TriTCE CPI: a novel trispecific T cell engager platform with integrated PD-1/PD-L1 checkpoint inhibition engineered for the treatment of immunosuppressed tumors

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Introduction

Immunosuppression in the tumor microenvironment limits antitumor responses of conventional CD3-engaging bispecific T cell engagers (TCEs) in solid tumors with immune-suppressed TMEs.

Trispecific TCEs with checkpoint inhibition (TriTCE CPI) are designed to increase T cell responses to address primary and acquired resistance mechanisms in the TME.

TriTCEs with integrated CD3 and PD-L1 engagement (via an engineered PD-1 domain) have the potential to enhance T cell responses in immunosuppressed and exhausted T cell microenvironments.

TriTCE CPI design is optimized for format and affinity

TriTCE CPI formats are screened for increased antitumor activity and T cell responses, PD-1/PD-L1 checkpoint blockade, and avidity-driven binding.

TriTCE CPI mediated enhanced binding and antitumor activity against tumor models with indolent PD-L1 expression

Upregulation of PD-L1 expression occurs following TCE treatment and is a mechanism of acquired resistance. TriTCE CPI may show enhanced antitumor activity in settings of acquired resistance.

Conclusions

TriTCEs have been formulated and designed to:

- Overcome PD-1 mediated tumor resistance mechanisms that can limit the efficacy of traditional bispecific TCEs.
- Promote increased antitumor activity in PD-L1+ tumors and with tumor-infiltrated PD-L1 upregulation and may improve responses in settings of acquired resistance.
- Avoid T cell exhaustion in the absence of tumor cell engagement.