Evaluation of NaPi2b Expression in a Well-Annotated Longitudinal Tissue Series of Ovarian Serous Carcinomas

Drapkin, Ronny[1]; Jung, Euihye[2]; Bradshaw, Chelsea[3]; DeMars, Leslie[3]; Mosher, Rebecca[3]

[1]Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA; [2]OCRC Tumor BioTrust Collection, University of Pennsylvania, Philadelphia, PA; [3]Mersana Therapeutics, Inc., Cambridge, MA

BACKGROUND

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

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

- Preliminary antitumor activity was reported in the platinum-resistant serous ovarian cancer Phase 1b expansion (EXP) cohort, including patients previously treated with bevacizumab and PARP inhibitors[5]
- Results suggest that clinical benefit may correlate with NaPi2b expression, with higher NaPi2b expression associated with higher likelihood of clinical benefit[5]
- Change in NaPi2b expression over the course of ovarian cancer has not been extensively evaluated; therefore, an analysis was performed to evaluate NaPi2b expression in a longitudinal tissue series

METHODS

- 11 patients with HGSOC had tissue sampled at multiple time points throughout the course of their disease:
  - 5 samples were evaluated at the time of primary debulking surgery and after chemotherapy
  - 2 samples were evaluated prior to chemotherapy, after neoadjuvant chemotherapy, and at the time of disease progression or recurrence
  - 4 samples were evaluated prior to chemotherapy and after neoadjuvant chemotherapy
  - Note that none of these treatments were UpRi
- NaPi2b expression was assessed by IHC by QualTek Molecular Laboratories (Discovery Life Sciences) using the GLP assay employed in the Phase 1b UpRi DES/EXP study (NCT03319628) and a TPS calculated
  - In a retrospective analysis, TPS ≥75% was shown to identify patients with a higher likelihood of response, and thus was determined as the cutoff for "NaPi2b-positive"[6]
- Tumor tissue samples were obtained from the Ovarian Cancer Research Center (OCRC) Tumor BioTrust Collection at the University of Pennsylvania

OCRC Tumor BioTrust Collection

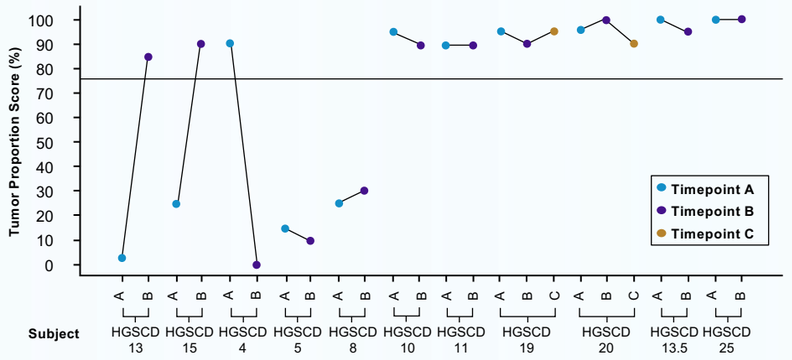
- The OCRC Tumor BioTrust Collection was established in 2007 at the University of Pennsylvania to support cancer research
- The OCRC collects human biospecimens, including cancer tissue, plasma, serum, peripheral blood mononuclear cells, blood, and other biological samples from all cases of patients with ovarian cancer
- Services offered include collection, processing, storage, and distribution of primary and recurrent ovarian tumor samples, and they can work with investigators to prospectively collect specific samples to support their research
- More information can be found at www.med.upenn.edu/OCRCBioTrust

RESULTS

- NaPi2b levels were evaluated by IHC and correlated through the disease course in matched (from the same patient) tissue samples
- 7/11 (64%) had an initial NaPi2b-positive biopsy
  - 6 of these 7 subjects (86%) remained NaPi2b-positive through their matched samples
- 8/11 (73%) maintained NaPi2b status over their treatment course
- 3/11 (27%) had a change in NaPi2b expression status over their treatment course
  - Samples that shifted status had >60% change in intensity

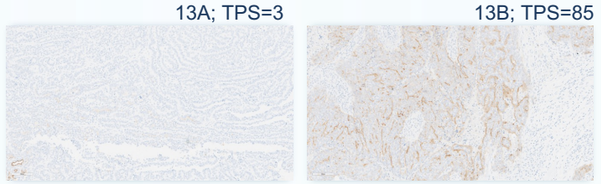
RESULTS

Longitudinal NaPi2b Expression in Matched HGSOC Tissue Samples

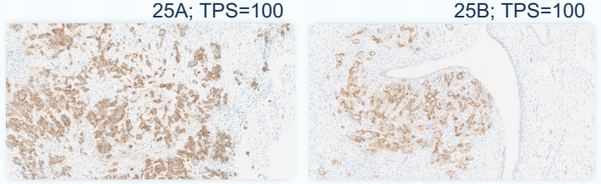


Samples are sequential in time, but "first" may not be from ovary anatomic site.

Representative IHC of Matched HGSOC Tissue Samples

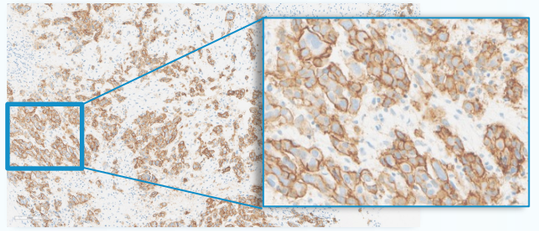


First debulking and recurrence



Original biopsy and post neoadjuvant

TPS=100 HGSOC Tissue Sample IHC (25A)



CONCLUSIONS

- Approximately two-thirds (64%) of patient tissue sampled for clinical evaluation presented with NaPi2b-positive tumors
- NaPi2b expression status was maintained over the course of treatment in the majority (73%) of evaluated individuals
- NaPi2b appears to remain consistent throughout the course of HGSOC and is a rational target for ongoing clinical trials
- UpRi is being evaluated in platinum-resistant ovarian cancer in the UPLIFT (NCT03319628) study and in platinum-sensitive ovarian cancer in the UP-NEXT (NCT05329545) and UPGRADE (NCT04907968) studies

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REFERENCES

1. Lin K et al. *Clin Cancer Res.* 2015;21(22):5139–5150. **2.** Bodyak ND et al. *Mol Cancer Ther.* 2021;20(5):896–905. **3.** Richardson DL et al. SGO Annual Meeting on Women's Cancer 2022; Abstract 585. **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

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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; NaPi2b, sodium-dependent phosphate transport protein 2B; PARP, poly (ADP-ribose) polymerase; SLC34A2, solute carrier family 34 member 2 gene; TPS, tumor proportion score; UpRi, upifitamab rilsodotin.