High-Risk, HR+, HER2- Early Breast Cancer:
Identifying Patients at High Risk of Recurrence

Unmet Need for Patients With HR+, HER2- Early Breast Cancer

Even after 5 years of adjuvant endocrine therapy (ET), **up to 41% of patients** with estrogen receptor (ER)-positive early breast cancer (EBC) **remained at risk for disease recurrence** for the next 20 years[1]

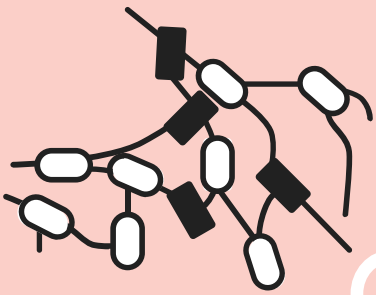
Tumor size (T) and nodal status (N) are independent prognostic variables for patient risk of recurrence (ROR)[2]

Risk of Distant Recurrence[1]

	N0	N1 (1-3 ALN)	N2 (4-9 ALN)
T1	13%	20%	34%
T2	19%	26%	41%

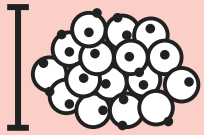
Key Factors for ROR in Patients With HR+, HER2- EBC

Nodal Status
is among the **most significant prognostic markers** for disease recurrence[3,4]



Patients with **N1 and N2** disease have a **1.6× and 3.0× increased ROR** compared with N0 patients, respectively[5]

Large Tumor Size
correlates with a **1.8×** increased ROR[5]



High Tumor Grade
elevates patient risk of disease recurrence by **2.4×**[5]

Biomarkers
such as high Ki-67 indicate the aggressiveness of cancer cells[6]

Age
at diagnosis may indicate aggressive disease for young patients and limit treatment options for older patients[6,7]

The combination of these factors may categorize patients with HR+, HER2- EBC as having a high risk of disease recurrence[8]

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Real-World Data Demonstrate N+ and High-Risk Impact on Prognosis[a,9]

N+ High-Risk

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

OR

4+ ALN (N2, N3)

Non–High-Risk

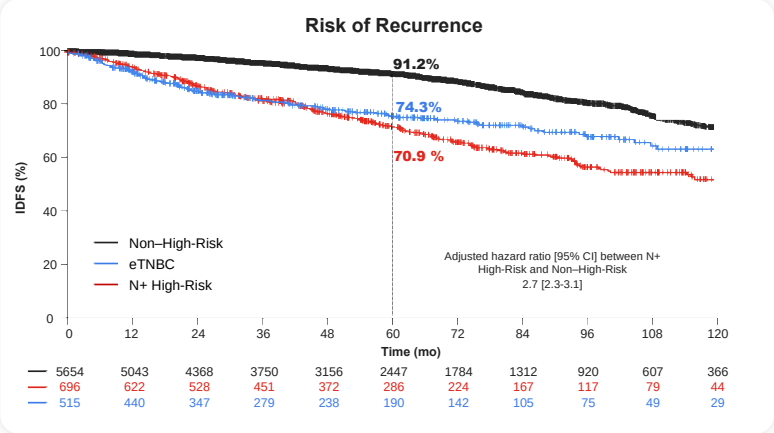
Patients not meeting N+ high-risk criteria

AT 5 YEARS

Patients with **N+, high-risk** disease have a

3.3× increase

in their ROR rate compared with those with non–high-risk disease, which is like those with early TNBC



- The **5-year risk of mortality** is **3.0× greater** for patients with **N+, high-risk disease** than those with **non–high-risk** features

N1 High-Risk

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

N1 Non–High-Risk

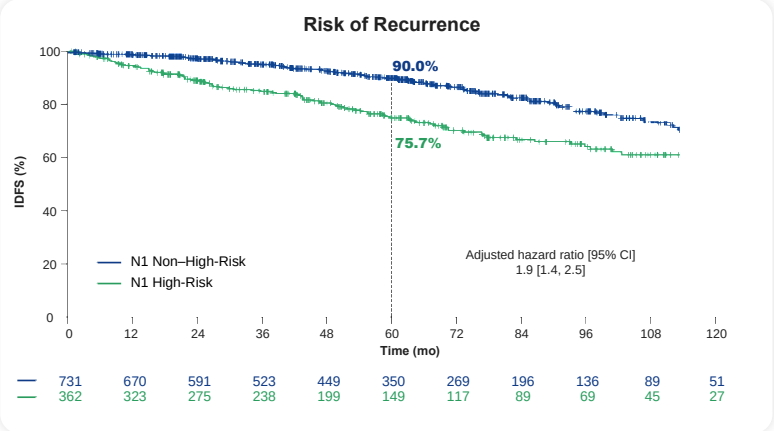
N1/N1mi: 1–3 ALN with Grade <3, tumor <5 cm, and Ki-67 <20%

AT 5 YEARS

Patients with **N1, high-risk** disease have a

14% increase

in their ROR rate compared with those with **N1, non–high-risk disease**



- The **5-year risk of mortality** is **1.9× greater** for patients with N1, **high-risk features**, such as tumor size ≥5 cm and Ki-67 ≥20%, compared with **N1, non–high-risk** disease

Adjuvant Therapy for Patients With High-Risk, HR+, HER2- EBC

The addition of **cyclin-dependent kinase 4/6 inhibitors (CDK4/6i) to adjuvant ET** in these patients has demonstrated **reduced recurrence** and **improved outcomes**[10,11]

Patients may be eligible for different therapies depending on their tumor characteristics[12,13]

It is critical to identify patients at high risk of recurrence to inform clinical decisions and optimize clinical outcomes[6,8]

[a]The ROR and OS rates are based on US Flatiron real-world data.

References: **1.** Pan H, et al. *N Engl J Med*. 2017;377(19):1836-1846. **2.** Győrffy B, et al. *Breast Cancer Res.* 2015;17(1):11. **3.** Tolaney S, et al. Poster presentation at: *SABCS 2024.* Abstract P1-11-02. **4.** Tonellotto F, et al. *Eur J Breast Health.* 2019;15(2):76-84. **5.** Colleoni M, et al. *J Clin Oncol.* 2016;34(9):927-935. **6.** Fasching PA, et al. *GebFra Science*. 2024; 84:164-184. **7.** Dang CM, Giuliano AE. *Oncology (Williston Park)*. 2011;25(10): 895-896, 899. **8.** Nelson D, et al. *PLoS One.* 2022;17(2):e0264637. **9.** Rugo HS, et al. Presented at: *ESMO Breast 2025.* Abstract 215P. **10.** Johnston S, et al. *J Clin Oncol*. 2020; 38(34):3987-3998. **11.** Hortobagyi G, et al. *Annals of Oncology*, 2025;36(2): 149 – 157. **12.** Abemaciclib [US PI]. Indianapolis, IN, USA: Eli Lilly USA LLC, 2025. **13.** Ribociclib [US PI]. East Hanover, NJ, USA: Novartis Pharmaceuticals Corporation, 2025.

Abbreviations: ALN=axillary lymph node; CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; EBC=early breast cancer; ER=estrogen receptor; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; IDFS=invasive disease-free survival; mi=micrometastases; mo=month; N=nodal status; N0=no ALN involvement; N1=1-3 ALNs; N2=4-9 ALNs; N3=≥10 ALNs; OS=overall survival; ROR=risk of recurrence; T=tumor size; TNBC=triple-negative breast cancer.

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