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Overall survival from the phase 3 postMONARCH trial of abemaciclib + fulvestrant vs placebo + fulvestrant for HR+, HER2-advanced breast cancer following progression on a prior CDK4/6 inhibitor + endocrine therapy

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Background

The phase 3 postMONARCH trial demonstrated a statistically significant improvement in progression-free survival (PFS) with abemaciclib + fulvestrant vs placebo + fulvestrant in HR+, HER2- advanced breast cancer (ABC) following progression on a prior CDK4/6i + endocrine therapy (ET). Here we report the final overall survival (OS) analysis.

Methods

postMONARCH was a global, double-blind, placebo-controlled study. Eligible patients had disease progression on a CDK4/6i + aromatase inhibitor as initial therapy for ABC or recurrence on/after adjuvant CDK4/6i + ET; no other prior therapy for ABC was permitted. Patients were randomized 1:1 to receive abemaciclib + fulvestrant or placebo + fulvestrant. The final OS analysis was pre-specified at 200 OS events (one-sided p-value boundary $p = 0.023$). Time-to-event analyses used Kaplan-Meier methods and stratified Cox models to estimate the HR and 95% confidence intervals (CI).

Results

368 patients were randomized 1:1 (abemaciclib + fulvestrant, $n = 182$; placebo + fulvestrant, $n = 186$). At data cutoff (06 Mar 2026), median follow-up was approximately 36 months with 200 events observed (90 [49.5%] vs 110 [59.1%]). Median OS was numerically longer with abemaciclib + fulvestrant vs placebo + fulvestrant: 32.1 months (95% CI 27.2–38.1) vs 24.6 months (95% CI 22.5–28.8); however, statistical significance was not reached (HR: 0.80, 95% CI 0.60–1.06; $p=0.1145$). Consistent OS differences were observed across subgroups. Updated PFS was consistent with the primary analysis (HR: 0.78, 95% CI 0.62–0.99; nominal $p = 0.0390$). PFS by blinded independent central review, time to second progression, and chemotherapy-free survival also favored abemaciclib. Safety was consistent with the established abemaciclib profile; no new signals were identified.

Conclusions

Abemaciclib + fulvestrant resulted in numerically longer median OS vs placebo + fulvestrant, however statistical significance was not reached. While absolute PFS benefit was modest, the overall evidence supports consideration of abemaciclib-based treatment for patients with HR+, HER2- ABC after disease progression on prior CDK4/6i + ET.

Clinical trial identification

NCT05169567.

Legal entity responsible for the study

Eli Lilly and Company.

Funding

Eli Lilly and Company.

Disclosure

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