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monarchE: Primary overall survival (OS) results of adjuvant abemaciclib + endocrine therapy (ET) for HR+, HER2-, high-risk early breast cancer (EBC)

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Background

Two years (yrs) of adjuvant abemaciclib+ET demonstrated statistically significant and clinically meaningful improvement over ET alone in invasive disease-free survival (IDFS) and distant relapse-free survival (DRFS) in patients (pts) with HR+, HER2-, node-positive, high-risk EBC. Here, we report primary OS (secondary endpoint) and updated IDFS and DRFS.

Methods

monarchE is an open-label, randomized, phase 3 trial in pts with HR+, HER2-, high-risk EBC. Pts were randomized (1:1) to receive ET for at least 5 yrs ± abemaciclib for the first 2 yrs. High-risk EBC was defined as either ≥4 positive axillary lymph nodes (ALN), or 1-3 ALN + either Grade 3 disease and/or tumor ≥5 cm (Cohort 1). Pts with 1-3+ ALN and central Ki67 ≥20% were enrolled to Cohort 2. The intent-to-treat (ITT) population consisted of Cohorts 1 (n=5120) and 2 (n=517). Hazard ratios (HRs) for efficacy endpoints were estimated using the Cox proportional hazard model. The primary OS analysis was triggered by approx. 650 deaths in the ITT population to allow adequate follow-up time.

Results

In the ITT population (median follow-up: 6.3 yrs) 301 pts in the abemaciclib+ET and 360 pts in the ET arm had died. The addition of abemaciclib to ET reduced the risk of death by 15.8% vs ET (HR 0.84; 95% CI, 0.72–0.98; *P* = 0.027), meeting the prespecified boundary for significance. OS benefit was consistent across prespecified subgroups. IDFS and DRFS benefit persisted up to 7 yrs (HR 0.73; 95%CI, 0.66-0.82 and 0.75, 0.66-0.84, respectively). At 7 yrs, IDFS was 77.4% with abemaciclib+ET vs 70.9% with ET, and DRFS was 80.0% vs 74.9% (absolute benefit: 6.5% and 5.1%, respectively). More pts in the ET arm (52%) received subsequent CDK4/6 inhibitors in any line metastatic setting than in the abemaciclib+ET arm (34%). In Cohort 1, IDFS, DRFS, and OS were consistent with the ITT population. Long-term safety data did not support concerns of delayed toxicities.

Conclusions

The addition of 2 yrs of adjuvant abemaciclib to ET resulted in statistically significant and clinically meaningful improvement in OS over ET in pts with HR+, HER2–, node-positive, high-risk EBC. At 7 yrs, abemaciclib+ET demonstrated a sustained IDFS and DRFS benefit. The following experts also contributed to the abstract: Joohyuk Sohn, Frances Boyle, Chiun-Sheng Huang, Zhimin Shao, Irfan Cicin and Belen San Antonio.

Clinical trial identification

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