Phase 1 analysis of ubamatamab (MUC16xCD3 bispecific antibody) in patients with recurrent ovarian cancer

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Objectives

• There is a high unmet need for improved therapies for patients with recurrent ovarian cancer.
• In immune-deficient mice, ubamatamab combined with human immune cells led to dose-dependent antitumour activity.
• Ubamatamab (REGN4018) is a MUC16 x cluster of differentiation 3 (MUC16xCD3) bispecific antibody that targets the epithelial ovarian cancer cell and T cells and triggers T-cell activation.
• There was no apparent relationship between ubamatamab dose and clinical safety or efficacy responses in the Phase 1 study.
• The regimens will not exceed the maximum concentration (Cmax) of 800 mg QW which was well tolerated and can be escalated.

Methods

• Normal age ≥18 years with relapsed advanced epithelial ovarian, primary peritoneal, or fallopian tube cancer.
• Patients received ubamatamab 0.3–800 mg IV weekly (QW) after step-up dosing, which was utilised to mitigate risk of CRS via gradual increase in drug exposure.
• Patients were aged ≥18 years with relapsed advanced epithelial ovarian, primary peritoneal, or fallopian tube cancer.
• There was no apparent relationship between ubamatamab dose and clinical safety or efficacy responses in the Phase 1 study.
• The regimens will not exceed the maximum concentration (Cmax) of 800 mg QW which was well tolerated and can be escalated.

Results

Baseline characteristics

Table 1. Baseline patient and tumour characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
<th>Median (IQR)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>78 (100)</td>
<td>69 (60–80)</td>
<td>–</td>
</tr>
<tr>
<td>Gender (female)</td>
<td>78 (100)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>CA-125 response rate (complete response + partial response)</td>
<td>24% (95% CI: 12–40%)</td>
<td>24% (95% CI: 12–40%)</td>
<td>–</td>
</tr>
<tr>
<td>ORR (complete response + partial response)</td>
<td>10% (95% CI: 41–72)</td>
<td>10% (95% CI: 41–72)</td>
<td>–</td>
</tr>
<tr>
<td>DCR (complete response + partial response + stable disease)</td>
<td>22% (95% CI: 5–29%)</td>
<td>22% (95% CI: 5–29%)</td>
<td>–</td>
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</tbody>
</table>

Safety

Table 2. Safety summary

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>n (%)</th>
<th>Median duration (weeks)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with any TEAE, n (%)</td>
<td>78 (100)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Patients with any TEAE resulting in death, n (%)</td>
<td>1 (1)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Patients with any TEAE, n (%)</td>
<td>78 (100)</td>
<td>–</td>
<td>–</td>
</tr>
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Key takeaways

• Ubamatamab resulted in an acceptable safety profile and durable responses in a heavily pretreated recurrent ovarian cancer population.
• There was no apparent relationship between ubamatamab dose and clinical safety or efficacy responses in the Phase 1 study.
• The regimens will not exceed the maximum concentration (Cmax) of 800 mg QW which was well tolerated and can be escalated.

Conclusion

The lowest full dose of administered ubamatamab was 0.3 mg IV QW; some patients received 0.1 mg IV QW.

Background

- There is a high unmet need for improved therapies for patients with recurrent ovarian cancer.
- Median overall survival of 25 months and 5 years of follow-up has not yet been reached.
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Pharmacokinetics

- Observed ubamatamab concentration-time profiles in serum across dose-escalation cohorts in patients are depicted in Figure 4.
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