Poster #13 | UPGRADE: Phase 1 Combination Trial of the NaPi2b-directed Antibody Drug Conjugate (ADC) Upifitamab Rilsodotin (UpRi; XMT-1536) in Patients with Ovarian Cancer

Topic: Ovarian

Objectives
Upifitamab rilsodotin (UpRi), is a first-in-class antibody drug conjugate targeting NaPi2b, a sodium-dependent phosphate transporter protein broadly expressed in solid tumors including high-grade serous epithelial ovarian, fallopian tube and primary peritoneal cancer (OC), and limited expression in healthy tissues. Preliminary antitumor activity from the Phase 1b expansion cohort of heavily pretreated patients with OC has been reported (Richardson et al., SGO 2022). Data through June 2021 demonstrated clinically meaningful activity in a population of recurrent ovarian cancer, with notable activity in patients with NaPi2b-high tumors (TPS≥75) treated at the optimized dose of 36 mg/m2, leading to the design of an ongoing single-arm registrational study in platinum-resistant OC (UPLIFT; NCT03319628). Based on the encouraging single-agent safety and efficacy data, we hypothesize that UpRi in combination with other therapies can provide additional clinical benefit, offer improved tolerability over current standard of care approaches, and may provide patients with an option for earlier lines of treatment. UPGRADE was designed as a Phase 1 dose escalation and expansion umbrella study to evaluate UpRi combinations in recurrent OC. UPGRADE-A is the first cohort under this umbrella, evaluating UpRi in combination with carboplatin in patients with platinum sensitive recurrent OC who have received 1-2 prior lines of therapy.

Methods
The UPGRADE-A cohort is enrolling patients with recurrent, platinum-sensitive high-grade serous OC. The trial consists of a dose escalation (DES) and an expansion portion (EXP). In both portions of the study, participants will be treated with UpRi in combination with carboplatin, IV every 28 days for 6 cycles, followed by UpRi monotherapy until disease progression or unacceptable toxicity. Approximately 18 patients will be enrolled in the DES; the primary endpoint is to identify the maximum tolerated dose (MTD) and to assess the feasibility of the combination. Approximately 30 patients will be enrolled in the expansion portion. Secondary endpoints include safety and tolerability, pharmacokinetics, and preliminary anti-neoplastic activity. Patients are not selected by NaPi2b status, but baseline tumors samples (fresh or archived) are collected for central lab analysis. NCT04907968

Results
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Conclusions
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