Poster:
TPS5627

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

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BACKGROUND

- Advanced/recurrent endometrial cancer (EC) is associated with a poor prognosis, with limited disease control in patients who relapse after first-line treatment[1,2]
- Molecular characterization is important to inform treatment decisions for patients with endometrial cancer (EC)[3]
- Wild type *TP53* (*TP53*wt) is found in ~75% of newly diagnosed EC and 50% of advanced/recurrent tumors; there are no specific targeted therapies for patients with *TP53*wt EC [3,4]
- Selinexor is an investigational oral XPO1 inhibitor that drives nuclear retention and functional activation of wild type tumor suppressor proteins, including p53[5]

RATIONALE

- ENGOT-EN5/GOG-3055/SIENDO (NCT03555422) is a phase 3 study evaluating selinexor as maintenance therapy in patients with advance/recurrent EC. Preliminary analysis of a pre-specified exploratory subgroup of patients with *TP53*wt EC showed a decrease in risk for progression or death with a median PFS of 13.7 months with selinexor as maintenance therapy vs 3.7 months with placebo at the time of primary PFS analysis (Figure 1)[6]
- The most common Grade 3 treatment-related adverse events were nausea, neutropenia, and thrombocytopenia[6]
- Efficacy and safety of selinexor as a maintenance therapy in patients with advance/recurrent EC will be evaluated in in the XPORT-EC-042 Study (NCT05611931)

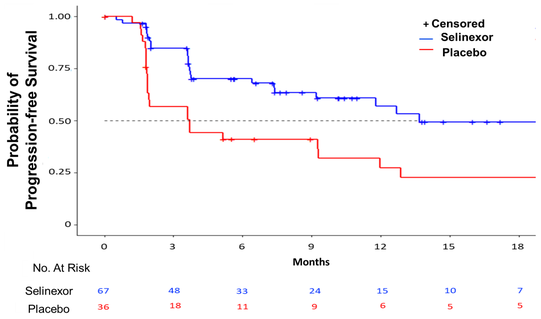

Figure 1. Progression-Free Survival of patients with wild type p53 endometrial cancer

STUDY DESIGN

ENGOT-EN20/GOG-3083/XPORT-EC-042 (NCT05611931)
A prospective, multicenter, double-blind, placebo-controlled, randomized Phase 3 study

N = 220

Key Eligibilities
- Known *TP53wt* EC by central NGS
- Primary stage IV disease or first recurrent EC
- Received at least 12 weeks of platinum-based chemotherapy ± immunotherapy

PR/CR Per RECIST v1.1

R 1:1

- **Selinexor 60mg PO QW**
- **Continued until PD, toxicity, or 3 years if in CR**
- **Placebo QW**

Stratified by:
- Primary stage IV vs recurrent
- PR vs CR

Primary Objective: To evaluate the efficacy of selinexor compared to placebo as maintenance therapy in patients with *TP53*wt advanced or recurrent endometrial cancer

CR, complete response; EC, endometrial cancer, HR, hazard ratio; NGS, next generation sequencing; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; QW, once weekly; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors

ENDPOINTS

Primary Endpoint: Investigator assessed PFS

Key Secondary Endpoint: Overall Survival

Secondary Endpoints
- Safety and tolerability
- TFST
- TSST
- PFS2
- PFS, assessed by BICR
- HR-QoL

Exploratory Endpoints
- PFS
  - per histologic subtypes
  - per other molecular features
- CR rate among pts who entered as PR
- Duration of CR
- Tumor biomarkers
- PK exposure parameters and efficacy/safety endpoints

BICR, Blinded Independent Central Review; HR-QoL, Health-related quality of life; PFS2, progression-free survival after consecutive treatment; PD, pharmacodynamics; PK, pharmacokinetics; TFST, time to first subsequent therapy; TSST, time to second subsequent treatment.

ELIGIBILITY CRITERIA

Select Inclusion Criteria
- Patients ≥18 years of age
- Histologically confirmed EC including: endometrioid, serous, undifferentiated, and carcinosarcoma.
- *TP53* wt confirmed by next generation sequencing (NGS) assessed by Foundation Medicine (FMI)
  - If *TP53* status was previously assessed by FMI, results may be used via data piping from the original source
- Completed at least 12 weeks of platinum-based therapy ± immunotherapy and achieved confirmed partial or complete response (PR or CR)
  - Primary Stage IV disease. OR
  - At first relapse
- Eastern Cooperative Oncology Group (ECOG) performance status of 0-1.
- Patients must have adequate bone marrow function and organ function within 2 weeks before starting study drug

Select Exclusion Criteria
- Uterine sarcomas (carcinosarcomas – not excluded), clear cell or small cell carcinoma with neuroendocrine differentiation
- Received a blood or platelet transfusion during the 2 weeks prior to C1D1
- Patients unable to tolerate two forms of antiemetics for at least 2 cycles will not be eligible for the trial.
- Previous treatment with an XPO1 inhibitor
- Stable disease or progressive disease (PD) or clinical evidence of progression prior to randomization
- Patients who received concurrent systemic anti-cancer therapy including investigational agents ≤3 weeks prior to C1D1

PARTICIPATING LOCATIONS

- Australia
- Belgium
- Canada
- Czech Republic
- Georgia
- Germany
- Greece
- Hungary
- Ireland
- Israel
- Italy
- New Zealand
- Slovakia
- Spain
- United States

STUDY INFORMATION

Study Contact: clinicaltrials@karyopharm.com

References: **1** Brooks RA, Fleming GF, Lastra RR, et al. CA Cancer J Clin 69:258–279, 2019 **2** Madariaga A, Rustin GJS, Buckanovich RJ, et al: Am Soc Clin Oncol Educ book Am Soc Clin Oncol Annu Meet 39:e152–e166, 2019 **3** Levine DA. Nature. 2013;497(7447):67–73. **4** Leslie KK, Filiaci VL, Mallen AR, et al. Gynecol Oncol. Apr 1;161(1):113, 2021. **5** Kashyap T, Argueta C, Aboukameel A, et al. Oncotarget. Nov 29; 7(48): 78883–78895. 2016. **6** Vergote I, Perez Fidalgo A, Hamilton E, et al., SGO 2022 Annual Meeting on Women's Cancer.

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