BOLERO-2: efficacy, safety, and quality of life with everolimus plus exemestane as first-line therapy in advanced breast cancer

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Background: In the BOLERO-2 study (NCT00863655), the combination of everolimus and exemestane (EVE+EXE) more than doubled progression-free survival (PFS) versus...
placebo (PBO) and EXE (median PFS 7.8 vs 3.2 mo; hazard ratio = 0.45; \( P < 0.0001 \)).

These efficacy results were consistent in all predefined subgroups, including patients with visceral metastases and in those whose disease recurred after adjuvant endocrine therapy (alone or with chemotherapy). This analysis of BOLERO-2 examines efficacy, safety, and quality of life (QOL) in the subgroup of patients who received EVE+EXE as first-line therapy in the advanced setting.

**Materials and Methods:** BOLERO-2 enrolled patients with hormone receptor–positive (HR+) advanced breast cancer who experienced disease recurrence or progression after prior nonsteroidal aromatase inhibitor therapy, and compared EVE (10 mg/d) + EXE (25 mg/d) versus PBO+EXE. The primary end point was PFS by local investigator review. QOL was assessed using the EORTC QLQ C-30 questionnaire, with definitive deterioration defined as a 5% decrease in global health status versus baseline, with no subsequent increase during the study.

**Results:** Of 724 patients in BOLERO-2, 137 (19%) received first-line EVE+EXE (n = 100; 14%) or PBO+EXE (n = 37; 5%) after disease progression in the adjuvant setting. The EVE+EXE group had significantly longer PFS than the PBO+EXE group (by local assessment: 11.50 vs 4.07 mo, respectively; hazard ratio = 0.39; 95% confidence interval, 0.25-0.62; by central assessment: 15.24 vs 4.21 mo, respectively; hazard ratio = 0.32; 95% confidence interval, 0.18-0.57). The safety profile was consistent with the established profiles of each agent. Median time to definitive deterioration in global
health status was numerically longer in the EVE+EXE arm than in the PBO+EXE arm (11.07 vs 7.23 mo, respectively; \( P = 0.1715 \)).

**Conclusions:** EVE+EXE significantly prolonged PFS while maintaining QOL in patients with HR+ advanced breast cancer who received this treatment as first-line therapy after disease recurrence after adjuvant therapy). The robust results observed in this population (PFS by local assessment 7.4 mo longer with EVE+EXE) support using the combination of EVE+EXE earlier in the advanced setting. The ongoing phase 2 trial, BOLERO-4, is prospectively evaluating the efficacy of EVE plus letrozole as a first-line therapy in patients with HR+ advanced breast cancer (target N = 200).