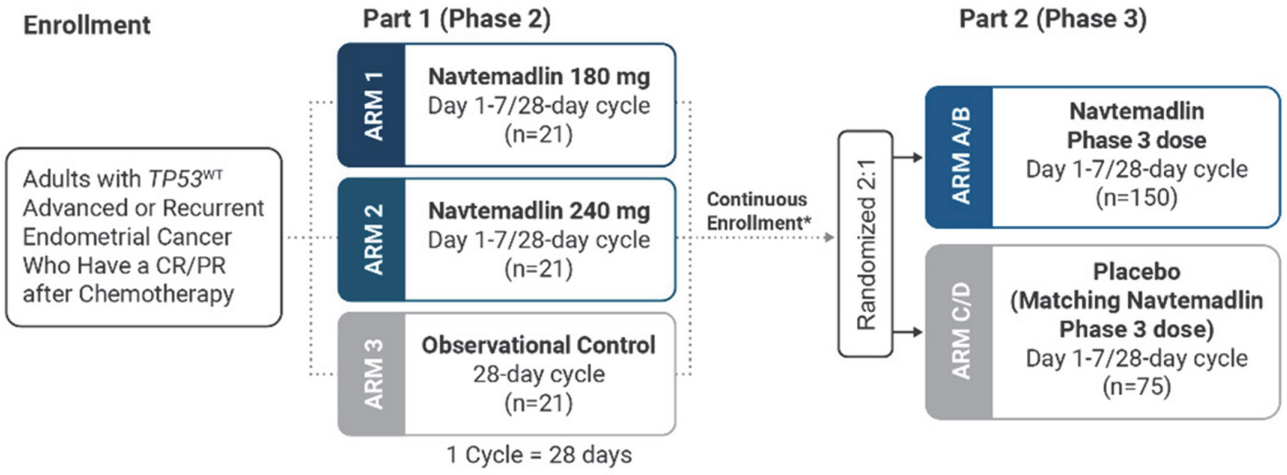


**Abstract TP008/#1500 Figure 1** Study schema of KRT-232–118

double minute 2 (MDM2), a key negative regulator of p53, is upregulated in ~50% of EC patients (Jeczen 2007) due to loss of $p14^{ARF}$, a critical modulator of intranuclear MDM2 levels, thus preventing p53 tumor suppressor function. Navtemadlin is a potent, selective MDM2 inhibitor that restores p53-mediated apoptosis in $TP53^{WT}$tumors. The sensitivity of EC to genotoxic chemotherapy (Miller 2020) suggests susceptibility to p53-mediated apoptosis. Post-chemotherapy maintenance with navtemadlin may provide a non-genotoxic way to maintain p53-driven activity and tumor cell control in the ~50% of $TP53^{WT}$EC patients (Nakamura 2019). KRT-232–118 is a Global 2-part Phase 2/3 study evaluating the safety and efficacy of navtemadlin maintenance therapy in $TP53^{WT}$ advanced/recurrent EC patients following response to chemotherapy (EudraCT 2022–5002196-31; NCT05797831).

**Methods** Adults with ECOG PS 0–1 who completed up to 6 cycles of chemotherapy excluding adjuvant/neo-adjuvant therapy and achieved CR or PR (RECIST v1.1) are eligible. The open-label Phase 2 randomizes patients to oral navtemadlin at a dose of 180 mg or 240 mg QD (Day 1–7/28-day cycle), or observation; primary endpoint is recommended Phase 3 dose (RP3D). The double-blind Phase 3 will randomize patients (2:1) to the RP3D vs placebo QD (Day 1–7/28-day cycle); stratification is by response and disease stage. Primary endpoint for Phase 3 is PFS by blinded independent review.

**Current Trial Status** This study is now open to enrollment.

## TP009/#1495 A PHASE 2, OPEN-LABEL, SINGLE-ARM, PROSPECTIVE, MULTI-CENTER STUDY OF NAB-SIROLIMUS PLUS LETROZOLE IN ADVANCED OR RECURRENT ENDOMETRIOID ENDOMETRIAL CANCER

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**Introduction** Despite recent pivotal data demonstrating improved outcomes with immunotherapy plus chemotherapy, regardless of mismatch repair status, alternative treatment options for advanced or recurrent endometrial carcinoma (EC) remain necessary. Dysregulation of mTOR signaling is implicated in the pathology of EC, particularly in endometrioid EC (EEC) in which >80% harbor PTEN or PI3K/AKT/mTOR pathway alterations. Moreover, crosstalk between mTOR and estrogen receptor signaling pathways is associated with

endocrine resistance. GOG-3007 and other phase 2 studies have demonstrated that the combination of conventional mTOR inhibitors (mTORi) and endocrine therapy provides clinical benefit in patients with EC. nab-Sirolimus is a nanoparticle injectable form of mTORi approved for malignant perivascular epithelioid cell tumor. Preclinical data with nab-sirolimus demonstrated improved tumor accumulation, mTOR inhibition, and tumor growth suppression compared with conventional mTORi. We hypothesize that nab-sirolimus in combination with letrozole may produce synergistic antitumor activity in patients with recurrent EEC.

**Methods** In this phase 2, open-label, single-arm, multi-center study (NCT05997017), nab-sirolimus (100 mg/m$^2$, IV, days 1 and 8 of each 21-day cycle) and letrozole (2.5 mg, oral, daily) are administered to patients (~29 planned) with clinically confirmed, advanced or recurrent EEC. Eligibility criteria include age ≥18 years, 0–1 prior chemo-based regimens, ECOG 0–1, mTORi naïve, and RECIST-measurable disease. The primary endpoint is best ORR by RECIST v1.1; key secondary endpoints include duration of response, PFS, OS, and safety. The relationship between biomarkers and response outcomes is an exploratory endpoint.

**Current Trial Status** Open for enrollment.

TP010/#397

### ENGOT-EN20/GOG-3083/XPORT-EC-042 A PHASE 3, RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND, MULTICENTER TRIAL OF SELINEXOR IN MAINTENANCE THERAPY FOR PATIENTS WITH P53 WILD-TYPE, ADVANCED OR RECURRENT ENDOMETRIAL CARCINOMA

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**Introduction** Selinexor is FDA-approved for use in multiple myeloma and diffuse large B-cell lymphoma. In the ENGOT-EN5/GOG-3055/SIENDO study (NCT03555422), preliminary analysis of a pre-specified exploratory subgroup of patients with TP53wt EC showed a decrease in risk for progression or death with a median PFS of 13.7 months with selinexor vs 3.7 months with placebo. of the EC molecular subtypes, TP53 wild type (wt) tumors represent 50% of advanced and recurrent tumors.

**Methods** XPORT-EC-042 (NCT05611931) is a phase 3 randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of selinexor as maintenance therapy in patients with TP53wt primary stage IV or recurrent EC, who achieved a partial or complete response per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 after completing at least 12 weeks of platinum combination chemotherapy±immunotherapy. Among other inclusion/exclusion criteria, eligible patients must be ≥18 years of age, have histologically confirmed EC, and TP53wt tumor confirmed by NGS sequencing. Patients will be randomized 1:1 with selinexor 60 mg or placebo once-weekly in 28-day cycles until progressive disease, toxicity, or 3-years if in complete response. A total of 220 patients are estimated to be enrolled globally. The primary endpoint is PFS based on RECIST v1.1 criteria as assessed by the Investigator. The key secondary endpoint is overall survival. Select secondary endpoints include safety assessments and PFS assessed by a blinded independent central review.

**Current Trial Status** Patient enrollment is ongoing.

## AS11. Ovarian cancer

TP011/#1536

### A DOUBLE-BLIND PLACEBO-CONTROLLED PHASE III CHEMO-IMMUNOTHERAPY (PACLITAXEL-CARBOPLATIN-OREGOVOMAB [PCO]) VS CHEMOTHERAPY (PACLITAXEL-CARBOPLATIN-PLACEBO [PCP]) IN PATIENTS WITH NEWLY DIAGNOSED, ADVANCED EPITHELIAL OVARIAN CANCER (EOC): FLORA-5/GOG-3035 STUDY

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**Introduction** Oregovomab, a murine IgGκ1 MAb, binds to the circulating tumor associated antigen CA125, resulting in development of immunogenic complexes with CA125, which are subsequently processed by dendritic cells and macrophages leading to downstream CA125-specific antitumor activity by T and B lymphocytes. In a randomized Phase 2 study in previously untreated EOC patients, immunization with oregovomab with paclitaxel and carboplatin (PC) demonstrated significant improvement in mPFS (months) 41.8 for PCO and 12.2 for PC (p = 0.0027, HR 0.46) and mOS has not yet been