Background

Anti-programmed death 1/ligand 1 (PD-1/PD-L1) therapies have been established as standard treatment for multiple tumor types. However, the key challenge of these therapies is resistance caused by immunosuppressive factors in the tumor microenvironment (TME). TGF–β is a multi-functional cytokine that is involved in the tight regulation of either anti-tumor immunity or tumor immunosuppression. TGF–β promotes an immune exclusion TME thus renders PD-L1 blockade ineffective. Therefore, dual targeting PD-L1 and TGF–β represents a rational synergistic strategy to enhance clinical outcome relative to each agent alone. TST005 is a novel bi-functional fusion protein combining a high affinity PD-L1 monoclonal antibody (mAb) in a fragment crystallizable (Fc) silenced immunoglobulin G1 (IgG1) backbone and a differentiated transforming growth factor beta (TGF–β) trap with improved stability. This study will investigate TST005’s safety, tolerability and preliminary anti-tumor activity in solid tumors.

Methods

This Phase 1, first in human (FIH) study is an open-label, multicenter trial that consists of a dose escalation phase in patients with advanced solid tumors who has failed prior therapy followed by a dose expansion phase in human papillomavirus (HPV) related malignancies that is not amenable to surgeryand have received prior standard therapy(ies). The primary objectives are to evaluate the safety and tolerability and determine the maximum tolerated dose or recommended Phase 2 dose(s) of TST005. Secondary objectives include pharmacokinetic, pharmacodynamic and preliminary anti-tumor activity of TST005. The dose escalation phase comprises five dose cohorts: accelerated titration of 1 subject in the starting dose cohort (1 mg/kg), and then four dose cohorts (3 mg/kg, 10 mg/kg, 20 mg/kg, 30 mg/kg) following classic 3+3 design. No more than one prior immune checkpoint inhibitor (ICI) treatment is allowed for eligible subjects. In the dose expansion phase, up to 30 patients with locally advanced or metastatic HPV+ malignancies, including cervical cancers, P16+ Oropharyngeal cancers, and other tumors that are known HPV+, and who are ICI treatment naive will be enrolled. Subjects will receive TST005 intravenous infusion every 3 weeks (Q3W) until disease progression per RECIST v1.1 and/ or immune RECIST or unacceptable toxicity. Subjects may continue to receive TST005 beyond RECIST v1.1 defined progression at the discretion of the Investigator. This study is ongoing at 4 sites in the US and China. As of the 30 June, 2022, the first two dose cohorts evaluation has been completed and no DLT was observed. Clinical trial information: NCT04958434. Study Sponsor: Suzhou Transcenta Therapeutics Co., Ltd.

Ethics Approval

The study obtained sites’ IRB approval for as listed below. All participants gave informed consent before taking part.

- Salus IRB (NXSAT20.69)
- Advarra IRB (SSU00157936)
- Mary Crowley Medical Research Center IRB (21-37)
- Shanghai Cancer Center IRB (2112248-1-2203)