Not all pN1 ER-pos HER2-neg breast cancers are equal: why careful patient selection is key for adjuvant ribociclib

B. Salaets, A. Deblander, L. De Sutter, K. Van Baelen, M. Van Houdt, N. Willers, T. Baert, A. Baten, F. Derouane, G. Floris, S. Han, H. Janssen, N. Nevelsteen, C. Remmerie, A. Smeets, J. Verhoeven, Y. Van Herck, C. Van Ongeval, C. Weltens, H. Wildiers, P. Neven

San Antonio Breast Cancer Symposium
December 9-12, 2025

Background

For patients with high-risk ER-pos, HER2-neg breast cancer, adding abemaciclib (2 years) or ribociclib (3 years) to standard endocrine therapy improves invasive disease-free survival (IDFS). We hypothesize that not all patients who meet the eligibility criteria of the NATALEE trial will derive a clinically meaningful benefit from 3 years of adjuvant ribociclib. Previously, we demonstrated that patients with grade 3 pT2N0 tumors have a high risk of recurrence and might benefit from this additional treatment[1]. Contrarily, patients with a pT0-2N1 tumor with more favorable tumor biology (grade 1-2), might have a low risk of recurrence irrespective of adjuvant treatment with a CDK4/6 inhibitor.
The RxPONDER trial[2] showed that 2497 patients with pN1, genomically low-risk tumors achieved a 94% 5-year distant disease-free survival (DDFS) with endocrine therapy alone. Here, we present real-world outcomes for patients with grade 1–2, pT0–2N1, ER-pos, HER2-neg tumors.

Inclusion criteria

- Patients diagnosed and/or treated at UZLeuven
- Early-stage ER-pos, HER2-neg breast cancer
- Surgery between 2000 and 2023
- NATALEE trial eligibility criteria for adjuvant ribociclib following local therapy.

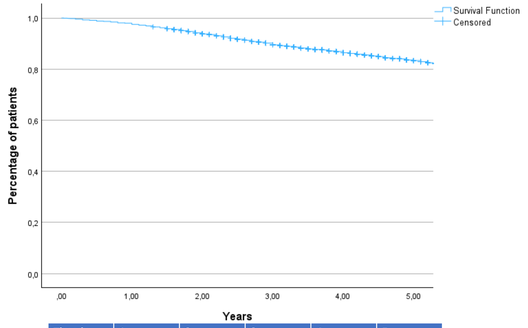
- **Cohort 1**: stage III disease (AJCC 8th edition) or stage II including either pN1 (excluding pT1N1mi) or pT2N0 tumors with grade 3, or grade 2 tumors with Ki-67 >20%

- **Cohort 2:** predefined lower-risk subgroup, characterized as patients with stage II, pT0–2N1 (excluding pT1N1mi), grade 1 or 2 tumors

Table 1. Patient and tumor characteristics

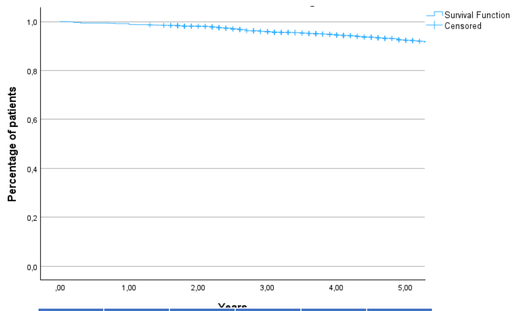
	COHORT 1. ALL NATALEE ELIGIBLE (N= 3980)	COHORT 2. STAGE II N1 GRADE 1-2 (N= 1357)
MEDIAN AGE IN YEARS	58	58
ANATOMICAL STAGE - NO. (%)		
STAGE II	2658 (66,8%)	1357 (100%)
STAGE III	1322 (33,2%)	0 (0%)
TUMOR SIZE – NO. (%)		
T1	732 (18,4%)	497 (36,6%)
T2	2385 (59,9%)	860 (63,3%)
T3	592 (14,9%)	0 (0%)
T4	264 (6,6%)	0 (0%)
T0 OR TX	7 (0,2%)	0 (0%)
NODAL STATUS - NO. (%)		
N0	819 (20,6%)	0 (0%)
N1	2327 (58,5%)	1357 (100%)
N2-3	831 (20,9%)	0 (0%)
NX	3 (0,1 %)	0 (0%)
HISTOLOGIC GRADE – NO. (%)		
1	337 (8,5%)	261 (19,2%)
2	2084 (69,9%)	1096 (80,8%)
3	1543 (38,8%)	0 (0%)
UNKNOWN	16 (0,4%)	0 (0%)
CHEMOTHERAPY – NO. (%)		
NEO-ADJUVANT	402 (10,1%)	37 (2,7%)
ADJUVANT	1957 (49,1%)	493 (36,3%)

IDFS all NATALEE eligible patients (Cohort 1)



Time in years	1	2	3	4	5
Events	100	247	412	529	639
No. at risk	3875	3690	3439	3182	2936

IDFS stage II, pT0–2N1, grade 1-2 tumors (Cohort 2)



Time in years	1	2	3	4	5
Events	19	34	68	85	114
No. at risk	1338	1297	1219	1134	1053

Figure 1. Kaplan-Meier Curves Invasive Disease Free Survival

Methods and Statistics

It concerns a retrospective single centre cohort study.

We assessed both IDFS and DDFS in this NATALEE-eligible population and compared (Cohort 1) to a predefined lower-risk subgroup (Cohort 2), characterized as patients with stage II, pT0–2N1, grade 1 or 2 tumors (excluding pT1N1mi).
Kaplan–Meier curves were used for the estimation of the DDFS and IDFS for both cohorts. Analyses have been performed using SPSS software. The 4-year outcome was chosen in accordance with the ESMO 2024 updated analysis of NATALEE with a 44.2 median follow-up.

Results

We identified 3980 patients eligible for adjuvant ribociclib according to NATALEE-criteria (Cohort 1); 66,8% were stage II and 1357 of them met the lower-risk subgroup criteria (Cohort 2). Median age at diagnosis was 58 years for both cohorts and median follow-up time was 17,6 years for Cohort 1 and 18,8 years for Cohort 2. Analysis showed a 4-year IDFS for Cohort 1 of 87,6% as compared to 93,5% for patients for Cohort 2. DDFS was 86.4 % and 94.5% respectively. At 10 years of follow-up the absolute difference in DDFS increased to 9,9% (70,1% vs. 80,0%).

Conclusion

We found that lower-risk, NATALEE eligible patients, already have an encouraging 4-year IDFS and DDFS. These data emphasize the need for careful patient selection, to derive a clinically meaningful benefit, balancing efficacy against potential toxicity.

Contact

Babette Salaets
UZ Leuven
Email: babette.Salaets@uzleuven.be

References

1. Van Severen R et al. Clinicopathological feature based risk recurrence in pT2N0 HR-positive and HER2-negative early breast cancer: a retrospective, real-world, monocentric study. Presented at: San Antonio Breast Cancer Symposium; December 5-8, 2024; San Antonio,TX.
2. Kalinsky K et al. 21-Gene Assay to Inform Chemotherapy Benefit in Node-Positive Breast Cancer. N Engl J Med. 2021 Dec 16;385(25):2336-2347. doi: 10.1056/NEJMoa2108873. Epub 2021 Dec 1. PMID: 34914339; PMCID: PMC9096864.

This presentation is the intellectual property of the author/presenter

© POSTER TEMPLATE BY GENIGRAPHICS® 1.800.790.4001 WWW.GENIGRAPHICS.COM