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A double-blind placebo controlled randomized phase III trial of fulvestrant and ipatasertib as treatment for HER-2 negative and estrogen receptor positive (ER+) metastatic breast cancer (MBC): Overall survival results of the CCTG/BCT MA.40/FINER study

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Background

The MA.40/FINER Study compared the efficacy and safety of the pan-AKT inhibitor ipatasertib versus (vs) placebo plus fulvestrant in patients with ER+/HER2-negative MBC immediately following progression on a CDK4/6 inhibitor (CDK4/6i) plus aromatase inhibitor (AI). Both the primary objective comparing investigator-assessed progression-free survival (PFS) between treatment arms in the ITT population and key secondary objective comparing PFS in the AKT pathway-altered cohort demonstrated statistically and clinically significant improvements. Here we report on the overall survival (OS) analysis.

Methods

Pre-, peri-, and postmenopausal women and men with ER+/HER-2-negative MBC were randomly assigned 1:1 to receive ipatasertib (400mg PO daily, days 1-21) plus fulvestrant (500mg IM, days 1 and 15, cycle 1 then day 1 of subsequent cycles) vs placebo plus fulvestrant. Randomization was stratified by AKT pathway altered (PIK3CA/AKT1/PTEN genomic alteration determined by cfDNA NGS assay) vs wild type/unknown and primary (<6 months (mo) CDK4/6i) vs secondary (>=6 mo CDK4/6i) endocrine resistance. OS was a secondary endpoint.

Results

250 participants were randomized to ipatasertib (125) or placebo (125). At a median follow-up of 35.0 mo, 3.2% ipatasertib vs 2.4% placebo arm participants remained on protocol treatment. Median OS for ITT populations were 26.68 mo (95% CI: 21.42 to 30.78 mo) vs 25.76 mo (95% CI: from 19.98 to 28.88 mo) for ipatasertib vs placebo arms (HR = 0.97, 95% C.I. 0.70 to 1.33, p = 0.83). In an exploratory analysis, median OS for AKT pathway-altered cohorts were 23.66 mo (95% CI: 18.53 to 28.65 mo) vs 25.23 mo (95% CI: 16.99 to 28.88 mo) [HR = 1.14 95% CI: 0.72 to 1.80; p=0.58]. No new safety signals were observed with longer duration follow-up.

Conclusions

Despite meaningful PFS improvements, the addition of ipatasertib to fulvestrant for the second-line treatment of ER+/HER-2-negative MBC after CDK4/6i plus AI did not impact OS for either total or AKT pathway-altered patient cohorts.

Clinical trial identification

NCT04650581.

Legal entity responsible for the study

Canadian Cancer Trials Group (CCTG).

Funding

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Disclosure

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