New Insights into Targeting the CD200R1 Pathway in T and NK Cells Using 23ME-00610 as a Single Agent or in Combination

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Background

CD200R1 is broadly expressed on tumor-infiltrating immune cells and is a candidate immune checkpoint. It is a member of the immunoglobulin superfamily and is expressed on immune cells, including T cells, B cells, and macrophages.

Objectives

1. Characterize the expression of CD200R1 and PD-1 pathway components on different cell subsets within various cancers.
2. Investigate the potential of 23ME-00610 to enhance immune cell activation.
3. Evaluate the synergistic effects of 23ME-00610 with other immune checkpoint inhibitors.

Results

CD200 has a Differentiated Expression Pattern from PD-L1

Figure 1. Immunophenotyping of Distinctive Tumor Cell Revenues

Differentiated Expression Pattern between CD200 and PD-L1

Figure 2. CD200R1 and PD-L1 Have Distinct Expression Profiles Across Tumor-Infiltrating Immune Cell Subsets

Figure 3. 23ME-00610 Differentially Activates Immune Cells Compared to Anti-PD-1

Figure 4. 23ME-00610 Enhances T Cell Antitumor Activity

Figure 5. 23ME-00610 Rescues the Immunosuppressive Activity of CD200 on T Cells

Figure 6. 23ME-00610 Synergizes with Anti-PD-1 to Enhance IFN Secretion from Primary Human T Cells

Conclusions

CD200R1 is a promising therapeutic target for immune checkpoint therapy. The potential of 23ME-00610 as a single agent or in combination with other immune checkpoint inhibitors warrants further investigation.

Acknowledgements

The authors would like to thank Jay Davis for spectral flow support and Teresa Hsiong for statistical support.

References

Coles, S. et al. Leukemia; 25(5):792


NK cells were isolated from human primary PBMCs and stimulated with 100 nM of 23ME-00610, anti-PD-1, or isotype control and stimulated with phytohemagglutinin (PHA) for 5 days. Expression of CD107a and CD200R1 was evaluated by flow cytometry.

Table 1: Ratio of adjusted area under the Curve (AUC)

<table>
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<tr>
<th>Test</th>
<th>Observed Ratio (Y/Y)</th>
<th>Upper 95% CI</th>
<th>FDR Adjusted P-Value</th>
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<td>Anti-CD200</td>
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<tr>
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<td>Anti-VEGF</td>
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Potential for 23ME-00610 to Combine with Anti-Angiogenics

Figure 7. 23ME-00610 Synergizes with Anti-VEGF to Inhibit Tumor Growth