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Overall survival (OS) of palbociclib (P) plus endocrine therapy (ET) versus capecitabine (CAP) in hormone-receptor+/HER2- metastatic breast cancer (MBC) that progressed on aromatase inhibitors (AIs): Final results of the PEARL study

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Background

PEARL study did not show superiority in progression-free survival (PFS) with P+ET versus (vs) CAP in patients (pts) with AI-resistant MBC, but P+ET was better tolerated and showed a significant delay in quality of life deterioration. Final OS data are reported here.

Methods

PEARL had two consecutive cohorts: cohort 1 (C1) with 296 pts randomized to P+exemestane vs CAP, and cohort 2 (C2) with 305 pts randomized to P+fulvestrant (F) vs CAP. Secondary endpoints included OS in C2 and in wild-type (wt) ESR1 (measured in ctDNA at baseline) pts (C1+C2). OS analysis was planned when 152 deaths occurred in C2, in order to have an 80% power to detect an increase of 50% in OS from 22 months (m) with CAP to 33 m with P+F or P+ET in wtESR1 pts. Adjusted hazard ratio (aHR) was calculated using a stratified Cox proportional hazard model with treatment arm, stratification factors and number of involved sites as covariates.

Results

At data cut-off (11Jan2021), the median follow-up of C2 and wtESR1 pts were 28.0 m and 30.3 m, respectively. Median OS in C2 was 31.1 m with P+F vs 32.8 m with CAP (aHR 1.10, 95% CI, 0.81–1.50; p=0.550). Median OS in wtESR1 pts was 37.2 m with P+ET vs 34.8 m with CAP (aHR 1.06, 95% CI, 0.81-1.37; p=0.683). None of the subgroup analyses showed superiority in OS for P+ET vs CAP. Subsequent therapy was given to 79.8% and 82.9% of pts with P+ET and CAP, respectively. The median number of subsequent lines was 3 (1-10) in the P+ET arm and 3 (1-9) in the CAP arm. First subsequent therapy was CDK4/6 inhibitor+ET in 26.1% of pts in the CAP arm and CAP in 36.1% of pts in the P+ET arm. The median PFS2 defined as time from randomization to the end of first subsequent therapy or death, was similar in both arms either in C2, 18.3 m with P+F vs 17.7 m with CAP (aHR 0.95, 95% CI, 0.73-1.25; p=0.728), and in wtESR1 pts, 18.3 m with P+ET vs 18.2 m with CAP (aHR 1.04, 95% CI, 0.83-1.31; p=0.717). PFS and response did not change in this final analysis. No new safety findings were observed with longer follow-up.

Conclusions

Palbociclib + endocrine therapy did not show a statistically superior OS compared to CAP in MBC pts progressing to AIs.

Clinical trial identification

NCT02028507.

Legal entity responsible for the study

GEICAM Spanish Breast Cancer Group.

Funding

Pfizer and AstraZeneca.

Disclosure

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