and for left colon compared to right colon procedures. Nevertheless, 16.3% of respondents were able to independently perform all bowel procedures surveyed. Future research should examine factors such as training and experience within these groups to address this disparity.

UPLIFT (ENGOT-OV67/GOG-3048) A PHASE I DOSE ESCALATION AND EXPANSION TRAIL OF UPFITAMAB RILSODOTIN (XMT-1536; UPRI), A NAPI2B-DIRECTED ANTIBODY DRUG CONJUGATE (ADC) IN PLATINUM-RESISTANT OVARIAN CANCER

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Introduction/Background UpRi is a first-in-class NaPi2b-targeting ADC with a novel scaffold-linker-payload that enables high drug-to-antibody ratio and controlled bystander effect. NaPi2b is a sodium-dependent phosphate transporter protein broadly expressed in high-grade serous epithelial ovarian, fallopian tube and primary peritoneal cancers (HGSO), with limited expression in healthy tissues. Preliminary antitumor activity from the Phase 1b expansion cohort of heavily pre-treated patients with recurrent HGSO has been reported (Richardson et al., SGO 2022). These data suggested clinically meaningful activity in patients, notably in those with NaPi2b-high tumors (TPS ≥75). Effective and well-tolerated treatments for platinum-resistant ovarian cancer (PROC) remain a substantial unmet medical need. The standard of care, single agent chemotherapy, has limited efficacy, significant toxicities, and short duration of response. UPLIFT was designed as a single-arm Ph2 registrational trial for UpRi monotherapy in PROC.

Methodology UPLIFT is enrolling patients with platinum-resistant HGSO with up to 4 prior lines of therapy (LoT). Prior bevacizumab is required for patients with 1–2 prior LoT only; it is not required for patients with 3–4 prior LoT. Patients may enroll regardless of NaPi2b expression; ≤ Grade 2 peripheral neuropathy is permitted. Primary platinum refractory patients are excluded. UPLIFT will enroll ~180 patients globally, including approximately 100 patients with NaPi2b-high expression. UpRi will be dosed intravenously at 36 mg/m² up to ~80 mg dose maximum every 4 weeks. Baseline tumor samples (fresh or archived) will be collected for central analysis of NaPi2b expression. Based on data from the Ph1b expansion cohort, the cut-off for high NaPi2b expression is Tumor Proportion Score (TPS) ≥75. The primary endpoint is ORR in NaPi2b-high expressing patients. Secondary endpoints include ORR in the overall population, duration of response, and safety. UPLIFT is being conducted in collaboration with ENGOT (ENGOT-Ov67) and GOG (GOG-3048). NCT03319628

Results N/A trial in progress

Conclusion N/A trial in progress

A PHASE I DOSE ESCALATION AND EXPANSION TRAIL OF CARBOPLATIN AND GEMCITABINE WITH THE ATR INHIBITOR BERZOSERTIB IN FIRST OR SECOND RECURRENCE PLATINUM SENSITIVE EPITHELIAL OVARIAN, PERITONEAL, AND FALLOPIAN TUBE CANCER

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Introduction/Background The combination of carboplatin and gemcitabine is a commonly used regimen for platinum-sensitive recurrent ovarian cancer. Preclinical studies showed that ATR knockdown in ovarian cancer cell lines sensitized to a wide variety of genotoxic stresses, including gemcitabine and cisplatin. A phase II study evaluating the addition of berzosertib to gemcitabine in platinum resistant ovarian cancer revealed an improvement in progression-free survival (PFS). We sought to assess the safety and preliminary efficacy signal of the triple combination therapy in high grade ovarian cancer (NCT02627443).

Methodology Eligible participants included women with histologically confirmed high grade serous or endometrioid epithelial ovarian, fallopian tube or peritoneal cancer in first or second resistant recurrence. Using a standard 3+3 design, participants were treated with carboplatin on day 1, gemcitabine on days 1 and 8, and escalating doses of berzosertib on days 2 and 9 of a 21 day cycle. An additional 22 participants enrolled at maximum tolerated dose (MTD). Tumor biopsies were obtained at 3 different timepoints in the expansion cohort.

Results Thirty-three eligible participants were enrolled across 7 institutions in the US, with 28 eligible patients treated at the MTD (6 during dose escalation, 22 during dose expansion). The MTD was deemed to be carboplatin AUC 4, gemcitabine 640 mg/m² and berzosertib 90 mg/m²/day with grade 4 thrombocytopenia as the only DLT. A confirmed response was observed in 14/28 (50%) participants. Median progression free survival was estimated to be 15.1 months (95% CI, 9.8-NE). The most common adverse events were cytopenias (96% grade 3–4 hematologic adverse event). Translational correlates from the expansion cohort are underway.