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Overall survival (os) results from SOLAR-1, a phase III study of alpelisib (ALP) + fulvestrant (FUL) for hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2–) advanced breast cancer (ABC)

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Background

Phosphatidylinositol 3-kinase (PI3K) pathway hyperactivation due to *PIK3CA* mutations contributes to poor survival in patients (pts) with HR+, HER2– ABC (Mosele 2020). In the phase III SOLAR-1 trial of pts with progression on/after aromatase inhibitor (AI), the PI3Kα inhibitor ALP together with FUL significantly improved progression-free survival (PFS) in the *PIK3CA*-mutant (mut) cohort (HR 0.65; 95% CI 0.50-0.85; $P<0.001$; median [m] PFS 11.0 mo with ALP + FUL vs 5.7 mo with placebo [PBO] + FUL), a population with poor prognosis. At final PFS analysis, the first interim OS results were immature.

Methods

Men/postmenopausal women (N=572) with HR+, HER2– ABC with no prior chemotherapy treatment (tx) and whose disease progressed on/after AI were randomized 1:1 to receive ALP (300 mg PO QD) or PBO, + FUL (500 mg IM on D1 and D15 of C1 then D1 of each 28-d cycle) and stratified by presence of lung and/or liver metastases and prior cyclin-dependent kinase 4/6 inhibitor. OS in the *PIK3CA*-mut cohort, a key secondary endpoint, was evaluated by Kaplan-Meier methodology; a 1-sided stratified log-rank test was performed with an O'Brien-Fleming efficacy boundary of $P\leq0.0161$.

Results

With mOS follow-up of 30.8 mo, mOS was 39.3 mo (95% CI 34.1-44.9) with ALP + FUL and 31.4 mo (95% CI 26.8-41.3) with PBO + FUL (HR 0.86; 95% CI 0.64-1.15; $P=0.15$); OS did not cross the prespecified boundary. Median time to chemotherapy (TTC) was 23.3 mo (95% CI 15.2-28.4) with ALP + FUL and 14.8 mo (95% CI 10.5-22.6) with PBO + FUL (HR 0.72; 95% CI 0.54-0.95). In pts with lung and/or liver metastases, mOS was 37.2 mo (95% CI 28.7-43.6) with ALP + FUL and 22.8 mo (95% 19.0-26.8) with PBO + FUL (HR 0.68; 95% CI 0.46-1.00). No new safety signals were observed with longer follow-up.

Conclusions

Though not statistically significant, OS was prolonged by a clinically relevant ≈8 mo with ALP when added to FUL in HR+, HER2–, *PIK3CA*-mut ABC. mTTC was also prolonged with ALP + FUL vs PBO + FUL. Coupled with the statistically and clinically significant PFS, these data further support ALP + FUL in this poorer prognostic population of pts with *PIK3CA*-mut ABC.

Clinical trial identification

NCT02437318.

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