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 pretreated 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 35 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
Conclusion The MTD of the triple combination was established and the study met its secondary endpoint of initial efficacy; however, significant cytopenias were noted with this regimen, which may limit further development.

LONG-TERM RESPONDERS (LTR) TO RUCAPARIB IN RECURRENT OVARIAN CANCER: A SUB-GROUP ANALYSIS FROM THE RUCAPARIB ACCESS (RAP) PROGRAM IN SPAIN BY GEICO

Introduction/Background Rucaparib is a PARPi approved as maintenance (MTN) for platinum (Pt)-sensitive recurrent HGOC, and as treatment (Tx) for BRCA-mutated recurrent HGOC patients. Real-world data about LTR patients from the RAP is analyzed here.

Methodology A retrospective GEICO study was performed at 22 hospitals that treated patients within the RAP. Women with HGOC received rucaparib (600 mg BID) in the MTN, Tx if Pt-sensitive, or Tx if Pt-resistant setting. In this subanalysis, long-term response was defined as progression-free survival (PFS) ≥12 months for the MTN group and ≥6 months for the Tx group.

Results In the study 51 patients were recruited: 18 received rucaparib as MTN and 33 as Tx. In the MTN group, 6 patients (33.3%) were LTR. Of them, 2 patients (33.3%) harbored BRCA or RAD51C mutations. The median number of prior lines was 3 (2–6), being ≥5 in 33.2%, 66.6% had measurable disease and 50.0% achieved PR to prior Pt-based chemotherapy. In the Tx group, 10 patients (30.3%) were LTR. All of them harbored BRCA and/or RAD51C mutations. The median number of prior lines was 6 (2–9), with 60.0% receiving ≥5 prior lines, 60.0% were Pt-resistant and 60.0% had measurable disease. The median PFS of LTR was not achieved in the MTN group and was 10.9 months (95% CI: 7.0–16.7) in the Tx group. Adverse events (AE) of any grade were reported in 66.6% of LTR within the MTN group and in 100.0% within the Tx group, while AE of grade ≥3 occurred in 16.6% and 50.0%, respectively. No new safety signals were detected. At present, 3 and 1 patients are still receiving rucaparib as MTN and Tx, respectively.

Conclusion A durable response was achieved in a notable proportion of patients, despite their unfavorable conditions at time of treatment initiation. The safety profile of rucaparib in this real-world setting is consistent with that previously reported.