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Preoperative window-of-opportunity study with giredestrant or tamoxifen (tam) in premenopausal women with estrogen receptor-positive (ER+)/human epidermal growth factor receptor 2-negative (HER2-) and Ki67≥10% early breast cancer (EBC): The EMPRESS study

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Background

Giredestrant is a potent, nonsteroidal, oral selective ER degrader (SERD) and antagonist with antitumor activity in patients (pts) with ER+/HER2- advanced breast cancer. In pre and perimenopausal women, it is administered in combination with gonadotropin-releasing hormone (GnRH) analogs. EMPRESS (NCT05659563) evaluated if short-term preoperative giredestrant, without GnRH analogs, is superior to tam in reducing Ki67 in premenopausal ER+/HER2– EBC pts.

Methods

This is a multicenter, international, open-label, randomized phase II, window-of-opportunity trial conducted in Spain and France. Eligible pts had untreated ER+/HER2- EBC (cT1–T3, N0–1, Ki67 ≥10% locally assessed). Pts were randomized (1:1) to 30 mg oral giredestrant or 20 mg oral tam daily. After 15 days (D), surgery or breast biopsy were performed. The primary endpoint was the absolute Ki67 change from baseline to D15 in pts with centrally confirmed Ki67 ≥10%. Key secondary endpoints included complete cell cycle arrest (Ki67 ≤2.7%) at D15 and changes in ER/progesterone receptor (PgR) expression. The study was powered at 80% using a two-sided Wilcoxon test (5% significance level).

Results

Between Jul 2023 and Dec 2024, 92 pts from 20 sites were enrolled (46 pts in each arm). Baseline characteristics were well balanced between the two arms. At data cutoff (January 30th, 2025), 41 pts in arm A and 44 in arm B had completed the study treatment. The absolute change of Ki67 from baseline to D15 was -14.5 (95% CI; -17.5, -13) with giredestrant and -10.0 (95% CI; -12.3, -8.5) with tam (p= 0.002), meeting the primary endpoint. The complete cell cycle arrest rate at D15 was numerically higher with giredestrant than tam (17.5% versus 4.5%, p=0.074). Giredestrant treatment also resulted in a strong and significant decrease in ER (p<0.001) and PgR (p<0.001) expression between baseline and D15. Additional endpoints will be reported at the meeting.

Conclusions

Giredestrant, administered without LHRH analogs, demonstrated superior antiproliferative activity than tam in terms of Ki67 reduction in premenopausal women with ER+/HER2- EBC.

Clinical trial identification

NCT05659563.

Legal entity responsible for the study

The authors.

Funding

F. Hoffmann-La Roche Ltd.

Disclosure

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