UP-NEXT (GOG-3049/ENGOT-ov71-NSGO-CTU): A Study of Upifitamab Rilsodotin (UpRi), a NaPi2b-directed Antibody-Drug Conjugate (ADC) in Platinum-Sensitive Recurrent Ovarian Cancer

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BACKGROUND

Unmet Medical Need in Platinum-Sensitive Recurrent High-Grade Serous Ovarian Cancer (HGSOC)

- Standard of care for patients with platinum-sensitive recurrent HGSOC consists of platinum-based doublet chemotherapy, with or without bevacizumab, followed by bevacizumab monotherapy or PARPi maintenance[1]
- Recent changes in the treatment landscape with the use of PARP inhibitors in patients with platinum-sensitive recurrent ovarian cancer, and more recently in frontline setting, have created a new unmet need for patients who exhaust these options earlier in their disease course, either because they take them in combination or sequentially[2–4]
- In addition, many patients are not appropriate candidates for these agents due to tolerability concerns, particularly in patients with comorbidities
- PARPi maintenance is not indicated for patients who achieve only stable disease after platinum therapy

NaPi2b Is a Sodium-Dependent Phosphate Transporter Broadly Expressed in Ovarian Cancer With Limited Expression in Healthy Tissues[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]
- NaPi2b is a lineage antigen and not an oncogene; its expression remains consistent throughout the course of disease[7]

Upifitamab Rilsodotin (UpRi) – Investigational First-in-Class NaPi2b-targeting ADC With a Novel Scaffold-Linker-Payload[6–8]

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

METHODS

Study Design and Eligibility

- **UP-NEXT** is a global Phase 3, double-blind, randomized, placebo-controlled study of UpRi monotherapy maintenance in patients with NaPi2b-positive platinum-sensitive recurrent ovarian cancer

Key Enrollment Criteria

- Patients with platinum-sensitive recurrent HGSOC[a]
- 2–4 prior platinum-containing chemotherapy regimens[b]
- Best response to last line of treatment: NED, CR, PR, or SD[c]
- ECOG PS = 0–1
- NaPi2b-positive (TPS ≥75%) tumor (archival or fresh biopsy)
- Prior PARPi required for patients with known deleterious *BRCA* mutations
- Patients who received bevacizumab in combination with their last platinum-containing regimen are excluded

UP-NEXT

N=350 Randomized 2:1

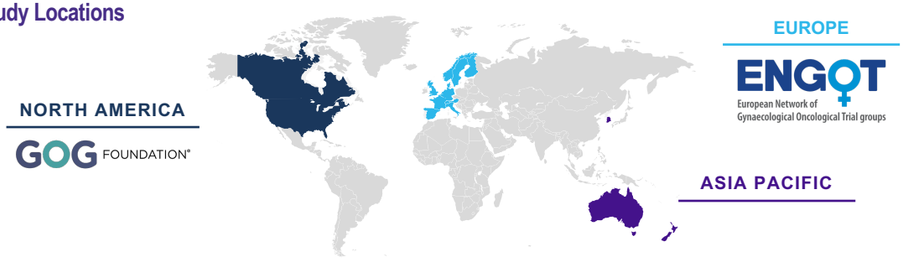
- **UpRi 30 mg/m^2** (capped at BSA 2.2 m^2) **IV q4w**
- **Placebo q4w**

All patients continue until PD or unacceptable AE, or up to 18 months

Primary Endpoint
- PFS by BICR

Secondary Endpoints
- PFS by investigator
- ORR by investigator
- OS
- Safety

Study Locations



CONCLUSIONS

- Upifitamab rilsodotin (UpRi) is an investigational first-in-class NaPi2b-targeting ADC with a novel scaffold-linker-payload that is designed with high DAR and a controlled bystander effect
- UP-NEXT is a global Phase 3 study of UpRi monotherapy maintenance in patients with NaPi2b-positive platinum-sensitive recurrent ovarian cancer
- Primary endpoint is PFS by BICR. Secondary endpoints include PFS by investigator, ORR by investigator, OS, and safety
- Trial is currently open for enrollment and is being conducted in collaboration with GOG (GOG-3049) and ENGOT (ENGOT-ov71-NSGO-CTU)
- ClinicalTrials.gov registry: NCT05329545

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ADDITIONAL INFORMATION

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For more information on UP-NEXT, visit ClinicalTrials.gov page NCT05329545 via QR code provided or contact medicalinformation@mersana.com

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[a] HGSOC, including fallopian tube and primary peritoneal cancer. [b] Carboplatin or cisplatin ± paclitaxel, docetaxel, pegylated liposomal doxorubicin, or gemcitabine. [c] For SD, no increase in disease confirmed by central review of imaging and absence of CA-125 rise >15% in 7 days prior to first dose.

ADC, antibody-drug conjugate; AE, adverse event; AF-HPA, auristatin F-hydroxypropylamide; BICR, blinded independent central review; *BRCA*, BRCA DNA repair associated gene; BSA, body surface area; CA, cancer antigen; CR, complete response; DAR, drug-to-antibody ratio; ECOG, Eastern Cooperative Oncology Group; ENGOT, European Network of Gynaecological Oncological Trial groups; GOG, GOG Foundation; HGSOC, high-grade serous ovarian cancer; HR, hazard ratio; IHC, immunohistochemistry; IV, intravenous; NaPi2b, sodium-dependent phosphate transport protein 2B; NED, no evidence of disease; ORR, objective response rate; OS, overall survival; PARP, poly (ADP-ribose) polymerase; PARPi, PARP inhibitor; PD, progressive disease; PFS, progression-free survival; PR, partial response; PS, performance status; q4w, every 4 weeks; SLC34A2, solute carrier family 34 member 2 gene; SD, stable disease; TPS, tumor proportion score; UpRi, upifitamab rilsodotin.

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