Non-clinical tumor models reveal broad combination potential of ICOS agonist antibodies

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Abstract

The combination potential of ICOS agonist antibodies is being explored, both in vitro and in vivo. The current study investigated whether ICOS agonist mAb can augment the efficacy of checkpoint inhibitors and chemotherapies in non-clinical models.

Background

ICOS is a CD28 superfamily receptor, predominantly expressed on subsets of T cells shortly after TCR activation. In addition to promoting T-cell collaboration, ICOS signaling has been shown to enhance T-cell antitumor activity and result in durable tumor rejection.

Methods

1. ICOS monoclonal antibody (mAb): Münzized 7E1709 (mAbG1) with fragment crystallizable (Fc) characteristics analogous to GS-K3359609 (Fc-engineered mAbG4 ICOS agonist).
2. Tumor models evaluated: EMT6 (breast), CT26 (colon), H22 (liver).
3. Combinations evaluated: anti-programmed cell death protein-1 (PD-1), CTLA-4, death receptor 4 (TRAIL) and CD40 agonists, chemo, and focal irradiation (RT).

Results

1. Anti-ICOS mAb demonstrated complementarily with various therapeutic strategies, across different non-clinical tumor models.
2. Combination effects with PD-1, CTLA-4, and RT were pronounced.
3. Focal RT enhanced ICOS efficacy in an ICOS-intensive tumor model (CT26).

Acknowledgments

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References


Conclusions

1. ICOS agonist mAb demonstrated broad mono and combo activity across divergent therapeutic modalities and tumor models.
2. These data highlight the combination potential of anti-ICOS agonist mAbs.
3. Combinations, such as those presented, are or will be incorporated into the ICOS clinical program, including in the IND/1E-1 (204691; NCT02339559), a first-in-human clinical trial evaluating ICOS agonist GS-K3359609 as monotherapy and in combination with other regimens in selected solid tumors.

Table 1. Tabulated mono and combo survival (%) across models

<table>
<thead>
<tr>
<th>Model</th>
<th>Focal RT (5 Gy x 4)</th>
<th>Combination</th>
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</thead>
<tbody>
<tr>
<td>PBS</td>
<td>Anti-ICOS</td>
<td>85%</td>
</tr>
<tr>
<td></td>
<td>Focal RT (5 Gy x 4)</td>
<td>85%</td>
</tr>
<tr>
<td>Anti-ICOS</td>
<td>PBS</td>
<td>85%</td>
</tr>
<tr>
<td></td>
<td>Anti-ICOS + vehicle</td>
<td>85%</td>
</tr>
<tr>
<td>Anti-ICOS</td>
<td>Focal RT (5 Gy x 4)</td>
<td>85%</td>
</tr>
<tr>
<td></td>
<td>Anti-ICOS + vehicle</td>
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<td>Anti-ICOS + vehicle</td>
<td>85%</td>
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Antigenic neo-epitopes following monotherapy (mono), and combination therapy (combo), across associated biotherapeutic.

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