UPGRADE-A: Phase 1 Expansion Trial of the NaPi2b-Directed Antibody Drug Conjugate Upifitamab Rilsodotin in Combination With Carboplatin in Patients With High-Grade Serous Ovarian Cancer

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BACKGROUND

Unmet Medical Need in Platinum-Sensitive Recurrent High-Grade Serous Ovarian Cancer (HGSOC)3-5

- Standard of care for patients with newly diagnosed and platinum-sensitive recurrent HGSOC often consists of platinum-based chemotherapy with or without bevacizumab, often followed by bevacizumab and/or PARP inhibitor maintenance therapy
- Platinum-containing combination therapies are associated with decreased response rates with successive lines of therapy
- The development of effective, novel platinum-based combinations are needed as there is an opportunity to improve outcomes following standard of care

Upifitamab Rilsodotin (UpRi): Investigational First-in-Class Sodium-Dependent Phosphate Transport Protein 2 (NaPi2b)-Targeting Antibody-Drug Conjugate (ADC)6,5

- UpRi is a first-in-class NaPi2b-targeting ADC with a novel scaffold-linker-payload that is designed to enable high drug-to-antibody ratio and controlled bystander effect
- NaPi2b is a sodium-dependent phosphate transport protein broadly expressed in solid tumors, including HGSOC, with limited expression in normal tissue
- Prior studies suggest that the majority of patients with HGSOC have NaPi2b-positive disease based on an IHC tumor proportion score (TPS) ≥75%
- Interim data from the Phase 1b study in heavily pretreated platinum-resistant HGSOC patients reported clinically meaningful activity for UpRi as a monotherapy, most notably in patients with NaPi2b positive tumors (TPS≥75%)
- Based on these emerging single-agent safety and efficacy data, it is hypothesized that UpRi in combination with carboplatin may provide additional clinical benefit for patients in earlier lines of treatment

RATIONALE FOR COMBINATION THERAPY WITH CARBOPLATIN

- To address the unmet medical need in platinum-sensitive recurrent HGSOC, novel platinum-based combinations must be developed that:
  – Can drive meaningful and durable responses
  – Can be continued as maintenance treatment following completion of platinum-based chemotherapy
  – Specifically contain targeted agents with a favorable therapeutic index that lack appreciable overlapping toxicity with carboplatin
  – Have non-overlapping mechanisms of action with other agents typically combined with carboplatin
  – ADCs, such as UpRi, may represent a promising strategy in combination with carboplatin to optimize outcomes

STUDY DESIGN AND ELIGIBILITY

Key Enrollment Criteria

- Platinum-sensitive recurrent/metastatic HGSOC, including fallopian tube or primary peritoneal cancer
- ≥3 prior lines of therapy
- Up to 1 non-platinum based prior chemotherapy regimen
- Tissue (fresh or archival) will be collected for retrospective assessment of NaPi2b expression
- ECOG PS 0–1

Dose Expansion

Primary Endpoints

- Feasibility of UpRi + carboplatin at 30 mg/m²
- Safety/tolerability, pharmacokinetics, ORR, OS and PFS

Secondary Endpoints

- Association between NaPi2b expression and response

REFERENCES

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