Society of Gynecologic Oncology
ANNUAL MEETING ON WOMENS' CANCER®
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SGO // PHOENIX, ARIZONA // MARCH 18 – 21, 2022

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

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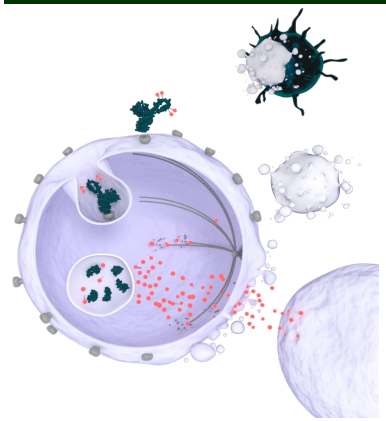
BACKGROUND

- Treatment options for platinum-resistant ovarian cancer (PROC) are limited, consisting primarily of single-agent chemotherapy, which has limited activity (ORR 4%-13%) and considerable toxicity[1-12]
- Ovarian cancer overexpresses folate receptor alpha (FRα) with little to no expression in normal tissue;[13-15] this tumor-specific expression provides an attractive candidate for targeted therapeutic approaches
- Mirvetuximab soravtansine (MIRV) is an antibody-drug conjugate 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 FRα-expressing ovarian cancer[11, 16-19]
- MIRV has encouraging activity as a monotherapy in PROC in patients whose tumors express high levels of FRα
  - SORAYA:[19] Objective response rate (ORR) by investigator 32.4% (95% CI: 23.6%, 42.2%), including five complete responses; duration of response (DOR) will be presented SGO 2022 (Matulonis et al.)
  - FORWARD I:[17] ORR by investigator 38% (95% CI: 27%, 49%)

MECHANISM OF ACTION



The antibody portion of MIRV binds to FRα-receptor on the surface of epithelial ovarian cancer cells and has been engineered to minimize its immunogenicity

MIRV is internalized via endocytosis

MIRV is degraded within the lysosome to release its cytotoxic payload (DM4)

DM4, a second-generation maytansine derivative disrupts tubulin resulting in mitotic arrest and apoptosis—100-1000 fold more potent than vinca alkaloids

DM4 also diffuses through the cell membrane allowing bystander killing of adjacent tumor cells

TRIAL SCHEMA

MIRASOL

Enrollment and Key Eligibility

- Platinum-resistant disease (PFI ≤ 6 mo)
  - 1° platinum refractory disease excluded (primary PFI < 3 mo)
- Prior bevacizumab and PARPi allowed
- 1-3 prior lines of therapy
- Patients with BRCA mutations allowed
- FRα-high by PS2+ scoring (≥75% PS2+)

Statistical Assumptions

- 430 patients/ 330 events for PFS by INV
- α=0.05 (two-sided)
- Power=90%; HR=0.7; control arm mPFS 3.5 mo

Mirvetuximab Soravtansine
6 mg/kg AIBW (calculated using adjusted ideal body weight) intravenously once every 3 weeks

1:1 Randomization
STRATIFICATION FACTORS
Investigator's Choice (IC) Chemotherapy (Paclitaxel, PLD, Topotecan)
Prior Therapies (1 vs 2 vs 3)

Investigator's Choice (IC) Chemotherapy
Paclitaxel, PLD,[†] or Topotecan
Paclitaxel: 80 mg/m2 weekly; PLD: 40 mg/m² every 4 weeks; Topotecan: 4 mg/m² on days 1, 8, and 15 every four weeks; or 1.25 mg/m² on days 1-5 every 3 weeks

Primary Objective

- To compare the progression-free survival (PFS) of patients randomized to MIRV vs IC chemo

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

Key Inclusion Criteria:

- Advanced platinum-resistant high-grade epithelial ovarian, primary peritoneal, or fallopian tube cancers
- 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
- Progressed on or after most recent line of therapy
- At least one lesion that meets the definition of measurable disease by RECIST v1.1
- Tumor demonstrated FRα-high membrane staining with IHC PS2 scoring
  - ≥75% of cells staining positive with ≥2+ staining intensity
- 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

Evaluation:

- Disease progression will be evaluated by the Investigator using Response Evaluation Criteria in Solid Tumors (RECIST, version 1.1). Computerized tomography (CT) or magnetic resonance imaging (MRI) scans will be collected and held for sensitivity analysis by a blinded independent central review (BICR)

TRIAL ENDPOINTS

Primary Endpoint:

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

Secondary Endpoints:

- Objective response includes best response of complete response or partial response as assessed by the investigator
- OS defined as the time from date of randomization until the date of death
- Primary PRO assessment, defined as the number of patients achieving at least 15-point absolute improvement at Week 9 in the abdominal/GI scale of EORTC QLQ-OV28

FUTURE DIRECTIONS FOR RESEARCH

The trial is open and enrolling at centers globally

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

For additional information please contact: medicalaffairs@immunogen.com

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