Poster **292P**

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Real-world evidence on risk of recurrence in patients with node-negative and node-positive HR+/HER2− early breast cancer from US electronic health records

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KEY FINDINGS & CONCLUSIONS

- This large, retrospective real-world study demonstrated considerable risk of recurrence in patients with N1 or N2-3 disease and patients with N0 disease with additional high-risk features
- N0 high-risk and N1 groups had similar risk profiles over time and both groups had substantially higher chemotherapy use than the N0 group. For N0 high-risk and N1 groups at 7 years:
  - Overall recurrence risk was 16.9% and 17.1%, respectively
  - Distant recurrence risk was 13.6% and 13.7%, respectively
- Patients with N0 disease and high-risk features had worse recurrence and mortality than patients with N0 disease without high-risk features at all time points. In patients with N0 disease with and without high-risk features at 7 years:
  - Overall recurrence risk was 2.9× greater (16.9% vs 5.9%)
  - Distant recurrence risk was 4.4× greater (13.6% vs 3.1%)
  - Mortality risk was 1.6× greater (16.8% vs 10.4%)
- Treatments to improve short- and long-term outcomes are needed for a broad population of patients with HR+/HER2− EBC, including a select group of N0 patients with high-risk features

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INTRODUCTION

- Despite the benefit of adjuvant endocrine therapy (ET), the risk of recurrence (ROR) in hormone receptor–positive (HR+)/human epidermal growth factor receptor 2–negative (HER2−) early breast cancer (EBC) remains a relevant concern
- Meta-analyses and population-based observational studies of patients with HR+/HER2− EBC have found that ROR peaks at 5 years and persists over time[1-3]
- Despite these studies, contemporary information on ROR and mortality in a broad range of patients, including those without nodal involvement, is limited
- The NATALEE trial demonstrated a 25% invasive disease-free survival proportional benefit with adjuvant ribociclib plus ET in patients with HR+/HER2− EBC vs ET alone. Similar benefit was found in the node-negative (N0) subgroup with high-risk features[4,5]
- While a cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitor is approved for high-risk N1 (and G3 or tumor size ≥50 mm), N2 or N3 HR+/HER2− EBC, it is not approved for N0 disease[6]
- Here, we used real-world data to estimate ROR and mortality for patients with HR+/HER2− EBC, including a subset of patients with high-risk N0 features

METHODS

- Patients aged ≥18 years with American Joint Committee on Cancer (AJCC) stage I-III HR+/HER2− EBC in the US Flatiron Health EBC de-identified electronic health records-derived database (2011-2023) were included
- The following endpoints were evaluated:
  - **Overall recurrence:** any locoregional or distant recurrence, excluding mortality as an event
  - **Distant recurrence:** any event involving distant recurrence only, excluding mortality as an event
  - **All-cause mortality:** death from any cause
- Subgroups of patients with N0 disease with and without high-risk features were extracted (“N0 high-risk” and “N0 non–high-risk”)
  - High-risk was defined by NATALEE eligibility criteria: T4N0, T3N0, or T2N0 with additional criteria (grade 2 with Ki-67≥20% or high genomic risk, or grade 3). All other patients with N0 disease were non–high-risk
- Kaplan-Meier methods were used to calculate survival and incidence rates of ROR and all-cause mortality at 3, 5, and 7 years, with patients censored on their last activity date
- Differences in ROR and mortality based on nodal groups were evaluated using log-rank tests

RESULTS

- Of 15,017 patients diagnosed with EBC in the Flatiron database, 7564 met inclusion criteria (**Figure 1**):
  - **N0 disease**: 5557 (73.5%)
    - **N0 high-risk**: 679/5557 (12.2%)
    - **N0 non–high-risk**: 4878/5557 (87.8%)
  - **N1 disease**: 1560 (20.6%)
  - **N2-3 disease**: 447 (5.9%)
- Median follow-up was **79.1 mo** (quartile [Q]1-Q3 45.7-113.6 mo) **(Table 1)**

Figure 1. Flowchart of Cohort Attrition

IHC, immunohistochemistry; TNM, tumor, lymph nodes, metastasis.
[a] Anatomic stage was derived based on the 8th edition AJCC Cancer Staging Manual using TNM stage. If both clinical and pathological stage values were recorded, the more severe value was used.
[b] Biomarker test results occurring any time before the initial treatment start date were considered. The test result closest to the initial treatment start date was prioritized. If there were conflicting test results on the same date, positive results were prioritized.
[c] HER2-negative includes IHC0, IHC1+, and IHC2+.
[d] Comorbidities were identified between 365 days before up to 90 days after the initial diagnosis date (inclusive). Patients with potential second malignancy or metastatic disease were excluded.

Overall and Distant Recurrence Risk

- Overall and distant ROR differed significantly between N0, N1, and N2-3 groups (log-rank *P*<.0001) (**Figure 2**)
- Patients with N1 disease and patients with N0 high-risk features had numerically similar and considerable overall and distant ROR across the 3- to 7-year time points. N1 and N0 high-risk groups were not statistically different in overall (*P*=.617) or distant (*P*=.438) ROR (**Table 2**).
- N0 non–high-risk group had significantly lower overall and distant ROR vs N1 (*P*<.0001) and N0 high-risk (*P*<.0001) groups.

Table 1. Characteristics of Patients by Nodal Status

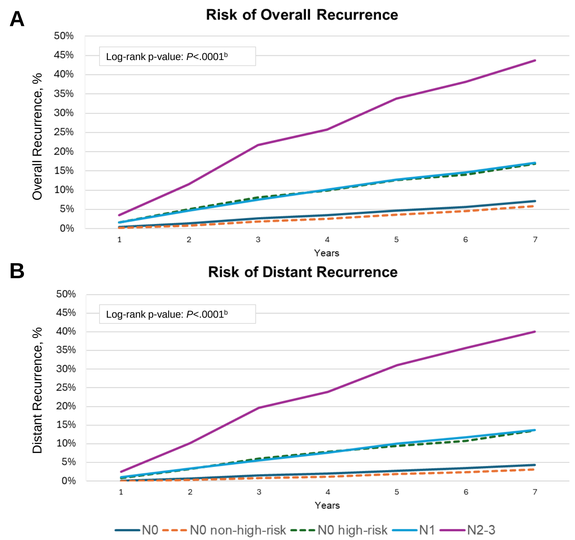
	Overall (n=7564)	N0 (all) (n=5557)	N0 non–high-risk (n=4878)	N0 high-risk (n=679)	N1 (n=1560)	N2-3 (n=447)
Age at initial diagnosis, median (range), years	64.0 (22.0-85.0)	65.0 (25.0-85.0)	65.0 (25.0-85.0)	62.0 (25.0-85.0)	61.0 (22.0-85.0)	61.0 (28.0-85.0)
Sex, n (%)						
Female	7505 (99.2)	5521 (99.4)	4851 (99.4)	670 (98.7)	1543 (98.9)	441 (98.7)
Male	59 (0.8)	36 (0.6)	27 (0.6)	9 (1.3)	17 (1.1)	6 (1.3)
Race, n (%)						
White	5142 (68.0)	3827 (68.9)	3380 (69.3)	447 (65.8)	1041 (66.7)	274 (61.3)
Black/African American	618 (8.2)	409 (7.4)	347 (7.1)	62 (9.1)	156 (10.0)	53 (11.9)
Asian	205 (2.7)	152 (2.7)	133 (2.7)	19 (2.8)	43 (2.8)	10 (2.2)
Hispanic or Latino	12 (0.2)	7(0.1)	6 (0.1)	1 (0.1)	5 (0.3)	0
Other/Unknown	1587 (21.0)	1162 (20.9)	1012 (20.7)	150 (22.1)	315 (20.2)	110 (24.6)
Menopausal status, n (%)						
Pre/Perimenopausal	1487 (19.7)	974 (17.5)	812 (16.6)	162 (23.9)	412 (26.4)	101 (22.6)
Postmenopausal	5589 (73.9)	4234 (76.2)	3768 (77.2)	466 (68.6)	1046 (67.1)	309 (69.1)
NA (male patient)	58 (0.8)	35 (0.6)	26 (0.5)	9 (1.3)	17 (1.1)	6 (1.3)
Unknown	430 (5.7)	314 (5.7)	272 (5.6)	42 (6.2)	85 (5.4)	31 (6.9)
Received (neo)adjuvant ET, n (%)						
Yes	7059 (93.3)	5262 (94.7)	4672 (95.8)	590 (86.9)	1417 (90.8)	380 (85.0)
No	505 (6.7)	295 (5.3)	206 (4.2)	89 (13.1)	143 (9.2)	67 (15.0)
Received (neo)adjuvant CT, n (%)						
Yes	1888 (25.0)	878 (15.8)	556 (11.4)	322 (47.4)	702 (45.0)	308 (68.9)
No	5676 (75.0)	4679 (84.2)	4322 (88.6)	357 (52.6)	858 (55.0)	139 (31.1)
Duration of follow up, median (Q1-Q3), months	79.1 (45.7-113.6)	77.0 (44.9-112.9)	77.3 (45.0-112.8)	75.4 (42.9-113.0)	83.1 (48.5-115.5)	85.5 (50.3-120.1)
Anatomic T-stage, n (%)						
T0	5 (0.1)	0	0	0	4 (0.3)	1 (0.2)
T1	4914 (65.0)	4213 (75.8)	4213 (86.4)	0	631 (40.4)	70 (15.7)
T2	2132 (28.2)	1197 (21.5)	665 (13.6)	532 (78.4)	724 (46.4)	211 (47.2)
T3	392 (5.2)	121 (2.2)	0	121 (17.8)	155 (9.9)	116 (26.0)
T4	121 (1.6)	26 (0.5)	0	26 (3.8)	46 (2.9)	49 (11.0)
Anatomic AJCC group stage, n (%)						
Stage I	4360 (57.6)	4213 (75.8)	4213 (86.4)	0	147 (9.4)	0
Stage II	2530 (33.5)	1318 (23.7)	665 (13.6)	653 (96.2)	1212 (77.7)	0
Stage III	674 (8.9)	26 (0.5)	0	26 (3.8)	201 (12.9)	447 (100)

CT, chemotherapy; NA, not applicable.

Table 2. Overall and Distant Recurrence Risk by Nodal Status

Incidence (95% CI), %	N0	N0 non–high-risk	N0 high-risk	N1	N2-3
Overall recurrence					
3-year	2.7 (2.2-3.2)	1.9 (1.5-2.4)	8.1 (6.0-10.7)	7.5 (6.2-9.0)	21.7 (17.7-26.3)
5-year	4.7 (4.1-5.5)	3.7 (3.0-4.4)	12.6 (9.9-16.1)	12.8 (11.0-15.0)	33.8 (28.8-39.4)
7-year	7.2 (6.3-8.3)	5.9 (4.9-6.9)	16.9 (13.3-21.3)	17.1 (14.7-19.8)	43.7 (37.9-50.0)
Distant recurrence					
3-year	1.5 (1.1-1.9)	0.8 (0.6-1.2)	6.0 (4.2-8.4)	5.5 (4.3-6.8)	19.7 (15.9-24.2)
5-year	2.8 (2.3-3.4)	1.9 (1.5-2.5)	9.4 (7.0-12.4)	10.0 (8.3-12.0)	31.1 (26.2-36.7)
7-year	4.3 (3.6-5.2)	3.1 (2.4-3.9)	13.6 (10.3-17.8)	13.7 (11.5-16.2)	40.1 (34.4-46.4)

Figure 2. Overall (A) and Distant (B) Recurrence Risk[a]



[a] Kaplan-Meier analysis started at initial diagnosis date. Patients without an event were censored on their last confirmed structured activity date.
[b] Overall and distant ROR log-rank differences were evaluated between N0, N1, and N2-3 groups.

All-cause Mortality Risk

- All-cause mortality risk differed significantly between N0, N1, and N2-3 groups (log-rank *P*<.0001) (**Table 3**)
- N1 and N0 high-risk groups had numerically similar and considerable risk of all-cause mortality across time points. N1 and N0 high-risk groups were not statistically different for overall mortality risk (*P*=.635)
- N0 non–high-risk group had significantly lower risk of all-cause mortality vs N1 (*P*<.0001) and N0 high-risk (*P*=.0003) groups.

Table 3. All-cause Mortality Risk by Nodal Status

Incidence (95% CI), %	N0	N0 non–high-risk	N0 high-risk	N1	N2-3
3-year	2.5 (2.1-3.0)	2.4 (1.9-2.9)	3.7 (2.4-5.6)	3.8 (2.9-5.0)	11.3 (8.5-15.0)
5-year	5.8 (5.0-6.6)	5.4 (4.7-6.3)	8.1 (5.9-11.1)	9.1 (7.6-11.0)	21.5 (17.4-26.4)
7-year	11.2 (10.0-12.5)	10.4 (9.2-11.7)	16.8 (13.0-21.4)	15.9 (13.5-18.6)	34.9 (29.5-41.0)

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