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

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BACKGROUND
NaPi2b is a Sodium-Dependent Phosphate Transporter Broadly Expressed in Ovarian Cancer, With Limited Expression in Healthy Tissues1

- NaPi2b is a lineage antigen and not an oncogene; its expression remains consistent throughout the course of disease2
- It is believed that approximately two-thirds of patients with HGSOCS have high NaPi2b expression based on an IHC tumor proportion score (TPS) of at least 75%3

Upfittamab Rilsodotin (UpRI) - Investigational First-in-Class NaPi2b-targeting Antibody-Drug Conjugate (ADC) With a Novel Scaffold-Linker-Payload

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 bevazcumab and PARP inhibitors
- Results suggest that clinical benefit may correlate with NaPi2b expression, with higher NaPi2b expression associated with higher likelihood of clinical benefit
- 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 HGSOCS 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
  - 4 samples were evaluated prior to chemotherapy, after neoadjuvant chemotherapy, and at the time of disease progression or recurrence

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 >50% change in intensity

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 HGSOCS and is a rational target for ongoing clinical trials
- UpRI is being evaluated in platinum-resistant ovarian cancer in the UPLIFT (NCT02316283) study and in platinum-sensitive ovarian cancer in the UP-NEXT (NCT05329545) and UPGRADE (NCT04970862) studies

ACKNOWLEDGMENTS

We would like to thank patients for making this study possible by contributing samples to the Ovarian Cancer Research Center (OCRC) Tumor BioTrust Collection at the University of Pennsylvania. 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


ADDITIONAL INFORMATION

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