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BUILDING BRIDGES // BREAKING BARRIERS
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PICCOLO: A phase 2, single arm study of mirvetuximab soravtansine in recurrent, platinum-sensitive, high-grade epithelial ovarian, primary peritoneal, or fallopian tube cancers with high folate receptor alpha (FRα) expression

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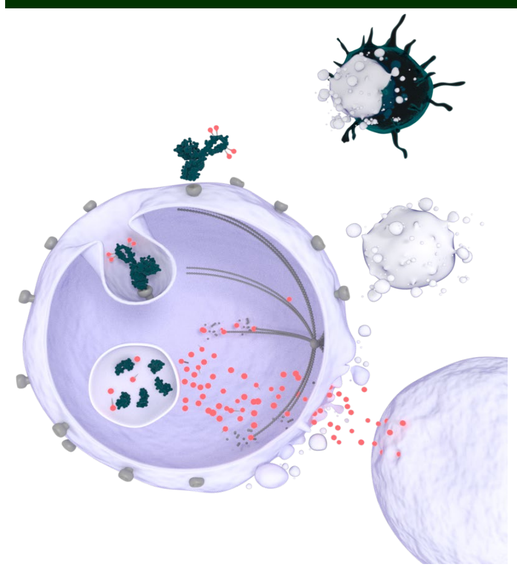
BACKGROUND

- 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 ovarian cancer
- Ovarian cancer overexpresses folate receptor alpha (FRα) with little to no expression in normal tissue;[1-3] 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[4-8]
- There is no generally accepted standard of care with a clear efficacy benchmark based on prospective trials in third-line or later patients with platinum-sensitive ovarian cancer (PSOC)
- MIRV has encouraging activity as a monotherapy in platinum-resistant ovarian cancer (PROC) in patients whose tumors express high levels of FRα
  - SORAYA:[8] 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:[5] ORR by investigator 38% (95% CI: 27%, 49%)
  - Data from a subset of patients who had PSOC and received ≥ 3 prior lines of therapy showed an ORR of 64% in FRα-high group[9]

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

PICCOLO

Enrollment and Key Eligibility

- Platinum-sensitive disease (PFI >6 mo)
- At least 2 prior lines of platinum-based therapy
  - Patients with documented platinum allergy require only 1 prior line of platinum
- FRα-high by IHC scoring (≥75% PS2+)
- Appropriate for single agent therapy as next line of therapy as determined by investigator

Statistical Assumptions

- N=75
- Null hypothesis: ORR is ≤ 28% tested using an optimal Simon's two-stage design w/o pause in enrollment

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

Primary Objective

- To determine efficacy of MIRV in patients with recurrent PSOC and high FRα expression

Secondary Objectives

- To determine the durability of response to MIRV in patients with PSOC
- To evaluate safety and tolerability of MIRV
- To characterize the clinical activity of MIRV in patients with PSOC and high FRα expression

Key Inclusion Criteria:
- Known BRCA status with prior PARPi required if BRCA mutation positive
- Patients may have received a non-platinum based line of therapy
- Progressed on or after most recent line of therapy
- At least one lesion that meets the definition of measurable disease by Response Evaluation Criteria in Solid Tumors (RECIST v1.1)
- Tumor demonstrated FRα-high membrane staining with IHC PS2 scoring
  - ≥75% of cells staining positive with ≥2+ staining intensity
- Prior bevacizumab allowed

Key Exclusion Criteria:
- Endometrioid, clear cell, mucinous, or sarcomatous histology, mixed tumors containing any of those histologies or low grade/borderline ovarian cancer

Evaluation:
- Objective response rate will be evaluated by the Investigator using RECIST v1.1. 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:
- ORR, which includes confirmed best response of CR or PR as assessed by the investigator

Secondary Endpoints:
- DOR, as defined as the time from initial investigator-assessed response (CR or PR) until progressive disease as assessed by the investigator
- PFS defined as time from first dose of MIRV until investigator assessed radiological progressive diesease or death
- OS defined as the time from first dose of MIRV until the date of death
- ORR, DOR, and PFS by blinded independent central review will be summarized as sensitivity analysis

FUTURE DIRECTIONS FOR RESEARCH

The trial is open and enrolling at centers globally

This study is registered at clinicaltrials.gov: **NCT05041257**

For additional information please contact: medicalaffairs@immunogen.com

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