Archival vs Fresh Tumor Samples for Assessing the Gene Expression of NaPi2b and Immune-Related Genes in the Phase 1 Study of Upifitamab Rilsodotin (UpRi) in Platinum-Resistant Ovarian Cancer

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BACKGROUND
Upifitamab rilsodotin (UpRi; XMT-1536) is an investigational first-in-class antibody-drug conjugate (ADC) targeting NaPi2b, a sodium-dependent phosphate transport protein broadly expressed in solid tumors, like ovarian cancer, with limited expression in normal tissue.¹⁻²

A Phase 1b UpRi single-agent study in platinum-resistant ovarian cancer (PROC) demonstrated encouraging efficacy and a tolerable safety profile, with more notable efficacy in patients with high NaPi2b expression (TPS ≥75%); data was presented at SGO 2022.³⁻⁴

Changes in NaPi2b expression over the course of ovarian cancer progression have not been extensively studied.¹ To address this, archival tumor tissue and/or fresh biopsy (if medically feasible) were collected from patients with PROC in this Phase 1 study (NCT03319628) to compare the gene expression levels of NaPi2b and other genes of interest.

METHODS
In this Phase 1 study:
- 70 patients had only archival tumor tissue collection
- 18 patients had only fresh biopsy collection
- 22 patients had both archival tumor tissue and fresh biopsy collection

Expression of SLC34A2 (gene name for NaPi2b) and other immune-related genes were assessed by NanoString using nCounter PanCancer IO 360 Panel plus a custom-designed gene set.

When comparing gene expression between lymph node (LN) and non-LN locations, only fresh samples were included in the group analysis.

When comparing gene expression between paired archival and fresh tissue:
1. Data from LN samples were first excluded due to differential gene expression
2. For patients who contributed both archival and fresh samples from non-LN locations, only fresh samples were included in the group analysis to ensure repeated sample collection

RESULTS
Figure 1: Differential gene expression between biopsies collected from LN and non-LN locations
1A: Immune-related genes have higher expression in LN compared to non-LN
1B: NaPi2b gene expression in LN vs non-LN

Figure 2: NaPi2b gene expression is not significantly different between archival and fresh biopsy samples
2A: NaPi2b gene expression in archival and fresh samples
2B: NaPi2b gene expression analysis from paired archival and fresh samples

Figure 3: Genes related to antigen presentation and T-cell function are decreased in fresh samples compared to archival samples
3A: HLA-B
3B: CD8A
3C: GZMK

CONCLUSIONS
RNA level (assessed by NanoString) and protein level (assessed by IHC) of NaPi2b remains stable between archival and fresh samples, suggesting a new biopsy may not be required for the determination of NaPi2b status. This would spare patients from the burden and risks associated with repeated sample collection.

Antigen presentation and T-cell function-related genes showed decreased expression in fresh samples, suggesting tumors may evade immune surveillance during disease progression.

Clinical trial information: NCT03319628

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ADDITIONAL INFORMATION
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*For more information on UPLIFT, visit ClinicalTrials.gov page NCT03319628 or QR code provided or contact medicalinformation@mersana.com