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Adjuvant ribociclib (RIB) plus nonsteroidal aromatase inhibitor (NSAI) in patients (pts) with HR+/HER2– early breast cancer (EBC): NATALEE 5-year outcomes

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Background

The phase 3 NATALEE trial demonstrated that adjuvant RIB + NSAI led to a statistically significant invasive disease–free survival (iDFS) benefit in pts with stage II and III HR+/HER2– EBC. We present a protocol-specified 5-year efficacy analysis.

Methods

Pts with HR+/HER2– EBC were randomized 1:1 to RIB (400 mg/d; 3 weeks on/1 week off for 3 y) + NSAI (letrozole 2.5 mg/d or anastrozole 1 mg/d for 5 y) or NSAI alone. Men and premenopausal women received goserelin. Pts were included if they had anatomical stage IIA (if N1 [1-3 axillary lymph nodes] or N0 with additional high-risk factors), stage IIB, or stage III disease per AJCC, 8th ed. The primary end point of iDFS and secondary efficacy end points of distant disease–free survival (DDFS), distant relapse–free survival (DRFS), and overall survival (OS) were evaluated using Kaplan-Meier methods. Statistical comparisons were made by stratified log-rank test.

Results

At data cutoff (May 28, 2025), all pts were off RIB treatment, and a similar proportion had completed 5 years of NSAI treatment in both arms (RIB + NSAI, 36.5%; NSAI alone, 34.4%). With a median iDFS follow-up of 55.4 months, RIB + NSAI demonstrated persistent iDFS benefit over NSAI alone (hazard ratio [HR], 0.716; 95% CI: 0.618-0.829; nominal 1-sided *P*<.0001). Absolute iDFS rates were 90.8% vs 88.0% at 3 y, 88.3% vs 83.9% at 4 y, and 85.5% vs 81.0% at 5 y (absolute improvement of 2.7%, 4.4%, and 4.5%, respectively). iDFS benefit was observed across subgroups, including N0 (HR, 0.606; 95% CI: 0.372-0.986). RIB + NSAI also demonstrated continued DDFS (HR, 0.709; 95% CI: 0.608-0.827) and DRFS (HR, 0.699; 95% CI: 0.594-0.824) benefit vs NSAI alone. A positive trend for OS favoring RIB + NSAI (HR, 0.800; 95% CI: 0.637-1.003; nominal 1-sided *P*=.026) continues to emerge. No new safety signals were observed with a median follow-up time of approximately 2 years after RIB completion.

Conclusions

In this 5-year landmark analysis with mature efficacy data, RIB + NSAI reduced the risk of invasive and distant disease recurrence compared with NSAI alone, including in pts with high-risk N0 disease. A positive trend for OS in favor of RIB + NSAI continues to emerge.

Clinical trial identification

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