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Adjuvant ribociclib (RIB) + nonsteroidal aromatase inhibitor (NSAI) in patients (pts) with HR+/HER2- early breast cancer (EBC): NATALEE 6-y overall survival (OS) and efficacy outcomes

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Background

The phase 3 NATALEE trial demonstrated a statistically significant invasive disease-free survival (iDFS) benefit with adjuvant RIB + NSAI in pts with high-risk stage II/III HR+/HER2- EBC. We present a prespecified analysis of OS and efficacy outcomes with 6 y of follow-up.

Methods

Pts with HR+/HER2- EBC were randomized 1:1 to receive RIB (400 mg/d; 3 wk on/1 wk off for 3 y) + NSAI (letrozole 2.5 mg/d or anastrozole 1 mg/d for 5 y) or NSAI alone. Premenopausal women and men also received goserelin. Pts had stage IIA (if N1 or if N0 with additional high-risk factors), stage IIB, or stage III disease per *AJCC, 8th ed.* OS, breast cancer-specific survival (BCSS), iDFS, distant disease-free survival (DDFS), and distant recurrence-free survival (DRFS) were evaluated via Kaplan-Meier methods. Statistical comparisons were conducted by stratified log-rank test.

Results

At the data cutoff (15 May 2026), all pts were off RIB for a median of 38 mo and beyond the predefined NSAI study regimen. With a median OS follow-up of 66.5 mo, RIB + NSAI showed an OS benefit over NSAI alone (HR, 0.809 [95% CI: 0.661-0.989]; nominal 1-sided $P=0.019$), with increasing absolute benefit over time from 1.2% (93.89% vs 92.73%) at 5 y to 2.1% (91.86% vs 89.73%) at 6 y, that was consistent across key subgroups. BCSS (HR, 0.706 [95% CI: 0.559-0.890]) was supportive of OS benefit. With a median iDFS follow-up of 66.3 mo, RIB + NSAI demonstrated a persistent iDFS benefit over NSAI alone (HR, 0.741 [95% CI: 0.646-0.849]; nominal 1-sided $P<.0001$), with the absolute iDFS benefit increasing from 4.1% (85.32% vs 81.24%) at 5 y to 5.3% (83.23% vs 77.92%) at 6 y. DDFS (HR, 0.744 [95% CI: 0.646-0.858]) and DRFS (HR, 0.738 [95% CI: 0.634-0.858]) benefits were also maintained. No new safety signals were observed.

Conclusions

With 6 y of follow-up and all pts off RIB (median, ≈ 3 y), the sustained reduction in recurrence risk and positive OS results with RIB + NSAI over NSAI alone continue to demonstrate a substantial and clinically relevant benefit for pts with high-risk stage II/III HR+/HER2- EBC, supporting the use of RIB + NSAI in the adjuvant setting across the broad NATALEE-eligible population.

Clinical trial identification

NCT03701334.

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Legal entity responsible for the study

Novartis Pharmaceuticals Corporation.

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Disclosure

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