**Abstract**

220307 is a novel small-molecule IL4I1 inhibitor that inhibits the enzyme that catabolizes phenylalanine and produces phenylpyruvate, leading to a reduction in IL4I1 activity and tumor growth. Combined with immune checkpoint blockade, 220307 further reduces tumor growth.

**Background**

IL4I1 is an enzyme that is upregulated in ovarian and B-cell tumors. It can be produced by both myeloid and T cells, particularly high expression in ovarian and B-cell tumors.

**IL4I1 Is Highly Expressed in Ovarian and B-Cell Tumors**

- **A**. Phenylpyruvate + H₂O₂ = NH₂
- **B**. H₂O₂ + Amplex Red (fluorescent)

**Activity of 220307 in Syngeneic Lymphoid and Solid Tumor Models**

- **A**. Phenylpyruvate + H₂O₂ = NH₂
- **B**. H₂O₂ + Amplex Red (fluorescent)

**IL4I1 Expression Is Elevated in Tumor versus Normal Tissue**

- **A**. IL4I1 is expressed in tumor cells and myeloid cells.
- **B**. IL4I1 enzyme activity is toxic to T cells.

**Anti-Tumor Activity of 220307 in the A20 B Cell Lymphoma Model**

- **A**. Phenylpyruvate + H₂O₂ = NH₂
- **B**. H₂O₂ + Amplex Red (fluorescent)

**Conclusions**

- IL4I1 is an enzyme that catabolizes phenylalanine and produces phenylpyruvate.
- IL4I1 expression is elevated in multiple tumor types and is particularly high in ovarian and B-cell tumors.
- IL4I1 can be produced by both tumor cells and myeloid cells.
- **220307** is a small-molecule inhibitor of IL4I1 that has single-agent and tumor activity.
- **220307** reduces tumor growth, particularly in ovarian and B-cell tumors.