# Abstract 4062: A Phase I Study of TST001, a High Affinity Humanized Anti-CLDN18.2 Monoclonal Antibody, in Combination with Capecitabine and Oxaliplatin (CAPOX) as the First Line Treatment of Advanced and Metastatic G/GEJ Cancer

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## Background

- TST001 is a recombinant humanized IgG1 antibody specifically against human Claudin18.2 (CLDN18.2) with high affinity and enhanced FcR engaging of NK cell
- *In vivo* pharmacology of TST001 in gastric PDX tumor model with CLDN18.2 medium expression: TST001 dose dependently inhibits tumor growth, TST001 exhibits more potent antitumor activity than IMAB362-analog at the same dose (10mg/kg), and more mice reached tumor complete regression. (*Figure 1*)
- TST001 monotherapy dose-escalation study has been completed in China and promising anti-tumor activities were observed in patients with advanced G/GEJC with CLDN18.2 expression who had failed multiple lines of prior therapies.

**Figure 1. *In Vivo* Pharmacology of TST001 in Gastric PDX Tumor Model with CLDN18.2 Medium Expression**


**7/10 of TST001 group vs. 0/10 of IMAB362 group achieved tumor clearance**



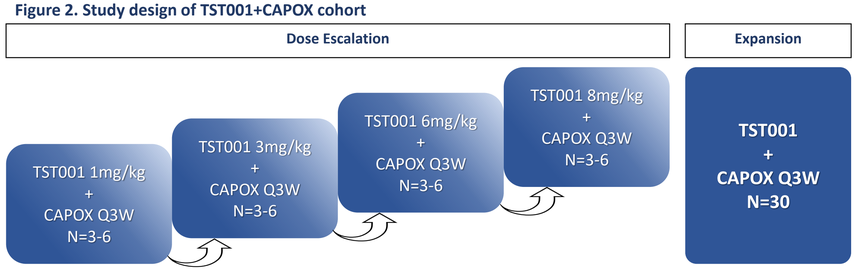
## Methods

- This cohort aimed to evaluate the safety, tolerability and preliminary efficacy of TST001 in combination with CAPOX as the 1st line treatment of patients with advanced G/GEJ cancer. (ClinicalTrials.gov Identifier: NCT04495296)
- Chinese patients with advanced G/GEJ cancer who had not received prior systemic treatment were enrolled regardless of Claudin18.2 expression in the dose escalation phase following 3+3 design; the safety and efficacy profile was being further evaluated in the dose expansion phase.(*Figure 2*)

## Results

- As of April 5, 2022, **14** patients had been dosed with TST001 at 1, 3, 6 or 8 mg/kg plus CAPOX Q3W in the dose escalation phase, and **12** patients at 6 mg/kg Q3W in the expansion phase. (*Table 1*) No subjects experienced dose-limiting toxicities.
- Treatment-emergent adverse events (TEAEs) (*Table 2*) were mostly grade 1-2, including nausea, hypoalbuminemia, anemia, vomiting and AST increased.
- Grade 3 treatment-related AEs included hypertension (11.5%), and nausea, vomiting, anemia, hypoalbuminemia (at 8 mg/kg dose), WBC count decreased, hypocalcemia, ALT increased, AST increased (3.8%, respectively), with no AEs of grade 4 or higher.
- The most common TEAE in TST001 6mg/kg (*Table 3*) are nausea, hypoalbuminemia, anemia, vomiting and AST increased.
- Among the **9** subjects (*Figure 3*) in the dose-escalation phase with CLDN18.2 unselected who had measurable lesions and had received at least one post-treatment tumor assessments, **5** achieved partial response and **3** achieved stable disease as the best overall response per RECIST1.1.

**Figure 2. Study design of TST001+CAPOX cohort**




**TST001** -a humanized CLDN18.2 mAb demonstrated manageable safety profile and preliminary clinical efficacy in combination with chemotherapy in Claudin18.2 non-selected 1st line advanced and metastatic G/GEJ Cancer patients.

**Table 1. Demographic and Baseline Characteristics TST001+CAPOX**

| | 1 mg/kg n=3 | 3 mg/kg n=3 | 6 mg/kg n=15* | 8 mg/kg n=5 | Overall n=26 |
|---|---|---|---|---|---|
| Age (Median, years) | 56 | 51 | 53 | 64 | 55 |
| Sex, n (%) | | | | | |
| Male | 2 (66.7) | 1 (33.3) | 12 (80.0) | 5 (100) | 20 (76.9) |
| Female | 1 (33.3) | 2 (66.7) | 3 (20.0) | 0 | 6 (23.1) |
| ECOG performance Status, n (%) | | | | | |
| 0 | 0 | 0 | 2 (13.3) | 2 (40.0) | 4 (15.4) |
| 1 | 3 (100) | 3 (100) | 13 (86.7) | 3 (60.0) | 22 (84.6) |
| Primary tumor, n | | | | | |
| Stomach | 3 (100) | 2 (66.7) | 13 (86.7) | 4 (80.0) | 22 (84.6) |
| GEJ | 0 | 1 (33.3) | 2 (13.3) | 1 (20.0) | 4 (15.4) |
| Gastrectomy, n (%) | | | | | |
| None | 1 (33.3) | 3 (100) | 8 (53.3) | 5 (100) | 17 (65.4) |
| Partial | 1 (33.3) | 0 | 5 (33.3) | 0 | 6 (23.1) |
| Radical or total | 1 (33.3) | 0 | 2 (13.3) | 0 | 3 (11.5) |
| Metastatic status at initial diagnosis | | | | | |
| M1 | 1 (33.3) | 3 (100) | 5 (33.3) | 3 (60.0) | 12 (46.2) |
| M0 or unknown | 2 (66.7) | 0 | 10 (66.7) | 2 (40.0) | 14 (53.8) |
| Ongoing, n (%) | 1 (33.3) | 2 (66.7) | 12 (80.0) | 3 (60.0) | 18 (69.2) |

* 5 subjects out of the 15 in TST001 6mg/kg subgroup had CLDN18.2 tested

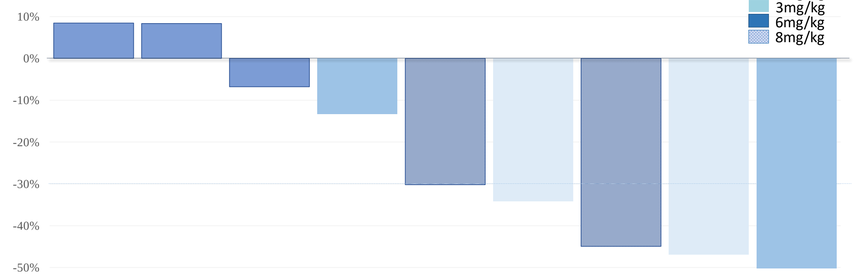
**Table 2. TEAEs by SOC and PT in the Dose Escalation & Expansion Phase (≥20% patients)**

| | 1 mg/kg n=3 | 3 mg/kg n=3 | 6 mg/kg n=15 | 8 mg/kg n=5 | Overall n=26 |
|---|---|---|---|---|---|
| Subjects with at least one TEAE | 3 ( 100) | 3 ( 100) | 15 ( 100) | 5 ( 100) | 26 ( 100) |
| Nausea | 3 ( 100) | 2 (66.7) | 12 (80.0) | 5 ( 100) | 22 (84.6) |
| Hypoalbuminaemia/hypoproteinemia | 2 (66.7) | 2 (66.7) | 10 (66.7) | 4 (80.0) | 18 (69.2) |
| Anaemia | 3 ( 100) | 3 ( 100) | 8 (53.3) | 2 (40.0) | 16 (61.5) |
| Vomiting | 1 (33.3) | 2 (66.7) | 7 (46.7) | 4 (80.0) | 14 (53.8) |
| Aspartate aminotransferase increased | 2 (66.7) | 3 ( 100) | 6 (40.0) | 0 | 11 (42.3) |
| Decreased appetite | 1 (33.3) | 0 | 6 (40.0) | 2 (40.0) | 9 (34.6) |
| Hyponatraemia | 1 (33.3) | 2 (66.7) | 4 (26.7) | 2 (40.0) | 9 (34.6) |
| Alanine aminotransferase increased | 2 (66.7) | 3 ( 100) | 4 (26.7) | 0 | 9 (34.6) |
| Oedema peripheral | 1 (33.3) | 2 (66.7) | 4 (26.7) | 0 | 7 (26.9) |

**Table 3. TEAE in ≥10% patients and ≥G3 TEAEs in 6mg/kg**

| | Any grade (≥10% patients) n=15 (100.0%) | ≥G3 n=6 (40.0%) |
|---|---|---|
| Nausea | 12 (80.0) | 1 ( 6.7) |
| Hypoalbuminaemia/hypoproteinemia | 10 (66.7) | 0 |
| Anaemia | 8 (53.3) | 0 |
| Vomiting | 7 (46.7) | 1 ( 6.7) |
| Aspartate aminotransferase increased | 6 (40.0) | 0 |
| Decreased appetite | 6 (40.0) | 0 |
| Hyponatraemia | 4 (26.7) | 2 (13.3) |
| Alanine aminotransferase increased | 4 (26.7) | 1 ( 6.7) |
| Oedema peripheral | 4 (26.7) | 0 |
| Fatigue/Asthenia/Malaise | 3 (20.0) | 0 |
| Hypocalcaemia | 2 (13.3) | 1 ( 6.7) |
| Hypertension | 2 (13.3) | 2 (13.3) |
| Peripheral sensory neuropathy | 2 (13.3) | 0 |
| Constipation | 2 (13.3) | 0 |
| Abdominal pain | 2 (13.3) | 1 ( 6.7) |
| Hyperglycaemia | 2 (13.3) | 0 |
| Abdominal distension | 2 (13.3) | 0 |
| Dyspepsia | 2 (13.3) | 0 |
| Weight decreased | 2 (13.3) | 0 |

**Figure 3. Best changes (%) from baseline of target lesions in dose escalation phase**




## Conclusion and Future Directions for Research

- TST001 in combination with CAPOX as the first line treatment of patients with advanced and metastatic G/GEJ cancer is well tolerated and encouraging preliminary anti-tumor activities have been observed.
- The recruitment for the current cohort is ongoing and the safety and efficacy of the combination of TST001+CAPOX as first line treatment for patients with advanced and metastatic G/GEJ cancer will be further evaluated.