CDK4/6 INHIBITORS + ET IN HR+, HER2- EARLY BREAST CANCER

THIS PRESENTATION WAS COMMISSIONED BY LILLY MEDICAL AND IS INTENDED TO BE USED BY HCPs FOR MEDICAL, SCIENTIFIC, AND EDUCATIONAL PURPOSES

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- NATALEE

CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; FDA=US Food and Drug Administration; HER2=human epidermal growth factor receptor 2; HR=hormone receptor.

Learning Objectives

After reviewing this educational slide deck on key concepts in high-risk HR+, HER2- EBC, HCPs will be able to:

Address Unmet Need:
Understand the critical unmet need in the treatment of high-risk HR+, HER2- EBC, and explore strategies to address these gaps in practice

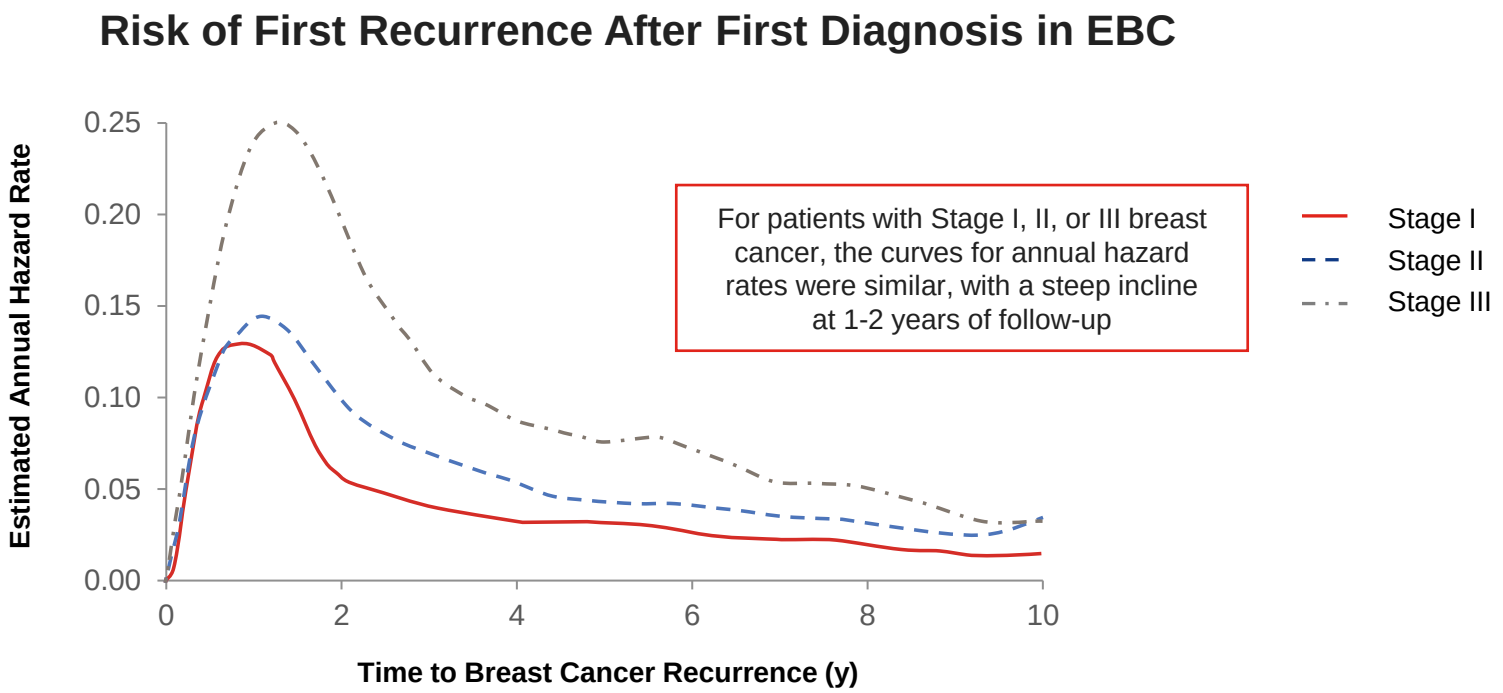
Identify Patients With High-Risk:
Learn to accurately identify patients with HR+, HER2- EBC who are at high risk of disease recurrence

Incorporate Emerging Data Into Clinical Practice:
Gain practical insights into ongoing clinical trials involving CDK4/6i combined with ET for HR+, HER2- EBC

CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; EBC=early breast cancer; ET=endocrine therapy; HCP=healthcare provider; HER2=human epidermal growth factor receptor 2; HR=hormone receptor.

UNMET NEED IN HIGH-RISK, HR+, HER2- EARLY BREAST CANCER

Risk of Recurrence Peaks Within 1-3 Years After Diagnosis in Patients With EBC



These data highlighted the **need for additional therapies** during the time when breast cancer recurrence peaks

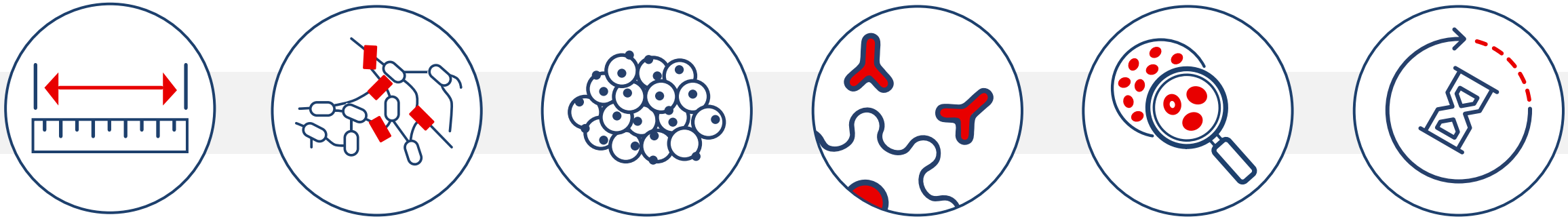
EBC=early breast cancer; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; y=year.

Cheng L, et al. *Cancer Epidemiol Biomarkers Prev*. 2012;21(5):800-809.

Identification of Patients With HR+, HER2- EBC at High Risk of Disease Recurrence

Not all patients with EBC will experience recurrence. It is important to identify patients with HR+, HER2- EBC at high risk of recurrence and their **appropriate treatment** while still in the **adjuvant setting**[1]

Clinical and Pathological Factors That Influence Risk of Recurrence Include[2,3]:



- Tumor size
- Lymph node involvement
- Tumor grade
- PR and ER expression; HER2 status
- Other biomarkers (eg, Ki-67)
- Age

EBC=early breast cancer; ER=estrogen receptor; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; PR=progesterone receptor.

1. Johnston SRD, et al. *J Clin Oncol*. 2020;38(34):3987-3998. 2. Győrffy B, et al. *Breast Cancer Res*. 2015;17(1):11. 3. Dang CM, Giuliano AE. *Oncology* (Williston Park). 2011;25(10):895-896, 899.

Recurrence Risk in Patients With Node-Positive, High-Risk, HR+, HER2- EBC vs Early TNBC

N+ High-Risk

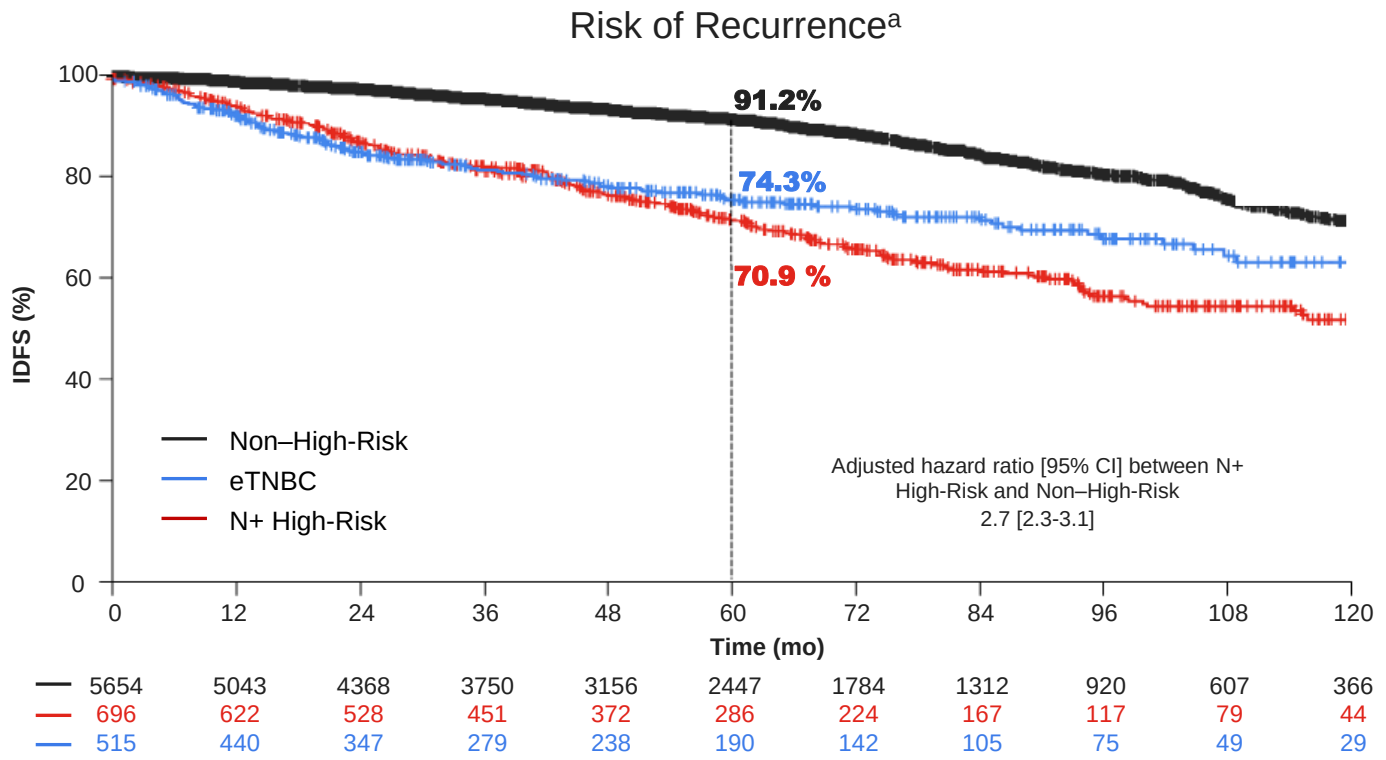
N1/N1mi high-risk:
1–3 ALN;
Grade 3 or tumor ≥5 cm

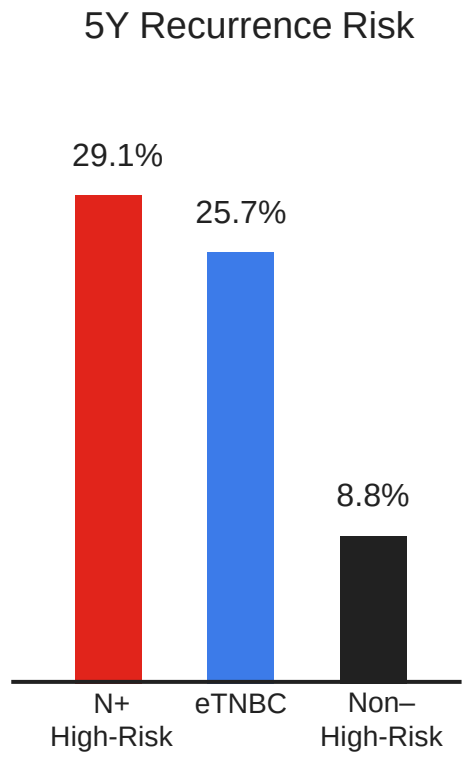
OR

4+ ALN
(N2, N3)

Non–High-Risk

Patients not meeting
N+ high-risk criteria





[a]Based on US Flatiron RW data.
ALN=axillary lymph node; EBC=early breast cancer; eTNBC=early triple-negative breast cancer; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; IDFS=invasive disease-free survival; mo=month; N=node; N1mi=micrometastases; N1=1–3 ALN; N2=4–9 ALN; N3=10+ ALN; RW=real-world; TNBC=triple-negative breast cancer; y=year.
Rugo HS, et al. Presented at: ESMO Breast Cancer Conference 2025. Poster 215P.

Mortality Risk in Patients With Node-Positive, High-Risk, HR+, HER2- EBC vs Early TNBC

N+ High-Risk

N1/N1mi high-risk:
1–3 ALN;
Grade 3 or tumor ≥5 cm

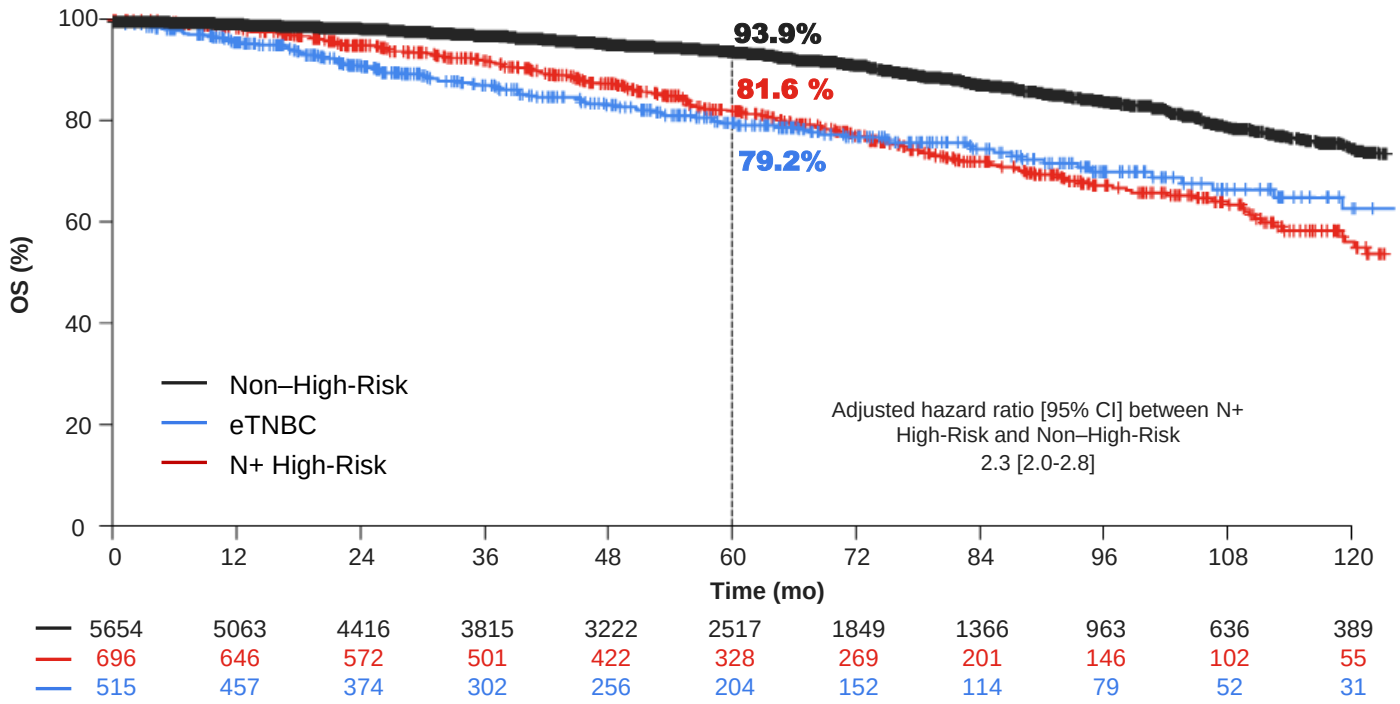
OR

4+ ALN
(N2, N3)

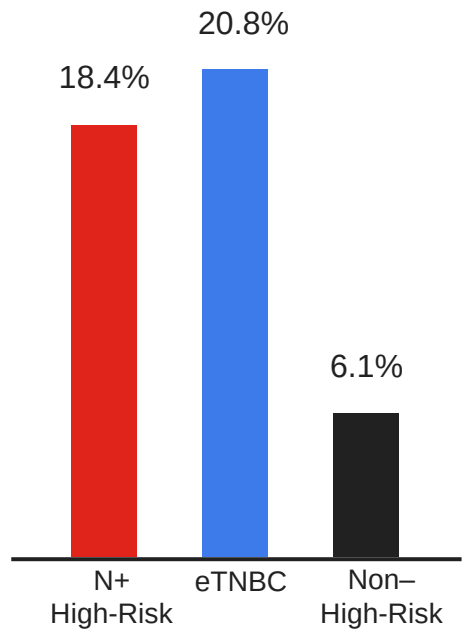
Non–High-Risk

Patients not meeting
N+ high-risk criteria

Overall Survival[a]



5Y Mortality Risk



[a]Based on US Flatiron RW data.
ALN=axillary lymph node; EBC=early breast cancer; eTNBC=early triple-negative breast cancer; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; mo=month; N=node; N1mi=micrometastases; N1=1–3 ALN; N2=4–9 ALN; N3=10+ ALN; OS=overall survival; RW=real-world; TNBC=triple-negative breast cancer; y=year
Rugo HS, et al. Presented at: ESMO Breast Cancer Conference 2025. Poster 215P.

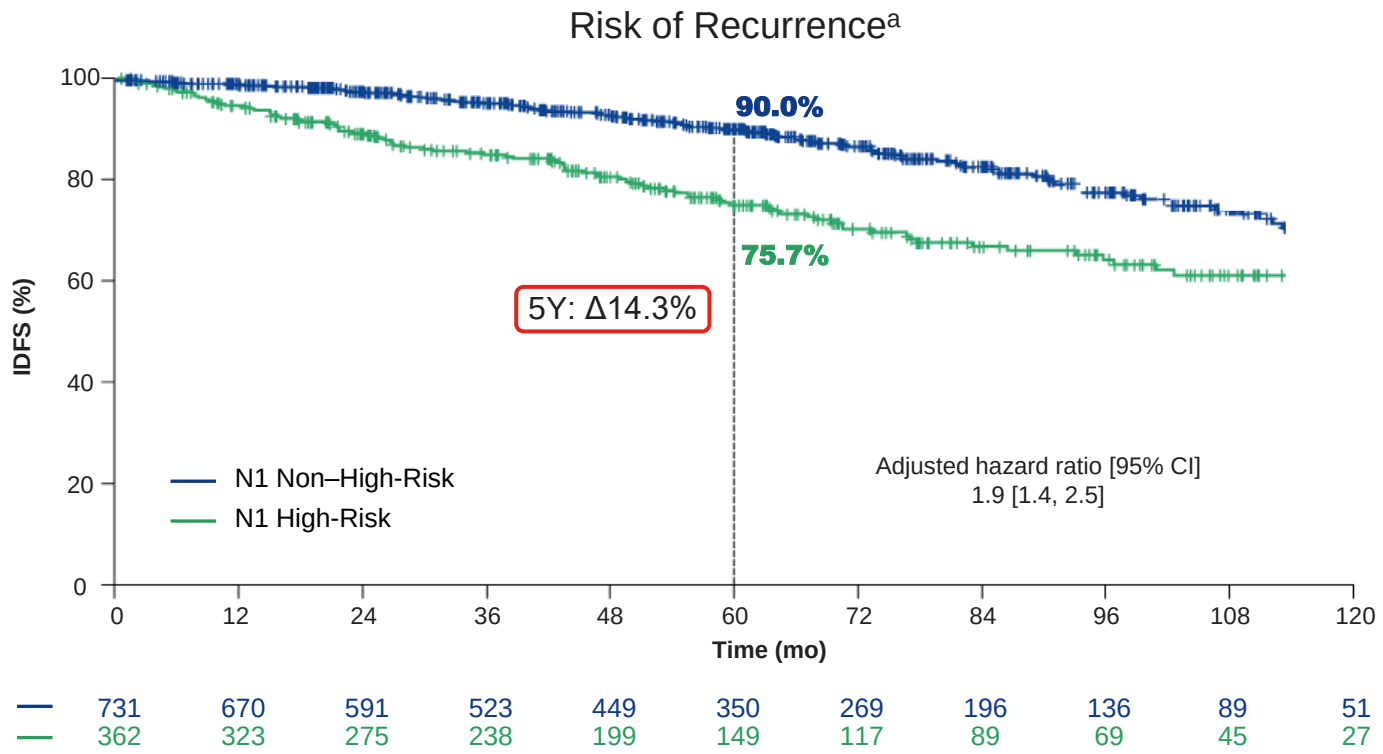
Recurrence Risk in Patients With N1/N1mi High-Risk, HR+, HER2- EBC vs N1/N1mi Non–High-Risk at 5Y

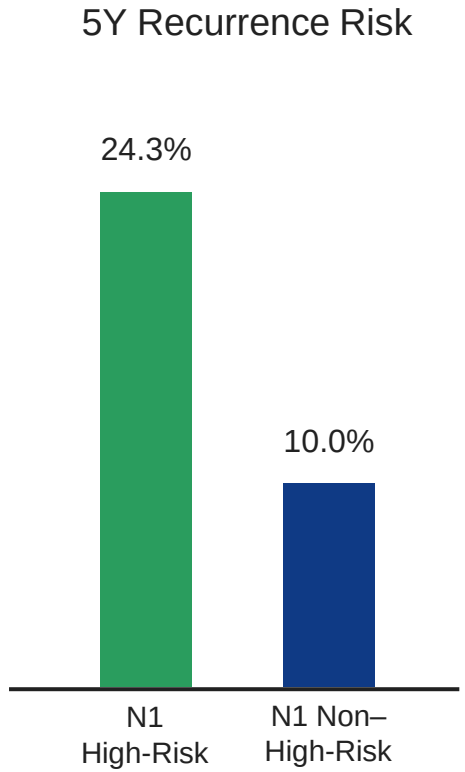
N1 High-Risk

N1/N1mi high-risk:
1–3 ALN;
Grade 3 or tumor ≥5 cm

N1 Non–High-Risk

N1/N1mi:
1–3 ALN +
Grade <3, tumor <5 cm, and Ki-67<20%





[a]Based on US Flatiron RW data.
ALN=axillary lymph node; EBC=early breast cancer; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; IDFS=invasive disease-free survival; mo=month; N=node; N1mi= micrometastases; N1=1–3 ALN; RW=real-world; y=year.
Rugo HS, et al. Presented at: ESMO Breast Cancer Conference 2025. Poster 215P.

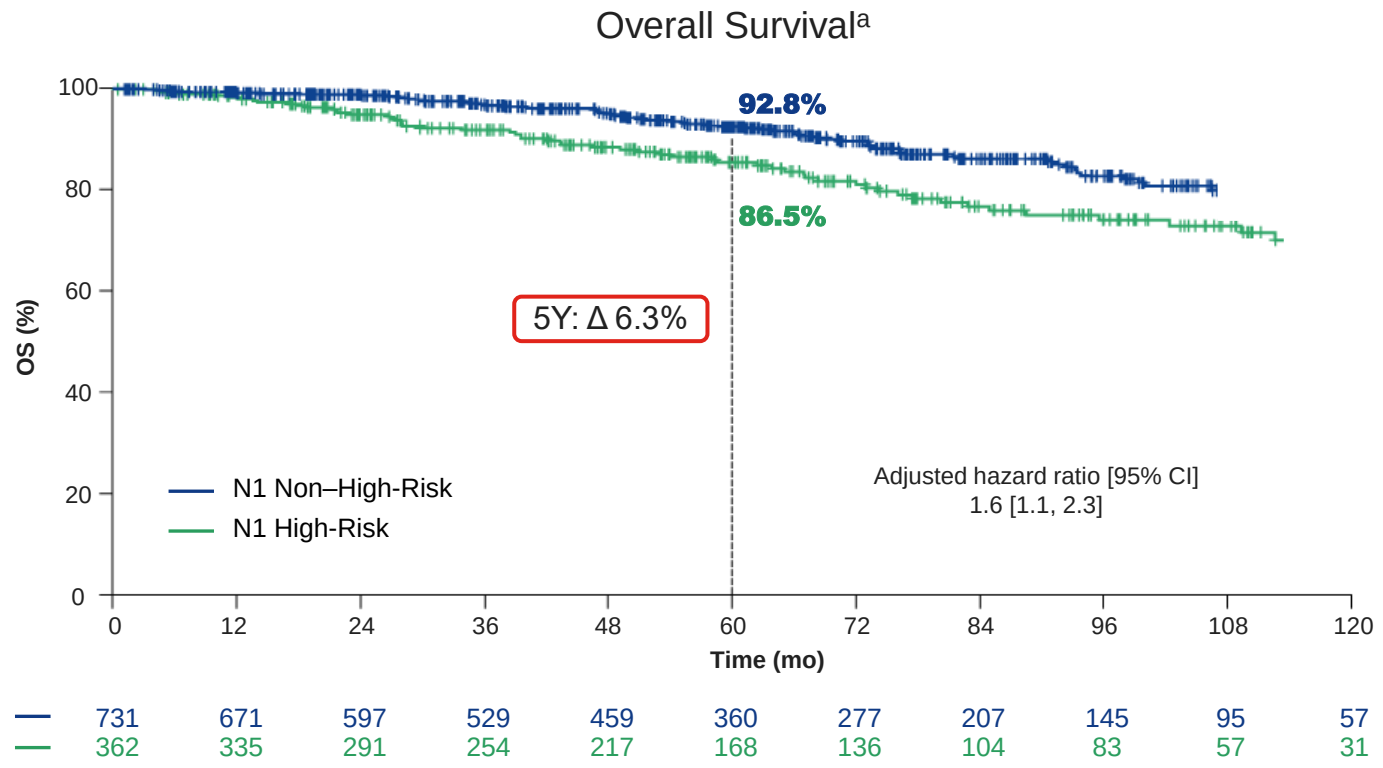
Mortality Risk in Patients With N1/N1mi High-Risk, HR+, HER2- EBC vs N1/N1mi Non–High-Risk at 5Y

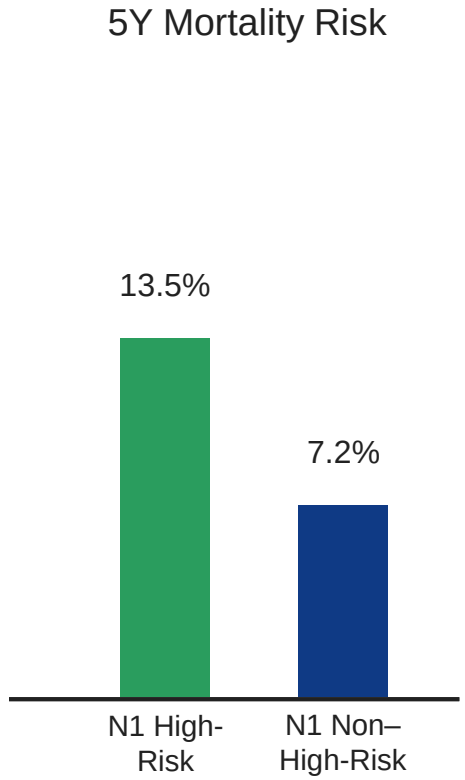
N1 High-Risk

N1/N1mi high-risk:
1–3 ALN;
Grade 3 or tumor ≥5 cm

N1 Non–High-Risk

N1/N1mi:
1–3 ALN +
Grade <3, tumor <5 cm, and Ki-67<20%





[a]Based on US Flatiron RW data.
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Rugo HS, et al. Presented at: ESMO Breast Cancer Conference 2025. Poster 215P.

Patients With High-Risk, Node-Positive EBC and Risk of Being Undertreated

HR+, HER2- EBC: **N+ High-Risk**

N1/N1mi High-Risk:
1-3 ALN + Grade 3 or tumor ≥5 cm

OR

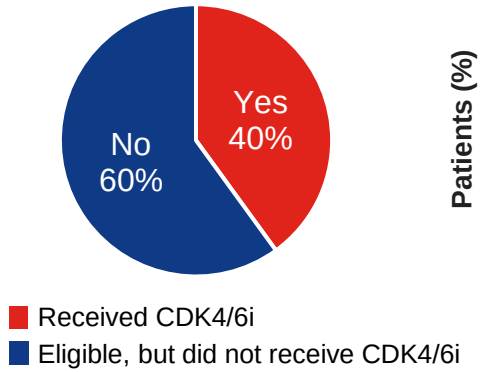
≥4 ALN (N2, N3)

Methods

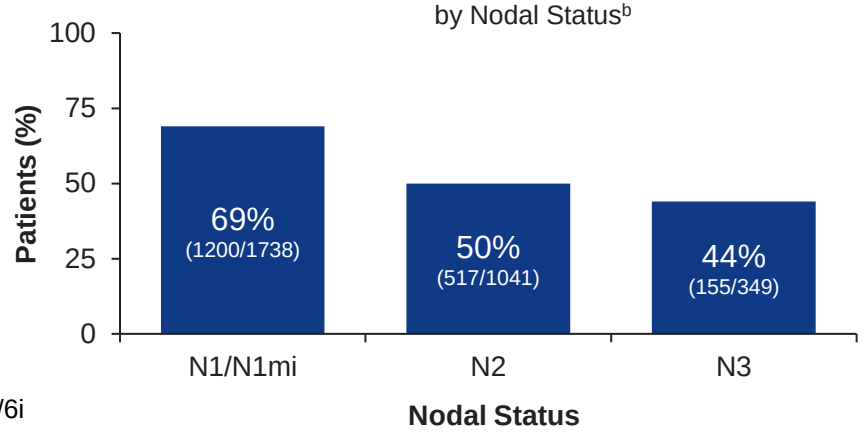
January 2023-March 2024
- Patients initiating adjuvant oral ET
- Multivariable logistic regression to identify factors associated with CDK4/6i utilization

Adjuvant CDK4/6i Use in US in Patients With Node-Positive High-Risk EBC[a]

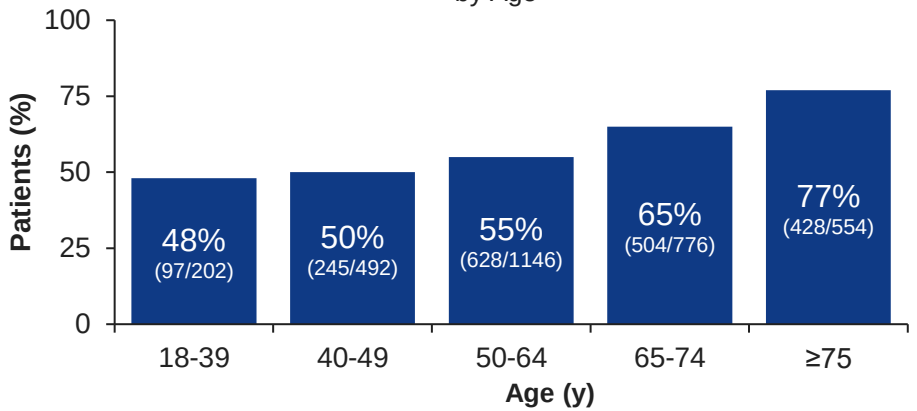
Node-Positive High-Risk EBC (N=3170)



Patients Who Did Not Receive a CDK4/6i by Nodal Status[b]



Patients Who Did Not Receive a CDK4/6i by Age



N+ High-Risk:

3 of 5 eligible patients did not receive a CDK4/6i

>2 of 3 eligible patients with N1/N1mi high-risk disease did not receive a CDK4/6i

70% eligible patients ≥65 years did not receive a CDK4/6i

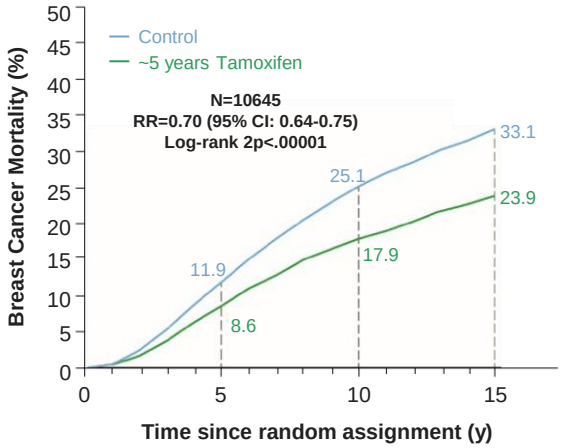
[a]Based on US Flatiron RW data. [b]N1/N1mi was high-risk with Grade 3 and/or tumor size ≥5 cm.
ALN=axillary lymph node; CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; EBC=early breast cancer; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; N=node; N1mi=micrometastases; N1=1-3 ALN; N2=4-9 ALN; N3=10+ ALN; RW=real-world; US=United States; y=year.
Sandoval-Leon A, et al. Presented at Miami Breast Cancer Conference (MBCC) 2025. Poster 42.

Improving Overall Survival in HR+ EBC: Challenges

Overall survival (OS) is a clinically meaningful measure of both efficacy and safety
and is considered the gold standard for establishing the clinical benefit of cancer treatments

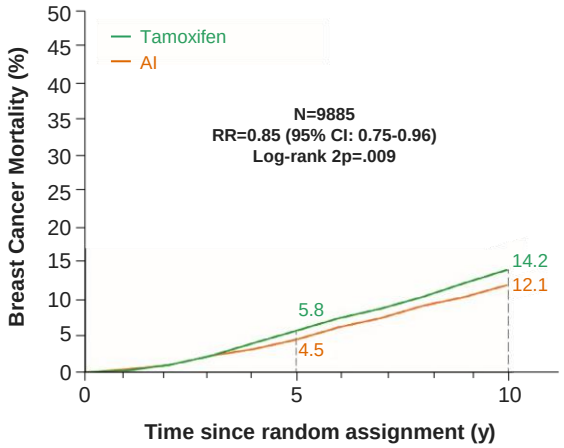
It has taken meta-analyses with large patient numbers to demonstrate improvement in breast cancer–specific mortality in HR+ EBC; changes in treatment standards have been based on reductions in the risk of recurrence and incremental improvements in mortality rates at 10-15 years[1-4]

Tamoxifen vs No Treatment[1]



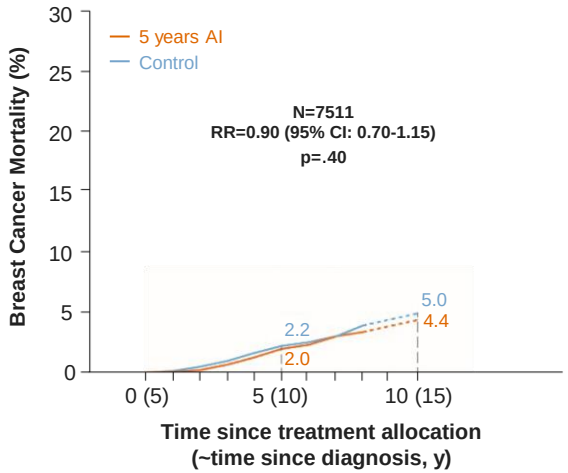
Breast cancer mortality benefit: **Δ at 15 years: 9.2%**

AI vs Tamoxifen[2]



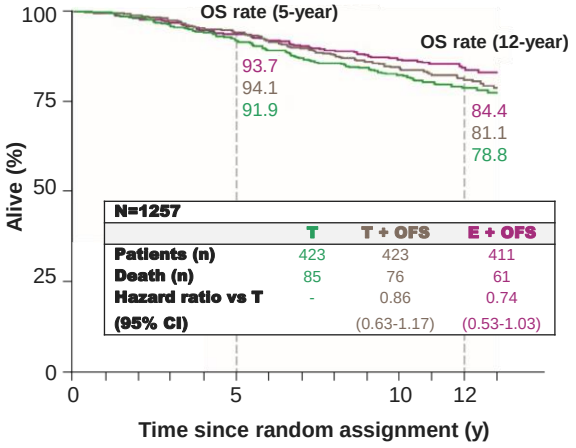
Δ at 10 years: 2.1%

5-Y ET vs Extended AI[3]



Δ at 15 years: 0.6%

Exemestane + OFS vs Tamoxifen[4]



Δ at 12 years: 5.6%

AI=aromatase inhibitor; E=exemestane; EBC=early breast cancer; ET=endocrine therapy; HR=hormone receptor; OFS=ovarian function suppression; OS=overall survival; RR=rate ratio; T=tamoxifen; y=year.

1. Early Breast Cancer Trialists' Collaborative Group. *Lancet*. 2011;378(9793):771-784. 2. Early Breast Cancer Trialists' Collaborative Group. *Lancet*. 2015;386(10001):1341-1352.
3. Early Breast Cancer Trialists' Collaborative Group. *Lancet*. 2025;406(10503):603-614. 4. Francis PA. *J Clin Oncol*. 2023;41(7):1370-1375.

HR+, HER2- EBC and Risk of Recurrence: Summary

Patients with N1 high-risk (N1 + Grade 3 or tumor ≥5 cm) have a 5-year risk of recurrence and death that is ~2 fold higher than patients with N1 and lower-risk features[1]

In patients meeting node-positive high-risk EBC criteria on standard ET in real-world US practice: ~1:3 patients are at risk of recurrence at 5 years[1]

These risks are similar to early TNBC, considered the most aggressive breast cancer subtype[1]

Proper identification of patients at high risk of recurrent disease is vital for optimal escalation of therapy while in the adjuvant setting[2]

ALN=axillary lymph node; EBC=early breast cancer; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; N1=1–3 ALN; TNBC=triple-negative breast cancer; US=United States.

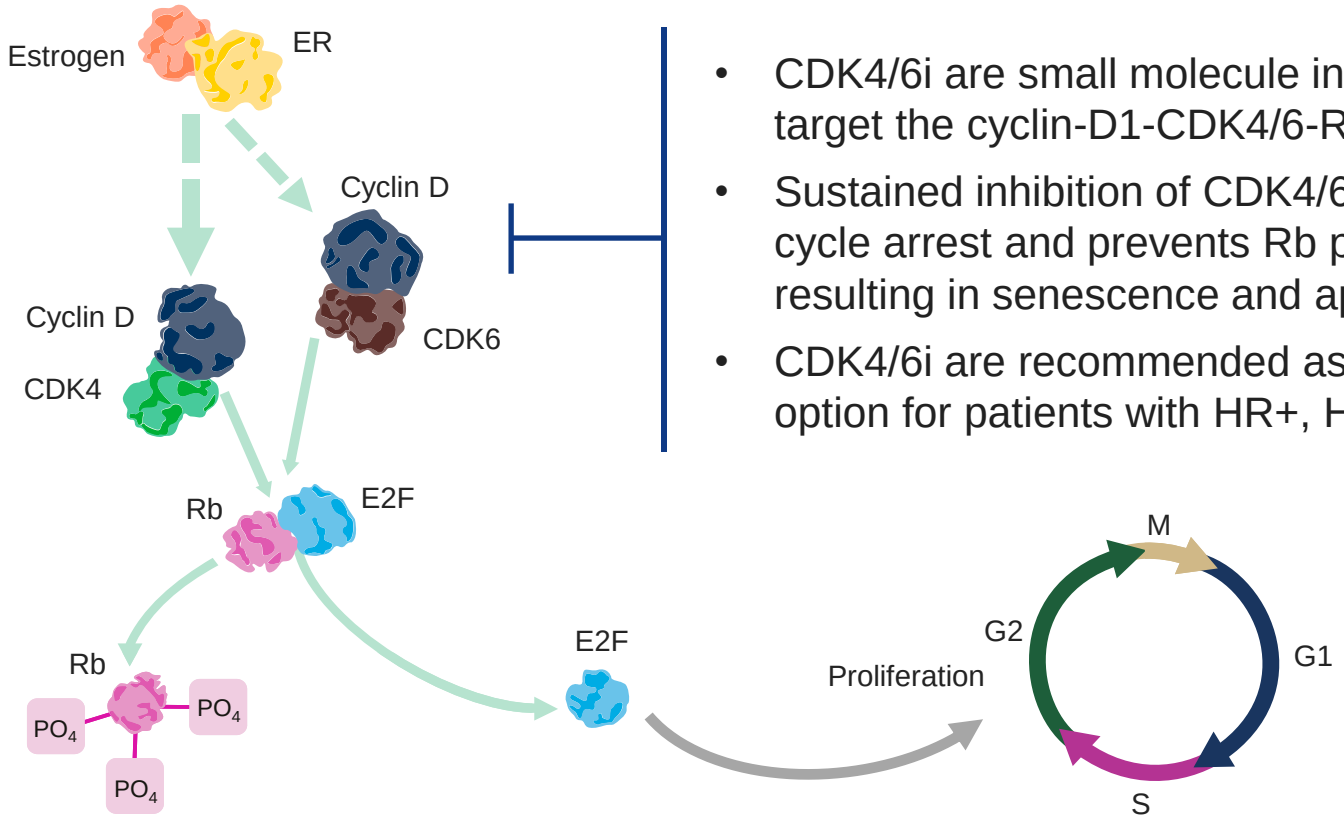
1. Rugo HS, et al. Presented at: ESMO Breast Cancer Conference 2025. Poster 215P. 2. Fasching PA, et al. *Geburtshilfe Frauenheilkd*. 2024;84(2):164-184.

THE USE OF CDK4/6i IN HR+, HER2- EARLY BREAST CANCER

CDK4/6i in Breast Cancer: Mechanism of Action

Activation of CDK4 and CDK6 through the cyclin D1-CDK4/6-Rb pathway leads to cellular proliferation[1]

This pathway is deregulated in most tumors[1,2]



- CDK4/6i are small molecule inhibitors that target the cyclin-D1-CDK4/6-Rb pathway[1,3]
- Sustained inhibition of CDK4/6 induces cell cycle arrest and prevents Rb phosphorylation, resulting in senescence and apoptosis[3,4]
- CDK4/6i are recommended as a treatment option for patients with HR+, HER2- MBC[1]

CDK4/6i are now a treatment option in the EBC setting in combination with adjuvant ET[1]

CDK4/6=cyclin-dependent kinase 4/6; CDK4/6i=CDK4/6 inhibitor; E2F=E2F transcription factor; EBC=early breast cancer; ER=estrogen receptor; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; M, G1, S, G2=phases of the cell cycle; MBC=metastatic breast cancer; PO_4=phosphate; Rb=retinoblastoma protein.

1. Braal CL, et al. *Drugs*. 2021;81(3):317-331. 2. Vermeulen K, et al. *Cell Prolif.* 2003;36(3):131-149. 3. Schettini F, et al. *Front Oncol*. 2018;8:608. 4. Torres-Guzmán R, et al. *Oncotarget*. 2017;8(41):69493-69507.

CDK4/6i in HR+, HER2- EBC: Trial Designs

	monarchE[a,1-3]	NATALEE[a,4-6]
CDK4/6i	Abemaciclib	Ribociclib
Design	Phase 3, randomized, open-label	Phase 3, randomized, open-label
Sample size	5637	5101
Study population	Stages IB-III Node-positive, high-risk N1/N1mi + Grade 3 and/or tumor ≥5 cm, N2/N3	Stage II-III Node-positive and N0 (Select higher-risk Stage IIA N0)
CDK4/6i dose	Abemaciclib 150 mg BID + ET (Continuous dosing)	Ribociclib 400 mg QD (3 wk on/1 wk off) + NSAI (Continuous dosing)
ET partner	Physician's choice (Tamoxifen or AI)[b]	NSAI (Letrozole or anastrozole)[c]
Duration of CDK4/6i treatment	2 years	3 years
First results reported	2020	2023
Primary endpoint	IDFS	

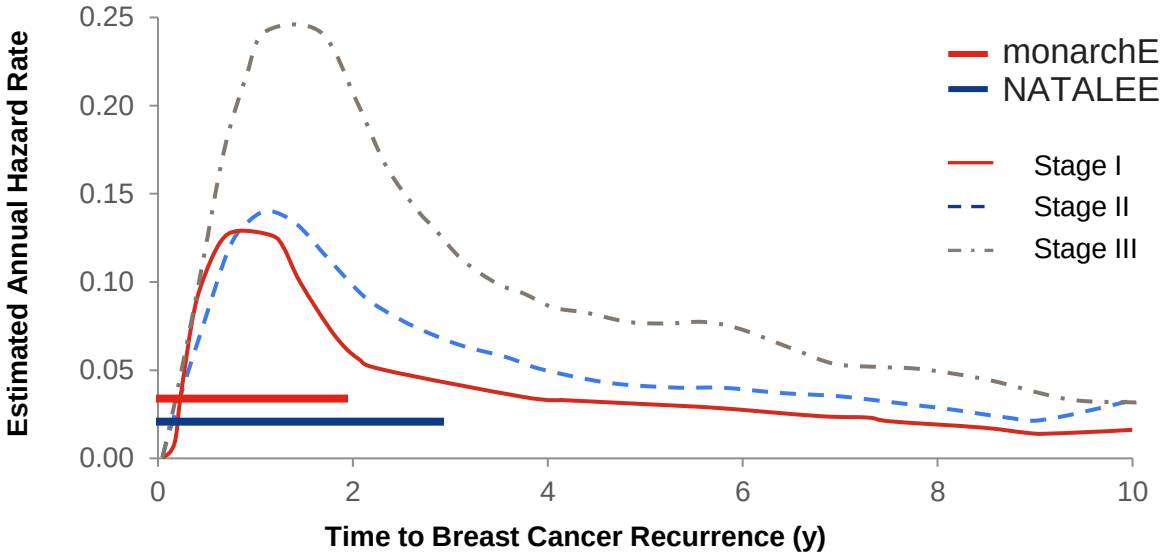
Note: The table above is not intended as a head-to-head trial comparison. Cross-trial comparison of efficacy, tolerability, and safety cannot be made.
Two Phase 3 trials that evaluated palbociclib (PENELOPE-B[7] and PALLAS[8]) in EBC did not meet statistical significance improvement in IDFS and are not shown above.

These trials were conducted in patients with HR+, HER2- EBC who had an increased risk of recurrence.
The trials differed in study design, patient populations, and treatment durations

[a]Trial met statistical significance. [b]With or without ovarian suppression per standard practice. [c]NSAI was investigator choice; men and premenopausal women also received LHRH agonists as per standard of care.
AI=aromatase inhibitor; BID=twice daily; CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; EBC=early breast cancer; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; IDFS=invasive disease-free survival; LHRH=luteinizing hormone–releasing hormone; N=node; N1mi= micrometastases; N1=1–3 ALN; N2=4–9 ALN; N3=10+ ALN; NSAI=nonsteroidal aromatase inhibitor; QD=once daily; wk=week.
1. https://www.clinicaltrials.gov/ct2/show/NCT03155997. (Accessed April 4, 2024). 2. Rastogi P, et al. Oral presentation at: SABCS 2020. Abstract GS1-01. 3. Johnston SRD, et al. *J Clin Oncol*. 2020;38(34):3987-3998.
4. https://clinicaltrials.gov/study/NCT03701334. (Accessed March 4, 2024). 5. Slamon DJ, et al. Oral presentation at: ASCO 2023. Abstract LBA500.
6. Slamon D, et al. *N Engl J Med*. 2024;390(12):1080-1091. 7. https://www.clinicaltrials.gov/ct2/show/NCT01864746. (Accessed April 24, 2023).
8. https://www.clinicaltrials.gov/ct2/show/NCT02513394. (Accessed April 3, 2024).

CDK4/6i in HR+, HER2- EBC: Duration of Treatment

Risk of First Recurrence After First Diagnosis in EBC[1]



	monarchE[2]	NATALEE[3]
CDK4/6i	Abemaciclib	Ribociclib
Duration of CDK4/6i treatment	2 years	3 years

Note: The table above is not intended for comparison as the information is not from any head-to-head trials. Cross-trial comparison of efficacy, tolerability, and safety cannot be made.

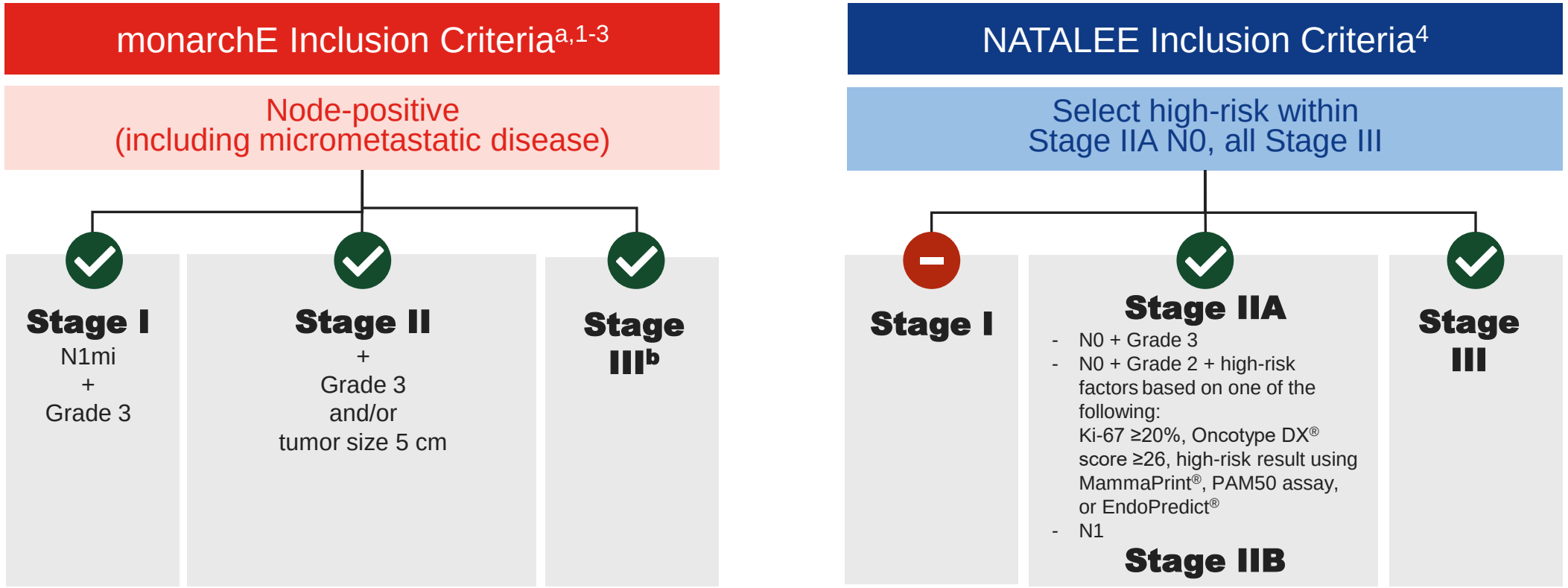
CDK4/6i trials in EBC have focused on 2-3 years of adjuvant treatment, during the time when recurrence peaks[2,3]

CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; EBC=early breast cancer; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; y=year.

1. Cheng L, et al. *Cancer Epidemiol Biomarkers Prev*. 2012;21(5):800-809. 2. https://clinicaltrials.gov/study/NCT03155997. (Accessed July 16, 2024).
3. https://clinicaltrials.gov/study/NCT03701334. (Accessed July 16, 2024).

High-Risk Criteria: monarchE and NATALEE

The criteria for defining and including patients with high-risk, HR+, HER2- EBC varied across adjuvant trials



Note: This table is not intended as a head-to-head trial comparison. Cross-trial comparison of efficacy, tolerability, and safety cannot be made. All the product/company names mentioned herein are trademarks of their respective owners.
[a]Patients in monarchE were required to have at least 1 positive ALN. In monarchE, AJCC stage was derived based on pathological tumor size and number of positive lymph nodes following primary surgery.[5] Cytological evaluation of lymph node status was used where patients received NAC. [b]Stage IIIB T4N1 can be included if Grade 3 and/or tumor ≥5 cm.
AJCC=American Joint Committee on Cancer; ALN=axillary lymph node; EBC=early breast cancer; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; N=node; N1=1–3 ALN; NAC=neoadjuvant chemotherapy; T=tumor.
1. Johnston SRD, et al. *J Clin Oncol.* 2020;38(34):3987-3998. 2. Rastogi P, et al. *J Clin Oncol*. 2024;42(9):987-93; 3. Abemaciclib [US PI]. Indianapolis, IN, USA: Eli Lilly USA LLC, 2025.
4. Slamon DJ, et al. *Ther Adv Med Oncol.* 2023;15:17588359231178125. 5. Amin MB, et al. *AJCC Cancer Staging Manual.* 8th ed. New York: Springer, 2017.

TRIALS OF FDA-APPROVED CDK4/6i IN HR+, HER2- EARLY BREAST CANCER

- monarchE
- NATALEE

Abemaciclib in EBC: FDA Prescribing Information

Abemaciclib Indication in EBC

Abemaciclib is indicated in combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive, early breast cancer at high risk of recurrence.

Warnings and Precautions

The FDA label carries warnings for diarrhea, neutropenia, ILD/pneumonitis, hepatotoxicity, venous thromboembolism, and embryo-fetal toxicity.

Blood count and liver function monitoring are recommended before treatment initiation, in the early treatment cycles, and as clinically indicated.

EBC=early breast cancer; FDA=US Food and Drug Administration; ILD=interstitial lung disease.

Abemaciclib [US PI]. Indianapolis, IN, USA: Eli Lilly USA LLC, 2025.

Abemaciclib in EBC: Guideline Recommendations

National Comprehensive Cancer Network® (NCCN®) Recommendation[1]

For the treatment of HR+, HER2-, node-positive, high-risk EBC, the NCCN recommends consideration of 2 years of abemaciclib in combination with ET as an **NCCN Category 1, Preferred** treatment option.[a]

American Society of Clinical Oncology® (ASCO®) Recommendation[2,3]

Abemaciclib for 2 years plus ET for ≥5 years may be offered to patients meeting the criteria of the ITT monarchE population with resected, HR+, HER2-, node-positive EBC at high risk of recurrence.[b]

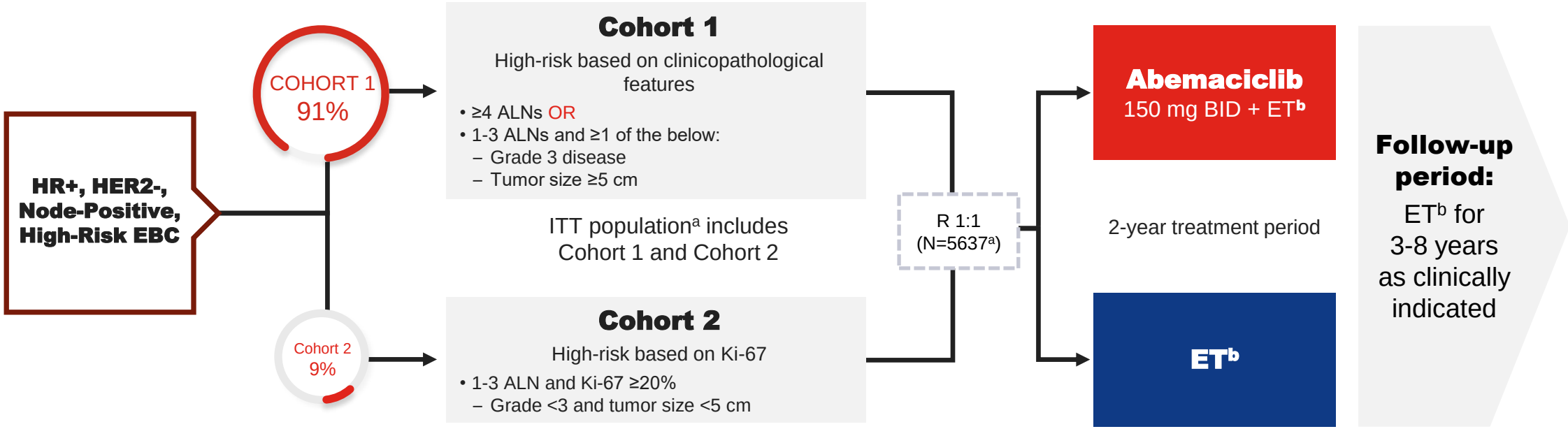
The panel promotes the use of abemaciclib primarily in those who would have been eligible for monarchE based on that trial's eligibility criteria.

(Evidence quality: **High**; strength of recommendation: **Strong**)

[a]Based on NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer Version 5.2025. High risk is defined as ≥4 positive ALNs (confirmed preoperatively and/or at surgery), or 1-3 positive ALNs with either Grade 3 disease or tumor size ≥5 cm (on preoperative imaging and/or at surgery). VTE risk should be considered when combining abemaciclib with tamoxifen. Category 1 is based upon high-level evidence (≥1 randomized Phase 3 trials or high-quality, robust meta-analyses), there is uniform NCCN® consensus (≥85% support of the Panel) that the intervention is appropriate. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
[b]Based on the ASCO 2024 Rapid Recommendation Update. High risk of recurrence is defined as having ≥4 positive ALNs or 1-3 positive ALNs with at least one of the following: Grade 3 disease, tumor size ≥5 cm, or Ki-67 ≥20%.
ALN=axillary lymph node; EBC=early breast cancer; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; ITT=intention-to-treat; VTE=venous thromboembolism.
1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.5.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed October 16, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. 2. Freedman RA, et al. *J Clin Oncol*. 2024;42(18):2233-2235. 3. Caswell-Jin JL, et al. *JCO Oncol Pract.* 2025;21(3):287-291.

monarchE: Study Design[1-5]

Phase 3, open-label study of abemaciclib in addition to ET in patients with high-risk, node-positive, HR+, HER2- EBC



Stratified for:
- Prior chemotherapy
- Menopausal status
- Region

Primary Objective: IDFS
Secondary Objectives: IDFS in high Ki-67 populations, DRFS, OS[c], safety, PK, PROs

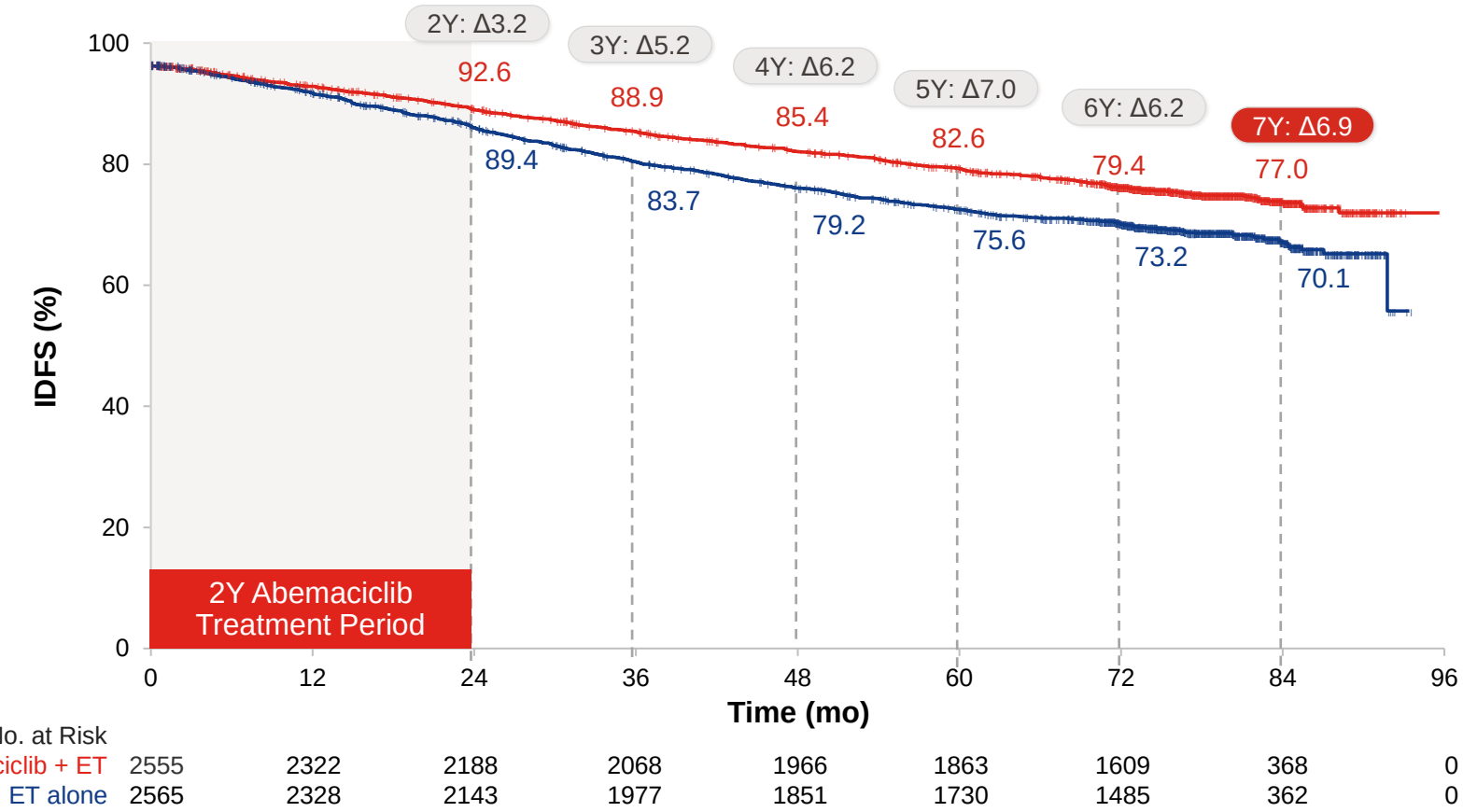
[a]Recruitment from July 2017 to August 2019. Data for the monarchE Cohort 1 population that forms the basis of multiple global approvals is in the supplement. [b]ET of physician's choice (eg, AI, tamoxifen, GnRH).
[c]After the primary IDFS analysis, following consultation with regulators, the target number of OS events was increased from 390 to 650, to ensure a minimum follow-up of ≥5 years and enable a more mature survival dataset.[6]
AI=aromatase inhibitor; ALN=axillary lymph node; BID=twice daily; DRFS=distant relapse-free survival; EBC=early breast cancer; ET=endocrine therapy; GnRH=gonadotropin-releasing hormone; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; IDFS=invasive disease-free survival; ITT=intention-to-treat; LHRH=luteinizing hormone–releasing hormone; OS=overall survival; PK=pharmacokinetics; PRO=patient-reported outcome; R=randomization.

1. ClinicalTrials.gov. Accessed April 24, 2023. https://www.clinicaltrials.gov/ct2/show/NCT03155997 2. Harbeck N, et al. *Ann Oncol*. 2021;32(12):1571-1581. 3. Johnston SRD, et al. *Lancet Oncol*. 2023;24(1):77-90.
4. Rastogi P, et al. *J Clin Oncol*. 2024;42(9):987-993. 5. Abemaciclib [US PI]. Indianapolis, IN, USA: Eli Lilly USA LLC, 2025. 6. Johnston S, et al. Presented at: ESMO 2025. LBA13.

Cohort 1

6.3Y mF/U

monarchE Cohort 1: IDFS[1,2]



27.4%

REDUCTION IN THE RISK OF DEVELOPING AN IDFS EVENT

Hazard ratio=0.726
(95% CI: 0.648-0.815),
nominal p<.0001

# IDFS Events	Abemaciclib + ET	512
	ET Alone	678

ET=endocrine therapy; IDFS=invasive disease-free survival; mF/U=median follow-up; mo=month; y=year.

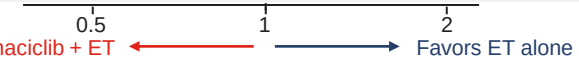
1. Johnston S, et al. Presented at: ESMO 2025. LBA13. 2. Johnston S, et al. *Ann Oncol*. Published online October 17, 2025. doi:10.1016/j.annonc.2025.10.005.

monarchE Cohort 1: IDFS for Key Prespecified Subgroups[a,1,2]

Cohort 1

6.3Y mF/U

	Abemaciclib + ET		ET		
	n	Events	n	Events	Hazard ratio (95% CI)	Interaction p value
Overall	2555	512	2565	678	0.726 (0.648-0.815)	
Menopausal status						.329
Premenopausal	1108	194	1112	265	0.681 (0.566-0.819)	
Postmenopausal	1447	318	1453	413	0.764 (0.660-0.885)	
Prior treatment						.440
Neoadjuvant chemotherapy	942	240	945	327	0.690 (0.584-0.815)	
Adjuvant chemotherapy	1514	247	1517	321	0.751 (0.636-0.886)	
Age, years						.339
<65	2150	409	2190	560	0.709 (0.624-0.805)	
≥65	405	103	375	118	0.814 (0.625-1.061)	
Baseline ECOG PS						.056
0	2182	425	2147	569	0.697 (0.614-0.790)	
1	371	87	413	108	0.940 (0.708-1.246)	
Primary tumor size						.177
<20 mm	676	98	656	150	0.612 (0.474-0.790)	
≥20 mm but <50 mm	1232	263	1278	332	0.800 (0.680-0.940)	
≥50 mm	600	140	606	191	0.692 (0.556-0.860)	
Number of positive lymph nodes						.822
1–3	873	142	888	188	0.752 (0.605-0.935)	
4–9	1104	197	1119	282	0.685 (0.571-0.821)	
10 or more	571	171	552	207	0.726 (0.593-0.889)	
Tumor grade						.780
Grade 1	186	27	190	42	0.645 (0.398-1.047)	
Grade 2	1181	234	1193	312	0.724 (0.611-0.858)	
Grade 3	1063	226	1050	281	0.770 (0.646-0.918)	
Tumor stage						.789
II	510	74	534	101	0.756 (0.560-1.021)	
III	2034	436	2027	576	0.720 (0.635-0.815)	
First ET						.076
Tamoxifen	783	142	805	218	0.620 (0.502-0.766)	
AI	1753	367	1725	458	0.776 (0.677-0.891)	



[a]Region of enrollment, race, and progesterone status data not shown.

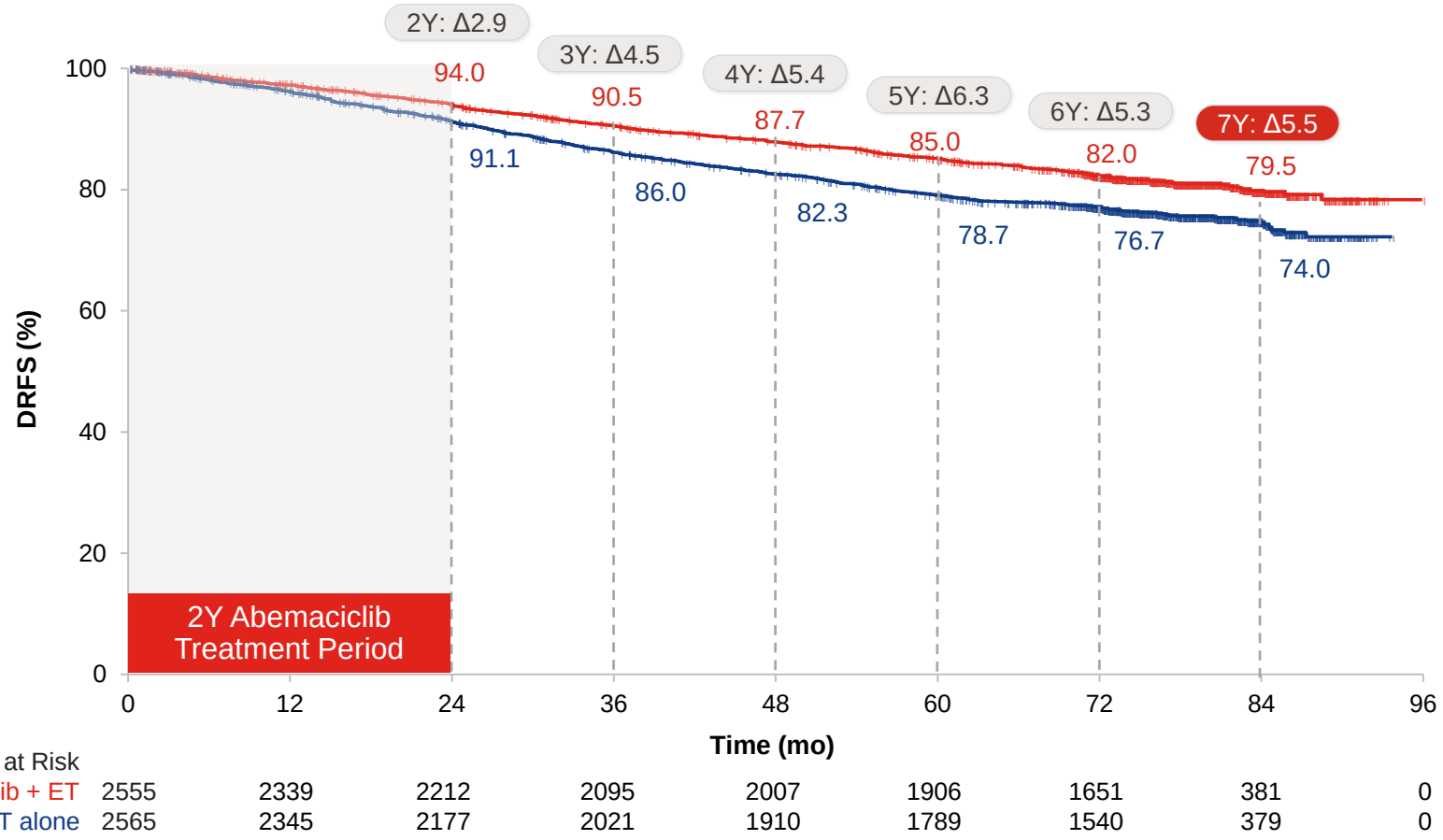
AI=aromatase inhibitor; ECOG PS=Eastern Cooperative Oncology Group performance status; ET=endocrine therapy; IDFS=invasive disease-free survival; mF/U=median follow-up; y=year.

1. Johnston S, et al. Presented at: ESMO 2025. LBA13. 2. Johnston S, et al. *Ann Oncol*. Published online October 17, 2025. doi:10.1016/j.annonc.2025.10.005.

Cohort 1

6.3Y mF/U

monarchE Cohort 1: DRFS[1,2]



26.4%

REDUCTION IN THE RISK OF DEVELOPING A DRFS EVENT

Hazard ratio=0.736
(95% CI: 0.651-0.832),
p<.0001

# DRFS Events	Abemaciclib + ET	448
	ET Alone	589

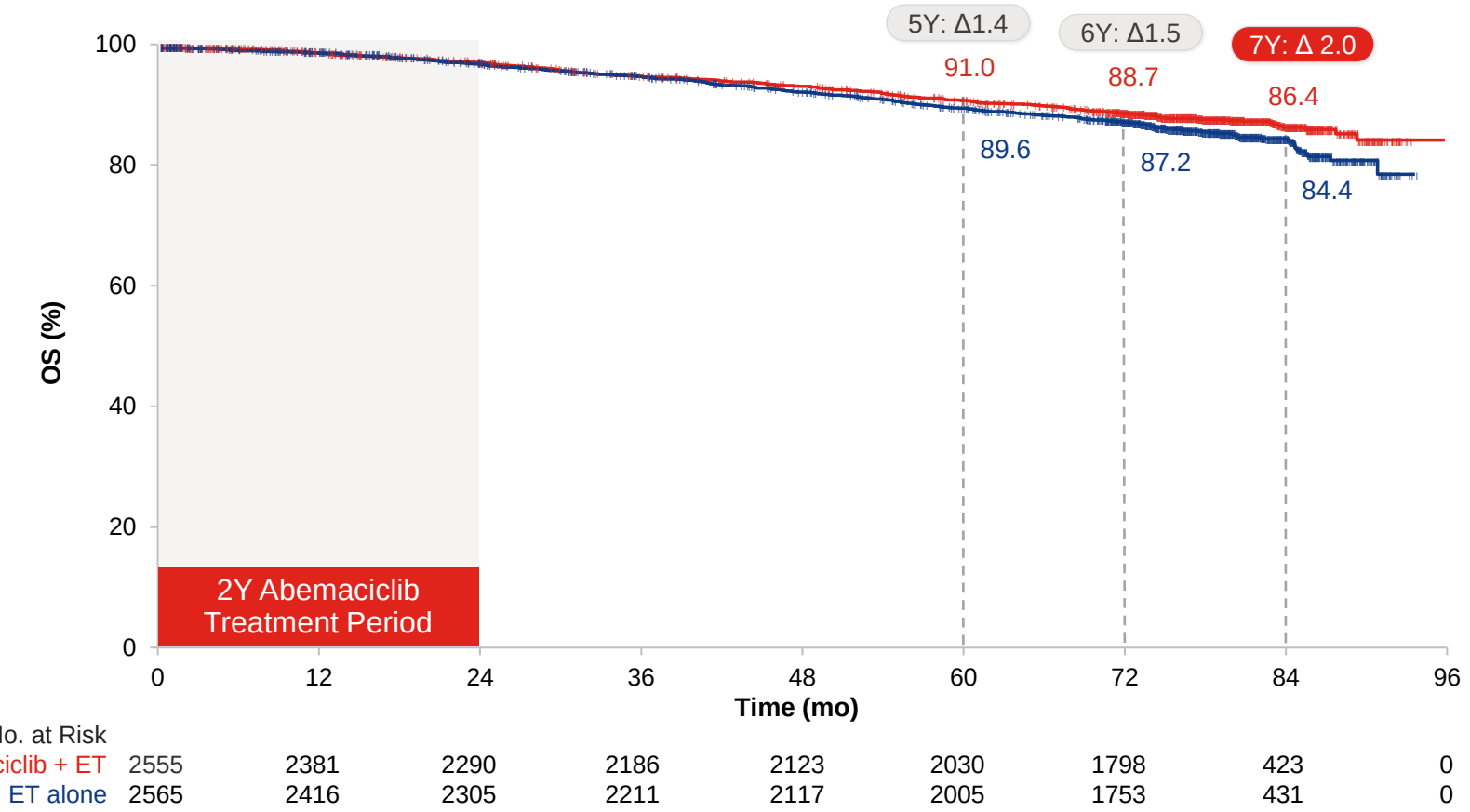
DRFS=distant relapse-free survival; ET=endocrine therapy; mF/U=median follow-up; mo=month; y=year.

1. Johnston S, et al. Presented at: ESMO 2025. LBA13. 2. Johnston S, et al. *Ann Oncol*. Published online October 17, 2025. doi:10.1016/j.annonc.2025.10.005.

Cohort 1

6.3Y mF/U

monarchE Cohort 1: OS[1,2]



16.5%

REDUCTION IN THE RISK OF DEATH

Hazard ratio=0.835
(95% CI: 0.713-0.977),
p<.0239

# OS Events	Abemaciclib + ET	286
	ET Alone	344

ET=endocrine therapy; mF/U=median follow-up; mo=month; OS=overall survival; y=year.

1. Johnston S, et al. Presented at: ESMO 2025. LBA13. 2. Johnston S, et al. *Ann Oncol.* Published online October 17, 2025. doi:10.1016/j.annonc.2025.10.005.

ITT

42-mo mF/U

monarchE: Treatment-Emergent AEs

AEs in Either Arm (≥20%), %	Abemaciclib + ET (n=2791)		ET Only (n=2800)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Diarrhea[a]	83.6	7.8	8.7	0.2
Neutropenia	45.9	19.6	5.6	0.9
Fatigue[b]	40.8	2.9	18.0	0.1
Leukopenia	37.7	11.4	6.6	0.4
Abdominal pain[b]	35.7	1.4	9.9	0.3
Nausea	29.6	0.5	9.0	0.1
Arthralgia[b]	26.5	0.3	37.9	1.0
Anemia	24.5	2.1	3.9	0.4
Hot flush[b]	15.4	0.1	23.0	0.4

[a]One Grade 5 event of diarrhea. [b]Patient has a maximum CTCAE Grade of 3.
AE=adverse event; CTCAE=Common Terminology Criteria for Adverse Events; ET=endocrine therapy; ITT=intention-to-treat; mF/U=median follow-up; mo=month.
Johnston SRD, et al. *Lancet Oncol*. 2023;24(1):77-90.

ITT

6.3Y mF/U

monarchE: SAEs and Fatal AEs[1,2]

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

- Safety was consistent with prior analyses, as all treated patients completed treatment ≥4 years ago
- No relevant differences in treatment arms in causes of deaths due to AEs

[a]During 2-year treatment period or within 30 days of study treatment discontinuation. [b]>30 days after study treatment discontinuation. [c]All SAEs up to 5 years from randomization collected regardless of causality. [d]All deaths not due to breast cancer in LTFU collected regardless of causality. Deaths due to unknown cause are excluded. Included SOC and PTs reported in ≥5 patients in either arm.
AE=adverse event; ET=endocrine therapy; ITT=intention-to-treat; LTFU=long-term follow-up; mF/U=median follow-up; N/A=not applicable; PT=primary therapy; SAE=serious adverse event; SOC=standard of care; y=year.
1. Johnston S, et al. Presented at: ESMO 2025. LBA13. 2. Johnston S, et al. *Ann Oncol*. Published online October 17, 2025. doi:10.1016/j.annonc.2025.10.005.

ITT

6.3Y mF/U

monarchE: Discontinuation Rates and Treatment Completion

100%
of monarchE patients are off abemaciclib treatment[1]

~80% have been followed for ≥2Y since treatment with abemaciclib[2]

Abemaciclib dose adjustments due to AEs
- Dose holds: 61.7%[1,4]
- Dose reductions: 43.6%[1,4]
- Discontinuations: 18.5% (8.9% after dose reduction)[3,4]

AE=adverse event; ITT=intention-to-treat; mF/U=median follow-up; y=year.

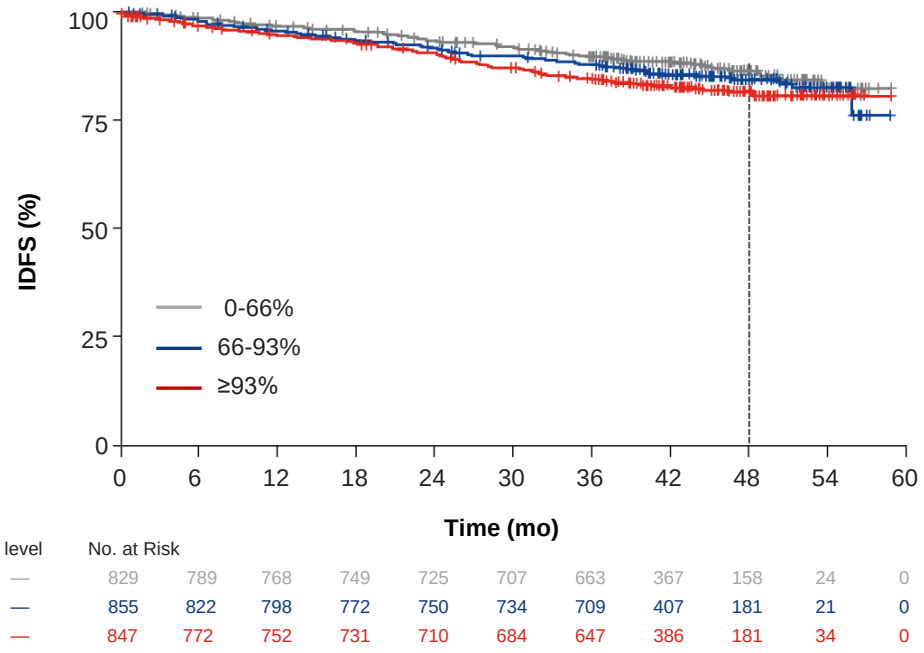
1. Johnston SRD, et al. *Lancet Oncol*. 2023;24(1):77-90. 2. Rastogi P, et al. *J Clin Oncol*. 2024;42(9):987-993. 3. Rugo HS, et al. *Ann Oncol.* 2022;33(6):616-627.
4. Johnston S, et al. *Ann Oncol*. Published online October 17, 2025. doi:10.1016/j.annonc.2025.10.005.

Cohort 1 | ITT

42-mo mF/U

monarchE Cohort 1: Dose Reductions

IDFS in Abemaciclib Arm by Relative Dose Intensity for Cohort 1[a,1]



Abemaciclib Exposure by the Number of Dose Reductions in ITT

	No Dose Reduction n=1570	1 Dose Reduction n=832	2 Dose Reductions n=389
Treatment Duration, mo			
Median (Q1-Q3)	23.7 (14.9-23.8)	23.7 (20.6-23.8)	23.7 (13.2-23.8)
>3 mo, %	86	95	94
>6 mo, %	81	90	86

Abemaciclib Recommended Dose[2]

150 mg BID

1st dose reduction: 100 mg BID

2nd dose reduction: 50 mg BID

In EBC, abemaciclib efficacy was not shown to be compromised by dose reductions[a,1]

[a]RDI was defined as the average daily dose of abemaciclib received by each patient over the treatment duration relative to the full dose (150 mg BID). Dose adjustments result in lower RDI. To explore the impact of dose adjustments on abemaciclib efficacy, patients treated with abemaciclib were classified into 3 equal-sized subgroups according to their RDI. IDFS rates were estimated within each subgroup.
BID=twice daily; EBC=early breast cancer; IDFS=invasive disease-free survival; ITT=intention-to-treat; mF/U=median follow-up; mo=month; Q=quartile; RDI=relative dose intensity.
1. Goetz MP, et al. *NPJ Breast Cancer*. 2024;10(1):34. 2. Abemaciclib [US PI]. Indianapolis, IN, USA: Eli Lilly USA LLC, 2025.

Cohort 1

6.3Y mF/U

monarchE: Efficacy Summary

Treatment benefit at 6.3 years median follow-up[1,2]

	IDFS	DRFS	OS
Relative risk reduction	27.4%	26.4%	16.5%
Absolute benefit at 7Y	6.9%	5.5%	2.0%

DRFS=distant relapse-free survival; IDFS=invasive disease-free survival; mF/U=median follow-up; OS=overall survival; y=year.

1. Johnston S, et al. Presented at: ESMO 2025. LBA13. 2. Johnston S, et al. *Ann Oncol*. Published online October 17, 2025. doi:10.1016/j.annonc.2025.10.005.

monarchE: Safety Summary[a]

Safety Data[1]

100% of patients are off abemaciclib treatment[b]

AEs were mainly low grade, and generally manageable with comedication and/or dose adjustments[1,2]

Most frequent AEs: any grade (Grade ≥3)[2]

Diarrhea	Neutropenia	Fatigue
83.6% (7.8%)	45.9% (19.6%)	40.8% (2.9%)

Serious AEs occurred in 15.5% of patients in the abemaciclib arm vs 9.1% in the ET only arm[1]

[a]Latest available safety data. [b]Includes patients (0.8%) who were randomized but never treated.
AE=adverse event; ET=endocrine therapy; ITT=intention-to-treat.
1. Johnston SRD, et al. *Lancet Oncol*. 2023;24(1):77-90. 2. Rugo HS, et al. *Ann Oncol*. 2022;33(6):616-627.

Ribociclib in EBC: FDA Prescribing Information

Ribociclib Indication in EBC

Ribociclib is indicated in combination with an aromatase inhibitor for the adjuvant treatment of adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative Stage II and III early breast cancer at high risk of recurrence.

Warning and Precautions

The FDA label carries warnings for ILD/pneumonitis, severe cutaneous adverse reactions, QT interval prolongation, increased QT prolongation with concomitant use of tamoxifen, liver toxicity, neutropenia, and embryo-fetal toxicity.

ECG, electrolytes, liver function tests, and blood counts should be performed before treatment initiation, in the early treatment cycles, and as clinically indicated.

EBC=early breast cancer; ECG=electrocardiogram; FDA=US Food and Drug Administration; ILD=interstitial lung disease.

Ribociclib [US PI]. East Hanover, NJ, USA: Novartis Pharmaceuticals Corporation, 2025.

Ribociclib in EBC: Guideline Recommendations

NCCN Recommendation[1]

For the treatment of HR+, HER2- EBC with any lymph node involvement (excluding microscopic nodal involvement), or if no nodal involvement either tumor size >5 cm, or if tumor size 2-5 cm, either Grade 2 (and high genomic risk or Ki-67 ≥20%), or Grade 3, the NCCN recommends consideration of 3 years of ribociclib with AI as an **NCCN Category 1, Preferred** treatment option.[a]

ASCO Recommendation[2,3]

The Panel recommends, based on the Phase 3 NATALEE trial, that adjuvant ribociclib (400 mg once daily, 3 weeks on followed by 1 week off) for 3 years plus ET may be offered to patients with anatomic Stage II or III breast cancer who would have met criteria for study entry and have a high risk of recurrence.

(Evidence quality: **High**; strength of recommendation: **Conditional**)

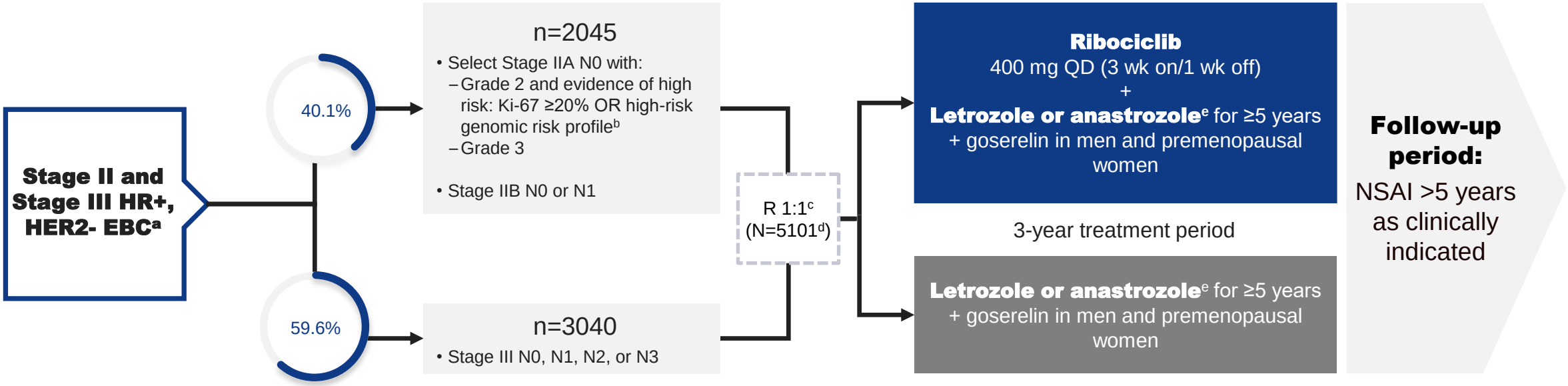
[a]Based on NCCN Guidelines® for Breast Cancer Version 5.2025. Category 1 is based upon high-level evidence (≥1 randomized Phase 3 trials or high-quality, robust meta-analyses), there is uniform NCCN® consensus (≥85% support of the Panel) that the intervention is appropriate. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

AI=aromatase inhibitor; ASCO=American Society of Clinical Oncology; EBC=early breast cancer; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; NCCN=National Comprehensive Cancer Network.

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.5.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed October 16, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. 2. Freedman RA, et al. *J Clin Oncol.* 2024;42(18):2233-2235. 3. Caswell-Jin JL, et al. *JCO Oncol* Pract. 2025;21(3):287-291.

NATALEE: Study Design[1-4]

Phase 3, open-label study of ribociclib in addition to ET in patients with HR+, HER2- EBC



Prior treatment:

Patients could have received up to 12 months of neoadjuvant or adjuvant ET to random assignment

Stratified for:

- Anatomical stage: II vs. III
- Menopausal status: men and premenopausal women vs. postmenopausal women
- Prior (neo)adjuvant chemotherapy: yes vs. no
- Geographic location: North America/Western Europe/Oceania vs rest of world

Primary Objective: IDFS using STEEP criteria[f]

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

Exploratory Endpoints: Locoregional RFS, gene expression and alterations in tumor ctDNA/ctRNA samples

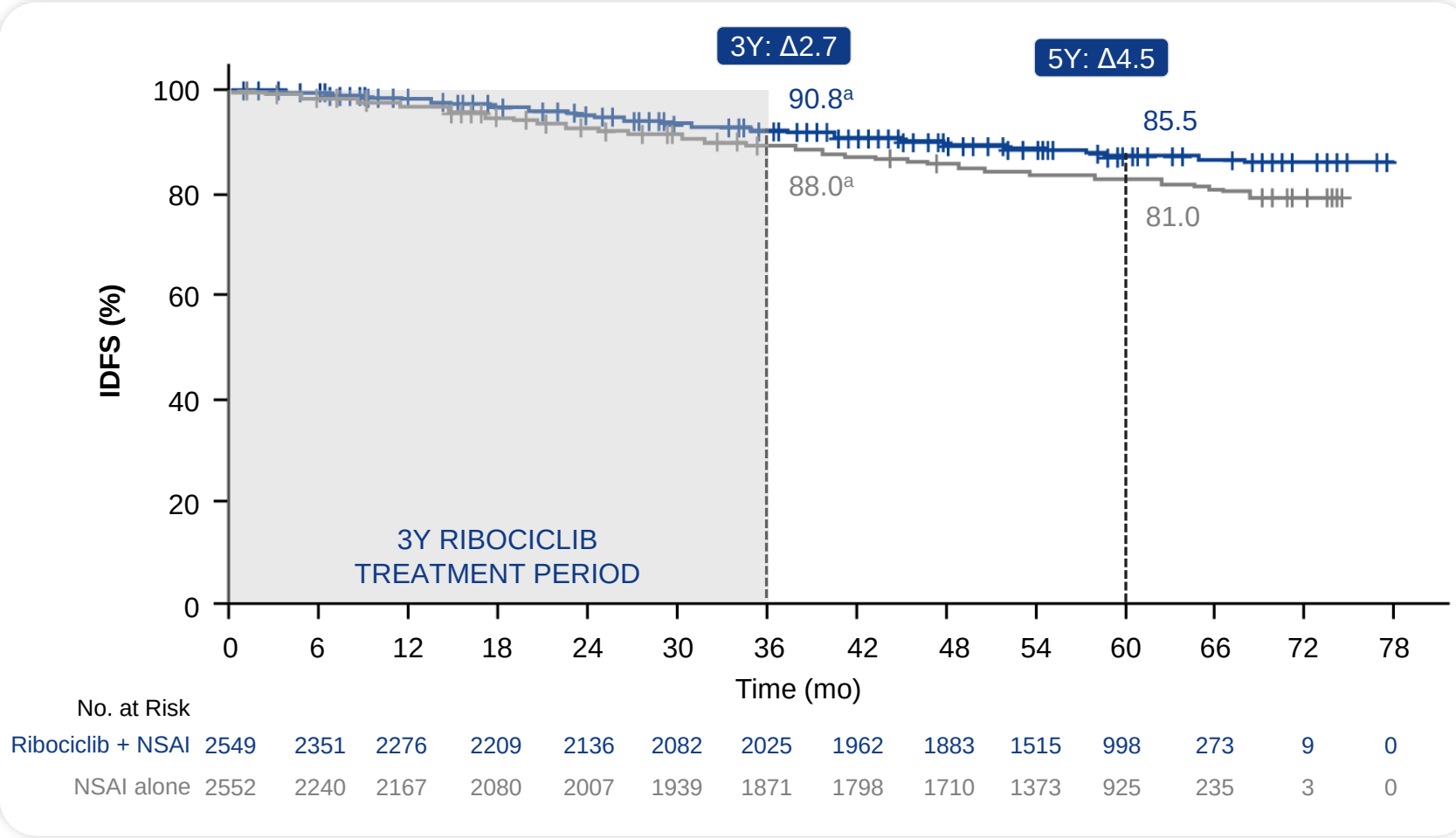
[a]Enrollment of patients with Stage II disease was capped at 40%. Fourteen patients had Stage I disease and 2 had missing data. [b]High genomic risk was based on one of the following assays: Oncotype DX score of ≥26, Prosigna PAM50, Mammaprint, or Endopredict. [c]Open-label design. [d]Between January 10, 2019, and April 20, 2021. [e]Depending on the investigator. [f]The primary endpoint was met at the second interim efficacy analysis with a medium follow-up of 27.7 months. ctDNA=circulating tumor DNA; ctRNA=circulating tumor RNA; DDFS=distant disease-free survival; EBC=early breast cancer; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; IDFS=invasive disease-free survival; N=node; NSAI=nonsteroidal aromatase inhibitor; OS=overall survival; PK=pharmacokinetics; PRO=patient-reported outcome; QD=once daily; R=randomization; RFS=recurrence-free survival; STEEP=Standardized Definitions for Efficacy Endpoints; wk=week.

1. https://www.clinicaltrials.gov/ct2/show/NCT03701334. (Accessed March 4, 2024). 2. Slamon D, et al. *N Engl J Med*. 2024;390(12):1080-1091. 3. Ribociclib [US PI]. East Hanover, NJ, USA: Novartis Pharmaceuticals Corporation, 2025. 4. Hortobagyi G, et al. Oral presentation at: SABCS 2023. Abstract GS03-03.

ITT

55.4-mo mF/U

NATALEE: IDFS



28.4%

REDUCTION IN THE RISK OF DEVELOPING AN IDFS EVENT

Hazard ratio=0.716
(95% CI: 0.618-0.829)
nominal 1-sided p<.0001

# IDFS Events	Ribociclib + NSAI	317
	NSAI alone	407

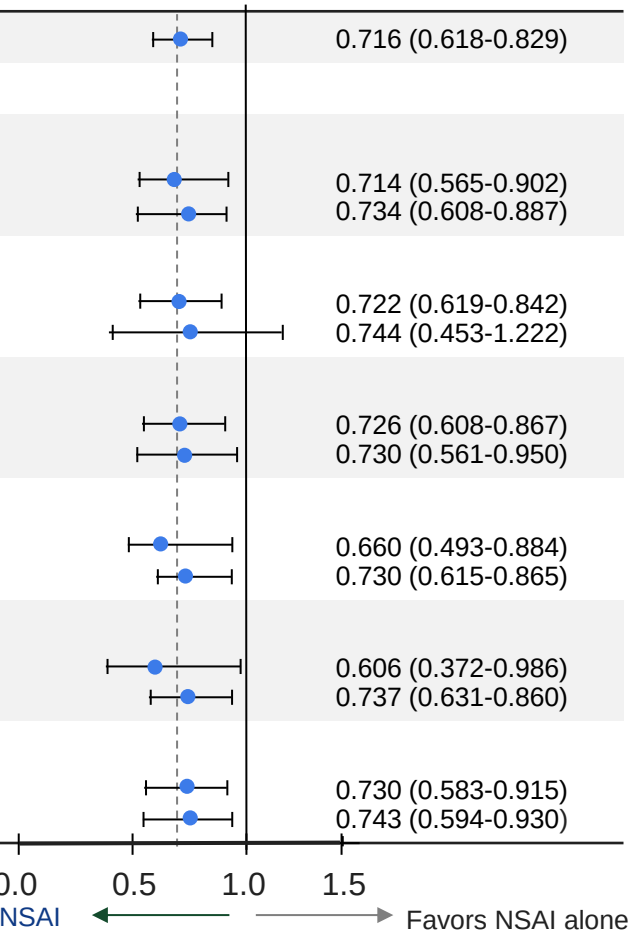
[a]The difference between percentages does not equal 2.7 due to rounding.
IDFS=invasive disease-free survival; ITT=intention-to-treat; mF/U=median follow-up; mo=month; NSAI=nonsteroidal aromatase inhibitor; y=year.
Crown J, et al. *ESMO Open*. 2025;10(11):105858.

ITT

55.4-mo mF/U

NATALEE: IDFS for Key Prespecified Subgroups

	Ribociclib + NSAI		NSAI alone			
	Events/n	5Y IDFS Rate, %	Events/n	5Y IDFS Rate, %	5YΔ, %	Hazard Ratio (95% CI)
ITT	317/2549	85.5	407/2552	81.0	4.5	0.716 (0.618-0.829)
Subgroups						
Menopausal status						
Men and premenopausal women	124/1126	87.1	162/1132	82.6	4.5	0.714 (0.565-0.902)
Postmenopausal women	193/1423	84.3	245/1420	79.7	4.5	0.734 (0.608-0.887)
Prior chemotherapy[a]						
Yes	290/2249	84.9	370/2245	80.2	4.7	0.722 (0.619-0.842)
No	27/300	89.6	37/307	86.6	3.0	0.744 (0.453-1.222)
Prior ET						
Yes	220/1832	85.8	278/1807	81.3	4.5	0.726 (0.608-0.867)
No	97/717	84.6	129/745	80.3	4.4	0.730 (0.561-0.950)
AJCC stage						
Stage II	75/1012	91.7	113/1034	87.9	3.7	0.660 (0.493-0.884)
Stage III	241/1527	81.2	294/1512	75.6	5.6	0.730 (0.615-0.865)
Nodal status[b]						
N0	25/285	90.3	46/329	84.6	5.7	0.606 (0.372-0.986)
N1-N3	292/2261	84.9	360/2218	80.5	4.4	0.737 (0.631-0.860)
Ki-67 status[c]						
Ki-67 ≤20%	132/1200	87.0	177/1241	83.0	4.1	0.730 (0.583-0.915)
Ki-67 >20%	138/919	83.2	172/932	78.1	5.1	0.743 (0.594-0.930)

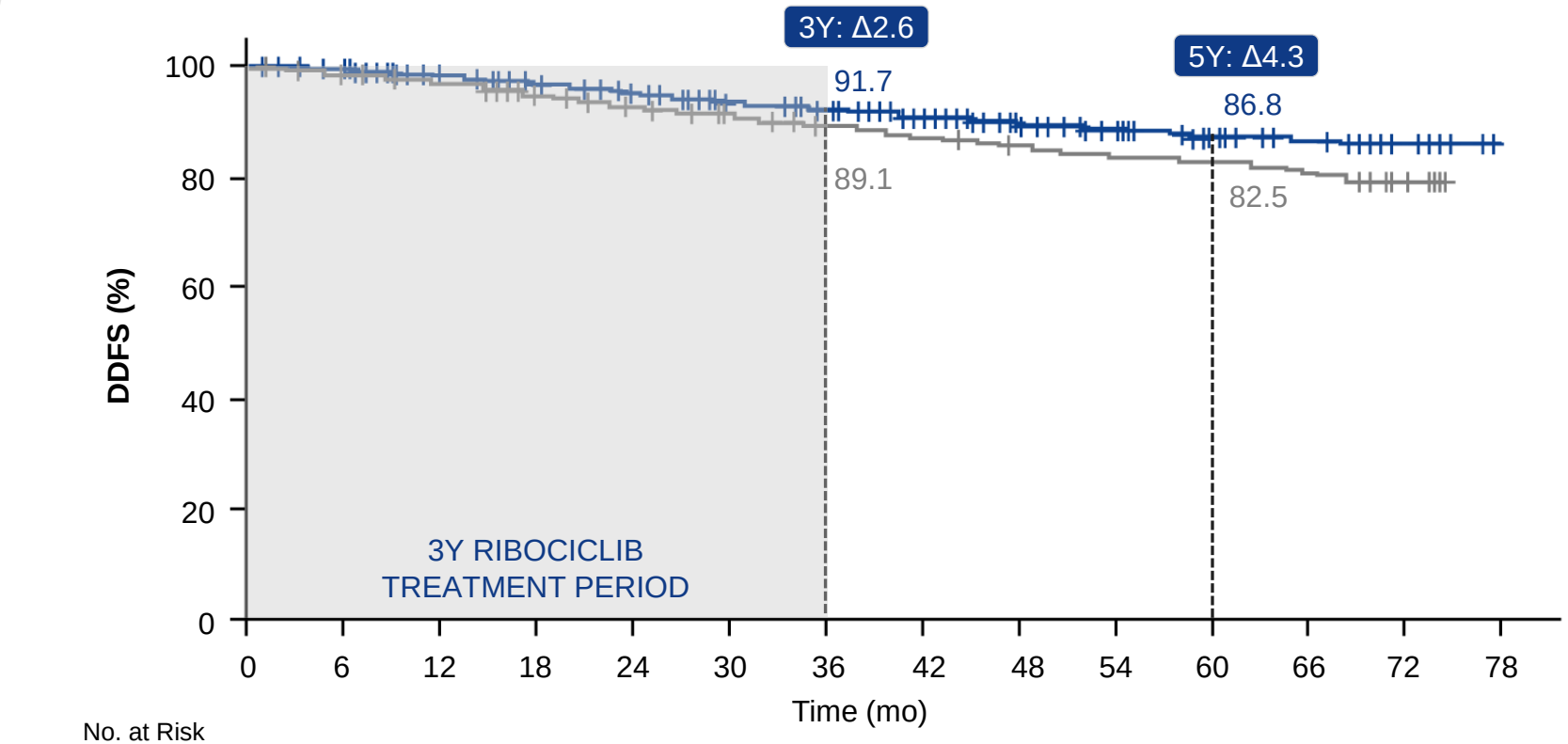


[a]Includes neoadjuvant and adjuvant chemotherapy. [b]Nodal status classification according to AJCC staging. Nodal status is from the most advanced stage derived per surgical specimen or at diagnosis.
[c]From archival tumor tissue.
AJCC=American Joint Committee on Cancer; ET=endocrine therapy; IDFS=invasive disease-free survival; ITT=intention-to-treat; mF/U=median follow-up; N=node; NSAI=nonsteroidal aromatase inhibitor.
Crown J, et al. *ESMO Open*. 2025;10(11):105858.

ITT

55.5-mo mF/U

NATALEE: DDFS



No. at Risk														
Ribociclib + NSAI	2549	2353	2283	2217	2149	2094	2038	1973	1891	1525	1005	274	9	0
NSAI alone	2552	2244	2171	2092	2023	1954	1888	1812	1723	1386	936	237	3	0

29.1%

REDUCTION IN THE RISK OF DEVELOPING A DDFS EVENT

Hazard ratio=0.709
(95% CI: 0.608-0.827)
nominal 1-sided p<.0001

# DDFS Events	Ribociclib + NSAI	289
	NSAI alone	375

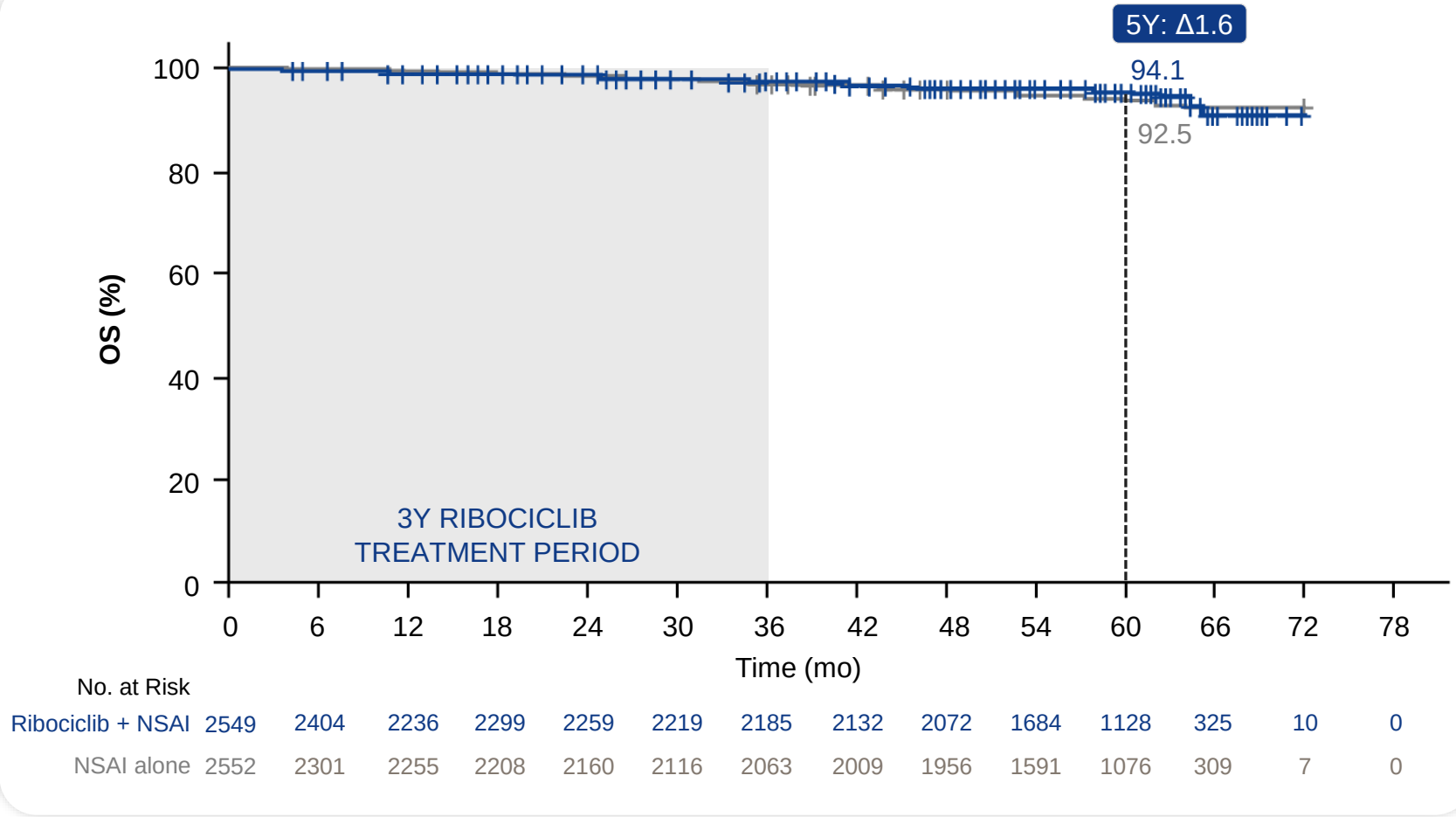
DDFS=distant disease-free survival; ITT=intention-to-treat; mF/U=median follow-up; mo=month; NSAI=nonsteroidal aromatase inhibitor.

Crown J, et al. *ESMO Open*. 2025;10(11):105858.

ITT

56.5-mo mF/U

NATALEE: OS



Hazard ratio=0.800
(95% CI: 0.637-1.003)
nominal 1-sided p=.026

# OS	Ribociclib + NSAI	138
Events	NSAI alone	162

ITT=intention-to-treat; mF/U=median follow-up; mo=month; NSAI=nonsteroidal aromatase inhibitor; OS=overall survival.
Crown J, et al. *ESMO Open*. 2025;10(11):105858.

ITT

44.2-mo mF/U

NATALEE: Treatment-Emergent AEs

AEs of Special Interest in Either Arm (≥15%), %[1]	Ribociclib + NSAI (n=2526)		NSAI Alone (n=2441)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Neutropenia[a]	62.8	44.4	4.5	0.9
Arthralgia	38.8	1.0	44.4	1.3
Nausea	23.5	0.2	7.9	<0.1
Headache	22.9	0.4	17.2	0.2
Fatigue	22.8	0.8	13.5	0.2
Alanine aminotransferase increase	19.7	7.7	5.7	0.7
Aspartate aminotransferase increase	17.2	4.6	5.9	0.6

12.9 months after the 4-year exploratory analysis[2]:

- 5 new deaths due to AEs occurred; however, these deaths were not considered treatment-related[2,3]
  - 3 patients in the ribociclib + NSAI arm (brain hemorrhage, myocardial infarction, gastric adenocarcinoma)
  - 2 patients in the NSAI-alone arm (rectal adenocarcinoma, aortic aneurysm rupture)
- The proportion of patients who developed secondary primary malignancies was similar in the 2 treatment arms (ribociclib + NSAI, 67 patients [2.7%]; NSAI alone: 74 patients [3.0%])[3]

[a]Includes neutropenia and neutrophil count decreased.
AE=adverse event; ITT=intention-to-treat; MedDRA=Medical Dictionary for Regulatory Activities; mF/U=median follow-up; mo=month; NSAI=nonsteroidal aromatase inhibitor.
1. Fasching PA, et al. *JAMA Oncol.* 2025;11(11):1364-1372. 2. Crown J, et al. *ESMO Open*. 2025;10(11):105858.
3. Crown J, et al. Oral presentation at: *ESMO* 2025. Abstract LBA14.

ITT

44.2-mo mF/U

NATALEE: Discontinuation Rates and Treatment Completion

100%
of NATALEE patients are off ribociclib treatment[1]

62.8% of patients completed the 3Y treatment with ribociclib[1]

Ribociclib dose adjustments due to AEs
- Dose reductions: 23.0%
- Discontinuations: 20.0%

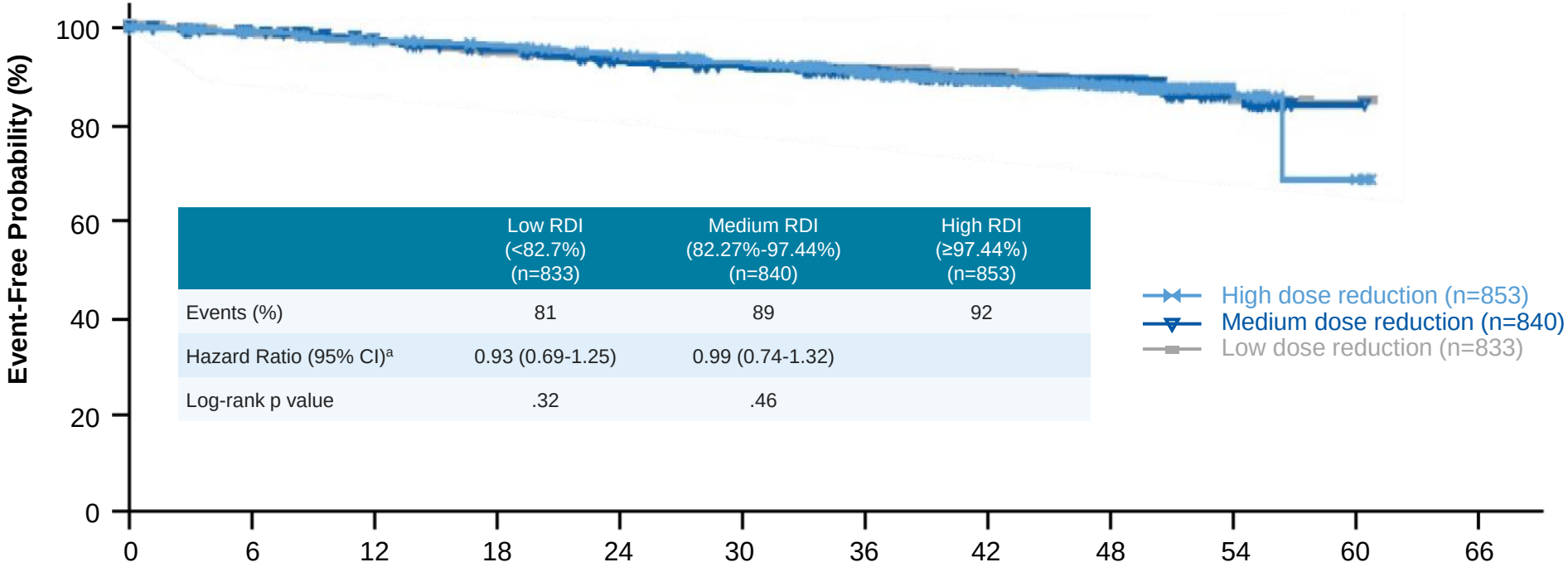
AE=adverse event; ITT=intention-to-treat; mF/U=median follow-up; mo=month; y=year.
Fasching PA, et al. *JAMA Oncol*. 2025;11(11):1364-1372.

ITT

44.2-mo mF/U

NATALEE: Dose Reduction

Invasive Disease-Free Survival by Relative Dose Intensity[1]



	Low RDI (<82.7%) (n=833)	Medium RDI (82.27%-97.44%) (n=840)	High RDI (≥97.44%) (n=853)
Events (%)	81	89	92
Hazard Ratio (95% CI)[a]	0.93 (0.69-1.25)	0.99 (0.74-1.32)	
Log-rank p value	.32	.46	

No. at risk												
High	853	789	769	756	735	716	640	518	317	52	4	0
Medium	840	801	774	749	717	701	610	495	307	45	1	0
Low	833	763	734	704	683	663	594	468	291	58	3	0

Ribociclib Recommended Dose[2]

400 mg QD

1st dose reduction: 200 mg QD

[a]High RDI group was used as reference group to calculate hazard ratio and p value.
IDFS=invasive disease-free survival; ITT=intention-to-treat; mF/U=median follow-up; mo=month; QD=once daily; RDI=relative dose intensity.
1. Hamilton E, et al. Poster presentation at SABCS 2024. Abstract P1-11-16. 2. Ribociclib [US PI]. East Hanover, NJ, USA: Novartis Pharmaceuticals Corporation, 2025.

ITT

55.4-mo mF/U

NATALEE: Efficacy Summary

Treatment benefit at 55.4 months median follow-up

	IDFS	DDFS[a]	OS[b]
Relative risk reduction	28.4%	29.1%	NR
Absolute benefit at 5Y	4.5%	4.3%	1.6%

[a]DDFS is reported for 55.5-mo mF/U. [b]OS is reported for 56.5-mo mF/U.
DDFS=distant disease-free survival; IDFS=invasive disease-free survival; ITT=intention-to-treat; mF/U=median follow-up; NR=not reported; OS=overall survival; Y=year.
Crown J, et al. *ESMO Open*. 2025;10(11):105858.

ITT

44.2-mo mF/U

NATALEE: Safety Summary

Safety Data[1]

100% of patients are off ribociclib treatment

AEs of special interest were mainly low grade, except for neutropenia, and the safety profile of ribociclib + NSAI remained stable with additional follow-up[1,2]

Most frequent AEs of special interest: any grade (Grade ≥3)[1]

Neutropenia	Arthralgia	ALT Increase	AST Increase
62.8% (44.4%)	38.8% (1.0%)	19.7% (7.7%)	17.2% (4.6%)

The most frequent reason for discontinuation of ribociclib due to AEs was liver-related AEs[1]

AE=adverse event; ALT=alanine transaminase; AST=aspartate aminotransferase; ITT=intention-to-treat; mF/U=median follow-up; mo=month; NSAI=nonsteroidal aromatase inhibitor.

1. Fasching PA, et al. *JAMA Oncol*. 2025;11(11):1364-1372. 2. Crown J, et al. *ESMO Open*. 2025;10(11):105858.

Summary

CDK4/6i + ET in HR+, HER2- EBC

1. Patients with high-risk, HR+, HER2- EBC may benefit from additional treatments to reduce their risk of disease recurrence[1-3]

2. Understanding features associated with node-positive and node-negative, high-risk, HR+, HER2- EBC will help identify patients who could benefit from a CDK4/6i in the adjuvant setting[4-6]

3. Two CDK4/6i are approved for patients with high-risk, HR+, HER2- EBC, offering a potential for improved clinical outcomes[7,8]

CDK4/6i=cyclin-dependent kinases 4/6 inhibitor; EBC=early breast cancer; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; HR=hormone receptor.

1. Burstein HJ, et al. *J Clin Oncol*. 2019;37(5):423-438. 2. Sheffield KM, et al. *Future Oncol*. 2022;18(21):2667-2682. 3. Caswell-Jin JL, et al. *JAMA*. 2024;331(3):233-241.
4. Colleoni M, et al. *J Clin Oncol*. 2016;34(9):927-935. 5. https://www.clinicaltrials.gov/ct2/show/NCT03155997. (Accessed April 4, 2023).
6. https://www.clinicaltrials.gov/ct2/show/NCT03701334. (Accessed March 4, 2024). 7. Ribociclib [US PI]. East Hanover, NJ, USA: Novartis Pharmaceuticals Corporation, 2025.
8. Abemaciclib [US PI]. Indianapolis, IN, USA: Eli Lilly USA LLC, 2025.

CDK4/6i USPI Links

Abemaciclib

https://e.lilly/3w30f5X

Ribociclib

https://e.lilly/3HInDZ9