TriTCE Co-Stim: A novel trispecific T cell engager platform, with integrated CD28 cosimulation, engineered to widen the therapeutic window for treatment of poorly infiltrated tumors

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Low T cell infiltration and T cell anergy are challenges for the treatment of solid tumors with conventional CD28-engaging bispecific T cell Engagers (TCEs) (Figure 1). Co-stimulatory trispecific TCEs (TriTCE Co-Stim) have the potential to provide more durable responses and reinvigorate low T cell infiltrates with higher T cell activation.

Anergy

Figure 2. T cells cultured with CLDN18.2 TriTCE Co-Stim in TAA-stimulated, or TAA-unstimulated T cell proliferation assays. No binding of CD28 observed in the presence of CD28-targeted TriTCE Co-Stim. (A) Lead CLDN18.2 TriTCE Co-Stim format is dependent on target expression to induce cytokine production by human immune cells and exhibits potent target cell lysis. (B) CLDN18.2 TriTCE Co-Stim does not elicit in vivo T cell engagement in vivo. (C) TriTCE Co-Stim does not result in body weight loss or systemic cytokine production relative to superagonist eCD28.

Therapeutic strategies to provide Signal 1 and Signal 2 (CD28) Co-Stim.

CLDN18.2 TriTCE Co-Stim mediates similar effects of tri-specific Co-Stim on CD8+ central memory (T_CM) and effector memory (T_EM) T cells and central memory (T_CM) T cells. (Figure 9)

Conclusions

- DMG-919 significantly enhanced T cell recruitment and engraftment of T cells in vivo
- Tumor-Cells + Tumor+DMG-919 co-engagement improved T cell recruitment and engraftment
- DMG-919 improved TIL and TCM cell engraftment
- DMG-919 significantly enhanced T cell recruitment and engraftment

References

- Weisser NE, et al. (2022) Targeting Solid Tumors with Bispecific T Cell Engager Immune Therapy. SITC 2023
- Escalante NK, et al. (2022) Targeting Solid Tumors with Bispecific T Cell Engager Immune Therapy (Vol. 6, pp.17-25)