UPLIFT (ENGOT-ov67/GOG-3048): A Pivotal Cohort of the XMT-1536-1 Trial of Upifitamab Rilsodotin (Upi; XMT-1536; UpRi), a NaPi2b-directed Antibody-Drug Conjugate (ADC), in Platinum-Resistant Ovarian Cancer

Richardson, Debra1; Perez-Fidalgo, Jose Alejandro2; Gonzalez Martin, Antonio2; Oaknin, Ana1; Hamilton, Erika1; Hays, John1; Pothuri, Bhavana3; Papadopoulos, Kyriakos4; Taylor, Sara5; Huang, Marilyn6; Lee, Yeh-Chen7; Krivak, Thomas2; Moreno Garcia, Victor8; Calvo, Emilianno9; Randall, Leslie10; Grimm, Bruce11; Starks, David5; Rose, Malcolm10; Duska, Linda12; Gao, Bo10; Peka, Robert11; Putim, Emily12; Barbieri, Rose4; Demars, Lorraine13; Concin, Nicole14
1Stephenson Cancer Center, University of Oklahoma Health Sciences Center and the Soon-Chung Yang Research Institute, Oklahoma City, OK; 2Hospital Universitario de Canarias, Tenerife, Tenerife, Spain; 3Eli Lilly and Company, Indianapolis, IN; 4Chao Medical Center of Oregon Health & Science University, Portland, OR; 5Karttunen Clinic, University of Helsinki, Finland; 6Glenbrook Hospital Medical Center, Chicago, IL; 7Astellas Pharma US, Inc., South San Francisco, CA; 8Hospital Universitario Miguel Servet, Zaragoza, Spain; 9Squash Cancer Center, University of Iowa, Iowa City, IA; 10DryShark Biotechnology, St. Louis, MO; 11Oncology Service, Detroit Receiving Hospital and Wayne State University, Detroit, MI; 12Rayoss Healthcare Network, Pittsburgh, PA; 13University Hospital Freiburg, Freiburg, Germany; 14Division of Gynecologic Oncology, Charlottesville, VA

BACKGROUND

- Effective and well-tolerated treatments for PROC remain a substantial unmet medical need, with SOC single-agent chemotherapy demonstrating response rates of 4–12%, median PFS of 3–4 months, and median OS of <12 months1–3
- NaPi2b is a sodium-dependent phosphate transport protein broadly expressed in solid tumors, including high-grade serous epithelial ovarian, fallopian tube, and primary peritoneal cancer, with limited expression in normal tissue5–6
- It is believed that approximately two-thirds of patients with HGSOC have high NaPi2b expression based on an IHC tumor proportion score (TPS) of at least 75%7
- Upifitamab rilsodotin (UpRi; XMT-1536) is an investigational first-in-class ADC targeting NaPi2b

METHODS

Rationale

- UPLIFT was designed as a Phase 2 single-arm registration trial for PROC as part of the ongoing Phase 1b study
- Designed to evaluate UpRi’s safety and efficacy in PROC
- Based on preliminary encouraging efficacy and safety data seen in Phase 1
- Built on Phase 1b data to move directly to pivotal Phase 2

Global

US, Europe, Australia, Canada

Key Inclusion Criteria

- Platinum-resistant HGSOC
- 1–4 prior lines of therapy
- Prior bevacizumab required if patient received only 1–2 prior lines of therapy
- ECOG PS 0–1
- Available archival or fresh tissue for NaPi2b expression assessment
- Grade 2 peripheral neuropathy

Key Exclusion Criteria

- 1–2 prior lines AND bevacizumab exposure
- Primary platinum-resistant disease

Primary Endpoint

- Investigator-assessed confirmed ORR in NaPi2b-positive (N~100)

Secondary Endpoints

- Investigator-assessed confirmed ORR in overall population (N~190-240, including 100 NaPi2b-positive) ORR
- DOR
- Safety

Statistical Considerations

- Sample size: N=180–240, including 100 patients with NaPi2b-positive tumors
- NaPi2b cutoff: Pre-defined threshold of TPS ≥75% in retrospectively evaluated tissue specimens
- Power: Sample size of ~100 for NaPi2b-positive expressions provides 95% power to rule out the maximum SOC-ORR of 12% using a 1-sided 97.5% exact binomial confidence interval

CONCLUSIONS

- UPLIFT will evaluate the efficacy and safety of upifitamab rilsodotin (UpRi) monotherapy in PROC
- UPLIFT will evaluate the relevance of NaPi2b as a biomarker in assessing ORR and DOR in the PROC population
- Tumor samples (fresh or archived) will be collected at enrollment for retrospective tumor tissue evaluation of NaPi2b expression
- Study is being conducted in collaboration with ENGOT (ENGOT-ov67) and GOG (GOG-3048)

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REFERENCES


ADDITIONAL INFORMATION

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For more information on UPLIFT, visit ClinicalTrials.gov page NCT03191628 or via QR code provided on this poster. For media information contact merusa.com.