Introduction

Molecular characterization is important to inform treatment decisions for patients with endometrial cancer (EC). Wild type TP53 (TP53wt) is found in ~50% of advanced/recurrent EC and of those, ~70% are microsatellite stable (MSS/pMMR).

Methods

ENGOT-ENS/GOG-3055/SIENDO (NCT03555422) is a randomized double-blind, phase 3 trial evaluating selinexor vs placebo as a maintenance treatment for advanced/recurrent EC following response to prior systemic therapy. Here we report the updated efficacy and safety of a prespecified exploratory subgroup analysis of patients with TP53wt EC.

Results

113 patients with TP53wt EC received selinexor (n = 77) or placebo (n = 36) as maintenance therapy. As of March 2023, the median follow-up was 25.3 months, and 26 patients remain on treatment. Median PFS (mPFS) was 27.4 months with selinexor vs 5.2 months with placebo (HR 0.42; 95% CI [0.25–0.70], nominal one-sided p = 0.0003). PFS improvement was observed regardless of microsatellite instability status; in the TP53wt/MSS(pMMR) subgroup, the mPFS was not reached with selinexor vs 4.9 months with placebo.

In patients with TP53wt, the most common adverse events (AEs) were nausea, vomiting, and diarrhea; most common grade 3/4 AEs were neutropenia, thrombocytopenia, and nausea; 16% of patients discontinued selinexor due to AEs. No grade 5 AEs occurred. No immune-related AEs were observed.

Conclusion/Implications

TP53wt status may represent a robust predictive biomarker for selinexor efficacy in EC. Additionally, a strong PFS signal was observed in the TP53wt/MSS(pMMR) subgroup, a patient population with high unmet need. Both additional data and updated data will be presented at the conference.