Real-world Risk of Recurrence by Nodal Status in Patients with HR+, HER2-, Node-Positive, High-risk Early Breast Cancer

OBJECTIVES

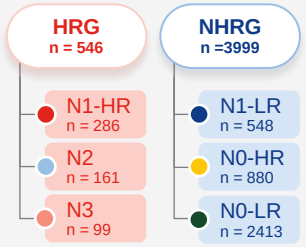
To describe real-world risk of recurrence by nodal status in patients with HR+ HER2- EBC:

1. who met node positive monarchE Cohort 1 clinicopathological criteria vs those who did not.
2. with N1 disease and at least one high-risk monarchE feature (tumor size ≥5cm or grade 3) versus those with (1) N1 disease with lower risk features and (2) N0 disease.

METHODS & STUDY DESIGN

HR=high risk
LR=lower risk

- Patients with HR+, HER2- EBC that received adjuvant ET were selected from the US Flatiron Health Database (Study period Jan 2011-Sep 2020)
- **High-risk group (HRG) is node positive:**
  N1 high risk (N1-HR); N2; N3
  - **N1-HR:** 1-3 LN (N1), tumor ≥5 cm or grade 3
- **Non-high-risk group (NHRG):** N1 with tumor <5cm, grade <3 and Ki-67<20% (or unknown) or N0
  - **N1-LR:** tumor <5 cm, grade <3, and Ki-67 <20% (or unknown)
  - **N0-HR*:** tumor ≥5 cm, grade 3, and/or Ki-67 ≥20%
  - **N0-LR:** tumor <5 cm, grade <3, and Ki-67 <20% (or unknown)



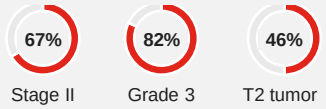
ANALYSES

- IDFS was used to assess recurrence risk measured from adjuvant ET initiation to recurrence or death and was estimated by Kaplan-Meier method.
- Adjusted hazard ratios (HRs) with 95% CI estimated by Cox proportional hazards regression models.

Key adjustment factors: age, race, menopausal status, ECOG PS

KEY BASELINE CHARACTERISTICS

- Median age of patients with node-positive disease was ~60 years (vs 51 years in monarchE).
- Prior neoadjuvant/adjuvant chemotherapy usage was 13%/53% in N1-HR and 4%/37% in N1-LR.
- In N1-HR:



**N0 with HR features was a subset of N0 and included in the analyses.
ALN, axillary lymph node; CI, confidence interval; EBC, early breast cancer; ET, endocrine therapy; HER2-, human epidermal growth factor 2-negative; HR, hazard ratio; HR+, hormone receptor-positive; HRG, high-risk group; IDFS, invasive disease-free survival; ITT, intention-to-treat, LN, lymph node; NHRG, non-high-risk group; PS, performance status; Y, years.

References: 1. Nelson D,R, et al. PLOS ONE.2022;17(2) e0264637; 2. Rastogi P, et al. J Clin Oncol.2024;42(9):987-93; 3. Data presented by Tolaney SM, et al at San Antonio Breast Cancer Conference 2024, Poster P1-11-02; Abstract SESS1880.

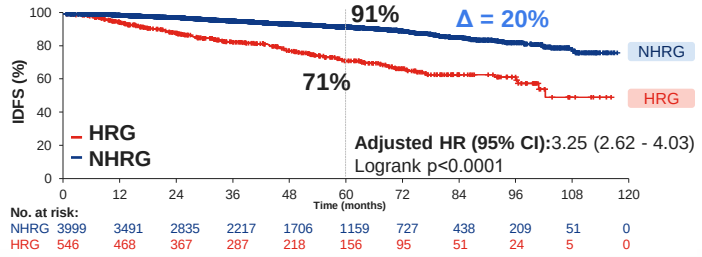
INTRODUCTION

- Tumor spread to lymph nodes is the most significant prognostic marker for recurrence.
- In node-positive HR+, HER2- EBC, most patients (72%) present with 1-3 ALN (N1) disease; however, outcomes for N1 disease are variable.
- The monarchE trial selected patients at **high risk of recurrence based on positive nodal status** [1-3 ALN (N1), 4-9 ALN (N2) or ≥10 ALN (N3)]. Patients in Cohort 1 (91% of the ITT population) with N1 disease required additional high-risk features: tumor ≥5 cm and/or grade 3 disease (N1 high risk). .
- In monarchE, 2 years of adjuvant abemaciclib plus ET showed ~8% improvement in 5-year IDFS in the FDA- and EMA-approved population (Cohort 1).
- In the present study, risk of recurrence among nodal subgroups was evaluated with a focus on patients with N1 disease and high risk clinical and pathological risk features..

UNDERSTANDING RISK OF RECURRENCE BY NODAL STATUS

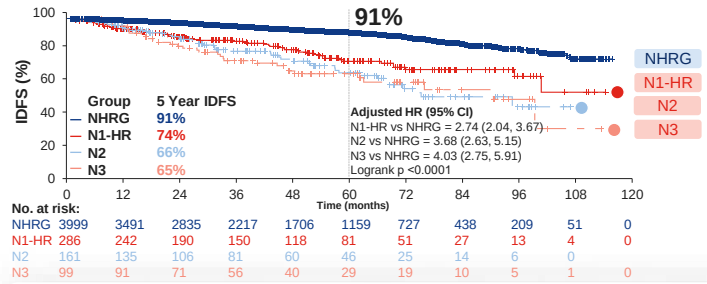
HR+, HER2- EBC

~1 in 3 patients with monarchE-like features are at risk of recurrence within 5 years when treated with ET alone



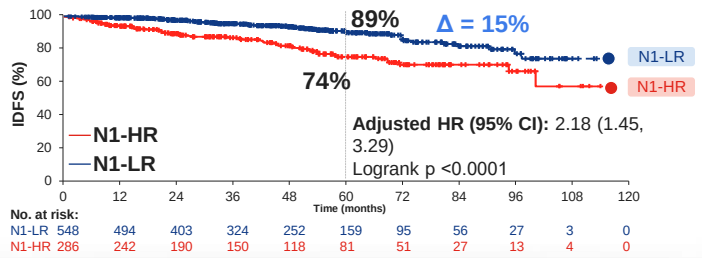
5Y risk of recurrence in HRG is 29% vs 9% in NHRG

Patients with N1 and high-risk features (N1-HR) have nearly as high risk of recurrence as those with 4+ positive nodes



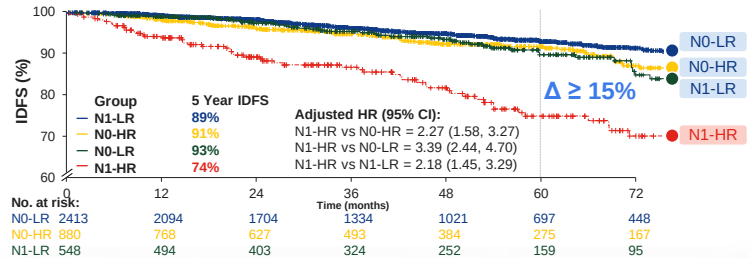
5Y risk of recurrence among N1-HR, N2 and N3 is ≥26% vs 9% in NHRG

Patients with N1-HR features have worse outcomes than patients with N1 without these high-risk features (N1-LR) at 5 years



5Y risk of recurrence in N1-HR is 26% vs 11% in N1-LR

Patients with N1-LR or N0 with high risk (N0-HR) or lower risk (N0-LR) have a similar risk of recurrence that is lower than N1-HR



5Y risk of recurrence in N1-HR is 26% vs ≤11% in N1-LR, N0-HR, N0-LR

KEY TAKEAWAYS FROM THIS REAL-WORLD STUDY

Compared to Patients with Non-High-Risk Features

Patients **with monarchE-like features** have **>3X increase in recurrence risk:**

- 5Y recurrence risk of **29%**
- **~1:3** patients will experience recurrence within 5Y

All node positive subgroups (N1 high-risk, N2, N3) representative of monarchE Cohort 1 **had an increased recurrence risk ≥2.7-fold higher**

Differentiating Risk in N1 disease

Patients with N1 high-risk disease (tumor ≥5 cm and/or grade 3) **had a distinctively higher risk of recurrence vs those with N1 disease without high-risk features:**

- **2.2X increased risk**
- an absolute **difference in IDFS of 15% at 5Y**

Implications for Clinical Practice

N1 high-risk patient identification
Particular attention should be paid to identify patients with N1 disease and high-risk features when evaluating **patients with node-positive disease for abemaciclib.**

Treatment considerations in patients at high risk

Risk of recurrence data shown here support the use of 2 years of adjuvant abemaciclib+ET in patients with node positive disease:

- N1 high-risk disease as they have a 2.2X increase in recurrence risk vs N1 low-risk.
- N2, N3 disease

Limitations

- Patients without Ki-67 results may be incorrectly classified as non-high-risk.
- Although potentially used more commonly in current practice to assess risk of recurrence, genomic testing was infrequent in this dataset of patients diagnosed 2011-2020.