Comparison of NaPi2b Expression From Paired Tissue Samples in a Clinical Study of Upifitamab Rilsodotin (UpRi; XMT-1536) Supports a Strategy of Testing in Archival Material

Richardson, Debra L[1]; Barve, Minal[2]; Saltos, Andreas[3]; Papadopolous, Kyriakos P[4]; Hays, John L[5]; Tolcher, Anthony[6]; Ellard, Susan[7]; Doroshow, Deborah[8]; Mitchell, Paul[9]; Zarwan, Corrine[10]; Werner, Theresa L[11]; Anderson, Charles[12]; Spira, Alexander I[13]; Mileshkin, Linda[14]; Bradshaw, Chelsea[15]; DeMars, Leslie[15]; Mosher, Rebecca[15]; Hamilton, Erika[16]

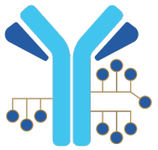
[1]Stephenson Cancer Center, University of Oklahoma Health Sciences Center and the Sarah Cannon Research Institute, Oklahoma City, OK; [2]Mary Crowley Cancer Research and Texas Oncology, Dallas, TX; [3]Moffitt Cancer Center, Tampa, FL; [4]START San Antonio, San Antonio, TX; [5]The Ohio State University Wexner Medical Center, Columbus, OH; [6]NEXT Texas Oncology, San Antonio, TX; [7]BC Cancer Agency, University of British Columbia, Vancouver, BC; [8]Icahn School of Medicine at Mount Sinai, New York, NY; [9]Austin Health - Olivia Newton-John Cancer Center, Australia; [10]Lahey Health Cancer Institute, Burlington, MA; [11]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; [12]Willamette Valley Cancer Institute and Research Center, Eugene, OR; [13]Virginia Cancer Specialists, Fairfax, VA; [14]Peter MacCallum Cancer Centre, Australia; [15]Mersana Therapeutics, Inc., Cambridge, MA; [16]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN

BACKGROUND

NaPi2b Is a Sodium-Dependent Phosphate Transporter Broadly Expressed in Ovarian Cancer, With Limited Expression in Healthy Tissues[1]

- 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%[2]
- NaPi2b is a lineage antigen and not an oncogene; its expression remains consistent throughout the course of disease[3]

Upifitamab Rilsodotin (UpRi) – Investigational First-in-Class NaPi2b-targeting Antibody-Drug Conjugate (ADC) With a Novel Scaffold-Linker-Payload[2–4]



Antibody: Humanized monoclonal anti-SLC34A2 (NaPi2b)

Linker: Fleximer polymer scaffold; cleavable ester linker stable in circulation

Payload: AF-HPA (DolaLock-controlled bystander effect); selectively toxic to rapidly dividing cells

Drug-to-Antibody Ratio (DAR): ~10

UpRi Phase 1b Ovarian Cancer Cohort Study[5]

- A Phase 1b UpRi single-agent dose escalation (DES) and expansion (EXP) study (NCT03319628) enrolled patients with high-grade, platinum-resistant serous ovarian cancer with 1 to 3 prior lines of therapy, or 4 prior lines of therapy regardless of platinum status
  - Preliminary antitumor activity was reported including patients previously treated with bevacizumab and PARP inhibitors
- The study collected both freshly biopsied and archival tissue samples for retrospective NaPi2b evaluation, if available, but only required a single specimen
- To determine if archival material would be sufficient to classify biomarker status, NaPi2b expression was evaluated in paired freshly biopsied and archival material from patients participating in the UpRi Phase 1b ovarian cancer EXP cohort

METHODS

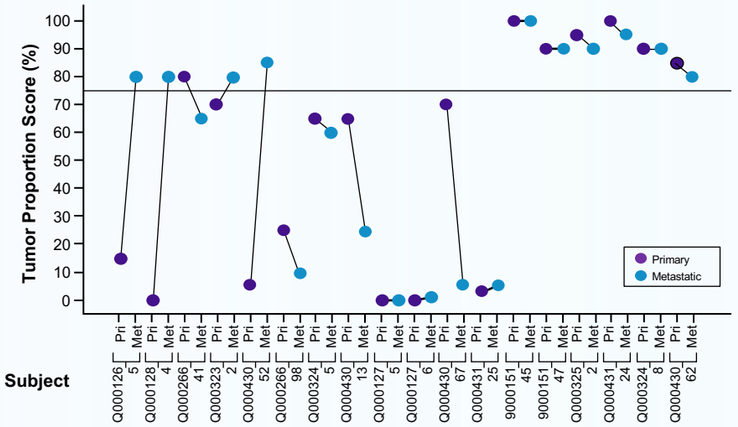
- 2 ovarian cancer sample sets were evaluated for NaPi2b expression using an IHC assay, and a TPS was calculated
  - The first set (18 pairs) was procured from tissue banks, representing synchronous sampling of primary and metastatic lesions to establish a reference NaPi2b heterogeneity rate[a].
  - The second set included matched metachronous samples ("archival" and "fresh") from 56 patients enrolled in the Phase 1b study, sampled prior to UpRi administration
- NaPi2b expression was assessed by QualTek Molecular Laboratories (Discovery Life Sciences) using the GLP assay employed in the Phase 1b UpRi DES/EXP study (NCT03319628)
  - In a retrospective analysis, TPS ≥75% was shown to identify patients with a higher likelihood of response and was thus determined as the cutoff for "NaPi2b-positive"[6]
- Concordance rates and kappa values were calculated

RESULTS

- In the first set of samples, synchronous primary and metastatic lesions from an archival tumor bank showed a concordance rate of 72%
  - 13 of 18 pairs (72%) maintained their NaPi2b status across primary and metastatic tissue samples
  - 7 of the 18 (39%) primary tumor samples were NaPi2b-positive (TPS ≥75%)
  - 10 of the 18 (56%) metastatic tumor samples were NaPi2b-positive (TPS ≥75%)
- In the second set of 56 metachronous samples, high concordance was demonstrated between fresh and archival tissue samples
  - Of 29 patients who were NaPi2b-positive in archival tissue, 22 were NaPi2b-positive in fresh tissue (76% concordance) and 7 were NaPi2b-negative (24%)
  - Of 27 patients who were NaPi2b-negative in archival tissue, 20 were NaPi2b-negative in fresh tissue (74% concordance) and 7 were NaPi2b-positive (26%)

RESULTS (continued)

NaPi2b Status in Primary/Synchronous Metastatic Paired Samples – Sample Set 1 (N=18 pairs)



NaPi2b Status in Fresh vs Archival Samples From Patients Participating in the Phase 1b UpRi Ovarian Cancer Cohort – Sample Set 2 (N=56 pairs), n (%)[b]

- 64% of patients were NaPi2b-positive based on either archival or fresh tissue[c]

	Archival NaPi2b-Positive (TPS ≥75%)	Archival NaPi2b-Negative (TPS <75%)	Total Fresh Samples
Fresh NaPi2b-Positive (TPS ≥75%)	22 (39.3)	7 (12.5)	29 (51.8)
Fresh NaPi2b-Negative (TPS <75%)	7 (12.5)	20 (35.7)	27 (48.2)
Total Archival Samples	29 (51.8)	27 (48.2)	

Kappa 0.5 (0.27, 0.73, moderate agreement).

CONCLUSIONS

- High concordance of NaPi2b status was observed in both synchronous and metachronous samples from the Phase 1b UpRi study
- The high concordance of metachronous samples supports use of archival tissue for NaPi2b biomarker analysis despite intervening lines of therapy
- Fresh or archival tissue samples to evaluate NaPi2b status are requested in the ongoing clinical trials evaluating UpRi therapy in platinum-resistant and platinum-sensitive ovarian cancer
  - UPLIFT (NCT03319628), UP-NEXT (NCT05329545), and UPGRADE (NCT04907968)

ACKNOWLEDGMENTS

We thank the patients, their families, and caregivers for their contribution to this study. This study is sponsored by Mersana Therapeutics, Inc. IHC analyses were performed by QualTek Molecular Laboratories (Discovery Life Sciences). Editorial support for this poster was provided by BluPrint Oncology.

REFERENCES

1. Lin K et al. *Clin Cancer Res*. 2015;21(22):5139–5150. **2.** Richardson DL et al. SGO Annual Meeting on Women's Cancer 2022; Abstract 585. **3.** Bodyak ND et al. *Mol Cancer Ther*. 2021;20(5):896–905. **4.** Mersana Therapeutics. Accessed July 12, 2022. https://www.mersana.com/pipeline/xmt-1536 **5.** Richardson DL et al. SGO Annual Meeting on Women's Cancer 2022; Abstract 76. **6.** Mersana Therapeutics. Accessed July 12, 2022. https://www.mersana.com/wp-content/uploads/2022/06/MRSN-UpRi-NaPi2b-Diagnostic-Development-Path_FINAL-render.pdf

ADDITIONAL INFORMATION

Downloadable PDF copies of this poster obtained through Quick Response (QR) code are for personal use only and may not be reproduced without permission from IGCS and the author of this poster.

[a] One subject in this set was inadvertently included as 2 separate analysis pairs using different tissue blocks procured from the tissue bank; notably, the 2 primary samples from the subject, annotated as synchronous specimens taken from the ovary, have discordant NaPi2b status. [b] Percent shown as a proportion of total n of 56 paired samples. [c] 36/56 patients were NaPi2b-positive based on both fresh and archival tissue (n=22), fresh tissue alone (n=7), or archival tissue alone (n=7).

Abbreviations: ADC, antibody-drug conjugate; AF-HPA, auristatin F-hydroxypropyl amide; DAR, drug-to-antibody ratio; DES, dose escalation; EXP, expansion; GLP, good laboratory practice; HGSOC, high-grade serous ovarian cancer; IHC, immunohistochemistry; Met, metastatic; NaPi2b, sodium-dependent phosphate transport protein 2B; PARP, poly (ADP-ribose) polymerase; Pri, primary; SLC34A2, solute carrier family 34 member 2 gene; TPS, tumor proportion score; UpRi, upifitamab rilsodotin.