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GEICAM/2014-12 (FLIPPER) study: First analysis from a randomized phase II trial of fulvestrant (F)/palbociclib (P) versus (vs) F/placebo (PL) as first-line therapy in postmenopausal women with HR (hormone receptor)+/HER2– endocrine sensitive advanced breast cancer (ABC)

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Background

The role of P combined with F in improving outcomes of endocrine sensitive ABC patients (pts) in the first-line setting deserved clinical testing. To study this, postmenopausal HR+/HER2– ABC with *de novo* metastatic disease or relapsing after >12 months of completing ≥5 years of adjuvant endocrine therapy were included in FLIPPER study.

Methods

In this double-blind phase II study, pts were randomly assigned in 1:1 ratio to F 500mg/P vs. F/PL. Stratification criteria were: visceral vs. non-visceral and recurrent vs. de novo metastatic disease. The primary objective was progression-free survival (PFS) at 1 year (investigator's assessment by RECIST 1.1). With a sample size of 190 pts and a two-sided alpha of 0.2, the analysis has 80% power to detect a difference between both treatment groups, assuming PFS proportions of 0.545 and 0.695 for F/PL and F/P, respectively (constant HR of 0.6).

Results

From Feb'2016 to Jan'2019, 189 pts were randomised (94 F/P, 95 F/PL). Median age was 64 years, 45.5% of pts had *de novo* metastatic disease, 60.3% visceral involvement. The study met the pre-specified primary endpoint: PFS rates at 1-year were 83.5% and 71.9% in F/P and F/PL groups, respectively (HR 0.55; 80% CI 0.36-0.83, p=0.064). Median PFS was 31.8 mo (F/P) vs. 22.0 mo (F/PL) (HR 0.52; 95% CI 0.34-0.78; p=0.002). Overall response rates were 68.3% (F/P) vs. 42.2% (F/PL) (p=0.004). The most frequent G2/4 non-haematological toxicities were diarrhoea (3.2% vs. 2.1%) and fatigue (12.8% vs. 5.3%) with F/P and F/PL, respectively. G3/4 haematological toxicities were neutropenia (64.9% vs. 0%), leukopenia (26.6% vs. 0%) and lymphopenia (14.9% vs. 2.1%). There were no reported cases of febrile neutropenia nor treatment related deaths. OS data are immature.

Conclusions

P/F significantly improved 1-year PFS rate compared to F/PL in pts with HR+/HER2- endocrine sensitive ABC. P/F also improved median PFS and ORR. These data provide evidence for superiority of F/P vs. F/PL in an ABC population not represented in the pivotal PALOMA3 trial.

Clinical trial identification

NCT02690480.

Legal entity responsible for the study

GEICAM Spanish Breast Cancer Group.

Funding

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Disclosure

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