First-in-human Phase 1/2 study of ubamatamab, a MUC16xCD3 bispecific antibody, administered alone or in combination with cemiplimab in patients with recurrent ovarian cancer

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Background

In preclinical mouse model studies, ubamatamab demonstrated dose-dependent antitumour activity against MUC16-expressing ovarian tumour cells. Ubamatamab (REGN4018) is a mucin-16 x CD3 bispecific antibody (MUC16xCD3) that promotes T cell-mediated cytotoxicity by facilitating contact between target and TCR. In a phase 1 study, ubamatamab was well tolerated in healthy volunteers and patients with advanced solid tumours. In a phase 2 study, ubamatamab demonstrated antitumour activity in a cohort of women with platinum-resistant ovarian cancer and demonstrated nonclinical activity in combination with vemurafenib in advanced melanoma. In a phase 1b study, ubamatamab demonstrated dose-dependent antitumour activity against MUC16-expressing ovarian tumour cells. In a phase 2 study, ubamatamab demonstrated dose-dependent antitumour activity against MUC16-expressing ovarian tumour cells.

UBA01-004 is a phase 1/2 study to evaluate the safety, antitumour activity, and PK properties of ubamatamab as monotherapy and in combination with cemiplimab in patients with recurrent epithelial ovarian cancer.

Objectives

Primary objectives

- To determine the safety and tolerability of ubamatamab as monotherapy and in combination with cemiplimab.
- To assess the preliminary efficacy of ubamatamab as monotherapy and in combination with cemiplimab as measured by ORR based on RECIST 1.1 criteria.
- To assess the preliminary efficacy of ubamatamab as monotherapy and in combination with cemiplimab as measured by ORR based on IRBCT 1.1 criteria.

Secondary objectives

- To assess the safety and tolerability of cemiplimab as monotherapy and in combination with ubamatamab.
- To assess the relationship between exposure and efficacy and safety endpoints.
- To assess the safety and tolerability of ubamatamab as monotherapy and in combination with trametinib, in combination with vemurafenib.

Methods

Study design

In a phase 1 study with a 2 × 2 design, patients with advanced ovarian cancer and measurable disease were treated with ubamatamab 250 mg IV Q3W or 800 mg IV Q3W as monotherapy or in combination with cemiplimab 350 mg Q3W. In a phase 2 study, eligible patients were randomized 1:1:1 to receive ubamatamab 250 mg IV Q3W or 800 mg IV Q3W as monotherapy or in combination with cemiplimab 350 mg Q3W. Patients who previously received a PARP inhibitor for patients with HRD-related ovarian cancer were eligible, as were patients who progressed on a prior treatment with a hedgehog pathway inhibitor.

Patient eligibility

Key inclusion and exclusion criteria are provided in Table 1.

Endpoints

In the dose expansion phase:
- Primary endpoint will be the objective response rate for each treatment arm as defined by RECIST 1.1 criteria.
- Secondary endpoints include:
  - Evaluation of duration of response and progression-free survival
  - Further evaluation of safety and pharmacokinetics.

In the combination phase:
- Additional objectives include:
  - Evaluation of antitumour activity as measured by ORR based on RECIST 1.1 criteria.
  - Evaluation of antitumour activity as measured by ORR based on IRBCT 1.1 criteria.

Table 1. Key inclusion and exclusion criteria for the randomised Phase 2 cohort

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
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<tr>
<td>Patients aged ≥18 years</td>
<td>Active malignancy (other than melanoma) within 5 years of study entry</td>
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<tr>
<td>Symptomatic ascites</td>
<td>&gt;1 prior systemic antitumour therapy</td>
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<tr>
<td>Eastern Cooperative Oncology Group (ECOG) performance status ≤1</td>
<td>History of severe allergic reaction to cemiplimab</td>
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<tr>
<td>Inactive second primary tumour</td>
<td>History of serous or mucinous neoplasms</td>
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<tr>
<td>Life expectancy of ≥3 months</td>
<td>Antihypertensive, anti-diabetic, or other medications that might affect safety or PK</td>
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References


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Disclosures

The authors declare no conflicts of interest.