Poster 245P

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Characteristics of real-world NATALEE- and monarchE-eligible populations: a US electronic health records database analysis

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KEY FINDINGS & CONCLUSIONS

- This sizeable, real-world study suggests that NATALEE-eligible patients constitute a larger number of patients at increased risk of recurrence vs monarchE-eligible patients (30.6% vs 14.5%, respectively), including select patients with N0 and all patients with macroscopic N1 disease
  - The N0 and N1 subgroups constitute ≈75% and ≈20% of the HR+/HER2- EBC patient population, respectively; 91.8% vs 45.9% of patients with N1 and 9.5% vs 0% of patients with N0 disease were eligible for NATALEE vs monarchE
- While both NATALEE (ribociclib) and monarchE (abemaciclib) showed statistically significant iDFS benefit, the broader eligibility criteria for NATALEE vs monarchE presents the potential opportunity for improving outcomes in additional patients with EBC at high risk of recurrence, beyond those eligible for monarchE

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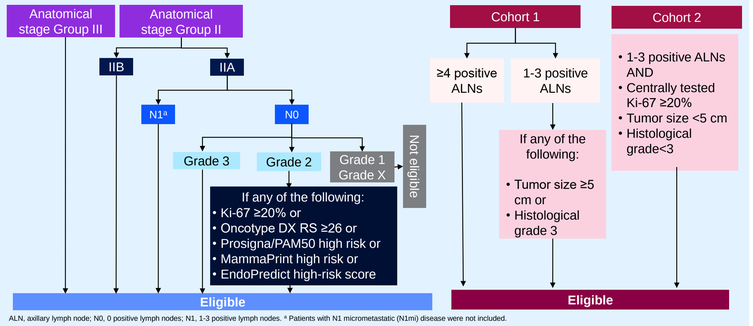
INTRODUCTION

- Despite standard-of-care adjuvant endocrine therapy (ET), short- and long-term risk of recurrence remains in patients with HR+/HER2– early breast cancer (EBC)[1-4]
- CDK4/6is have been studied in phase 3 trials in the HR+/HER2− EBC in the adjuvant setting
  - In NATALEE, ribociclib + a nonsteroidal aromatase inhibitor (NSAI) showed a statistically significant invasive disease-free survival (iDFS) benefit over NSAI alone (HR, 0.75; 95% CI: 0.62-0.91; *P*=.003), sustained with an additional follow-up at 33.3 months (HR, 0.749), in a broad stage II/III HR+/HER2− EBC patient population at risk of recurrence[5,6]
  - In monarchE, abemaciclib + ET showed a statistically significant iDFS benefit over ET alone (HR, 0.75; 95% CI: 0.60-0.93; *P*=.01), sustained with an additional follow-up at 54 months (HR, 0.680), in select patients with node-positive HR+/HER2− EBC[7,8]
  - In PENELOPE-B and PALLAS, no benefit with palbociclib + ET was noted in HR+/HER2– EBC[9,10]
- The eligibility criteria for the 2 positive adjuvant CDK4/6i trials were different: NATALEE included a broader EBC population than monarchE
- A real-world analysis was conducted to understand the distribution and characteristics of HR+/HER2− EBC patient populations eligible for NATALEE vs those eligible for monarchE

METHODS

- This retrospective analysis in patients from the ConcertAI Patient360 electronic health record database (January 2015 to January 2023) used deidentified electronic medical records from patients treated at US academic and community clinics
- Patients in the ConcertAI database with a curated diagnosis for BC (any recorded ICD-10 code for C50 or ICD-9 code for 174 or 175) were eligible
- Patients aged ≥18 years with a BC diagnosis who had surgery and stage I to III HR+/HER2− EBC at initial diagnosis and initiated adjuvant ET were included
  - NATALEE and monarchE eligibility criteria were used to identify patients eligible for either trial (**Figure 1**)
  - The data were analyzed at the date of first ET initiation post-resection surgery (index date)

Figure 1. Eligibility Criteria for NATALEE and monarchE



ALN, axillary lymph node; N0, 0 positive lymph nodes; N1, 1-3 positive lymph nodes. [a] Patients with N1 micrometastatic (N1mi) disease were not included.

RESULTS

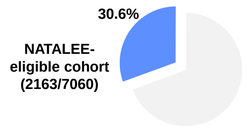
Patients who met selection criteria for NATALEE and monarchE

- A total of 22,621 patients were diagnosed with BC, of whom 7060 met the selection criteria and were included (**Figure 2**)
  - Patients with stage I disease (n = 4261; 60.4%) were the largest group, followed by patients with stage II (n = 2172; 30.8%) and stage III (n = 627; 8.9%) disease
  - Most patients had lymph node (LN)–negative disease (N0; n = 5286; 74.9%), followed by patients with 1 to 3 +LNs (N1; n = 1388; 19.7%), 4 to 9 +LNs (N2; n = 254; 3.6%) and ≥10 +LNs (N3; n = 132; 1.9%)

Figure 2. Patients in the ConcertAI Database Who Met Selection Criteria for the Analysis

- Of the 7060 patients, 2163 (30.6%) and 1023 (14.5%) met the eligibility criteria for NATALEE and monarchE, respectively; this is similar to real-world estimates (≈11%) that were previously reported for patients eligible for treatment with adjuvant abemaciclib[12] (**Figure 3**)
  - 14.2% (1001/7060) of patients met the eligibility criteria for both trials
- Patients with T2N0 grade 2 tumors who were eligible for NATALEE were likely undercounted
  - Among patients with T2N0 grade 2 tumors (n = 490) who required Ki-67/genomic tests to meet NATALEE criteria, only 248 (50.6%) had a reported test result, of whom 112 met the high-risk criteria

Figure 3. Number of Patients Meeting Inclusion Criteria for NATALEE and monarchE



NATALEE-Eligible Cohort

Category, n	Patients
Anatomical stage III	627
Anatomical stage IIB	662
Anatomical stage IIA (N1)	483
Anatomical stage IIA (N0 and grade 3)	279
Anatomical stage IIA (N0 and grade 2 and meeting NATALEE testing criteria)	112

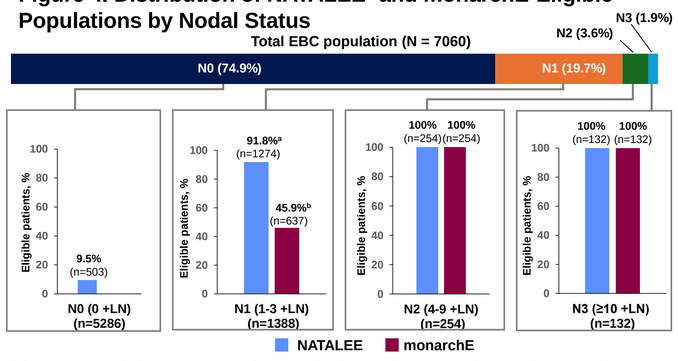
monarchE-Eligible Cohort

Category, n	Patients
Cohort 1 (≥4 +LNs or 1-3 +LNs and tumor size ≥5 cm/histological grade 3)	885
Cohort 2 (1-3 +LNs and centrally tested Ki-67 ≥20%; tumor size <5 cm, histological grade <3)	138

Eligibility for NATALEE and monarchE by nodal status

- A higher proportion of patients with N1 disease were eligible for NATALEE (91.8%) than for monarchE (45.9%) (**Figure 4**)
  - NATALEE did not include patients with micrometastatic disease (N1mi), which accounted for the 8.2% (114/1388) of patients with N1 disease who were not NATALEE eligible; 22 patients with N1mi disease were included in the monarchE-eligible N1 patient population (3.5% [22/637])

Figure 4. Distribution of NATALEE- and monarchE-Eligible Populations by Nodal Status



EBC, early breast cancer; LN, lymph node; N1mi, micrometastatic disease. [a] Patients with N1mi disease ([8.2%] 114/1388) were not included in NATALEE. [b] Includes 22 patients with N1mi disease.

Patient characteristics

- While NATALEE included all patients eligible for monarchE (except 22 patients with N1mi), the proportions of patients with grade 3 disease, larger tumor size (T3/4), and a Ki-67 score of ≥20% were lower in the NATALEE-eligible cohort, reflecting the broader real-world HR+/HER2− EBC population who are at risk of recurrence and eligible for NATALEE (**Table 1**)

Table 1. Features of NATALEE- vs monarchE-Eligible Patients

	NATALEE-eligible patients (n = 2163)	monarchE-eligible patients (n = 1023)
Age, years		
Median (range)	60 (24-87)	59 (25-86)
Race, n (%)[a]		
Asian	68 (3.1)	33 (3.2)
Black	235 (10.9)	112 (10.9)
White	1659 (76.7)	769 (75.2)
Menopausal status, n (%)		
Pre/perimenopausal	528 (24.4)	266 (26.0)
Postmenopausal	1351 (62.5)	617 (60.3)
Unknown	284 (13.1)	140 (13.7)
Tumor grade, n (%)[b]		
Grade 1	314 (14.5)	84 (8.2)
Grade 2	979 (45.3)	419 (41.0)
Grade 3	776 (35.9)	478 (46.7)
Tumor size, n (%)[c]		
T0	4 (0.2)	3 (0.3)
T1	541 (25.0)	235 (23.0)
T2	1160 (53.6)	439 (42.9)
T3	362 (16.7)	272 (26.6)
T4	95 (4.4)	73 (7.1)
Ki-67 score, n (%)		
Low (<20)	273 (12.6)	98 (9.6)
High (≥20)	598 (27.6)	389 (38.0)
Unknown	1292 (59.7)	536 (52.4)
Chemotherapy, n (%)[d]		
Yes	1202 (55.6)	691 (67.5)
Neoadjuvant therapy, n (%)		
Yes	474 (21.9)	297 (29.0)

[a] NATALEE- vs monarchE-eligible cohorts included 178 vs 95 patients with no race information; 22 vs 13 American Indian or Alaska Native patients; and 1 vs 1 Native Hawaiian or other Pacific Islander patient. [b] NATALEE- vs monarchE-eligible cohorts included 1 vs 0 patients with grade X tumor. [c] NATALEE- vs monarchE-eligible cohorts included 1 vs 1 patient with TX tumor size. [d] Received chemotherapy prior to initiating adjuvant ET.

- Among patients with N0 disease who were eligible for NATALEE, 48.9% received prior chemotherapy (**Table 2**)

Table 2. Characteristics of NATALEE-Eligible Patients With N0 Disease

	Patients with N0 disease eligible for NATALEE (n = 503)
Age, years	
Median (range)	60 (24-86)
Menopausal status, n (%)[a]	
Pre/perimenopausal	118 (23.5)
Postmenopausal	313 (62.2)
Tumor grade, n (%)[b]	
Grade 2	169 (33.6)
Grade 3	310 (61.6)
Ki-67 score, n (%)[c]	
High (≥20)	224 (44.5)
Chemotherapy, n (%)[d]	
Yes	246 (48.9)

[a] Overall, 72 patients (14.3%) had unknown menopausal status. [b] Overall, 20 patients (4.0%) had grade 1 tumors. [c] Overall, 33 patients (6.6%) had a Ki-67 score of <20, and 246 (48.9%) had an unknown Ki-67 score. [d] Received chemotherapy prior to initiating adjuvant ET.

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