Abstract

Background: SCH 717454 is a fully human antibody directed against the insulin-like growth factor I receptor (IGF-1R), which is heightened in the growth and metastatic potential of many pediatric solid tumors. In vitro and preclinical testing has shown SCH 717454 has a potent effect on IGF-1R signaling, which is a key regulator of cell cycle progression, cell survival, and tumor growth.

Methods: A pediatric preclinical testing panel (PPTP) was used to evaluate the efficacy of SCH 717454 in a panel of 16 solid tumor xenografts and 1 acute lymphoblastic leukemia (ALL) cell line, MOLT-4.

Results: SCH 717454 reduced xenograft tumor volume compared to control in 10 of the 16 xenografts and in MOLT-4. Three xenografts with CR or MCR responses had high IGF-1R expression.

Conclusions: SCH 717454 is a promising single agent on a number of pediatric solid tumors. Further clinical testing is warranted.

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Methods for PPTP in Vivo Testing

SCH 717454 in Vivo Activity

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Tumor</th>
<th>Response</th>
<th>Mean Tumor Volume</th>
<th>EFS T/C</th>
<th>Median T/C</th>
<th>P-value</th>
<th>Overall Group</th>
<th>CR</th>
<th>MCR</th>
<th>PD1</th>
<th>PD2</th>
<th>PD3</th>
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</thead>
<tbody>
<tr>
<td>Control</td>
<td>NB-1643</td>
<td>CR</td>
<td>0.56</td>
<td>2.2</td>
<td>0.24</td>
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<td>RTV</td>
<td>0</td>
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<tr>
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<td>NB-1643</td>
<td>MCR</td>
<td>0.16</td>
<td>2.3</td>
<td>0.04</td>
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<td>RTV</td>
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<td>0</td>
<td>0</td>
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<td>1</td>
</tr>
</tbody>
</table>

IGF-1R Expression

- 3 xenografts with low IGF-1R expression did not respond (2, 6, 8).
- The 3 xenografts with high IGF-1R expression had high activity against SCH 717454.

CONCLUSIONS

The activity of SCH 717454 as a single agent in the PPTP panel suggests a potential clinical utility for selected pediatric solid tumors. SCH 717454 was able to control tumor growth in approximately one-third of the solid tumors tested. Further testing and dose escalation are warranted to determine the optimal activity of SCH 717454 in combination with other molecular-targeted agents.