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

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BACKGROUND

NaPi2b is a Sodium-Dependent Phosphate Transporter Broadly Expressed in Ovarian Cancer, With Limited platinum status expansion (EXP) study (NCT03319628) enrolled patients with freshly biopsied and archival material from patients participating in biomarker status, NaPi2b expression was evaluated in paired tissue samples. To determine if archival material would be sufficient to classify platinum resistance status, 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 status. • 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". 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 (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 (55%) 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%).

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

<table>
<thead>
<tr>
<th>Subject</th>
<th>Total Fresh Samples</th>
<th>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 (%)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>NaPi2b Positive (TPS ≥75%)</td>
<td>NaPi2b Negative (TPS &lt;75%)</td>
</tr>
<tr>
<td>Fresh</td>
<td>22 (39.3)</td>
<td>7 (12.5)</td>
</tr>
<tr>
<td>Fresh</td>
<td>7 (12.5)</td>
<td>20 (35.7)</td>
</tr>
</tbody>
</table>
| Total   | 29 (51.8)             | 27 (48.2)                     | \n
Kappa 0.5 (0.27, 0.73, moderate agreement).

RESULTS (continued)

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 required in the ongoing clinical trials evaluating UpRi therapy in platinum-resistant and platinum-sensitive ovarian cancer.

UPRIFT (NCT03319628), UP-NEXT (NCT03529945), and UPGRADE (NCT0497968)

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REFERENCES


ADDITIONAL INFORMATION

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