GOG-3073, ENGOT-OV72/MITO: A PHASE 3 STUDY OF RELACORILANT + NAB-PACLITAXEL VS. NAB-PACLITAXEL IN ADVANCED, PLATINUM-RESISTANT OVARIAN CANCER

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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 aberrantly expressed in ovarian tumors, and high GR expression is associated with poor outcomes.
- 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.

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

- Improved PFS (HR 0.66; 3-year PFS 34.2% vs 20.5% in control arm).
- Improved ORR (44.0% vs 28.8%)
- Trend toward improved OS (HR 0.67; median OS 13.9 vs 12.2 months).

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

Inclusion Criteria

- ≥18 years old

- Diagnosed:
  - High-grade (grade 3) serous, epithelial ovarian, primary peritoneal, or fallopian tube carcinoma

- Platinum-resistant disease (progression <6 months from completion of a platinum-containing therapy)

- Prior therapies:
  - 1-3 lines of prior systemic anticancer therapy
  - ≤1 prior line of platinum chemotherapy and prior bevacizumab required

- 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
  - ALT or AST ≤5 × ULN or ≤5 × ULN in context of liver metastases
  - Total bilirubin ≤1.5 × ULN
  - Albumin ≥3 g/dL
  - Creatinine clearance ≥60 mL/min/1.73 m²

Key Inclusion & Exclusion Criteria

- Diagnosed:
  - High-grade endometrioid, clear-cell carcinoma, mucinous or serous carcinoma, or mixed tumors containing any of these histologies, or low grade or borderline ovarian tumor

- Primary platinum-resistant-refractory disease

- Prior therapies:
  - Chemotherapy and other treatments for disease under study within 28 days before the first dose of nab-paclitaxel

- 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

Primary Endpoint

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

Key Secondary & Exploratory Endpoints

- Safety, pharmacodynamics, pharmacokinetics, and patient-reported outcomes

References


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