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Abemaciclib in high risk early breast cancer

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Background

Over 90% of patients with breast cancer are diagnosed with early breast cancer (EBC). While many patients with HR+ disease will not recur or have distant relapse with standard therapies, up to 30% of patients whose cancer has high risk clinical and/or pathological features may experience distant relapse, many in the first 2 years. Novel treatment options are needed to prevent early recurrences and development of metastases for these patients. Abemaciclib is an oral, continuously dosed CDK4 & 6 inhibitor approved for use in HR+, HER2- advanced breast cancer (ABC). Efficacy and safety of abemaciclib in ABC supported phase III evaluation in the adjuvant setting.

Methods

monarchE, an open-label, phase III study, included patients with HR+, HER2-, high risk EBC, who completed primary treatment. Patients with ≥4 positive nodes, or 1-3 nodes and at least one of the following: tumor size ≥5 cm, histologic grade 3, or central Ki-67 ≥20%, were eligible, and randomized (1:1) to abemaciclib (150 mg BID for 2 years) plus endocrine therapy (ET) or ET alone. A prespecified interim analysis was planned at ☒293 IDFS events. The primary endpoint was invasive disease-free survival (IDFS) per STEEP criteria. Secondary endpoints included distant relapse-free survival (DRFS), overall survival, and safety.

Results

5,637 patients were randomized. With 323 IDFS events observed in the intent-to-treat population, positive efficacy required a 2-sided p-value <0.0264. Abemaciclib plus ET demonstrated a statistically significant improvement in IDFS versus ET alone (p=.0096, HR: 0.747, 95% CI: 0.598, 0.932), corresponding to a 25.3% reduction in the risk of an IDFS event. The 2-year IDFS rates were 92.2% vs 88.7%, respectively. A similar improvement was observed for DRFS (HR: 0.717, 95% CI: 0.559, 0.920) with 2-year DRFS rates of 93.6% and 90.3%, respectively. Consistent benefit was seen in all prespecified subgroups. The most frequent AEs were diarrhea, neutropenia and fatigue in the abemaciclib arm and arthralgia, hot flush and fatigue in the control arm. Safety was consistent with the known profile of abemaciclib.

Conclusions

Abemaciclib when combined with ET is the first CDK4 & 6 inhibitor to demonstrate a statistically significant improvement in IDFS in patients with HR+, HER2-, high risk EBC.

Clinical trial identification

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