.gov. NCT05952557. 2. ABCSG. CAMBRIA-2 study details. Available at:https ://www.abcsg.org/en/abcsg-studien/studies-open-for-enrollment/abcsg-62-cambria-2-2/abcsg-62-cambria-2-studiendetails (accessed on March 05, 2025).
3. Ascione L, et al. *Curr Opin Oncol*. 2024;36(6):465–473.

# The CAMBRIA-1 trial is evaluating camizestrant as single-agent therapy in intermediate/high risk ER+/HER2− eBC following 2–5yrs of adjuvant ET[1-3]

Switch strategy | Intermediate/high risk

**Patient population**

ER+/HER2− eBC patients with intermediate/high-risk disease who completed definitive locoregional therapy and standard adjuvant ET (± CDK4/6i) for 2–5 years (+ 3 mo) without recurrence

N=4,300

R 1:1

**Phase 3[a]**

**ARM A: continue standard ET[b]**

**ARM B: camizestrant[c]** 75 mg QD

5 years

**Phase 3 objectives**

**Primary:** IBCFS

**Secondary:** IDFS, OS, DRFS, safety, PK, and PROs

**STRATIFICATION FACTORS**

- Risk (intermediate vs high)
- Duration of prior adjuvant ET
- Menopausal status
- Prior adjuvant CDK4/6i (yes/no)

OFS is required for men and pre/perimenopausal women

## KEY INCLUSION CRITERIA

- Women or men aged ≥18 years
- Confirmed ER+/HER2− eBC without evidence of distant metastasis
- Receiving SOC adjuvant ET ≥24 mo but ≤60 mo
- Prior (neo)adjuvant CDK4/6i + ET is permitted but must be completed
- ECOG PS 0–1
- Considered at intermediate- or high-risk (≥T3 [T4d excluded]; ≥2 LN; T1c–T2 N0 [mic], or 1 LN and G3, or poor genomic risk, or Ki-67 ≥20%)

## KEY EXCLUSION CRITERIA

- Inoperable locally advanced BC or distant metastatic disease (including contralateral ALN)
- History of any other cancer (except non-melanoma skin cancer or *carcinoma in situ* of the cervix) unless in complete remission with no therapy for ≥5 years
- History of previous BC (except ipsilateral DCIS treated with locoregional therapy alone ≥5 years ago/contralateral DCIS treated with locoregional therapy at any time; patients must have completed ET ≥5 years prior to randomization)

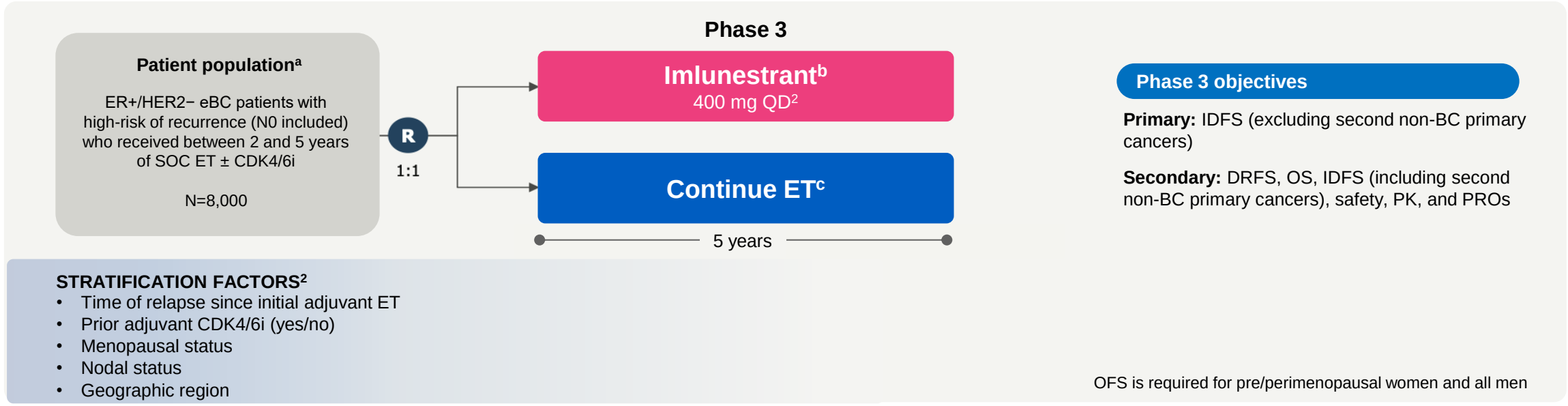
[a]The clinical trial study design presented aligns with clinical study protocol global amendment 2 v3 (July 20, 2023). [b]Endocrine therapy (investigator's choice of tamoxifen, anastrozole, letrozole, or exemestane) is administered per local label once daily. [c] Administered orally.

ALN, axillary lymph node; BC, breast cancer; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; DCIS, ductal carcinoma *in situ*; DRFS, distant relapse-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 2; IBCFS, invasive breast-cancer-free survival; IDFS, invasive disease-free survival; LN, lymph node; mic, microinvasion; mo, months; , node status; OFS, ovarian function suppression; OS, overall survival; PK, pharmacokinetics; PROs, patient-reported outcomes; QD, once daily; SOC, standard of care; T, tumor size.

1. ClinicalTrials.gov. NCT05N774951. 2. Ascione L, et al. *Curr Opin Oncol*. 2024;36(6):465–473. 3. Hamilton EP, et al. ESMO 2023. Abstract 354TiP.

# The EMBER-4 trial is evaluating imlunestrant as single-agent therapy in patients with high-risk ER+/HER2− eBC following 2–5yrs of adjuvant ET[1,2]

Switch strategy | High risk




## KEY INCLUSION CRITERIA

- Women or men aged ≥18 years
- Confirmed ER+, HER2− eBC, resected, invasive BC, without evidence of distant metastasis
- At increased risk of recurrence based on clinical-pathological features at diagnosis (N0 T ≥5 cm, or G3 T 2–5 cm; N1 T ≥5 cm, or G2/3 T2–5 cm; N2, N3)
- Received ≥24 mo but ≤60 mo of any adjuvant ET
- May have received (neo)adjuvant ChT and/or CDK4/6i or PARPi
- ECOG PS 0–1

## KEY EXCLUSION CRITERIA

- Metastatic disease (including contralateral ALN)
- Inflammatory BC
- >6 mo consecutive gap in therapy during prior adjuvant ET
- Completed or discontinued prior adjuvant ET >6 mo prior to screening
- History of previous BC, except for ipsilateral DCIS treated by locoregional therapy alone ≥5 years ago
- Prior ET of any duration for BC prevention (tamoxifen or AIs) or raloxifene

[a]The clinical trial is being conducted globally. [b]Administered orally. [c]Endocrine therapy (investigator's choice of tamoxifen, anastrozole, letrozole, or exemestane) is administered per local label.

AI, aromatase inhibitor; ALN, axillary lymph nodes; BC, breast cancer; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; ChT, chemotherapy; DCIS, ductal carcinoma *in situ*; DRFS, distant recurrence-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; IDFS, invasive disease-free survival; mo, months; N, node status; OS, overall survival; PARPi, poly-adenosine diphosphate-ribose polymerase inhibitor; PK, pharmacokinetics; PROs, patient-reported outcomes; QD, once daily; SOC, standard of care; T, tumor size.



1. ClinicalTrials.gov. NCT05514054. 2. Ascione L, et al. *Curr Opin Oncol*. 2024;36(6):465–473.

# 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 greatly reduced ER availability, showing reduction in tumors regardless of *ESR1* mutation status[2]
  - **agonistic properties**: at lower doses, elacestrant can function as a SERM and has estrogen-like effects, which can both reduce hot flashes and protect against bone loss[1,3]


Adapted from: McDonnell DP, et al., 2021

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



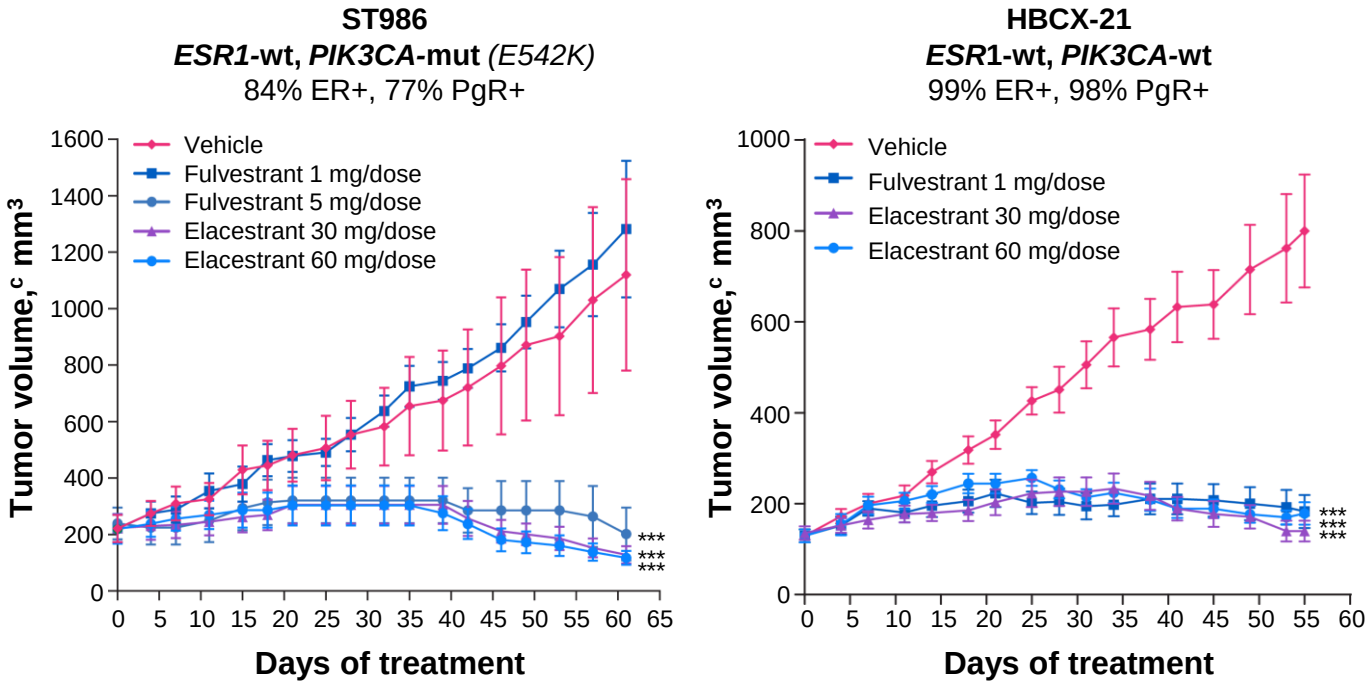
1. Garner F, et al. *Anticancer Drugs.* 2015;26(9):948–956. 2. Bardia A, et al. *J Clin Oncol*. 2021;39(12):1360–1370. 3. McDonnell DP, et al. *J Clin Oncol*. 2021;39(12):1383–1388.

# Elacestrant demonstrated activity in *ESR1* wild-type tumors

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

| | Elacestrant (N=124) | SOC (N=125) |
|---|---|---|
| **Event** | 82 | 78 |
| **Hazard ratio (95% CI)** | 0.86 (0.63–1.19) | |
| **p-value** | 0.31 | |
| **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[b] resistant to CDK4/6i[2]




Asterisks represent significant differences in the indicated treatment groups relative to vehicle control at end of treatment

[a]The EMERALD study was not powered to demonstrate statistical significance for *ESR1*-wt. [b]PDX models ST986 and HBCX-21 were selected based on relatively high expression levels of wt-type ER and PR.
[c]Mean tumor volumes ± SEM of indicated PDX models treated with elacestrant or fulvestrant at the indicated dose.

CDK4/6i cyclin-dependent kinase 4/6 inhibitor; CI, confidence interval; ER, estrogen receptor; *ESR1,* estrogen receptor 1; mut, mutation; PDX, patient-derived xenograft; PFS, progression-free survival; *PIK3CA,* phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; PgR, progesterone receptor; SEM, standard error of the mean; SOC, standard of care; wt, wild type.

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

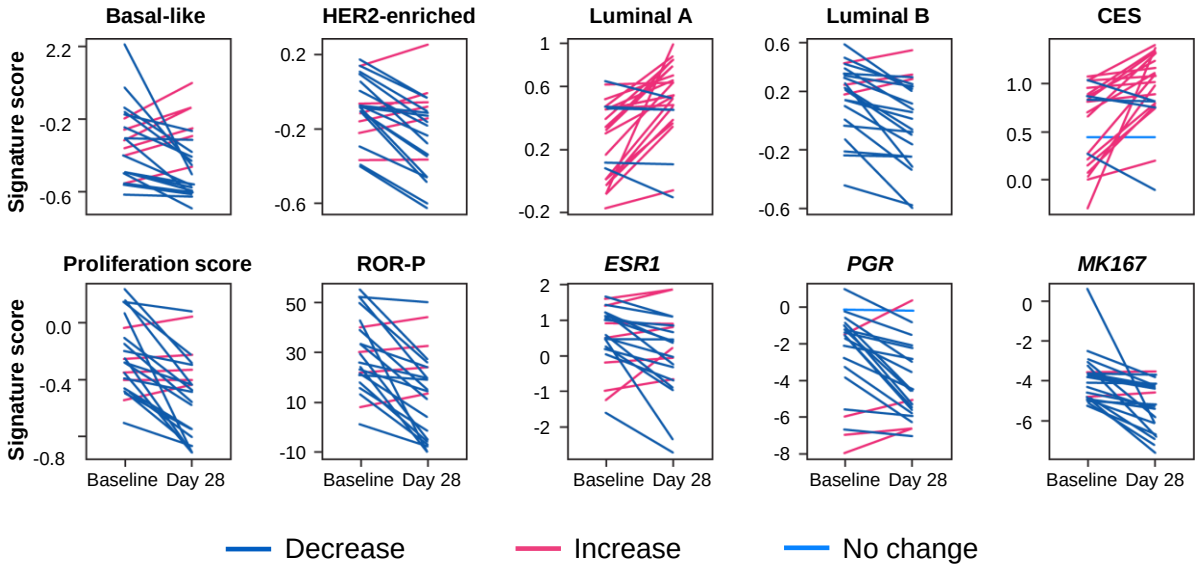
# ELIPSE: elacestrant demonstrated relevant biological and molecular responses in eBC, supporting further investigation[1]

## Treatment with elacestrant results in a 27% CCCA[a] rate, and substantial Ki-67 suppression

| Baseline characteristics | Overall population |
|---|---|
| **n** | 22 |
| *Histologic type (%)* | |
| Ductal | 17 (73.9) |
| Lobular | 4 (17.4) |
| Other | 2 (8.6) |
| *Centralized baseline Ki-67* | |
| Median | 13 |
| Range | 5–70 |

| Results | Overall population | Luminal A (n=12) |
|---|---|---|
| n | 22 | 11 |
| CCCA at day 28, n (%) | 6 (27.3)<br>(95% CI 10.7–50.2) | 5 (41.7) |
| Ki-67 ≤10% at day 28, n (%) | 14 (63.7) | 11 (100.0) |
| Ki-67 geometric mean change, %<br>(95% CI) | -52.9<br>(95% CI -67.4 to -32.1) | -64.6<br>(95% CI -79.4 to -39.3) |

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




[a]Complete cell cycle arrest (Ki-67 ≤2.7%).

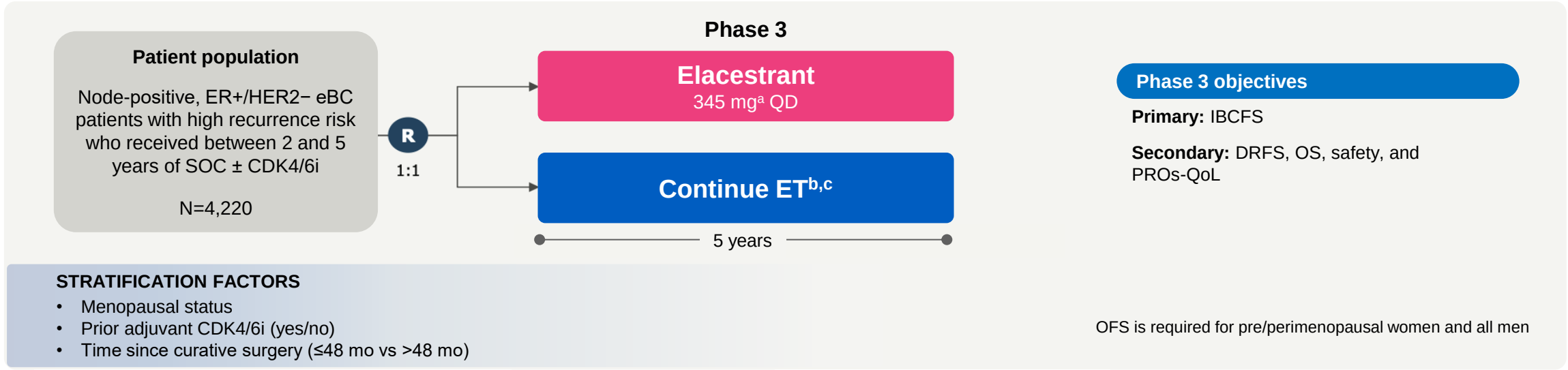
CCCA, complete cell cycle arrest; CES, chemo-endocrine score; CI, confidence interval; eBC, early breast cancer; *ESR1*, estrogen receptor 1; HER2, human epidermal growth factor receptor 2; MK167, marker of proliferation Ki-67; *PGR*, progesterone receptor gene; ROR-P, PAM50-derived risk of recurrence plus a proliferation index



1. Vidal M, et al. *Clin Cancer Res*. Published online January 16, 2025. doi:10.1158/1078-0432.CCR-24-2460 (including supplementary data).

# ELEGANT trial evaluates elacestrant as single-agent therapy in ‘pure high-risk’ ER+/HER2- eBC patients following 2-5yrs of adjuvant ET[1,2]

Switch strategy | High risk




## KEY INCLUSION CRITERIA

- Women or men aged ≥18 years
- Confirmed ER+, HER2− early stage II–III resected invasive BC without evidence of recurrence or distant metastases[d]
- High-risk of recurrence defined at initial staging as ≥4 positive ALN or 1–3 positive ALN and histologic grade 3 disease or tumor size ≥5 cm
- ECOG PS 0–1
- 2–6 years from date of curative surgical resection
- Received ≥24 mo but ≤60 mo of ET (AIs or tamoxifen) ± CDK4/6i[e]
- Pre/perimenopausal women and all men will be administered an LHRH agonist
- Considered a candidate for an additional 5 years of ET

## KEY EXCLUSION CRITERIA

- Stage IV metastatic BC
- Inflammatory BC
- 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
- History of any prior (ipsilateral and/or contralateral) invasive BC except for ipsilateral DCIS treated by local regional therapy at any time
- >6 mo of continuous interruption of prior SOC adjuvant ET or discontinued adjuvant ET >6 mo prior to randomization

[a]Elacestrant 345 mg is equivalent to 400 mg elacestrant hydrochloride. [b]Anastrozole, letrozole, exemestane, or tamoxifen per local label once daily. [c]Change in endocrine therapy after randomization in the control arm from an AI to another AI or tamoxifen is allowed per investigator’s judgment. [d]Recurrence-free at baseline based on investigator’s best assessment and negative imaging completed within 6 mo prior to randomization. [e]Patients who received prior CDK4/6i or PARPi must have already completed or discontinued these treatments.

AI, aromatase inhibitor; ALN, axillary lymph node; BC, breast cancer; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; DCIS, ductal carcinoma *in situ*; DRFS, distant recurrence-free survival; eBC, early breast cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; ER, endocrine receptor; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; IBCFS, invasive breast cancer-free survival; LHRH, luteinizing hormone-releasing hormone; mo, months; OFS, ovarian function suppression; OS, overall survival; PROs, patient-reported outcomes; QD, once daily; QoL, quality of life; SOC, standard of care.

1. ClinicalTrials.gov. NCT06492616. 2. ELEGANT. STML-ELA-0422. 2024.

# Summary of ongoing studies investigating oral SERDs as adjuvant therapy for HR+/HER2− eBC

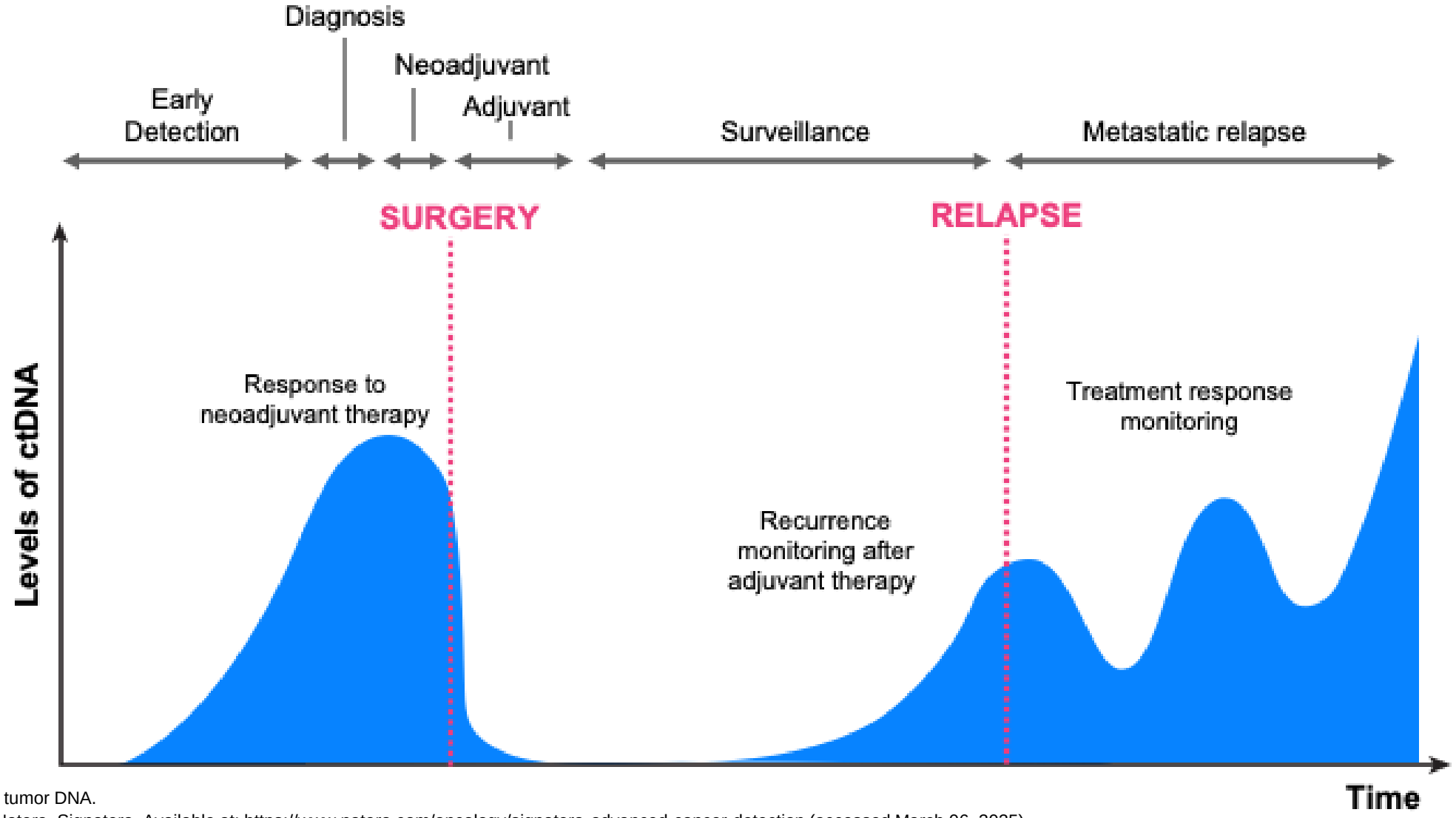
| Patient population | | | ELEGANT[1] | EMBER-4[2,3] | CAMBRIA-1[3,4] | lidERA[3,5,6] | CAMBRIA-2[3,7] |
|---|---|---|---|---|---|---|---|
| **N** | | | 4,220 | 8,000 | 4,300 | 4,200 | 5,500 |
| **Intervention** | | | Elacestrant | Imlunestrant | Camizestrant | Giredestrant | Camizestrant (± abema 2 y) |
| **Trial design** | | | TREATMENT SWITCH AFTER 2-5 YEARS OF ADJUVANT ET | | | UPFRONT ADJUVANT TREATMENT | |
| **Risk of recurrence** | | | +++ | ++ | + | + | + |
| **Patient population** | | | Pure high-risk | High-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% (incl N0 mic) | YES | If ≥2 ILN+, or grade 3, or genomic high-risk, or Ki-67 ≥20% (including N0 mic) |
| | | 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[c] or Ki-67 ≥20% | If grade 3, or genomic high-risk, or Ki-67 ≥20% |
| | IIB | T2 N1 | If tumor size 5 cm or grade 3 | If tumor size 5 cm or grade 2/3 | YES[a] | YES | YES[a] |
| | | 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[c] 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[b] | YES | YES |
| | | T4 N1 | If tumor size ≥5 cm or grade 3 | If tumor size ≥5 cm, or grade 3 or grade 2 and 2–5 cm | YES[b] | YES | YES |
| | | T4 N2 | YES | YES | YES[b] | 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**

[a]For 1 LN+ only if grade 3, or genomic high risk, or Ki-67 >20%.[b]T4d excluded. Abema, abemaciclib. [c]Oncotype DX or MammaPrint high. 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, node status; SERD, selective estrogen receptor degrader; T, tumor size; y, year.

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. Available at: https://www.clinicaltrialsregister.eu/ctr-search/search?query=LidERA (accessed March 2025). 7. ClinicalTrials.gov. NCT05952557.

# Monitoring of minimal residual disease through ctDNA is likely to prove beneficial for anticipating recurrence[1]

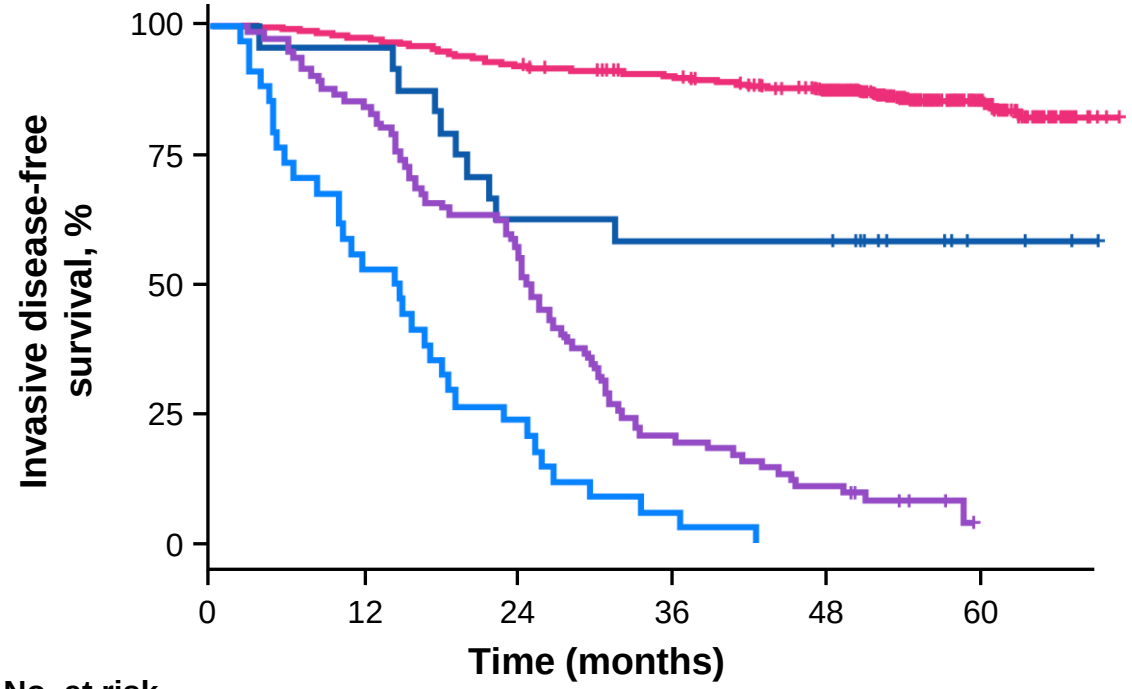



ctDNA, circulating tumor DNA.

1. Adapted from: Natera. Signatera. Available at: https://www.natera.com/oncology/signatera-advanced-cancer-detection (accessed March 06, 2025).

# 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 |

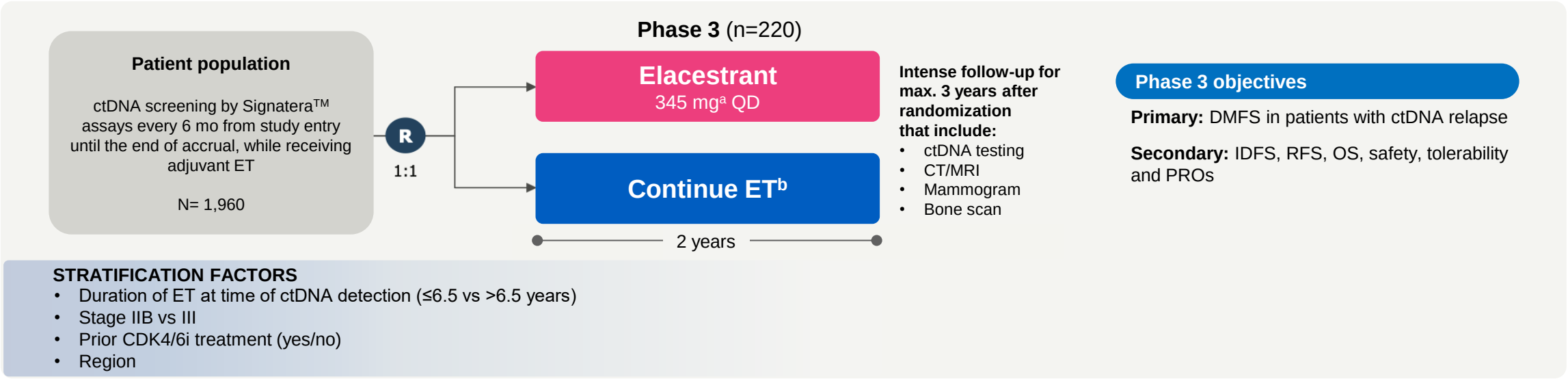
| | Longitudinal analysis (N=889)[a] | | | |
|---|---|---|---|---|
| | Baseline (−), undetected N=831 | | Baseline (+), detected N=58 | |
| | Persistently − | Became + | Persistently + | Became − (undetected) |
| N | 749 (90) | 82 (10) | 34 (60) | 24 (40) |
| IDFS event, n (%) | 107 (14) | 76 (93) | 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) |

[a]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/a, not available

1.Loi et al. ASCO 2024. Abstract LBA507

# TREAT ctDNA study evaluated elacestrant efficacy in ER+/HER2− eBC patients with ctDNA relapse[1,2]




## KEY INCLUSION CRITERIA

- Women or men age ≥18 years
- Confirmed ER+[c], HER2− eBC without evidence of distant metastasis
- Stage IIb or III and completed adjuvant ChT
- Completed ≥4 cycles of neoadjuvant ChT and ≥ypT1C or ypN+
- Received 2-7 years of ET
- Prior CDK4/6i or PARPi allowed if completed ≥12 mo prior to enrolment
- ctDNA+ per the Signatera assay (Randomization phase)

## 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[d]
- Any history of coagulopathy in the past 6 mo

[a]Elacestrant 345 mg is equivalent to 400 mg elacestrant hydrochloride. [b]Anastrozole, letrozole, exemestane, or tamoxifen per local label once daily. [c]≥10% staining. [d]Grade 3 per CTCAE v5.0.

BC, breast cancer; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; ChT, chemotherapy; CT, computed tomography; ctDNA, circulating tumor deoxyribonucleic acid; DMFS, distant metastasis-free survival; eBC, early breast cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; ER, estrogen receptor; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; IDFS, invasive disease-free survival; mo, months; MRI, magnetic resonance imaging; OS, overall survival; PARPi, poly-ADP ribose polymerase inhibitor; PRO, patient-reported outcome; RFS, relapse-free survival.



1.Clinicaltrials.gov. NCT05512364. 2.TREAT ctDNA. EORTC-2129-BCG. 2023.

# Key takeaways

**Risk assessment enables personalized treatment approaches**, optimizing 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 the only oral SERD with agonistic properties being investigated as a switch strategy in a "pure high-risk population"** following demonstration of CCCA rate reduction, substantial Ki-67 suppression, and activity in *ESR1* wild-type breast cancer[6,9–11]

CCCA, complete cell cycle arrest; CDK4/6, cyclin dependent kinase 4/6; *ESR1*, estrogen receptor 1; ET, endocrine therapy; SERD, selective estrogen receptor degrader; SOC, standard of care.

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. ClinicalTrials.gov. NCT06492616. 10. Vidal M, et al. *Clin Cancer Res*. Published online January 16, 2025. doi:10.1158/1078-0432.CCR-24-2460. 11. Kaklamani VG, et al. ASCO 2023. Poster 291.

# Discussion and Q&A

Prof. Michael Gnant

Medical University of Vienna, Austria

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# Thank you!

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