Poster # **366P**

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Impact of neoadjuvant chemotherapy response on adjuvant ribociclib benefit in HR+/HER2− EBC: a NATALEE analysis

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KEY FINDINGS & CONCLUSIONS

- This subgroup analysis of NATALEE demonstrated a consistent iDFS benefit with ribociclib + NSAI regardless of NACT response
- In the NSAI-alone arm, NACT responders had prolonged iDFS compared with non-responders
- NACT responders generally had more aggressive disease features compared with non-responders
- These findings suggest that further investigation is warranted regarding the incorporation of cyclin-dependent kinase 4 and 6 inhibitors as a potential therapeutic strategy to optimize NACT use in HR+/HER2− EBC

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INTRODUCTION

- The European Society for Medical Oncology (ESMO) Clinical Practice Guidelines recommend that neoadjuvant chemotherapy (NACT) be used for select patients with hormone receptor–positive (HR+)/human epidermal growth factor receptor 2–negative (HER2−) early breast cancer (EBC) who are at high risk of recurrence[1]
  - Given the toxicity of CT and the availability of effective targeted therapies with more manageable toxicity profiles, CT de-escalation has become an important goal for patients with HR+/HER2− EBC[2,3]
- In the phase 3 NATALEE trial, ribociclib + nonsteroidal aromatase inhibitor (NSAI) significantly improved 4-year invasive disease–free survival (iDFS) compared with NSAI alone (HR, 0.72; 95% CI: 0.61–0.84; *P*<.0001) in patients with high-risk HR+/HER2− EBC[4]
  - Furthermore, a consistent iDFS benefit with ribociclib + NSAI vs NSAI alone has been shown regardless of whether patients had any prior CT, including NACT[5]
- Here, we evaluated the impact of NACT response on clinical outcomes in NATALEE

METHODS

- Patients who received NACT in NATALEE were evaluated for outcomes based on whether they responded to NACT
- Since pathologic complete response was not collected in NATALEE, NACT response was determined using a composite scoring system based on changes in tumor size, nodal status, and Ki67 from baseline to surgery; patients with a score ≥1 were classified as responders, while patients with a score <1 were classified as non-responders (**Table 1**)
  - Scores for the 3 parameters were added to produce a score that ranged from −3 (worsening of all 3 parameters) to 3 (improvement of all 3 parameters)
- iDFS was analyzed for responders and non-responders using a multivariate Cox proportional hazards model that was stratified by region, menopausal status, nodal status, and stage

Table 1. Criteria for Defining Response to NACT

Parameter	Improvement (1)	Worsening (−1)	No change (0)
Tumor size	Decreased (eg, T2 to T1)	Increased (eg, T0 to T1)	Either surgery or diagnosis is TX or missing
Nodal status	Decreased (eg, N1 to N0)	Increased (eg, N1 to N2)	Either surgery or diagnosis is NX or missing
Ki67	Changed from >20% at diagnosis to ≤20% at surgery	Changed from ≤20% at diagnosis to >20% at surgery	Same Ki67 (categorical) at diagnosis and surgery or either is missing

N, nodal; NX, nodal status cannot be assessed; T, tumor; TX, tumor can't be assessed.

RESULTS

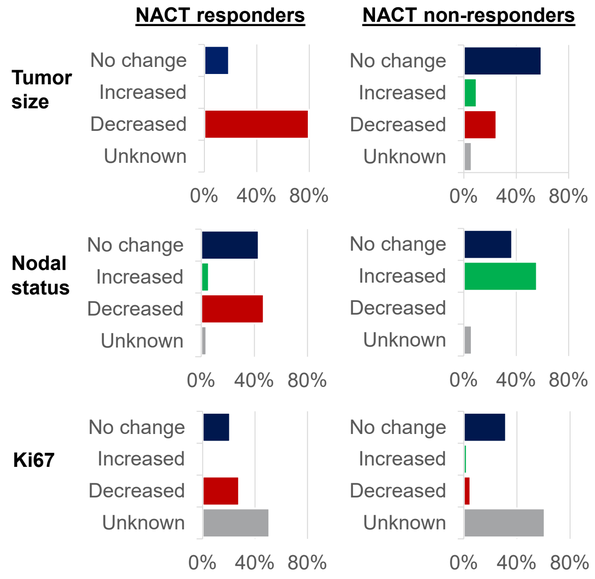
Classifying NACT Response in NATALEE

- In NATALEE, 2180 patients received NACT (n=1085 patients in the ribociclib + NSAI arm; 1095 in the NSAI-alone arm; **Table 2**)
- Among patients in NATALEE who received NACT, 519/1085 (47.8%) in the ribociclib + NSAI arm and 519/1095 (47.4%) in the NSAI-alone arm were classified as responders (**Table 2**)
- Among NACT responders in the ribociclib + NSAI arm, 79.6% had decreased tumor size, 47.1% had decreased nodal status, and 27.8% had decreased Ki67 score (**Figure 1**)

Table 2. Classifying NACT Responders and NACT Non-Responders

	Non-responders				Responders		
Score	**−3**	**−2**	**−1**	**0**	**1**	**2**	**3**
Ribociclib + NSAI, n (%)	1 (0.1%)	19 (1.8%)	169 (15.6%)	377 (34.7%)	306 (28.2%)	185 (17.1%)	28 (2.6%)
NSAI alone, n (%)	0	28 (2.6%)	156 (14.2%)	392 (35.8%)	286 (26.1%)	207 (18.9%)	26 (2.4%)

Figure 1. Summary of Responses to NACT in the Ribociclib + NSAI Arm



NACT Responder vs Non-Responder Characteristics in the Ribociclib + NSAI and NSAI-Alone Arms

- Within the NACT responder and non-responder groups, baseline characteristics at diagnosis were generally balanced between treatment arms; however, several differences were noted when comparing responders with non-responders (**Table 3**)
  - In both treatment arms, the NACT responder vs non-responder group had larger tumors, higher-grade tumors, greater nodal status, and a greater proportion of premenopausal patients

Table 3. NACT Baseline Patient Characteristics

	Ribociclib + NSAI		NSAI-alone	
Characteristic	**NACT responders (n=519)**	**NACT non-responders (n=566)**	**NACT responders (n=519)**	**NACT non-responders (n=576)**
Median age, years	48.0	50.5	49.0	50.0
Sex, n (%)				
Male	0	2 (0.4)	2 (0.4)	1 (0.2)
Female	519 (100.0)	564 (99.6)	517 (99.6)	575 (99.8)
Menopausal status, n (%)				
Premenopausal	290 (55.9)	260 (45.9)	291 (56.1)	280 (48.6)
Postmenopausal	229 (44.1)	306 (54.1)	228 (43.9)	296 (51.4)
T stage, n (%)				
TX	2 (0.4)	19 (3.4)	4 (0.8)	25 (4.3)
T0	0	2 (0.4)	0	3 (0.5)
T1	22 (4.2)	65 (11.5)	26 (5.0)	67 (11.6)
T2	231 (44.5)	246 (43.5)	230 (44.3)	234 (40.6)
T3	174 (33.5)	144 (25.4)	158 (30.4)	177 (30.7)
T4	89 (17.1)	85 (15.0)	101 (19.5)	68 (11.8)
Missing	1 (0.2)	5 (0.9)	0	2 (0.3)
Histological grade, n (%)				
GX	9 (1.7)	6 (1.1)	4 (0.8)	7 (1.2)
G1	16 (3.1)	34 (6.0)	17 (3.3)	42 (7.3)
G2	268 (51.6)	325 (57.4)	290 (55.9)	340 (59.0)
G3	170 (32.8)	132 (23.3)	169 (32.6)	144 (25.0)
Not done or missing	56 (10.8)	69 (12.2)	39 (7.5)	43 (7.5)
N stage, n (%)				
NX	17 (3.3)	25 (4.4)	16 (3.1)	35 (6.1)
N0	52 (10.0)	78 (13.8)	56 (10.8)	97 (16.8)
N1	263 (50.7)	338 (59.7)	259 (49.9)	332 (57.6)
N2	120 (23.1)	83 (14.7)	103 (19.8)	77 (13.4)
N3	66 (12.7)	35 (6.2)	85 (16.4)	33 (5.7)
Missing	1 (0.2)	7 (1.2)	0	2 (0.3)
Histological subtype, n (%)				
Ductal	435 (83.8)	431 (76.1)	444 (85.5)	446 (77.4)
Lobular	52 (10.0)	98 (17.3)	47 (9.1)	90 (15.6)
Other	31 (6.0)	37 (6.5)	28 (5.4)	40 (6.9)
Missing	1 (0.2)	0	0	0

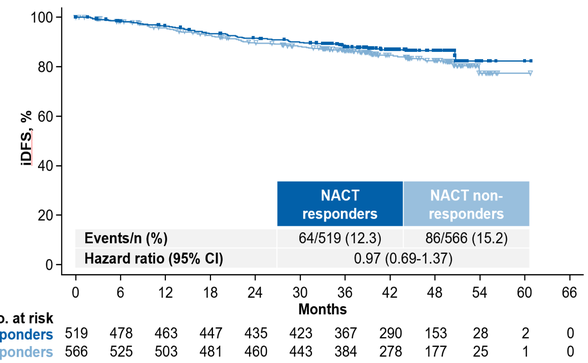
G, grade; GX, grade cannot be assessed; N, nodal; NX, nodal status cannot be assessed; T, tumor; TX, tumor cannot be assessed.

Multivariate Cox Regression Analysis of NACT Responders vs Non-Responders in the Ribociclib + NSAI and NSAI-Alone Arms

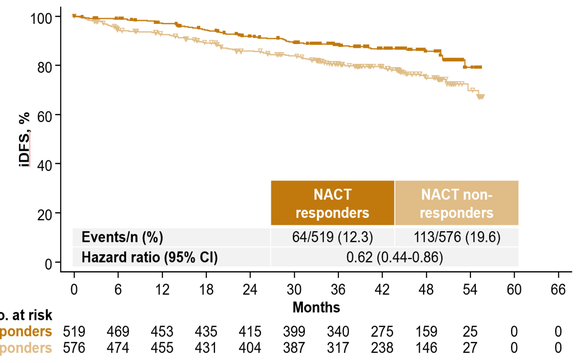
- After stratifying by region, menopausal status, nodal status, and stage and adjusting for histological subtype and grade, iDFS benefit with ribociclib + NSAI was similar for NACT responders and non-responders (4-year iDFS rates, 86.5% vs 82.4%; hazard ratio [HR], 0.97; 95% CI, 0.69–1.37; **Figure 2A**)
- In the NSAI-alone arm, iDFS benefit was greater for NACT responders vs non-responders (4-year iDFS rates, 85.7% vs 74.8%; HR, 0.62; 95% CI, 0.45–0.86; **Figure 2B**)
- In a sensitivity analysis where patients with unknown T or N status at diagnosis or surgery were removed, a similar trend was observed with consistent iDFS benefit with ribociclib + NSAI for responders and non-responders (HR, 0.98; 95% CI, 0.69–1.40)
  - In the NSAI-alone arm, iDFS favored responders over non-responders (HR, 0.64; 95% CI, 0.45–0.91)

Figure 2. iDFS in NACT-Treated Patients

A. iDFS for NACT Responders vs Non-Responders in the Ribociclib + NSAI Arm



B. iDFS for NACT Responders vs Non-Responders in the NSAI-Alone Arm



References

1. Loibl S et al. *Ann Oncol*. 2024;35(2):159-182
2. Langeh U et al. *Health Sciences Review*. 2023;9:100119
3. Pavlovic D et al. *Ther Adv Med Oncol*. 2023; 15:17588359231205848
4. Fasching PA et al. Oral presented at: ESMO 2024; September 13-17, 2024; Barcelona, Spain. Oral LBA13
5. McAndrew N et al. Poster presented at: ESMO 2024; September 13-17, 2024; Barcelona, Spain. Poster 242P

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