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

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BACKGROUND

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

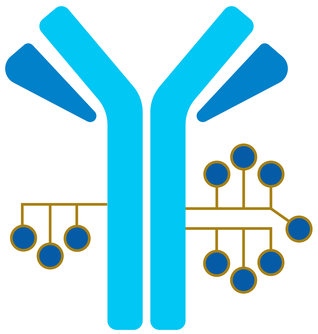
- Standard of care for patients with platinum-sensitive recurrent HGSOC consists of platinum-based doublet chemotherapy, with or without bevacizumab, followed by bevacizumab monotherapy or PARP inhibitor (PARPi) maintenance, or platinum-based doublet chemotherapy followed by observation[1]
- Recent changes in the treatment landscape with the use of PARPi in patients with platinum-sensitive recurrent ovarian cancer, and more recently in the 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 Transporter Broadly Expressed in Ovarian Cancer With Limited Expression in Healthy Tissues[5,6]

- It is estimated that at least a majority of patients with HGSOC express high levels of NaPi2b based on an immunohistochemistry (IHC) tumor proportion score (TPS) of ≥75[7,8]
- NaPi2b is a lineage antigen and not an oncogene, and its expression remains consistent throughout disease course[8,9]

Upifitamab Rilsodotin (UpRi) is a First-in-Class NaPi2b-Targeting ADC With a Novel Scaffold-Linker-Payload Designed to Enable High Drug-to-Antibody Ratio (DAR) and Controlled Bystander Effect[7,9,10]

UpRi



Antibody: Humanized monoclonal anti-SCL34A2 (NaPi2b)

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

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

DAR: ~10

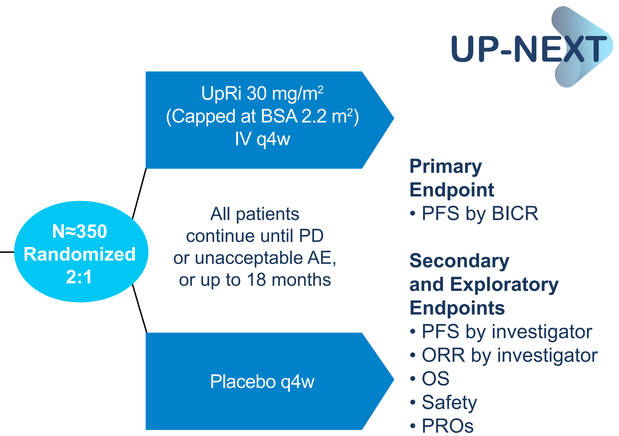
METHODS

Study Design and Eligibility

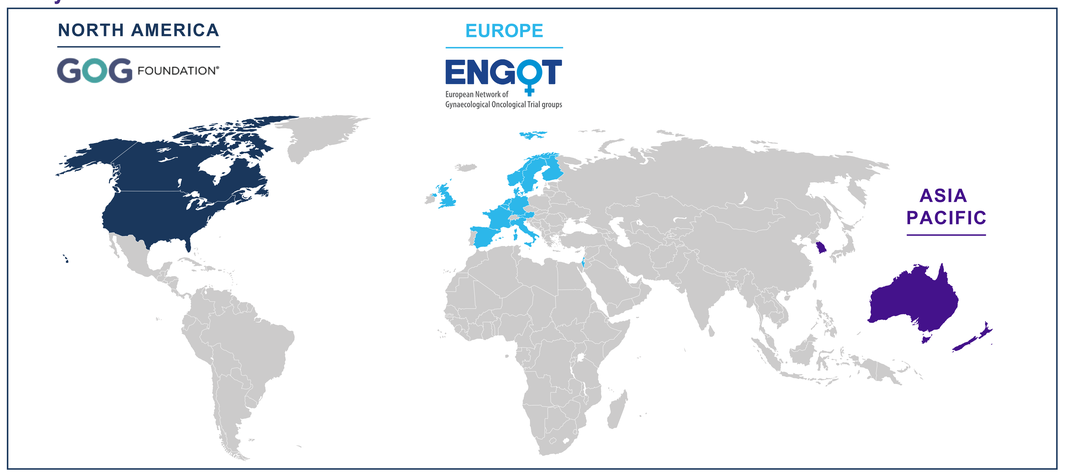
- **UP-NEXT** is a global Phase 3, double-blind, randomized, placebo-controlled study of UpRi monotherapy maintenance in patients with NaPi2b-positive platinum-sensitive recurrent ovarian cancer

Key Enrollment Criteria

- Patients with platinum-sensitive recurrent HGSOC[a]
- 4–8 cycles of platinum-based therapy in second to fourth line setting[b]
- Best response to last line of treatment: NED, CR, PR, or SD[c]
- ECOG PS 0–1
- NaPi2b-positive (TPS ≥75) tumor based on archival or fresh tumor 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



Study Locations



CONCLUSIONS

- 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
- The primary endpoint is PFS by BICR. Secondary and exploratory endpoints include PFS by investigator, ORR by investigator, OS, safety, and PROs
- The 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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[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; 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 PS, Eastern Cooperative Oncology Group performance status; ENGOT, European Network of Gynaecological Oncological Trial groups; GOG, GOG Foundation; HGSOC, high-grade serous ovarian cancer; IHC, immunohistochemistry; IV, intravenous; NaPi2b, sodium-dependent phosphate transport protein 2B; ORR, objective response rate; OS, overall survival; PARPi, poly (ADP-ribose) polymerase inhibitor; PFS, progression-free survival; PRO, patient-reported outcome; q4w, every 4 weeks; SLC34A2, solute carrier family 34 member 2 gene; TPS, tumor proportion score; UpRi, upifitamab rilsodotin.

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