**INTRODUCTION**

TCB cells engaging bispecific T-cell engaging antibodies (TCBs) have shown great activity in hematologic malignancies, but development of TCBs for solid tumors is challenging. Due to their high potency, TCBs can target normal organs and lead to off-target effects, resulting in significant toxicities. As a result, it has been difficult to reach the level of drug exposure required for efficacy without excessive toxicity. Therefore, several methods are needed to enable the potent and tumor-specific activity of TCBs while minimizing toxicity due to cytotoxic release and damage to healthy tissues.

**RESULTS**

**Picture 2:** TCBs have shown clinical activity in hematologic malignancies, but therapeutics which direct the activity of cytotoxic T cells to tumors.

**Figure 3:** Pb-TCB Demonstrates Reduced Binding to EGFR+ and CD3+ Cells in vitro

**Figure 4:** Pb-TCB Offers Substantial Protection in in vitro Functional Assays

**Figure 5:** Pb-TCB Sensitivity to Protease Cleavage Correlates with Tumor cell Infiltration and Efficacy in PBMC Engrafted NSG Mice

**Figure 6:** EGFR/CD3 Pb-TCB Induces Regressions of Established HT29 Tumors in PBMC Engrafted NSG mice

**Figure 7:** EGFR/CD3 Pb-TCB is Efficacious in HCT116 Established Tumor Model

**Figure 8:** Pb-TCB Provides Increased Safety relative to act-TCB in Cynomolgus Monkeys

**CONCLUSIONS**

- **EGFR/CD3** act-TCB demonstrates potent EGFR-dependent T-cell mediated killing in all cell types.
- **The Pb-TCB** attenuates EGFR and CD3 on solid cells and reduces target infiltration. **Pb-TCB and act-TCB induce regressions of established EGFR+ tumors in human PBMC engrafted NSG mice**.
- **Cytokine profiles correlate with both efficacy and tumor infiltration in PBMC engrafted NSG mice.**
- **The Pb-TCB demonstrates reduced T-cell activation relative to the unmasked TCB.**

**EGFR-CD3 Bispecific Probody™ Therapeutic Induces Tumor Regressions and Increases Maximum Tolerated Dose >60 fold in Preclinical Studies**

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