Abstract 4046

TST001 in Combination with Capecitabine and Oxaliplatin (CAPOX) as a First-Line Treatment of Advanced G/GEJ Cancer-updated data of Cohort C from a Phase I/IIa, Multi-center Study (TranStar102/TST001-1002)

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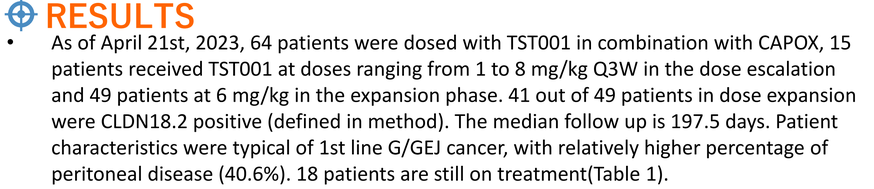
BACKGROUND

- Adding an anti-claudin18.2(CLDN18.2) antibody to a chemotherapy is a clinically validated approach for patients with high CLDN18.2 expressing gastric tumors.
- TST001 is a potential best-in-class antibody with higher CLDN18.2 binding affinity and lower fucose, resulting in enhanced antibody-dependent cellular cytotoxicity (ADCC) activity.
- Pre-clinical studies showed that TST001 has stronger tumor growth inhibition effect than the IMAB362-analog at the same dose, regardless of CLDN18.2 expression levels, which may lead to anti-tumor activity even in low to median CLDN18.2-expressing gastric cancer (Figure 1).

Figure 1. In Vivo Anti-Tumor Activity of TST001 on GC Xenograft Models with CLDN18.2 Expression



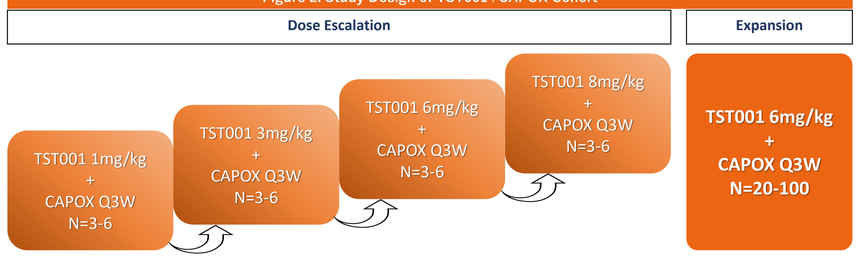
CLDN18.2 expression: IHC 2+, TC 40-50%

CLDN18.2 expression: IHC 2+, TC 40-70%

METHODS

- Cohort C of the phase I/IIa study (NCT04495296) is aimed at evaluating the efficacy and safety of TST001 plus CAPOX as the 1st line treatment for G/GEJ cancer, including a dose escalation phase and an expansion phase (Figure 2).
- Chinese patients with unresectable locally advanced or metastatic G/GEJ cancer who had not received prior systemic treatment for advanced disease were enrolled.
- Positive CLDN18.2 expression (membranous staining ≥1+ intensity in≥10% of tumor cells) as assessed centrally using the LDT assay was required in the expansion phase only.

Figure 2. Study Design of TST001+CAPOX Cohort



RESULTS

- As of April 21st, 2023, 64 patients were dosed with TST001 in combination with CAPOX, 15 patients received TST001 at doses ranging from 1 to 8 mg/kg Q3W in the dose escalation and 49 patients at 6 mg/kg in the expansion phase. 41 out of 49 patients in dose expansion were CLDN18.2 positive (defined in method). The median follow up is 197.5 days. Patient characteristics were typical of 1st line G/GEJ cancer, with relatively higher percentage of peritoneal disease (40.6%). 18 patients are still on treatment(Table 1).
- No patients experienced dose-limiting toxicity; Treatment-emergent adverse events (TEAEs) were mostly grade 1-2, including nausea, hypoalbuminaemia, anaemia and vomiting (Table 2). Only one patient experienced grade 3 nausea and vomiting at dose of 6mg/kg, one patient experienced grade 3 hypoalbuminaemia at dose of 8mg/kg. No patient experienced such event of grade 4.

Table 1. Demographic and Baseline Characteristics

		1 mg/kg (N=3)	3 mg/kg (N=3)	6 mg/kg (N=52)*	8 mg/kg (N=6)	Overall (N=64)
Age	Median	56	51	55.5	63.5	56
	Min, Max	54, 58	32, 65	21, 76	44, 75	21, 76
Sex, n (%)	Male	2(66.7)	1(33.3)	33(63.5)	6(100)	42(65.6)
	Female	1(33.3)	2(66.7)	19(36.5)	0	22(34.4)
ECOG PS, n(%)	0	0	0	9(17.3)	2(33.3)	11(17.2)
	1	3(100)	3(100)	43(82.7)	4(66.7)	53(82.8)
CLDN18.2 expression	Positive	0	0	41*(78.8)	1(16.7)	42(65.6)
	Not Done	3	3	11(21.2)	5(83.3)	22(34.4)
No. of Metastasis sites	0-2	2(66.7)	2(66.7)	33(63.5)	5(83.3)	42(65.6)
	≥3	1(33.3)	1(33.3)	19(36.5)	1(16.7)	22(34.4)
Sites of Metastasis	Peritoneum	0	1(33.3)	24(46.2)	1(16.7)	26(40.6)
	Hepatic	0	1(33.3)	11(21.2)	3(50.0)	15(23.4)
	Pulmonary	1(33.3)	1(33.3)	9(17.3)	1(16.7)	12(18.8)

*: Including 3 patients without CLDN18.2 testing in dose escalation , 8 patients without CLDN18.2 testing out of 49 patients in dose expansion

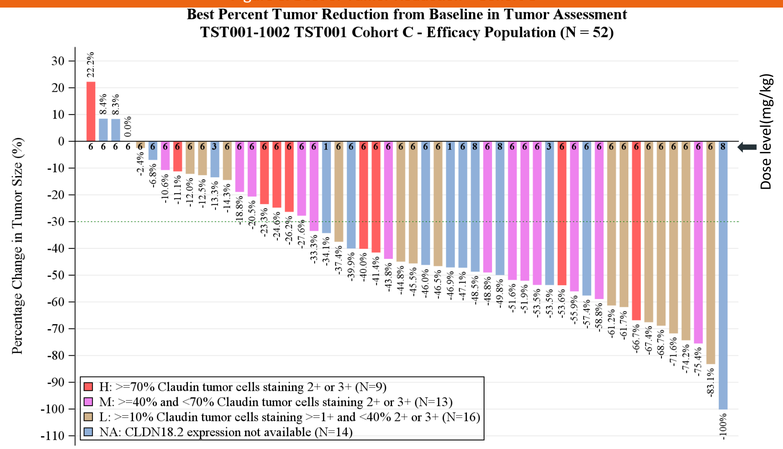
Table 2. TEAEs by PT, Any grade in ≥30% patients, regardless of causality

	1 mg/kg (N=3)	3 mg/kg (N=3)	6 mg/kg (N=52)	8 mg/kg (N=6)	Overall (N=64)
Subjects with at least one TEAE*	3(100)	3(100)	52(100)	6(100)	64(100)
Anaemia	3(100)	3(100)	43(82.7)	4(66.7)	53(82.8)
Hypoalbuminaemia	2(66.7)	2(66.7)	43(82.7)	6(100)	53(82.8)
Nausea	3(100)	2(66.7)	34(65.4)	6(100)	45(70.3)
Aspartate aminotransferase increased	2(66.7)	3(100)	34(65.4)	1(16.7)	40(62.5)
Platelet count decreased	1(33.3)	3(100)	28(53.8)	5(83.3)	37(57.8)
Neutrophil count decreased	2(66.7)	2(66.7)	28(53.8)	3(50.0)	35(54.7)
Vomiting	1(33.3)	2(66.7)	26(50)	5(83.3)	34(53.1)
Alanine aminotransferase increased	2(66.7)	3(100)	24(46.2)	1(16.7)	30(46.9)
Decreased appetite	1(33.3)	0	25(48.1)	3(50.0)	29(45.3)
Hyponatraemia	1(33.3)	2(66.7)	23(44.2)	3(50.0)	29(45.3)
White blood cell count decreased	1(33.3)	2(66.7)	24(46.2)	2(33.3)	29(45.3)
Weight decreased	1(33.3)	1(33.3)	19(36.5)	2(33.3)	23(35.9)
Hypokalaemia	1(33.3)	0	19(36.5)	2(33.3)	22(34.4)

*: 65.6% patient experienced at least one TEAE with grade 3 or higher.

•As of April 21, 2023, among the 49 patients of 6mg/kg dose expansion group, 42 patients had measurable lesions and at least one post treatment tumor assessment, 28 (66.7%) achieved partial response. Across all doses, the response rate (confirmed and unconfirmed) is 65.4%.

Figure 3. Best of Tumor Reduction – Cohort C



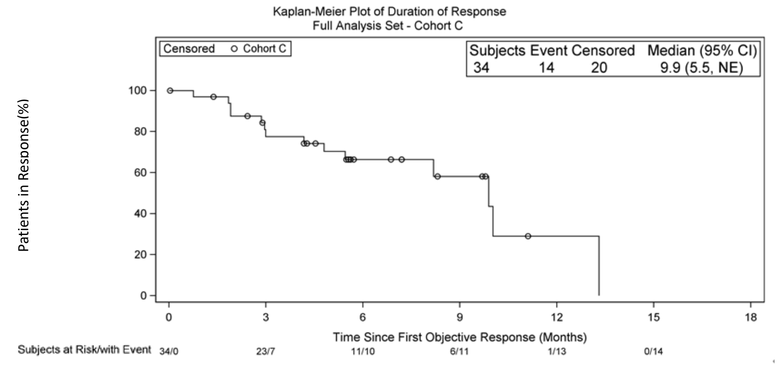
Values of changed from baseline are from target lesions

Extraction Date: 2023-04-21 Run Date: 2023-04-22

*:Including 10 patients in dose escalation at dose ranging from 1mg/kg to 8mg/kg and 42 patients in dose expansion at dose of 6mg/kg.

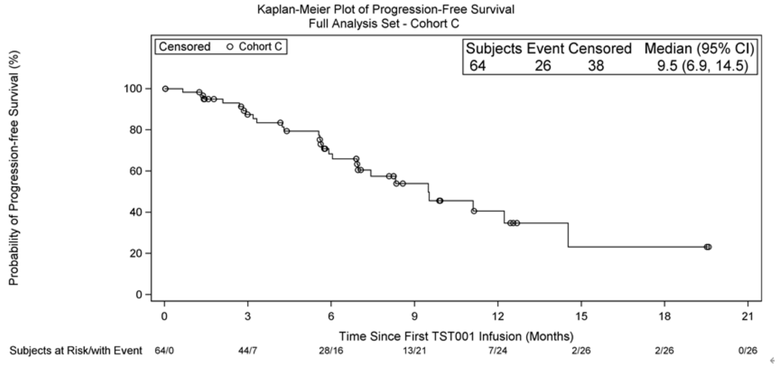
•Out of 34 responders from all dose groups in Cohort C, 14 had progression disease or death and the estimated median duration of response was 9.9 months.

Figure 4.Duration of Response – Cohort C



- As of cutoff date, 26 out of 64 patients had progression disease or death, with an estimated median progression-free survival 9.5 months (Figure 5).

Figure 5. Progression-Free Survival – Cohort C ITT



FUTURE DIRECTIONS FOR RESEARCH

- The safety profile of TST001 is mainly characterized by manageable on target, off tumor side effects; Most of these AEs are of grade 1 or 2.
- The addition of TST001 to CAPOX for first-line treatment of CLDN18.2 expressing (≥10%, ≥1+) patients with G/GEJ cancer leads to improved efficacy outcomes as compared to historical controls, with no obvious trend to lower efficacy with lower levels of expression.
- More detailed efficacy results of TST001 by CLDN18.2 expression will be published at upcoming meeting.

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