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A randomised double-blind placebo-controlled phase II trial of palbociclib combined with letrozole (L) in patients (pts) with oestrogen receptor-positive (ER+) advanced/recurrent endometrial cancer (EC): NSGO-PALEO / ENGOT-EN3 trial

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Background

Cyclins are proteins that activate cyclin-dependent kinases (CDKs) and are required for normal cell cycle transitions. Palbociclib is an oral selective inhibitor of the CDKs 4 and 6. EC endometrioid adenocarcinoma is hormone dependent and endocrine therapy with aromatase inhibitors is well established. This is the first randomised trial of a CDK4/6 inhibitor (P) vs placebo combined with L in pts with advanced or recurrent ER+ EC.

Methods

Eligible pts had ECOG PS 0/1, histologically confirmed endometrioid EC that was ER+ and measurable or evaluable per RECIST v1.1 and had received no prior CDK4/6 inhibitor therapy. Prior surgery, radiation therapy, chemotherapy or ≤1 line of endocrine therapy (MPA/megestrol acetate) was permitted. Pts were stratified according to number of prior chemotherapy lines, prior endocrine therapy and measurable vs evaluable disease. Pts were randomised 1:1 to receive L 2.5 mg OD orally d1–28 with either palbociclib 125 mg or placebo OD orally d1–21 in a 28-d cycle until progression. Tumours were assessed every 12 weeks. The primary endpoint was progression-free survival (PFS).

Results

Of 77 enrolled pts, 73 were evaluable (2 received no trial drug; 1 had brain metastases; 1 withdrew consent before starting treatment): 37 randomised to L + placebo and 36 to L + palbociclib combination. Major comorbidity: diabetes in 12%, hypertension in 41%. 88% had relapsed disease and only 15% had prior MPA/megestrol acetate. Palbociclib/placebo was interrupted in 25/ 8 pts and in 14 pts the dose of palbociclib was reduced. L + palbociclib significantly improved PFS compared with L + placebo: median 8.3 vs. 3.0 months, respectively; hazard ratio 0.56 (95% CI 0.32 to 0.98; p0.041). Disease control rate at 24 weeks: 64% vs. 38%. Treatment-emergent grade 3/4 adverse events were significantly more frequent with L + palbociclib (anaemia 8% vs 3%; neutropenia 42% vs 0%). Patient-reported outcomes were similar in the two treatment arms.

Conclusions

The L + palbociclib combination demonstrated clinically meaningful improvement in PFS with manageable toxicity, meriting phase III investigation.

Clinical trial identification

NCT02730429.

Legal entity responsible for the study

NSGO-CTU (Nordic Society of Gynaecological Oncology - Clinical Trial Unit).

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Disclosure

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