**Key Findings**

- Population PK model-based simulations indicate that domvanalimab flat doses of 1200 mg Q3W and 1600 mg Q4W will result in similar exposure to 15 mg/kg Q3W and 20 mg/kg Q4W, respectively.

- Flat doses of 1200 mg Q3W and 1600 mg Q4W are being studied in ongoing Phases 2 and 3 clinical trials in multiple cancer indications.

**Simulations indicate that flat doses of 1200 mg Q3W and 1600 mg Q4W result in similar exposure as 15 mg/kg Q3W and 20 mg/kg Q4W, respectively.**

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**INTRODUCTION**

Domvanalimab (AB154) is an Fc-silent humanised IgG1 mAb designed to block the interaction of T-cell immunoglobulin and ITM domain (TIGIT) with CD112 and CD155, reducing inhibition of T cells and NK cells and, thereby, promoting antitumour activity.

Domvanalimab, in combination with zimberelimab, an investigational anti-PD-1 mAb, is being developed in multiple oncology indications, including non-small cell lung cancer (NSCLC) and upper gastrointestinal tract cancers; clinically meaningful improvement in objective response rate & progression-free survival was demonstrated compared to zimberelimab monotherapy in NSCLC patients.

Domvanalimab was dosed based on body weight in early phase clinical studies; a model-informed drug development (MIDD) approach is used to provide justification for flat-dosing regimen, improving the ease of use and administration.

**OBJECTIVES**

- To develop a population pharmacokinetics (PK) model for domvanalimab
- To derive flat doses of domvanalimab using MIDD approach to employ in future clinical studies

**METHODS: Clinical Studies with Domvanalimab PK Data**

<table>
<thead>
<tr>
<th>Study</th>
<th>Population PK-PD Analysis</th>
<th>Study Design</th>
<th>Population</th>
<th>Number of subjectsa</th>
<th>Number of PK observations</th>
<th>O/W dosing regimen</th>
<th>Clinical Trial.gov identifier</th>
</tr>
</thead>
<tbody>
<tr>
<td>AB154C00001</td>
<td>phase 1 open-label, parallel group, dose-escalation study to evaluate the safety, pharmacology, PK, PD, and preliminary efficacy in patients with solid tumors</td>
<td>Patients with advanced solid tumors</td>
<td>40</td>
<td>42</td>
<td>0.5 mg/kg, 1 mg/kg, 2 mg/kg, 15 mg/kg, 20 mg/kg</td>
<td>Q3W</td>
<td>NCT03628677</td>
</tr>
<tr>
<td>AB154C00002</td>
<td>open-label, proof of concept study of domvanalimab monotherapy in combination with zimberelimab or domvanalimab+zimberelimab monotherapy</td>
<td>Metastatic G1a (squamous or non-squamous non-small cell lung cancer (NSCLC))</td>
<td>40</td>
<td>42</td>
<td>0.5 mg/kg, 1 mg/kg, 2 mg/kg, 15 mg/kg, 20 mg/kg</td>
<td>Q3W, Q4W</td>
<td>NCT04262856</td>
</tr>
</tbody>
</table>

*a: patients who have received at least one dose of non-maintenance phase; full data are available in the Table 1 analysis

**RESULTS**

- A two-compartment model with weight as covariate on clearance and central volume of distribution was selected as the final model
- Simulations indicated that the overall difference in geometric means of all summary exposure measures between the weight based and flat dose regimens was < 1% when comparing 1200 mg Q3W to 15 mg/kg Q3W, and 1600 mg Q4W to 20 mg/kg Q4W regimens.

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**METHODS: Population PK Model Structure**

**Parameter Estimates**

- The population PK-PD analysis was conducted using nonlinear mixed-effects modeling with the NONMEM software, version 7.5.
- Graphical and all other statistical analyses, including evaluation of NONMEM outputs, were performed using R version 3.6.2 for Windows

**REFERENCE**


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