TTI-622 (SIRPa-IgG4 Fc), a CD47-Blockading Innate Immune Checkpoint Inhibitor, Suppresses Tumor Growth and Demonstrates Enhanced Efficacy in Combination with Anti-Tumor Antibodies in Both Hematological and Solid Tumor Models

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TTI-622 (SIRPa-IgG4 Fc): A Novel Biologic that Blocks the CD47 "Do Not Eat" Signal

- CD47 binds to SIRPα on the surface of macrophages and delivers a "do not eat" signal to suppress phagocytosis.
- Tumor cells frequently overexpress CD47 and exploit this pathway to evade macrophage-mediated destruction.
- TTI-622 [human SIRPα linked to a human IgG4] is a soluble decoy receptor that neutralizes the suppressive effects of CD47 and promotes macrophage-mediated phagocytosis of tumor cells.
- Previous studies have shown that blockade of the CD47-SIRPα pathway using TTI-622, a soluble SIRPa-IgG4 Fc fusion protein, triggers macrophage phagocytosis of tumor cells in vitro, and potentially inhibits tumor growth in vivo.

In this study, the in vitro and in vivo efficacy of TTI-622, a soluble SIRPa-Fc variant protein containing an IgG4 Fc tail, was evaluated in multiple model systems.

TTI-622 Potently Induces Macrophage-Mediated Phagocytosis of Primary Malignant Human Cells

TTI-622 Potentiates the Efficacy of Daratumumab (anti-CD38 mAb) in a Head and Neck Squamous Cell Carcinoma Xenograft Model

Both Early and Delayed Administration of TTI-622 Decrease Tumor Growth and Improve Survival in a DLBCL Xenograft Tumor Model

TTI-622 Enhances the Efficacy of Cetuximab (anti-EGFR mAb) in a Head and Neck Squamous Cell Carcinoma Xenograft Model

Conclusions

- TTI-622 potently induces phagocytosis of a broad panel of tumor cells derived from patients with both hematological and solid tumors.
- Unlike CD47-blocking antibodies, TTI-622 binds minimally to human erythrocytes and does not induce hemagglutination in vitro.
- TTI-622 preferentially induces phagocytosis of tumor cells over platelets in a competitive phagocytosis assay.
- In a DLBCL xenograft tumor model, both early and delayed treatments resulted in statistically significant decreases in tumor growth, and improved survival relative to treatment with control Fc.
- TTI-622 potentiates the efficacy of cetuximab and daratumumab in solid and hematological xenograft tumor models, respectively.
- Based on these data, a clinical study of TTI-622 in patients with advanced lymphoma or myeloma is being initiated.