The phase II randomized, open-label acecLERA BC study (NCT04576455) evaluated giredestrant vs PCET (n = 103) giredestrant (n = 47) PCET (n = 90) Fulvestrant (n = 29) giredestrant (n = 39) PCET (n = 62) Figure 1: Exploratory analyses of efficacy in key subgroups A) CDK4/6i B) No CDK4/6i C) F) AI D) F) E) AI* F) No CDK4/6i G) AI* H) No chemotherapy I) No prior A/I J) F=AI* No CDK4/6i K) Fulvestrant* L) Fulvestrant* M) Fulvestrant* N) CDK4/6i* O) No chemotherapy P) No prior chemotherapy Q) No prior chemotherapy R) No prior chemotherapy S) No prior chemotherapy T) No prior chemotherapy U) No prior chemotherapy V) No prior chemotherapy W) No prior chemotherapy X) No prior chemotherapy Y) No prior chemotherapy Z) No prior chemotherapy

All patients were assessed for efficacy with investigator-assessed progression-free survival (INV-PFS). giredestrant demonstrated a numeric improvement vs PCET, with a hazard ratio (HR) of 0.81 (17% vs 9%) and clinical benefit rate (CBR): 32% vs 21%; objective response rate (ORR): 13% vs 7%.

In giredestrant-treated patients, median INV-PFS was 5.5 months (95% CI 4.2, 6.8) and median PFS was 3.6 months (95% CI 2.5, 4.5) vs 2.7 months (95% CI 1.6, 3.3) in PCET-treated patients. Of the 39 patients with prior chemotherapy, 27 (70%) achieved a CBR vs 17 (42%) in the PCET cohort (p = 0.01) and 13 (33%) had an ORR vs 7 (18%) (p = 0.07). Giredestrant was well tolerated in patients with prior chemotherapy, with a median (range) of 9 months (0.08–83) of exposure.

METHODS

Biomarkers were assessed in baseline circulating tumor (ct)DNA isolated from plasma using qualitative and quantitative methods. A total of 90 patients were enrolled in the ctDNA-evaluable cohort, with 47 evaluable patients in the giredestrant arm and 43 evaluable patients in the PCET arm. Short nucleotide variants were detected across 90 pts in both treatment arms, including 17% with ESR1 variants with known or likely impact on protein function based on their status in COSMIC. The most common mutations in ctDNA-evaluable ESR1 variants included mainly D538G and Y537S/N and PIK3CA mutations, mainly E545K and E545D.

CONCLUSIONS

Expansory subgroup analyses showed favorable outcomes with giredestrant in terms of INV-PFS, CBR, and ORR across patients with prior chemotherapy. The benefit was more pronounced in pts with ER+ tumors (both vs PCET overall and vs comparator choice of fulvestrant specifically), compared with an AI, and in pts who received prior fulvestrant. Clinical benefit was observed across different HER2 statuses.

CONFLICTS OF INTEREST

El reports consulting fees (e.g., advisor, consultant) from Lilly, Novartis, Pfizer, Roche, Gilead, Merck Sharp & Dohme, and Astellas; contracted research from Novartis and Pfizer; travel, accommodation, and expenses from Lilly and Roche; and is a scientific advisor for third-party writing assistance for this poster, furnished by Daniel Clyde, PhD, of Health Interactions, was provided by F Hoffmann-La Roche Ltd. GM reports consulting fees (e.g., advisor, consultant) from AbbVie, Amgen, AstraZeneca, Lilly, Novartis, Pfizer, and Roche; travel, accommodation, and expenses from Lilly and Roche; and is a scientific advisor for third-party writing assistance for this poster, furnished by Daniel Clyde, PhD, of Health Interactions, was provided by F Hoffmann-La Roche Ltd. This study is sponsored by F Hoffmann-La Roche Ltd.

REFERENCES


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