# 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

Lu, Min<sup>1</sup>; Shaw, Pamela<sup>1</sup>; Bradshaw, Chelsea<sup>1</sup>; Richardson, Debra<sup>2</sup>; Hamilton, Erika<sup>3</sup>; Bernardo, Patti<sup>1</sup>; Tolcher, Anthony<sup>4</sup>; Mosher, Rebecca<sup>1</sup> <sup>1</sup>Mersana Therapeutics, Inc., Cambridge, MA; <sup>2</sup>Stephenson Cancer Center, University of Oklahoma Health Sciences Center and the Sarah Cannon Research Institute, Oklahoma City, OK; <sup>3</sup>Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN; <sup>4</sup>NEXT Texas Oncology, San Antonio, TX

# 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<sup>1,2</sup>
- > 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  $\geq$ 75%); data was presented at SGO 2022<sup>1,a</sup>
- Changes in NaPi2b expression over the course of ovarian cancer progression have not been extensively studied.<sup>3,4</sup> 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 samples in archival group vs fresh group are independent

#### 34<sup>th</sup> EORTC-NCI-AACR SYMPOSIUM

<sup>a</sup> Data cutoff June 10, 2022.<sup>1</sup>

# 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



Figure 2: NaPi2b gene expression is not significantly different between archival and fresh biopsy samples

2A: NaPi2b gene expression in archival and fresh samples



CD8A, cluster of differentiation 8a molecule; GZMK, granzyme K; IHC, immunohistochemistry; HLA-B, major histocompatibility complex, class I, B; LN, lymph node; NaPi2b, sodium-dependent phosphate transport protein 2B; non-LN, non-lymph node; NS, not significant; PROC, platinum-resistant ovarian cancer; SGO, Society of Gynecologic Oncology; SLC34A2, solute carrier family 34 member 2 gene; TPS, tumor proportion score.

1B: NaPi2b gene expression in LN vs non-LN



	LN	Nor
Number of values	18	2
25% percentile	629.6	11
Median	1859	27
75% percentile	3133	69
Mean	2372	55

**2B:** NaPi2b gene expression analysis from paired archival and fresh samples

N=12	Archival	Fresh
25% percentile	1529	1545
Median	4566	3855
75% percentile	6285	7135
	0200	1100
Mean	5109	4621

## CONCLUSIONS

- RNA level (assessed by NanoString) and protein level (assessed by IHC) of NaPi2b remains stable between archival and fresh samples<sup>3,4</sup>, 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

## ACKNOWLEDGMENTS

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