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UPLIFT (ENGOT-ov67/GOG-3048): A Pivotal Cohort of Upifitamab Rilsodotin (XMT-1536; UpRi), an NaPi2b-directed Dolaflexin Antibody Drug Conjugate (ADC) in Platinum-Resistant Ovarian Cancer

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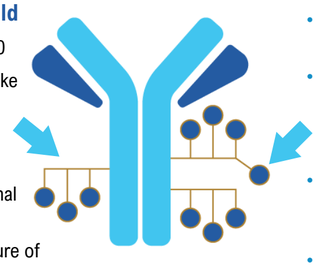
BACKGROUND

- NaPi2b is a sodium-dependent phosphate transport protein broadly expressed in solid tumors, including high-grade serous epithelial ovarian, fallopian tube, and primary peritoneal cancer, with limited expression in normal tissue
- Upifitamab rilsodotin (UpRi; XMT-1536) is an investigational first-in-class antibody drug conjugate (ADC) targeting NaPi2b

Upifitamab Rilsodotin (UpRi): First-in-Class ADC Targeting NaPi2b

Hydrophilic Polymer Scaffold

- High DAR of ~10
- Excellent drug-like properties
- Highly stable in circulation
- Dose-proportional exposure
- Very low exposure of free payload



DolaLock Payload With Controlled Bystander Effect

- Selectively toxic to rapidly dividing cells
- Initially released payload (AF-HPA) is freely cell permeable and bystander capable
- Intracellular conversion to AF diminishes permeability and controls bystander effect
- Accumulates in tumor, not a PgP substrate
- Induces immunogenic cell death

- Preliminary antitumor activity was reported in the platinum-resistant ovarian cancer Phase 1b expansion cohort, including in patients previously treated with bevacizumab and PARP inhibitors[1–3]
- Data as of June 2021 demonstrated 34% ORR, 5 months DoR, and 84% DCR in 38 patients with high NaPi2b expression (TPS ≥75)[a]
  - Prevalence of TPS ≥75 estimated to be two-thirds of patients with ovarian cancer (based on clinical experience and tissue bank evaluation)
  - Two patients with CR following prior treatment with bevacizumab and PARP inhibitors
  - A post-hoc analysis exploring drug exposure across 2 dose groups determined that, at the optimized dose of 36 mg/m^2, UpRi has a more favorable safety profile while maintaining similar efficacy
- Most frequently reported TRAEs were fatigue, nausea, transient AST increase, thrombocytopenia (transient in nature), and decreased appetite. Most frequently reported Grade 3+ TRAEs were fatigue, anemia, transient AST increase, and transient thrombocytopenia
- No Grade ≥3 (severe) TRAEs of neutropenia, peripheral neuropathy, or ocular toxicity

METHODS

RATIONALE

- Effective and well-tolerated treatments for platinum-resistant ovarian cancer remain a substantial unmet medical need
- SOC treatment, such as single-agent chemotherapy, have limited efficacy, with response rates of 4–12%, median PFS of 3–4 months, and median OS of less than 12 months[4–6]
- UPLIFT was designed as a Phase 2 single-arm registrational trial for platinum-resistant ovarian cancer as part of the ongoing Phase 1b study
  - Based on the available emerging safety and efficacy profile of UpRi
  - Designed to provide an opportunity for accelerated development and streamlined pathway to regulatory submission

Study Population for UPLIFT

Platinum-resistant ovarian cancer

- 1–4 prior lines in platinum-resistant
- High-grade serous histology
- Archived tumor and fresh biopsy (if medically feasible)
- Prior bevacizumab for those with 1–2 prior lines of therapy

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Assessments

- Tumor imaging (MRI or CT) baseline and every 8 weeks
- Response assessed per RECIST v1.1

STATISTICAL CONSIDERATIONS

- Sample Size: N=up to 180 total patients, including ~100 patients with tumors with high NaPi2b expression
- NaPi2b Cutoff: Pre-defined threshold of TPS ≥75% in retrospectively evaluated tissue specimens
- Power: Sample size of ~100 for high NaPi2b expressors provides ≥90% power to rule out the maximum SOC ORR of 12% using a 1-sided 97.5% exact binomial confidence interval

DOSING

- Single-agent UpRi dosed at 36 mg/m^2 up to a maximum of approximately 80 mg, administered IV Q4W

UPLIFT Cohort Key Eligibility Criteria

Primary Cancer	High-grade serous ovarian, fallopian tube, or primary peritoneal
Patient Population	Platinum-resistant (progressed within 6 months of last dose of platinum) • 1–4 prior lines of therapy • Prior bevacizumab required for patients with 1 or 2 prior lines of therapy, but not required for patients with 3–4 prior lines of therapy • Excludes primary platinum-refractory disease
Baseline Neuropathy	Allowed Grade 1–2; excludes patients with baseline neuropathy Grade 3 or higher
Tissue Availability	Fresh **OR** archival
Biomarker Positivity	Not required (retrospectively assessed)

OBJECTIVES

Primary Objective

- Investigator-assessed confirmed ORR in patients with platinum-resistant ovarian cancer and high NaPi2b expression

Secondary Objectives

- Investigator-assessed confirmed ORR in overall platinum-resistant ovarian cancer population
- DoR
- Safety

SUMMARY

- Upifitamab rilsodotin (UpRi) is an investigational first-in-class ADC targeting the sodium-dependent phosphate transport protein NaPi2b
- UPLIFT will evaluate the relevance of NaPi2b as a biomarker in both the NaPi2b-high and overall populations, with the goal of better understanding how NaPi2b can be used in further development to enrich patient outcomes
- Tumor samples (fresh or archived) will be collected prior to enrollment for retrospective tumor tissue evaluation of NaPi2b expression
- ≥90% power to rule out the maximum SOC ORR of 12%
- Study is being conducted in collaboration with ENGOT (ENGOT-ov67) and GOG (GOG-3048)
- ClinicalTrials.gov registry: NCT03319628

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REFERENCES

1. Tolcher AW et al. ASCO Annual Meeting 2019. Abstract 3010.
2. Richardson DL et al. ASCO Annual Meeting 2020. Abstract 3549.
3. Hamilton EP et al. ESMO Virtual Congress 2020. Abstract 2365.
4. Moore K et al. ESMO Congress 2019. Abstract 9920.
5. Pujade-Lauraine E et al. SGO Annual Meeting 2019. Abstract LBA1.
6. Gaillard S et al. ESMO Congress 2018. Abstract 2064.

ADDITIONAL INFORMATION

For more information on UPLIFT, visit ClinicalTrials.gov page NCT03319628 via QR code provided below.

[a] TPS as determined by an IHC method.

Abbreviations: AF, auristatin F; AF-HPA, auristatin F-hydroxypropylamide; AST, aspartate aminotransferase; CR, complete response; CT, computerized tomography; DAR, drug-to-antibody ratio; DCR, disease control rate; DoR, duration of response; ENGOT, European Network for Gynecological Oncological Trial Groups; GOG, Gynecology Oncology Group; IHC, immunohistochemistry; IV, intravenous; MRI, magnetic resonance imaging; NaPi2b, sodium-dependent phosphate transport protein 2B; ORR, overall response rate; OS, overall survival; PARP, poly (ADP-ribose) polymerase; PFS, progression-free survival; PgP, P-glycoprotein; Q4W, every 4 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; SOC, standard of care; TPS, tumor proportion score; TRAE, treatment-related adverse event.