DID YOU KNOW?

Beyond the Data

The Impact of Underutilization of CDK4/6 Inhibitors in Node-Positive, High-Risk, HR-Positive/HER2-Negative Early Breast Cancer

CDK4/6 Inhibitors: Sustained Long-Term Reduction of Disease Recurrence in the Adjuvant Setting

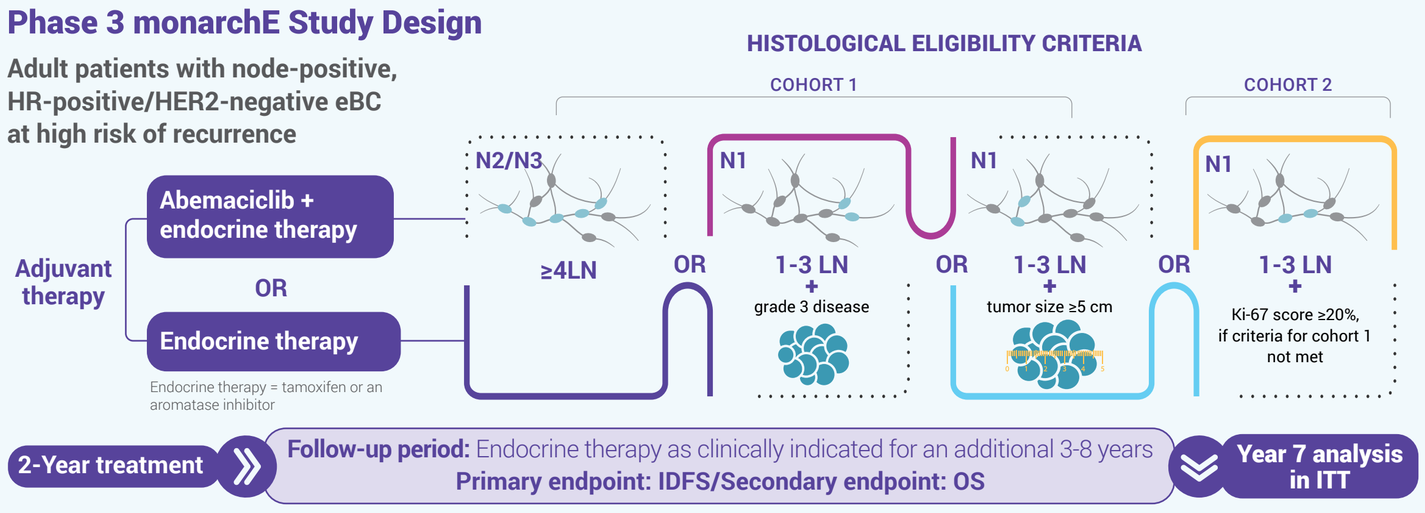
Currently, there are 2 cyclin-dependent kinase (CDK)4/6 inhibitors approved for adjuvant use in node-positive, high-risk, hormone receptor (HR)-positive/HER2-negative early breast cancer (eBC):

- Abemaciclib was approved in 2021 in combination with endocrine therapy (ET) (tamoxifen or an aromatase inhibitor [AI]) for the adjuvant treatment of adult patients with node-positive, HR-positive/HER2-negative eBC at high risk of recurrence based on data from the phase 3 monarchE study[1,2]
- Ribociclib was approved in 2024 in combination with an AI for the adjuvant treatment of adults with HR-positive/HER2-negative stage II and III eBC at high risk of recurrence based on the results of the phase 3 NATALEE study[3]

monarchE: 7-year Landmark Analysis Presented at ESMO 2025 Demonstrates Sustained Benefits in Key Outcomes[4,5]

Phase 3 monarchE Study Design

Adult patients with node-positive, HR-positive/HER2-negative eBC at high risk of recurrence



At 7 Years, IDFS Benefit Was Maintained for Abemaciclib Plus ET

Compared with ET alone

26.6% Reduction in risk of IDFS events

Δ6.5% IDFS benefit at 7 years

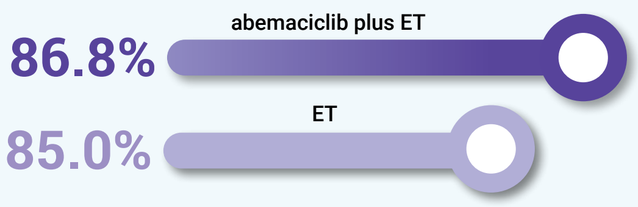
~30% Fewer patients living with metastatic disease

- **Hazard ratio**, 0.73; 95% CI, 0.66-0.82; *P*<.0001
- Median follow-up of 76 months

At 7 Years, a Statistically Significant OS Difference Was Demonstrated for Abemaciclib Plus ET

Compared with ET alone

- **Hazard ratio**, 0.84; 95% CI, 0.72-0.98; 2-sided *P*=.027
- Median follow-up of 76 months



15.8% reduced risk of death

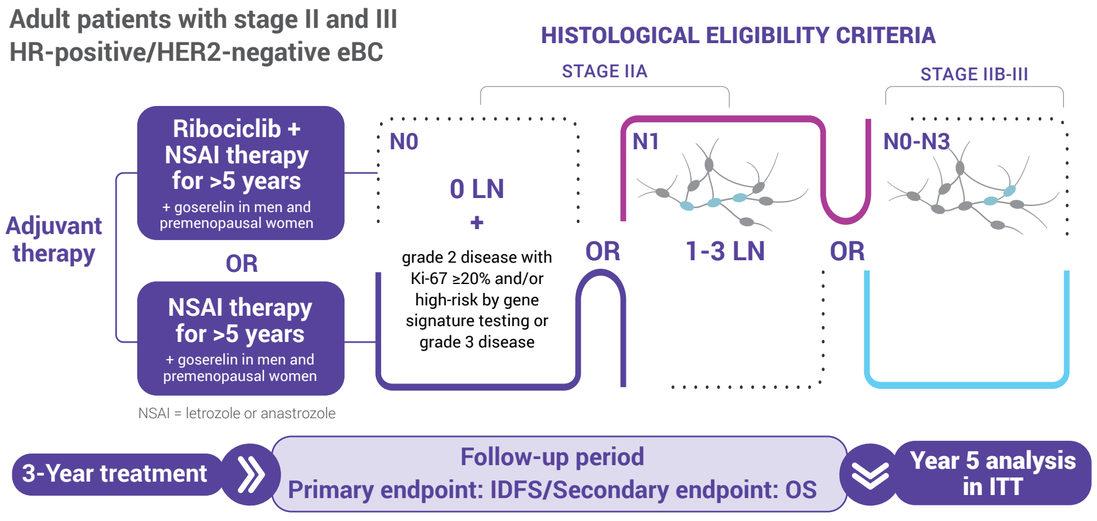
Safety was consistent with prior reports, and no new signals related to delayed toxicities were identified

CI, confidence interval; ET, endocrine therapy; IDFS, invasive disease-free survival; ITT, intent-to-treat; LN, lymph nodes; OS, overall survival.

NATALEE: 5-Year Follow-Up Presented at ESMO 2025 Demonstrates Continued Benefits in Key Outcomes[6,7]

Phase 3 NATALEE Study Design

Adult patients with stage II and III HR-positive/HER2-negative eBC



At 5 Years, IDFS Benefit Was Maintained for Ribociclib Plus NSAI

Compared with NSAI alone

- At median follow-up of 55.4 months, ribociclib continues to demonstrate a durable IDFS benefit
- **Hazard ratio**, 0.72; 95% CI, 0.62-0.83; *P*<.0001

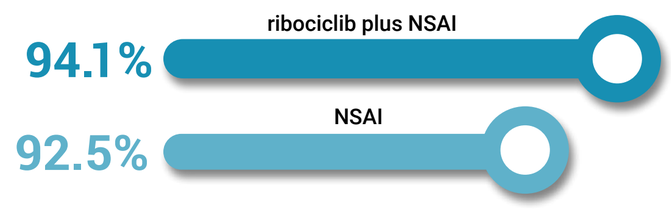
Δ4.5% IDFS benefit at 5 years

At 5 Years, an OS Difference Was Demonstrated for Ribociclib Plus NSAI

Compared with NSAI alone

- **Hazard ratio**, 0.80; 95% CI, 0.64-1.003; 1-sided *P*=.026
- Median follow-up of 56.5 months

There were fewer patients alive with metastatic disease (n=114) in the ribociclib plus NSAI arm than the NSAI arm (n=169)



No new safety signals were identified

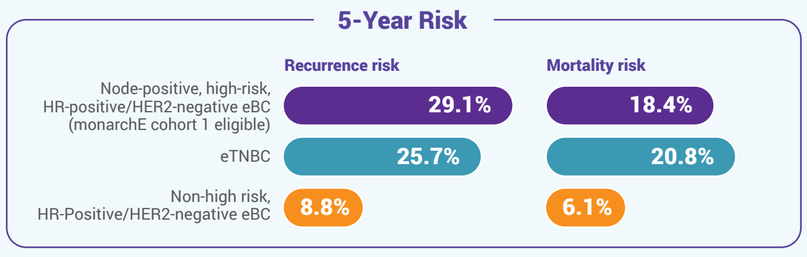
CI, confidence interval; ET, endocrine therapy; IDFS, invasive disease-free survival; ITT intent-to-treat; LN, lymph nodes; NSAI, nonsteroidal aromatase inhibitor; OS, overall survival.

Real-World Studies Show High Risk of Recurrence and Mortality Rates in Node-Positive, HR-Positive/HER2-Negative eBC Comparable With Triple-Negative Breast Cancer and Underutilization of Adjuvant CDK4/6 Inhibitors in Eligible Patients

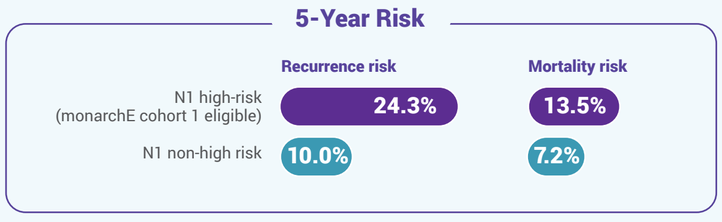
Findings Presented at ESMO Breast Cancer 2025[8]

A real-world, retrospective study evaluated the risk of recurrence and mortality in ~16,000 adult patients with eBC using the US Flatiron database. Electronic health records were analyzed between January 2011 and June 2024. During the study period, abemaciclib was the only approved therapy for node-positive, high-risk, HR-positive/HER2-negative eBC.

Patients Who Meet monarchE Histological Eligibility Features Have 5-Year Mortality and Recurrence Risks Comparable With eTNBC



5-Year Recurrence and Mortality Risks in Patients With N1 High-Risk Disease (1-3 Lymph Nodes Plus Grade 3 or Tumor ≥5 cm) are ~2-Fold Higher Relative to Non-High-Risk Disease



eBC, early breast cancer; eTNB, early triple-negative breast cancer; HR, hormone receptor.

Findings Presented at Miami Breast Cancer Conference 2025[9]

A real-world, retrospective study evaluated the utilization of abemaciclib across 280 institutions using the US Flatiron database. Electronic health records were analyzed for adults meeting monarchE inclusion criteria and who initiated adjuvant oral ET between January 2023 and March 2024. During the study period, abemaciclib was the only approved therapy for node-positive, high-risk, HR-positive/HER2-negative eBC.

Many Eligible Patients, Especially Older Adults and Those With High-Risk N1 Disease, Did Not Receive Abemaciclib

60% of eligible node-positive, HR-positive/HER2 negative eBC patients did not receive abemaciclib

70% of eligible patients ≥65 years did not receive abemaciclib, with utilization decreasing with age

2 in 3 eligible patients with N1 high-risk disease (with or without micrometastasis) did not receive abemaciclib

74% of these had grade 3 disease

Real-world data demonstrate a clear, clinical need for adjuvant treatment of node-positive, high-risk, HR-positive/HER2-negative eBC beyond ET alone. CDK4/6 inhibitors show significant long-term effectiveness in this setting. However, underutilization of CDK4/6 inhibitors leaves patients at risk of recurrence and death comparable with TBNC

References

1. VERZENIO [prescribing information]. 2021. Lilly USA, LLC; Indianapolis, IN.
2. VERZENIO [prescribing information]. 2025. Lilly USA, LLC; Indianapolis, IN.
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5. Johnston S, Martin M, O'Shaughnessy J, et al. Overall survival with abemaciclib in early breast cancer. *Ann Oncol*. 2025;S0923-7534:049488.
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7. Fasching PA, Stroyakovskiy D, Yardley DA, et al., Ribociclib plus endocrine therapy in hormone receptor–positive/ERBB2-negative early breast cancer: 4-year outcomes from the NATALEE randomized clinical trial. *JAMA* Oncol. 2025; e253700.
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9. Sandoval-Leon A, et al. Exploring the treatment gap in high-risk HR+, HER2- early breast cancer (EBC): eligible patients not receiving abemaciclib in the US. Presented at: 42nd Annual Miami Breast Cancer Conference. March 6-9, 2025; Miami, FL. Poster 42.

For full prescribing information see:
https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/208716s019lbl.pdf
https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/209092s024lbl.pdf

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