**Clinical Background**

- **TST001 combined with CAPDX as first-line therapy of patients with G/GEI cancer is being explored in the Cohort A study TranStar102.**
- **As of Aug 4th, 2022, 36 patients have been enrolled and treated with TST01 at 60mg/kg Q3W plus CAPDX in the expansion phase.**
- **Among the 15 patients with measurable disease and at least one post-treatment tumor assessment (Figure 3), 11 (73.3%) achieved partial response and 4 (26.6%) achieved stable disease as the best overall tumor response per RECIST1.1. Disease control rate is 100%.*
- **This cohort is still ongoing data will be presented in another poster in this meeting.**

**Primary Objectives**

- To evaluate the safety and tolerability of TST001 single agent in patients with locally advanced or metastatic solid tumor.
- To determine the maximum tolerated dose (MTD) and/or recommended Phase II dose (RP2D) of TST001 as monotherapy, in combination with nivolumab, in combination with nivolub and mFOLFOX6, or in combination with gemcitabine and albumin-bound paclitaxel.
- To evaluate the safety and tolerability of TST001 in combination with nivolub and mFOLFOX6 in patients with locally advanced or metastatic GE/GI cancer.
- To evaluate the safety and tolerability of TST001 in combination with gemcitabine and albumin-bound paclitaxel in patients with locally advanced or metastatic pancreatic cancer.

**Methods**

**Patient Selection**

- **Part A:** solid tumor patients progressed after standard therapies, or intolerant of standard therapies will be eligible for Part A Cohort A. Patients may up regulate PDL1 expression.
- **Part B and C:** Patients with G/GEI adenocarcinoma who have radiologically progressed following one or two prior systemic therapies; prior checkpoint inhibitors allowed.
- **Part B and C:** About 15 patients with histologically confirmed pancreatic adenocarcinoma who have received prior systemic therapies for advanced disease in each arm. There must be at least one evaluable lesion (dose escalation phase) or measurable lesion (Part B cohort A and C and dose expansion of cohort B) per RECIST v1.1.

**Study Population**

- **Part A:** solid tumor patients progressed after standard therapies, or intolerant of standard therapies, or with a tumor type without standard therapy.
- **Part B and C:** About 15 patients with histologically confirmed G/GEI adenocarcinoma in each arm, who have not received prior systemic therapies for advanced disease.
- **Part B and C:** Patients with G/GEI adenocarcinoma who have radiologically progressed following one or two prior systemic therapies; prior checkpoint inhibitors allowed.
- **Part B and C:** About 15 patients with histologically confirmed pancreatic adenocarcinoma who have received prior systemic therapies for advanced disease in each arm. There must be at least one evaluable lesion (dose escalation phase) or measurable lesion (Part B cohort A and C and dose expansion of cohort B) per RECIST v1.1.

**Dosage Schedule**

- **Part A:** TST001 will be administered as an IV infusion at 2 mg/kg or 4 mg/kg on Day 1 every 3 weeks for Part B.
- **Part B:** Q2W or Q3W.
- **Part C:** Q4W.

**Study Treatment**

- **TST001 is tested in Q2W and Q3W schedule separately in Part A.**
- **TST001 will be administered as an IV infusion at 2 mg/kg or 4 mg/kg on Day 1 every 3 weeks for Part B.**
- **Part C:** Q4W.

**Clinical Endpoint**

- **As of Apr 20, 2023, part A has been completed;** part B is ongoing.

**Background**

- Gastric cancer (GC) remained the 4th leading cause of cancer death worldwide, accounting for about 7.7% of all cancer related mortality.
- Combination of platinum and fluoropyrimidine are the preferred first-line chemotherapy regimen for patients with HER2 negative advanced gastric cancer. Nivolumab was approved in combination with chemotherapy for first-line treatment of patients with advanced or metastatic gastric cancer. Though treatment outcome being improved, the median overall survival of nivolumab plus chemotherapy was still less than 14 months.
- Claudin-18.2 isoform 2 (CLDN18.2) is a member of the human Claudin family of tetraspan membrane proteins that are crucial structural and functional components of tight junctions. CLDN18.2 expression is strictly limited to differentiated epithelial cells of gastric mucosa. CLDN18.2 is ectopically expressed at a significant level in multiple tumor types including gastric, esophageal, pancreatic and lung cancers, making it an attractive anti-cancer target. In G/GEI cancer, its expression is independent from PD-L2.
- Zebutilumab (IMAB362) is a clinical stage anti-CLDN18.2 antibody, significant improvement in PFS and OS was demonstrated when zebutilumab was added to mFOLFOX6 or to CapOx as compared to placebo plus mFOLFOX6 or CapOx. Results were limited to patients with CLDN 18.2 high expression (75%, 2+), which is about 38% of the population.

**Preclinical Data**

- TST001 is a humanized IgG1 monoclonal antibody with enhanced antibody-dependent cellular cytotoxicity (ADCC) activity via reduced fusocylation, and has stronger anti-tumor activities than IMAB362 analog. (Figure 1B and C), which is a humanized IgG1 monoclonal antibody with enhanced antibody-dependent cellular phagocytosis (ADCP) activities against CLDN18.2 expressing cells than IMAB362 analog. (Figure 1B and C).
- In vivo studies in mouse syngeneic tumor models demonstrated better efficacy of TST001 in low CLDN 18.2 expressing vs IMAB362 expressing cells. (Figure 1A) and may up regulate PD-L1 expression.
- In vivo studies in mouse syngeneic tumor models demonstrated better efficacy of TST001 in low CLDN 18.2 expressing vs IMAB362 expressing cells. (Figure 1A) and may up regulate PD-L1 expression.
- The anti-tumor efficacy of triple combination of TST001 plus anti-PD-1 antibody and chemotherapy was significantly better than anti-PD1 antibody in combination with chemotherapy or TST001 in combination with chemotherapy. (Figure 2B)

**Figure 1.** The cell killing activities of TST001 and IMAB362 analog were compared by using ADCC/CDC/ADCP assay. (A) PBMC-mediated ADCC activity against CLDN18.2 expressing Jurkat-NFAT-Luc. (B) IMAB362 antibody activity against CLDN18.2 expressing murine 4T1 cells target cell and naked NIH 3T3 fibroblast cell as effector cell. The luminescence signal of effector cell indicates ADCC activity.

**Figure 2A.** In vivo pharmacological activity of TST001 monotherapy or in combination in a PDAC tumor model.

**Figure 3.** Time course of tumor growth in vivo in a Capan2/IL21 tumor model. 

Reference:

- NCCN guidelines for gastric cancer version 2.2023
- NCT number: NCT04859296.

**Abstract**

A Multi-cohort Phase I/IIa Clinical Trial to Evaluate the Safety, Tolerability, and Pharmacokinetics of TST001 Administered as a Monotherapy, with Nivolumab or Standard of Care in Patients with Locally Advanced or Metastatic Solid Tumors (TranStar101/TST001-1001)