IMGC936, an investigational ADAM9-targeting antibody drug conjugate, is active against patient-derived ADAM9-expressing xenograft models

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Abstract 1841

ADAM9 is a cell surface protein that belongs to the ADAM (a disintegrin and metalloproteinase) family of proteins, which have been implicated in cytokine and growth factor shedding, and cell migration. Dysregulation of ADAM9 has been involved in tumor progression and metastasis, as well as pathological neovascularization. We have previously shown that ADAM9 is overexpressed in multiple solid tumor indications and that anti-ADAM9 antibodies are efficiently internalized and degraded by tumor cell lines making ADAM9 an attractive target for antibody-drug conjugate (ADC) development1,2.

IMGC936 is an investigational ADAM9-targeting ADC, comprised of a high-affinity humanized immunoreactive monoclonal antibody (mAb) specifically coupled to DM21 as a drug antibody ratio (DAR) of 2. DM21 is a next-generation linker/payload that combines a maytansine-derived microtubule-destabilizing payload with a stable triazolyl linker. IMGC936 is being investigated in a phase 1 dose escalation study evaluating safety and pharmacokinetics in patients with solid tumors (NCT04327774).

Here we explore ADAM9 expression and prevalence in solid tumors and evaluate the activity of IMGC936 in clinically relevant patient-derived xenograft (PDX) models with ADAM9 expression similar to that observed in human tumors.

INTRODUCTION

Efficacy in PDX Study

<table>
<thead>
<tr>
<th>Model Type</th>
<th>Model Description</th>
<th>DM21</th>
<th>ADC</th>
<th>Activity</th>
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</thead>
<tbody>
<tr>
<td>TNBC</td>
<td>CTG-0936</td>
<td>100</td>
<td>IMGC936</td>
<td>Active</td>
</tr>
<tr>
<td>NSCLC</td>
<td>CTG-0306</td>
<td>8.5</td>
<td>IMGC936</td>
<td>Inactive</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>CTG-0889</td>
<td>10</td>
<td>IMGC936</td>
<td>Inactive</td>
</tr>
<tr>
<td>Gastric</td>
<td>CTG-0353</td>
<td>5</td>
<td>IMGC936</td>
<td>Highly Active</td>
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</tbody>
</table>

IMGC936 was active against tumors with clinically relevant ADAM9 expression and was well tolerated across all models tested.

CONCLUSIONS

ADAM9 is expressed in multiple tumor types, including TNBC, pancreatic, gastric, and NSCLC.

- The expression is highly heterogeneous, both within and across tumor types; very few tumors are ADAM9-negative.

IMGC936 showed compelling anti-tumor activity against PDX models with clinically relevant expression levels and heterogeneity of ADAM9 expression.

- IMGC936 was active against all PDX models with a single dose of 3.4 mg/kg (100 µg/kg of DM21 payload); the dose was well tolerated.

These data support the current clinical evaluation of IMGC936 (NCT04622774).

References: 1AACR 2017, abstract 38, 2AACR 2019, abstract 1538

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