TROCEPT TUMOR-SPECIFIC TARGETING AND REPLICATION ENABLES IN-TUMOR PRODUCTION OF IMMUNE CHECKPOINT INHIBITORS FOLLOWING INTRAVENOUS DELIVERY

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Background
TROCEPT is a novel tumor-selective oncolytic adenovirus type 5 engineered to remove all natural tissue tropisms. This engineering addresses the main limitation of other viral therapies which infect normal tissues and are rapidly removed by the liver, thereby limiting tumour bioavailability. TROCEPT has been further engineered to specifically bind to αvβ6 integrin which is expressed at high frequency in the majority of epithelial cell derived cancers. In addition, the TROCEPT platform can encode transgenes which enables in-tumor production of powerful therapeutic drugs. The lead programme, TROCEPT-01, encodes a fully human, full length immune checkpoint inhibitor (ICI) antibody. TROCEPT-01 is currently undergoing IND-enabling studies and is expected to enter First in Human studies in 2024 in multiple solid tumor indications.

Methods
TROCEPT-01’s tumor selectivity was investigated in both in vitro and in vivo studies.

Results
Here we demonstrate in vitro that both viral replication and oncolytic cell death following infection with TROCEPT-01 is selective for tumor cells compared to a panel of normal human primary cells. In addition, following intravenous delivery in in vivo models comprising human αvβ6 integrin-positive tumors engrafted in immune-deficient mice, we demonstrate virus delivery and transgene expression in the tumor.

Conclusions
TROCEPT-01’s tumor selective transgene expression and in-tumor production of ICIs enables high local drug concentration in the tumor, potentially reducing systemic toxicity and 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. Thus, TROCEPT delivery of ICIs has the potential to generate a synergistic effect, first attracting and activating T cells, and then enabling tumor-localized production of ICIs to high concentrations to boost anti-tumor T cell responses and increase response rates. TROCEPT has the potential for the delivery of a variety of new and powerful therapeutic drugs to tumors. TROCEPT-01 is currently undergoing IND-enabling studies and is expected to enter First in Human studies in 2024 in multiple solid tumor indications.

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