TROCEPT MEDIATED IN-TUMOR DELIVERY OF IMMUNE CHECKPOINT INHIBITORS REDUCES SYSTEMIC TOXICITY RISKS AND BOOSTS IMMUNE ACTIVATION

Abstracts

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Background Immune checkpoint inhibitors (ICIs) have revolutionized immunotherapy, but their efficacy is limited to certain cancers, and response rates are largely dependent on the ability of the patients’ T cells to recognize and activate against tumor antigens. Additionally, systemic delivery can lead to dose limiting toxicity.1

TROCEPT is a novel tumor-selective delivery technology, based on type 5 adenovirus, engineered not enter normal human tissues. The removal of normal tissues tropisms addresses the main limitation of other viral therapies, which show limited efficacy due to rapid removal by the liver.2 TROCEPT has been further engineered to specifically bind to a tumor marker expressed on most carcinomas.3 The TROCEPT platform can be loaded with transgenes encoding protein-based drugs for in-tumor delivery (i.e., TROCEPT can deliver the transgene into the cancer cell, turning the cancer cell into a drug factory, which releases the payload into the local tumor environment). TROCEPT-01 enables tumor-localized generation of high concentrations of ICI payloads (figure 1).

Methods Selective cell entry of TROCEPT-01 was assessed in vitro using infectivity assays in target-positive and -negative tumor and healthy cell lines. Further in vitro assays confirmed the production of ICIs in multiple tumor cell lines, and functionality of the in-tumor generated ICI was confirmed using primary T cell activation experiments. Finally, an immune-deficient murine model, engrafted with a human tumor, was used to assess biodistribution of TROCEPT-01, after intravenous delivery, using a bioluminescence in vivo imaging system (IVIS®) and qPCR.

Results In vitro testing confirmed TROCEPT-01’s exquisite selectivity for tumor cells and demonstrated functional production of ICIs from treated tumor cells. In vivo experiments demonstrated tumor-localized biodistribution of TROCEPT-01, with a low amount of TROCEPT-01 detected in healthy organs (including the liver) and peripheral blood.

Conclusions TROCEPT’s tumor selective transgene delivery and in-tumor production of ICIs enables high local dosing only in the tumor, addressing systemic toxicity and potentially increasing efficacy. Additionally, several pre-clinical studies have demonstrated that oncolytic viruses can induce anti-viral immunity against infected tumor cells, recruiting cytotoxic T cells and other pro-inflammatory cell types.4 Thus, TROCEPT delivery of ICIs has the potential to generate a synergistic effect, first attracting and activating T cells, and then delivering tumor-localized ICIs at high concentrations to boost the anti-tumor T cell response and increase response rates in several tumor types. TROCEPT has the potential for delivery of new and powerful therapeutic drugs for the in-tumor treatment of cancer.

REFERENCES


Figure 1 Schematic of the mode of action of TROCEPT-01 encoding an immune checkpoint inhibitor