GOG 3045/ENGOT ov-55/MIRASOL: A randomized, open-label, phase 3 study of mirvetuximab soravtansine versus investigator's choice of chemotherapy in advanced high-grade epithelial ovarian, primary peritoneal, or fallopian tube cancers with high folate-alpha (FRα) receptor expression

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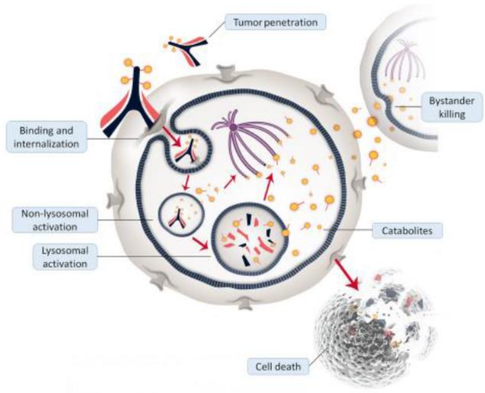
BACKGROUND

- Despite advances with PARP inhibitors and anti-angiogenic agents in newly diagnosed ovarian cancer, unmet need remains for additional active and well-tolerated therapies in recurrent disease
- Elevated FRα expression is a characteristic of several solid tumors, including epithelial ovarian cancer (EOC), thereby providing an attractive candidate for targeted therapeutic approaches
- Mirvetuximab soravtansine (MIRV) is an antibody-drug conjugate (ADC) comprising a FRα-binding antibody, cleavable linker, and the maytansinoid DM4, a potent tubulin-targeting agent that has shown consistent and meaningful single agent clinical activity, along with favorable tolerability, in patients with high FRα expressing ovarian cancer
- Mirvetuximab soravtansine has encouraging activity as a monotherapy in platinum resistant ovarian cancer (PROC) in patients whose tumors express medium and high levels of FRα
  Monotherapy: 24% to 47% confirmed overall response rate (ORR) in FRα high patients [1, 2]

MECHANISM OF ACTION



1. The fully humanized antibody portion of MIRV binds to FRα receptor found on the surface of epithelial ovarian cancer cells
2. MIRV is internalized via endocytosis
3. MIRV is degraded within the lysosome to release its cytotoxic payload (DM4)
4. DM4, a second-generation maytansine derivative disrupts tubulin resulting in mitotic arrest and apoptosis—100-1000 fold more potent than vinca alkaloids
5. DM4 also diffuses through the cell membrane allowing bystander killing on adjacent tumor cells

MIRASOL

Enrollment and Key Eligibility

- 430 patients/330 events for PFS by INV
- Platinum resistant disease (PFI < 6 mo)
  - 1* platinum refractory disease excluded (PPFI < 3 mo)
- Prior Bev and PARP allowed
- 1-3 prior lines
- BRCAmut patients allowed
- FRα high only

Statistical Assumptions

- α=0.05 (two-sided), Power = 90%, HR=0.7; control arm mPFS 3.5 mo

*BICR: Blinded Independent Central Review
†PLD: pegylated liposomal doxorubicin

Mirvetuximab Soravtansine

6 mg/kg (adjusted ideal body weight) once every 3 weeks

1:1 Randomization
STRATIFICATION FACTORS
IC Chemotherapy Choice (Paclitaxel, PLD, Topotecan)
Prior therapies (1 vs 2 vs 3)

Investigator's Choice Chemotherapy
Paclitaxel, PLD†, or Topotecan

Paclitaxel: *80 mg/m² weekly*
PLD: *40 mg/m² once every 4 weeks*
Topotecan: *4 mg/m² on Days 1, 8, and 15 every 4 weeks; or 1.25 mg/m² on Days 1-5 every 3 weeks*

Primary Endpoint

Progression-free survival by INV
BICR for sensitivity analysis*

Secondary Endpoints

Overall response rate by INV
Overall survival
Patient reported outcomes

Key Inclusion Criteria:

- Progressed on or after most recent line of therapy
  - Note: Progression must be determined radiographically and/or by CA-125 GCIG progression criteria
- At least one lesion that meets the definition of measurable disease by RECIST v1.1
- Tumor (archival or biopsy) must be positive for FRα expression as defined by the Ventana FOLR1 (FOLR-2.1) CDx assay (Only 'high' (FRα-high ≥75% PS2+) is reported as positive)
- Received at least 1 but no more than 3 prior systemic lines of anticancer therapy, and for whom single-agent therapy is appropriate as the next line of treatment
- Prior bevacizumab and PARPi allowed

- **Key Exclusion Criteria:**
- Primary platinum-refractory disease, defined as disease that did not respond to or has progressed within 3 months of the last dose of first line platinum-containing chemotherapy

REFERENCES
1. Moore et al ASCO 2017
2. Moore et al ESMO 2019

STUDY DESIGN

- MIRASOL is a randomized phase 3 study designed to evaluate the efficacy of MIRV compared with that of standard-of-care chemotherapy in adult patients with platinum-resistant EOC, primary peritoneal cancer, or fallopian tube cancer
- Confirmation of high FRα positivity by immunohistochemistry (high expression; ≥ 75% of cells with PS2+ staining intensity) and ≤ 3 prior lines of therapy
- MIRASOL is designed to randomize 430 patients, 1:1 to Arm 1 (MIRV at a dose of 6 mg/kg, calculated using adjusted ideal body weight, administered IV on Day 1 of a 21-day cycle) or Arm 2 (investigators' choice chemotherapy (IC Chemo): paclitaxel, pegylated liposomal doxorubicin, or topotecan)

TRIAL ENDPOINTS

Primary Endpoint

- PFS, defined as the time from date of randomization until investigator-assessed progressive disease (PD) or death, whichever occurs first

Secondary Objectives

- To compare the ORR of patients randomized to MIRV vs. IC Chemo
- To compare overall survival (OS) of patients randomized to MIRV vs. IC Chemo
- To compare the primary patient-reported outcome (PRO) using the EORTC QLQ-OV28 (abdominal/GI symptom scale) assessment from patients randomized to MIRV vs. IC Chemo

FUTURE DIRECTIONS FOR RESEARCH

The trial is open and enrolling at centers in the US and Europe

This study is registered at clinicaltrials.gov: **NCT04209855**

For additional information please contact:
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