Abstract #3016: First-in-human dose escalation and expansion study of SYSA1801, an antibody-drug conjugate targeting Claudin 18.2 in patients with resistant/refractory solid tumors

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Background
• SYSA1801 is a monomethyl auristatin E (MMAE) antibody-drug conjugate (ADC) targeting Claudin 18.2 (CLDN18.2), a tight junction protein broadly expressed in gastric, pancreatic, and other solid tumors.
• CLDN18.2 has a highly selective cell surface expression profile that is limited to normal gastric mucosa, making it a promising ADC therapeutic target.
• SYSA1801 has shown significant in vitro and in vivo anti-tumor activity in multiple cell lines and xenografts expressing CLDN18.2.

Methods
• In this open-label, multi-center, phase I study, patients with histologically confirmed resistant/refractory solid tumors that express CLDN18.2 who progressed on or were intolerant to standard treatment, or had no standard treatment were recruited.

Outcomes
• The primary endpoint was safety, adverse events were graded according to CTCAE 5.0.
• The secondary endpoints were pharmacokinetics profiles and efficacy as per RECIST 1.1.

Results
• Data cut-off date: November 5, 2022.
• 33 eligible patients were enrolled to receive up to SYSA1801 3.0 mg/kg.
• The demographics and baseline characteristics were summarized in Table 1.

Table 1. Demographics and baseline characteristics of enrolled patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>1.0 mg/kg (n=9)</th>
<th>1.5 mg/kg (n=6)</th>
<th>2.0 mg/kg (n=10)</th>
<th>2.5 mg/kg (n=7)</th>
<th>3.0 mg/kg (n=2)</th>
<th>Total (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>61 (38-79)</td>
<td>56 (39-74)</td>
<td>61 (35-82)</td>
<td>62 (46-81)</td>
<td>59 (39-70)</td>
<td>60 (35-82)</td>
</tr>
<tr>
<td>Sex</td>
<td>8 M, 2 F</td>
<td>4 M, 2 F</td>
<td>8 M, 2 F</td>
<td>6 M, 1 F</td>
<td>2 M, 0 F</td>
<td>24 M, 6 F</td>
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<tr>
<td>ECOG score</td>
<td>1 (0-2)</td>
<td>1 (0-2)</td>
<td>1 (0-2)</td>
<td>1 (0-2)</td>
<td>1 (0-2)</td>
<td>1 (0-2)</td>
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<tr>
<td>No. of prior lines, n (%)</td>
<td>2 (0-4)</td>
<td>2 (0-4)</td>
<td>3 (0-6)</td>
<td>2 (0-4)</td>
<td>2 (0-4)</td>
<td>2 (0-4)</td>
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<tr>
<td>Metastasis</td>
<td>Yes (n=14)</td>
<td>Yes (n=14)</td>
<td>Yes (n=10)</td>
<td>Yes (n=6)</td>
<td>Yes (n=2)</td>
<td>Yes (n=30)</td>
</tr>
<tr>
<td>No (n=16)</td>
<td>Yes (n=2)</td>
<td>Yes (n=2)</td>
<td>Yes (n=2)</td>
<td>Yes (n=4)</td>
<td>Yes (n=2)</td>
<td>Yes (n=16)</td>
</tr>
</tbody>
</table>

• Two DLTs (grade-3 nausea and vomiting) occurred at the 3.0 mg/kg dose.
• Treatment-related adverse events (TRAEs) of any grade occurred in 25 patients (75.8%), in which 8 (24.2%) were ≥ grade 3.

Safety
• Among 17 evaluable patients with gastric cancer, ORR and DCR were 47.1% (95% CI: 23.0-72.2%, 8 PRs) and 64.7% (95% CI: 38.3-86.5%, 3 SDs).

Conclusion
• SYSA1801 exhibited promising early signs of efficacy with a well-tolerated safety profile in patients with CLDN18.2-expressing resistant/refractory solid tumors, especially gastric cancer.
• Dose expansion study is ongoing with cohort expansion study to start when the optimized dose is determined in China; studies outside of Greater China including in the United States are being planned by Elevation Oncology.

Acknowledgment
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