**Blockade of the CD47 “Do Not Eat” Signal by TTI-621 (SIRPαFc) Leads to Enhanced Anti-Tumor CD8+ T Cell Responses In Vitro**

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**TTI-621 (SIRPαFc): 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
- Blocking CD47 using TTI-621, a suitable SIRPαFc decoy receptor fused to a human FcγI, mediates the suppressive effects of CD47 and triggers macrophage-mediated phagocytosis of tumor cells in vitro, and effectively controls tumor growth in vivo
- In this study we have investigated whether TTI-621-mediated phagocytosis results in augmented T cell responses

**To evaluate the T cell response to a model tumor antigen, Jurkat (a human leukemia cell line) was stably transfected with a construct containing the human cytomegalovirus phosphoprotein pp65 (CMV-Jurkat)**

**Macrophages that had phagocytosed CMV-Jurkat in the presence of TTI-621 were assessed for their ability to present tumor antigen and subsequently trigger tumor-specific autologous CD8+ T cell responses**

**Increased Macrophage Phagocytic Activity by TTI-621 Leads to Proliferation and Activation of Tumor-Specific CD8+ T Cells**

**Conclusion**

- TTI-621 potently triggers macrophage phagocytosis of a human leukemia cell line transfected with the human cytomegalovirus phosphoprotein pp65 (CMV-Jurkat)
- Macrophage phagocytosis of CMV-Jurkat leads to presentation of tumor antigen (pp65) on the surface of macrophages
- Macrophages presenting tumor antigen (CMVpp65) induce proliferation and activation of tumor-specific CD8+ T cells in vitro

**Collectively, our study demonstrates for the first time in a human culture system that blockade of the CD47 ‘do not eat’ signal in increased phagocytosis, augmented tumor antigen presentation and enhanced anti-tumor CD8+ T cell responses**

**Two Phase 1, multicenter studies have been initiated to evaluate TTI-621 in subjects with relapsed/refractory hemotological malignancies and solid tumors (NCT02663518 and NCT02695064)**

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**Blockade of CD47 Using TTI-621 Leads to Phagocytosis of CMVpp65-Transfected Tumor Cells**

**TTI-621-Mediated Phagocytosis Leads to Presentation of Tumor Antigen on the Surface of Macrophages**

**TTI-621-Mediated Phagocytosis Results in Expansion of Fully Functional Tumor-Specific CD8+ T cells that are Capable of Exhibiting Cytotoxicity**