Final Progression-Free Survival Analysis of BOLERO-2: A Phase III Trial of Everolimus for Postmenopausal Women With Advanced Breast Cancer

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ABSTRACT

Everolimus (EVE) is an mTOR inhibitor approved for the treatment of advanced breast cancer (BC) in the United States and Europe. In the phase III BOLERO-2 trial, EVE compared with placebo (PBO) plus exemestane (EXE) significantly prolonged progression-free survival (PFS) and overall survival in postmenopausal women with hormone receptor-positive (HR+) and HER2-negative advanced BC progressing after prior endocrine therapy. We provide an update on the final overall and progression-free survival analyses and report the first update on overall survival of patients randomized to EVE plus EXE (EVE+EXE) versus PBO plus EXE (PBO+EXE) at the time of data cut-off (July 19, 2011; median follow-up of 23.9 months).

METHODS

Study Design and Treatment

The BOLERO-2 trial compared EVE (10 mg/day) with PBO in postmenopausal women with advanced BC progressing after prior endocrine therapy with anastrozole or letrozole. After 2 years of adjuvant endocrine therapy, patients with residual disease were randomized in a 1:1 ratio to receive EVE+EXE or PBO+EXE.

RESULTS

Conclusions

EVE+EXE markedly prolonged PFS in the overall population and in all patient subgroups. The effect of EVE+EXE treatment was consistent among all prospectively defined subgroups. We report here final, protocol-defined progression-free survival (PFS) data after 2 years of adjuvant endocrine therapy. Consistent with previous reports, EVE+EXE significantly prolonged PFS versus EXE monotherapy as per local assessment (7.8 vs 3.2 months, respectively; HR=0.45 [95% CI, 0.38-0.54]; log-rank p=0.0001). Furthermore, EVE+EXE was non-inferior to PBO+EXE in PFS time, with a median of 8.5 vs 6.7 months, respectively (HR=0.64 [95% CI, 0.50-0.81], log-rank p=0.002). These findings were consistent across all subgroups defined by: Eastern Cooperative Oncology Group (ECOG) performance status, geographic region, visceral disease, measurable disease, hormone receptor status (HR+ vs HR-), weight change, and prior adjuvant therapy.

PFS Subgroup Analysis

Overall Survival

Final progression-free survival analysis of BOLERO-2: A phase III trial of everolimus for postmenopausal women with advanced breast cancer (BC) who relapse or progress on a nonsteroidal aromatase inhibitor (NSAI) are limited. Interim investigator and institutional review board approval were required before study enrollment. Women who had received prior chemotherapy and/or radiation therapy were included in the study. The primary endpoint was PFS, defined as the time from randomization to disease progression or death. Time to event was estimated by the Kaplan-Meier method. The effect of EVE+EXE treatment was consistent among all prospectively defined subgroups. We report here final, protocol-defined progression-free survival (PFS) data after 2 years of adjuvant endocrine therapy.

Secondary Endpoints

Patients without visceral metastases had an estimated 59% risk reduction for PFS events versus patients with visceral metastases (HR=0.41 [95% CI, 0.31-0.55]; log-rank p<0.0001). Median duration of exposure to EVE was 23.9 weeks (range, 1.0-123.3 weeks) in the EVE+EXE arm versus 4.6 weeks (range, 0.1-118.3 weeks) in the PBO+EXE arm. Median time to initiation of EVE and EXE was 2.8 and 5.1 months, respectively. PFS time was similar across all trials focused on BC progressing during or after NSAI therapy.

Conclusion:

EVE+EXE improved PFS in patients who received adjuvant endocrine therapy±chemotherapy and was non-inferior to PBO+EXE, consistent with previous reports. PFS time was similar across all trials focused on BC progressing after prior NSAI and may lead to a paradigm shift in treatment for this patient population.