1524P First-line TST001 plus Capecitabine and Oxaliplatin (CAPOX) for Advanced G/GEJ Cancer with CLDN18.2 Positive – Update Efficacy Data from Study TranStar102-Cohort C

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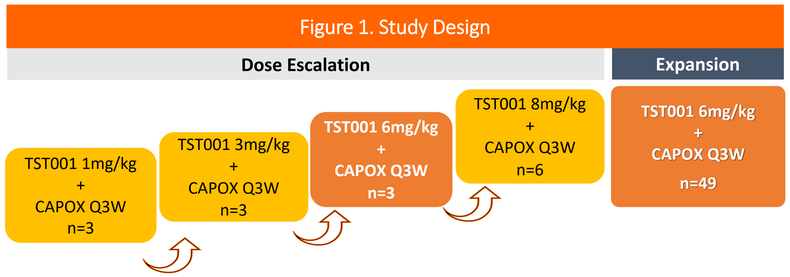
BACKGROUND

- Phase 3 studies (SPOTLIGHT and GLOW) showed that combining anti-CLDN18.2 antibody with chemotherapy significantly improved PFS and OS as first-line treatment for G/GEJ (gastric/gastroesophageal junction) cancer with CLDN18.2 expression above 75%, 2/3+ per Astellas CDx (~38% of all G/GEJ cancer patients).
- TST001 (osemitamab) is a potential best-in-class antibody with improved CLDN18.2 affinity and enhanced ADCC effect, leading to anti-tumor activity in low to medium CLDN18.2 expression gastric cancer animal models.
- The preliminary efficacy of TST001 in combination with CAPOX in the patients with advanced G/GEJ cancer was reported previously in ASCO and ESMO-GI. Here we present the updated analysis in the patients from dose expansion phase who had received TST001 at 6mg/kg Q3W and CAPOX.

METHODS

- Cohort C from Transtar102 study (NCT04495296) was designed to explore the safety and efficacy of TST001 plus CAPOX as first-line treatment in advanced G/GEJ cancer (Figure 1). Positive CLDN18.2 expression (defined as membranous staining intensity ≥1+ in ≥10% of tumor cells) was required in the expansion phase and performed retrospectively in dose escalation and safety run-in phase using the IHC 14G11 LDT assay in a central laboratory. Patients with CLDN18.2 expression ≥10% ≥1+ represent approximately 55% of all the G/GEJ cancer patients.

Figure 1. Study Design



RESULTS

- As of Sep 7, 2023, a total of 64 patients had been dosed with TST001 plus CAPOX: 15 patients were dosed with TST001 at 1 to 8 mg/kg Q3W in the dose escalation and 49 patients at 6 mg/kg in the dose expansion. The median follow-up for the 49 patients was 11.3 months with the longest treatment duration over 1.5 years. The study is still ongoing.
- 41 out of these 49 patients in dose expansion phase had CLDN18.2 positive tumor (High: n=9, Medium: n=13, Low: n=19, per CLDN18.2 expression levels *), and the other 8 patients didn't have the biomarker tested (unknown CLDN18.2 expression).
- The baseline demographics of these 49 patients are similar to the overall population of the 64 patients in this cohort, which was presented previously *(J Clin Oncol 41, 2023 , suppl 16; abstr 4046)*.
- 81.6% patients had ECOG performance status of 1 and 34.7% patients had 3 or more metastatic lesions. More than half of patients had peritoneum metastasis, which is one of clinical factors predicting poor prognosis (Table 1).

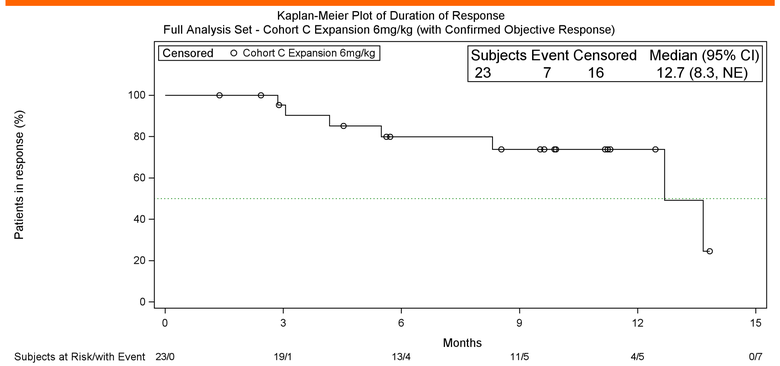
Table 1. Demographic and Baseline Characteristics

Parameter		Overall (N=49)
Age	Median	56.0
	Min, Max	21, 76
Sex, n(%)	Male	30(61.2)
	Female	19(38.8)
ECOG PS, n(%)	0	9(18.4)
	1	40(81.6)
Cancer Type, n(%)	GC	47(95.9)
	GEJ	2(4.1)
Gastrectomy, n(%)	None	28(57.1)
	Partial	10(20.4)
	Total	11(22.4)
Metastasis, n(%)	M0	2(4.1)
	M1	47(95.9)
No. of Metastasis sites, n(%)	0-2	31(63.3)
	>=3	17(34.7)
	Missing	1(2.0)
Sites of Metastasis, n(%)	Peritoneum	25(51.0)
	Hepatic	10(20.4)
	Pulmonary	8(16.3)
CLDN18.2 levels*, n(%)	High	9(18.4)
	Medium	13(26.5)
	Low	19(38.8)
	UK	8(16.3)
Measurable disease, n(%)	Yes	45(91.8)
	No	4(8.2)

* **High:** ≥70% tumor cells staining 2+ or 3+; **Medium**: ≥40% and ＜70% tumor cells staining 2+ or 3+; **Low**: ≥10% tumor cells staining ≥ 1+ and <40% 2+ or 3+ ; **UK**: unknow

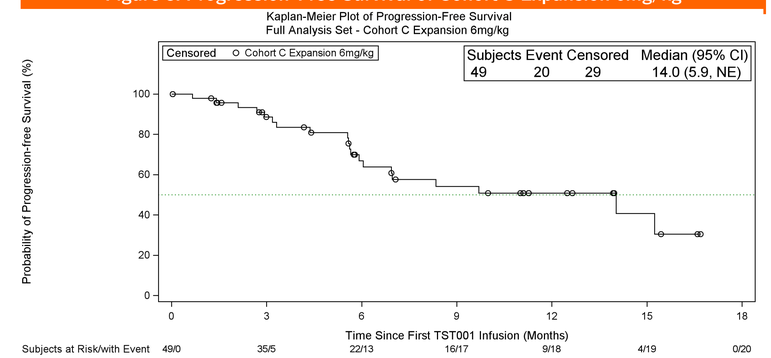
- The safety profile of these 49 patients are similar to the overall population of 64 patients in this cohort, which was presented previously (*J Clin Oncol 41, 2023 , suppl 16; abstr 4046*). It was mainly characterized by manageable on-target-off-tumor effects, including nausea, hypoalbuminaemia, and vomiting, most of them were grade 1 or 2 and occurred during the first 2 cycles.
- As of the cut-off date, among the 42 patients who had measurable lesions at baseline and at least one post-baseline tumor assessment, 28 achieved partial response, of which 23 (54.8%, 23/42) had been confirmed. The median duration of response (DoR) of these 23 responders was 12.7 months (Figure 2).

Figure 2. Duration of Response of Cohort C Expansion 6mg/kg



- As of the cut-off date, among the 49 patients, 20 patients had progression of disease or death, with an estimated median progression-free survival (PFS) of 14 months (Figure 3).

Figure 3. Progression-Free Survival of Cohort C Expansion 6mg/kg



- As of the cut-off date, the median OS was not reached because of the limited number of events, the 12-month survival rate for the overall population (64 patients) in this cohort was 88.9% (95% CI: 74.2, 95.4).

CONCLUSIONS

- TST001 plus CAPOX as first-line treatment in patients with G/GEJ cancer demonstrated good safety and tolerability.
- The addition of TST001 to CAPOX as first-line treatment in patients with CLDN18.2 expressing (defined as membranous staining intensity ≥1+ in ≥10% of tumor cells using IHC 14G11 LDT) G/GEJ cancer leads to encouraging and durable anti-tumor activities with longer DoR and PFS as compared to historical controls.
- The overall survival data is immature and requires further follow-up.

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