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Neoadjuvant giredestrant (GDC-9545) + palbociclib (palbo) vs anastrozole (A) + palbo in post-menopausal women with oestrogen receptor-positive, HER2-negative, untreated early breast cancer (ER+/HER2– eBC): Interim analysis of the randomised, open-label, phase II coopERA BC study

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Background

Endocrine therapy is the mainstay for ER+ BC while CDK4/6 inhibitors + A decrease Ki67 expression (a proliferation biomarker). Giredestrant, a highly potent, nonsteroidal, oral, selective ER antagonist and degrader (SERD), achieves robust ER occupancy, is well tolerated and has encouraging anti-tumour activity as monotherapy and in combination with palbo in metastatic BC. coopERA BC (NCT04436744) investigates giredestrant vs A (both + palbo) in post-menopausal women with ER+/HER2– eBC. We present an interim analysis.

Methods

Patients (pts) with measurable cT1c (≥1.5 cm)–cT4a–c ER+/HER2– eBC and baseline Ki67 score ≥5% are randomised 1:1 to 1 mg oral daily (PO QD) A or 30 mg PO QD giredestrant on Days (D)1–14 (window-of-opportunity [WOO] phase; 14D) followed by QD dosing for four 28-D cycles + 125 mg PO palbo on D1–21 (neoadjuvant phase; 16 weeks) pre-surgery. Stratification factors: T status; Ki67 score; progesterone receptor status. Primary efficacy endpoint: Centrally assessed geometric mean relative Ki67 score change from baseline to Week 2 during the WOO phase (scores reflect endocrine therapies' ability to suppress proliferation; a surrogate clinical outcomes marker). Complete cell cycle arrest rate (CCCA; pts with Ki67 score ≤2.7%) at Week 2 is a secondary efficacy endpoint. Safety is also assessed.

Results

83/202 planned pts were assessed. Two-week relative Ki67 reduction was greater with giredestrant (reduction from baseline to Week 2 geometric mean = 80%; 95% CI = 72%, 85%) than A (67%; 95% CI = 56%, 75%; P = 0.0222). Consistent Ki67 suppression was observed in pts with baseline Ki67 ≥20% (giredestrant: 83% reduction; A: 71%) or <20% (65% vs 24%). At Week 2, 25% of tumours exhibited CCCA with giredestrant vs 5% with A (Δ 20%; 95% CI = –37%, –3%). Fewer pts had giredestrant- vs A-related adverse events (AEs) (28% vs 38%); no grade ≥3 AEs or serious AEs were giredestrant-related.

Conclusions

Interim analysis data demonstrated superior anti-proliferative activity of giredestrant compared with A. Safety was consistent with the known giredestrant profile.

Clinical trial identification

NCT04436744.

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