UPLIFT (ENGOT-ov67/GOG-3048): A Pivotal Cohort of the XMT-1536-1 Trial of Upifitamab Rilsodotin (XMT-1536; UpRi), a NaPi2b-directed Antibody-Drug Conjugate (ADC), in Platinum-Resistant Ovarian Cancer

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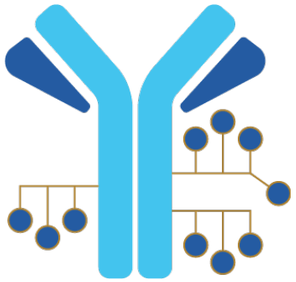
BACKGROUND

- Effective and well-tolerated treatments for PROC remain a substantial unmet medical need, with SOC single-agent chemotherapy demonstrating response rates of 4–12%, median PFS of 3–4 months, and median OS of <12 months[1–3]
- 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[4,5]
- It is believed that approximately two-thirds of patients with HGSOC have high NaPi2b expression based on an IHC tumor proportion score (TPS) of at least 75%[6]
- Upifitamab rilsodotin (UpRi; XMT-1536) is an investigational first-in-class ADC targeting NaPi2b

Upifitamab Rilsodotin (UpRi): Investigational First-in-Class NaPi2b-targeting ADC[5-7]



Antibody: Humanized monoclonal anti-SLC34A2 (NaPi2b)

Linker: Fleximer polymer scaffold; cleavable ester linker stable in circulation

Payload: AF-HPA (DolaLock-controlled bystander effect); selectively toxic to rapidly dividing cells

Drug-to-Antibody Ratio (DAR): ~10

- Preliminary antitumor activity was reported in the PROC Phase 1b expansion cohort, including in patients previously treated with bevacizumab and PARP inhibitors[6]
- Data as of June 2021 demonstrated 34% ORR, 5-month DOR, and 87% DCR in 38 patients with NaPi2b-positive tumors (TPS ≥75%)[6,a]
  - Two patients demonstrated CR following prior treatment with bevacizumab and PARP inhibitors
  - 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 occurred
- A post hoc analysis exploring drug exposure across 2 dose groups determined that, at the dose of 36 mg/m^2, UpRi has a more favorable safety profile while maintaining similar efficacy

METHODS

Rationale

- **UPLIFT** was designed as a Phase 2 single-arm registrational trial for PROC as part of the ongoing Phase 1b study
  - Designed to evaluate UpRi's safety and efficacy in PROC
  - Based on preliminary encouraging efficacy and safety data seen in Phase 1
  - Built on Phase 1b data to move directly to pivotal Phase 2

Global
US, Europe, Australia, Canada

UPLIFT

Key Inclusion Criteria
- Platinum-resistant[b] HGSOC[c]
- 1–4 prior lines of therapy
- Prior bevacizumab required if patient received only 1–2 prior lines of therapy
- ECOG PS = 0–1
- Available archived or fresh tissue for retrospective NaPi2b evaluation
- Grade ≤2 peripheral neuropathy

Key Exclusion Criteria
- 1–2 prior lines AND bevacizumab-naive
- Primary platinum-refractory disease

UpRi 36 mg/m^2 up to max 80 mg; **IV q4w**

Primary Endpoint
- Investigator-assessed confirmed ORR in NaPi2b-positive (N=~100)

Secondary Endpoints
- Investigator-assessed confirmed ORR in overall population (N=~180-240, including 100 NaPi2b-positive)
- DOR
- Safety

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

Statistical Considerations

- Sample size: N=~180-240, including 100 patients with NaPi2b-positive tumors
- NaPi2b cutoff: Pre-defined threshold of TPS ≥75% in retrospectively evaluated tissue specimens
- Power: Sample size of ~100 for NaPi2b-positive expressors provides ≥90% power to rule out the maximum SOC ORR of 12% using a 1-sided 97.5% exact binomial confidence interval

CONCLUSIONS

- UPLIFT will evaluate the efficacy and safety of upifitamab rilsodotin (UpRi) monotherapy in PROC
- UPLIFT will evaluate the relevance of NaPi2b as a biomarker in assessing ORR and DOR in the PROC population
- Tumor samples (fresh or archived) will be collected at enrollment for retrospective tumor tissue evaluation of NaPi2b expression
- Study is being conducted in collaboration with ENGOT (ENGOT-ov67) and GOG (GOG-3048)
- ClinicalTrials.gov registry: NCT03319628

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REFERENCES

1. Moore K et al. ESMO Congress 2019; Abstract 9920. **2.** Pujade-Lauraine E et al. SGO Annual Meeting on Women's Cancer 2019; Abstract LBA1. **3.** Gaillard S et al. ESMO Congress 2018; Abstract 2064. **4.** Lin K et al. *Clin Cancer Res*. 2015;21(22):5139–5150. **5.** Bodyak ND et al. *Mol Cancer Ther*. 2021;20(5):896–905. **6.** Richardson DL et al. SGO Annual Meeting on Women's Cancer 2022; Abstract 76. **7.** Mersana Therapeutics. Accessed August 4, 2022. https://www.mersana.com/pipeline/xmt-1536

ADDITIONAL INFORMATION

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For more information on UPLIFT, visit ClinicalTrials.gov page NCT03319628 via QR code provided or contact medicalinformation@mersana.com

[a] TPS as determined by an IHC method. [b] Platinum-resistant is defined as disease that has progressed within 6 months of last dose of platinum. [c] HGSOC, including fallopian tube and primary peritoneal cancer.

Abbreviations: ADC, antibody-drug conjugate; AF-HPA, auristatin F-hydroxypropylamide; AST, aspartate aminotransferase; CR, complete response; CT, computed tomography; DAR, drug-to-antibody ratio; DCR, disease control rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; ENGOT, European Network for Gynaecological Oncological Trial groups; GOG, Gynecologic Oncology Group; HGSOC, high-grade serous ovarian cancer; IHC, immunohistochemistry; IV, intravenous; MRI, magnetic resonance imaging; NaPi2b, sodium-dependent phosphate transport protein 2B; ORR, objective response rate; OS, overall survival; PARP, poly (ADP-ribose) polymerase; PFS, progression-free survival; PROC, platinum-resistant ovarian cancer; PS, performance status; q4w, every 4 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; SLC34A2, solute carrier family 34 member 2 gene; SOC, standard of care; TPS, tumor proportion score; TRAE, treatment-related adverse event; UpRi, upifitamab rilsodotin.

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