GOG-3073, ENGOT-OV72/MITO: A Phase 3 Study of Relacorilant + Nab-paclitaxel vs. Nab-paclitaxel in Advanced, Platinum-resistant Ovarian Cancer

ROSELLA
Relacorilant with Nab-paclitaxel in Ovarian Cancer

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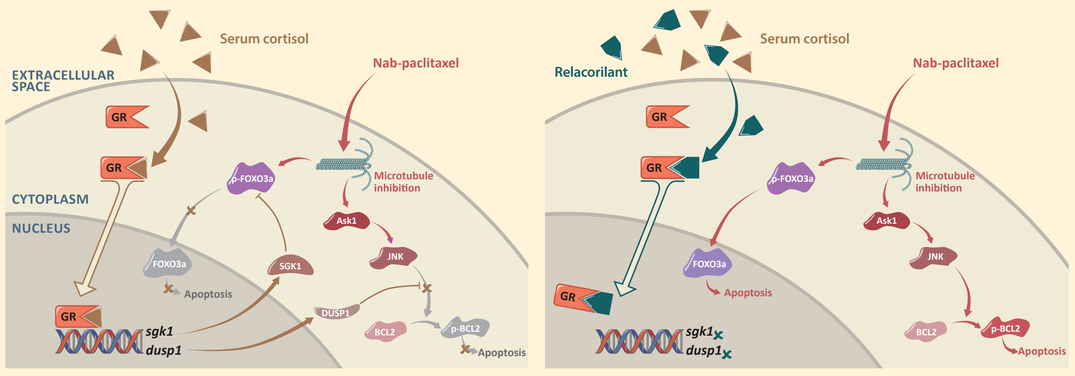
Poster number: PB-35

Background

- Platinum resistance occurs in virtually all patients with recurrent ovarian cancer.
- Single agent chemotherapies are commonly used in this setting, but outcomes are generally poor, leaving a large unmet need for treatments.
- Cortisol, which acts by binding to the glucocorticoid receptor (GR), can reduce the efficacy of chemotherapies by suppressing the apoptotic pathways used by cytotoxic agents.
- The GR is abundantly expressed in ovarian tumors and high GR expression is associated with poor outcomes.[1]
- Preclinical and clinical data indicate that modulation of GR signaling with relacorilant, a selective GR modulator, can reverse the anti-apoptotic effects of cortisol, thereby enhancing chemotherapy efficacy.[2–4]



A phase 2 study* of relacorilant + nab-paclitaxel in patients with recurrent, platinum-resistant/refractory ovarian cancer showed:[4]

- Improved PFS (HR 0.66; *P*=0.038; median PFS 5.6 vs. 3.8 months)
- Improved DOR (HR 0.36; *P*=0.006; median DOR 5.6 vs. 3.7 months)
- Trend toward improved OS (HR 0.67; median OS 13.9 vs. 12.2 months)
- Even greater improvement was seen in patients with 1–3 prior lines of therapy (including prior bevacizumab) and without primary platinum-refractory disease.

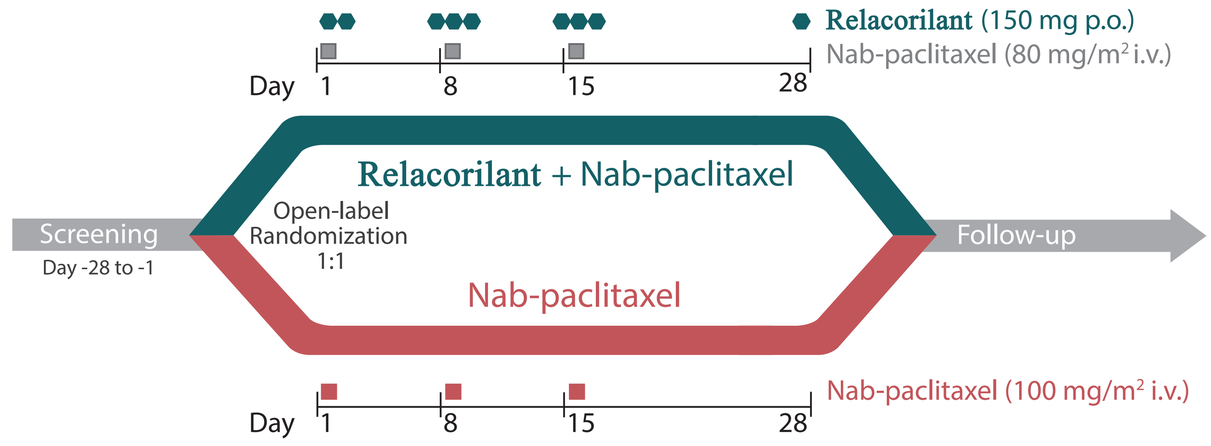
- **The phase 3 ROSELLA study** aims to confirm the findings of the phase 2 study in a larger patient population.

*Relacorilant dosed intermittently on the day before, day of, and day after nab-paclitaxel infusion; compared to nab-paclitaxel monotherapy. Results presented reflect data as of March 22, 2021 (PFS and DOR) and March 7, 2022 (OS). DOR, duration of response; HR, hazard ratio; OS, overall survival; PFS, progression-free survival.

Study Design

- **ROSELLA** (NCT05257408, EudraCT 2022-000662-18) is a confirmatory, phase 3, randomized, 2-arm, open-label, multicenter study of relacorilant + nab-paclitaxel compared to nab-paclitaxel monotherapy in patients with recurrent, platinum-resistant, high-grade serous epithelial ovarian, primary peritoneal, or fallopian tube cancer.
- The study is being conducted globally in collaboration with GOG FOUNDATION and ENGOT (European Network of Gynaecological Oncological Trial groups)

See ClinicalTrials.gov for more details:



- Approximately 360 patients randomized 1:1 to:
  - Relacorilant (150 mg the day before, day of, and day after nab-paclitaxel infusion) + nab-paclitaxel (80 mg/m² on days 1, 8, and 15 of each 28-day cycle)

  or
  - Nab-paclitaxel monotherapy (100 mg/m² on days 1, 8, and 15 of each 28-day cycle).

BICR, blinded independent central review; RECIST, Response Evaluation Criteria in Solid Tumors.

Primary Endpoint

- Progression-free survival by BICR per RECIST v1.1

Key Secondary & Exploratory Endpoints

- Overall survival per RECIST v1.1
- Safety, pharmacodynamics, pharmacokinetics, and patient-reported outcomes

Key Inclusion & Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• ≥18 years old	
• Diagnosis: ○ High-grade (grade 3) serous, epithelial ovarian, primary peritoneal, or fallopian tube carcinoma	• Diagnosis: ○ Low-grade endometrioid, clear-cell carcinoma, mucinous or sarcomatous histology, or mixed tumors containing any of these histologies, or low-grade or borderline ovarian tumor
• Platinum-resistant disease (progression <6 months from completion of a platinum-containing therapy)	• Primary platinum-refractory disease
• Prior therapies: ○ 1–3 lines of prior systemic anticancer therapy ○ ≥1 prior line of platinum chemotherapy and prior bevacizumab required	• Prior therapies: ○ Chemotherapy and other treatments for disease under study within 28 days before the first dose
• ECOG performance score of 0 or 1 • Adequate organ function: ○ Absolute neutrophil count ≥1500 cells/mm³ ○ Platelet count ≥100,000/mm³ ○ Hemoglobin ≥9 g/dL ○ AST or ALT ≤2.5 × ULN or ≤5 × ULN in context of liver metastases ○ Total bilirubin ≤1.5 × ULN ○ Albumin ≥3 g/dL ○ Creatinine clearance ≥40 mL/min/1.73 m²	• Clinically relevant toxicity from prior systemic anticancer therapies or radiotherapy that has not resolved to grade ≤1 • Any major surgery within 4 weeks prior to randomization • Treatment with chronic or frequently used corticosteroids ○ A short course of steroids for hypersensitivity reactions due to chemotherapy (eg, paclitaxel) is allowed

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ECOG, Eastern Cooperative Oncology Group; ULN, upper limit of normal.

Summary & Conclusions

- There remains a large unmet need for effective treatments for platinum-resistant ovarian cancer.
- A phase 2 study of the selective glucocorticoid receptor modulator relacorilant + nab-paclitaxel in patients with advanced ovarian cancer showed meaningful improvements in PFS, DOR, and OS with minimal added toxicity compared to nab-paclitaxel alone.[4]
- Here we introduce ROSELLA, a confirmatory phase 3 study comparing relacorilant + nab-paclitaxel to nab-paclitaxel monotherapy in patients with advanced, platinum-resistant ovarian cancer.

DOR, duration of response; PFS, progression-free survival; OS, overall survival.

The authors want to thank all those who are participating in this study: The study patients and their families, the investigators, and the sponsor team.

References

1. Veneris, JT et al. *Gynecol Onol*. 2017;146(1):153–160.
2. Greenstein, AE and Hunt, HJ. *Oncotarget*. 2021;12(13): 1243–1255.
3. Munster, P et al. *Clin Cancer Res*. 2022;28(15):3214–3224.
4. Colombo, N et al. *J Clin Oncol*. 2023 Jun 26;JCO2202624.

Acknowledgements

This study is sponsored by Corcept Therapeutics. Medical writing assistance was provided by Tina Schlafly, PhD, CMPP, and Valerie Hilliard, PhD, of Corcept Therapeutics.

Presenter Disclosures

DL: Grants/research support- Clovis Oncology, GSK, MSD, PharmaMa, AstraZeneca, genmab, Immunogen, Incyte, Roche, Seagen, Novartis. Honoraria or consultation fees- Clovis Oncology, GSK, MSD, PharmaMa, AstraZeneca, genmab, Immunogen, Incyte, Roche, Seagen, Novartis, Oncoinvest, Corcept, and Sutro. Participation in a company-sponsored speaker's bureau- Seagen, Immunogen, Genmab,AstraZeneca, Clovis Oncology, GSK, MSD, PharmaMar. Others (travel expenses)- AstraZeneca, Clovis Oncology, GSK.

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