PD-7
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Osemitamab plus Capecitabine and Oxaliplatin (CAPOX) as the First-Line Treatment of Advanced G/GEJ Cancer -Updated Efficacy Data per Claudin 18.2 Expression Level from Study TranStar102/TST001-1002-Cohort C

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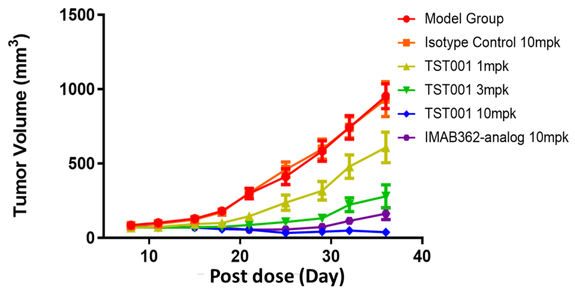
BACKGROUND

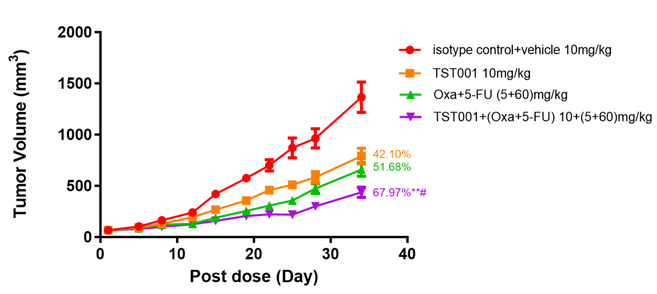
- Adding CLDN18.2 antibody to chemotherapy is a clinically validated approach to improve long term outcomes for patients with high CLDN18.2 expressing tumors (proved by GLOW and SPOTLIGHT).
- Osemitamab (TST001) is a potential best-in-class humanized antibody with high affinity for CLDN18.2 and enhanced ADCC (antibody-dependent cellular cytotoxicity), delivering potent anti-tumor activities in both low and high CLDN18.2 expressing tumors.
- Osemitamab monotherapy has stronger tumor growth inhibition effect than the zolbetuximab (IMAB362)-analog at the same dose, regardless of CLDN18.2 expression levels.
- Preclinical studies showed that TST001 plus chemotherapy had better inhibitory effects on tumor growth than chemotherapy.

Figure 1. In Vivo Anti-Tumor Activity of TST001 Monotherapy or Combination Therapy in Different CLDN18.2 Expressing Tumor Models

A: Tumor growth inhibition of TST001 monotherapy vs. IMAB362-analog in MKN45/hCLDN18.2 Tumor Model（CLDN18.2 expression IHC 2+, TC 40-50%）



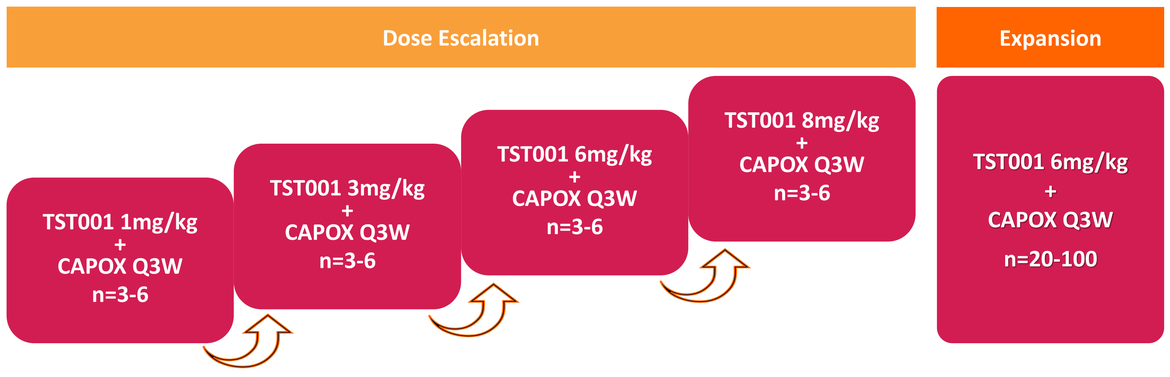
B. Efficacy of TST001+Oxaliplatin+5-FU in PDX GC-02-0004 mouse tumor models (CLDN18.2 expression IHC 2+, TC 40-70%)



METHODS

- The efficacy and safety of osemitamab plus CAPOX as first-line treatment with advanced G/GEJ cancer was explored in a dose escalation and expansion phase 1/2 study in China (Cohort C, NCT04495296). In the expansion phase (except 8 patients from a safety run-in), CLDN18.2 positive was required, which is defined as IHC membrane staining intensity ≥1+ in ≥10% tumor cells per LDT assay, selecting approximately 55% of the screened patients.

Figure 2. Study Design



RESULTS

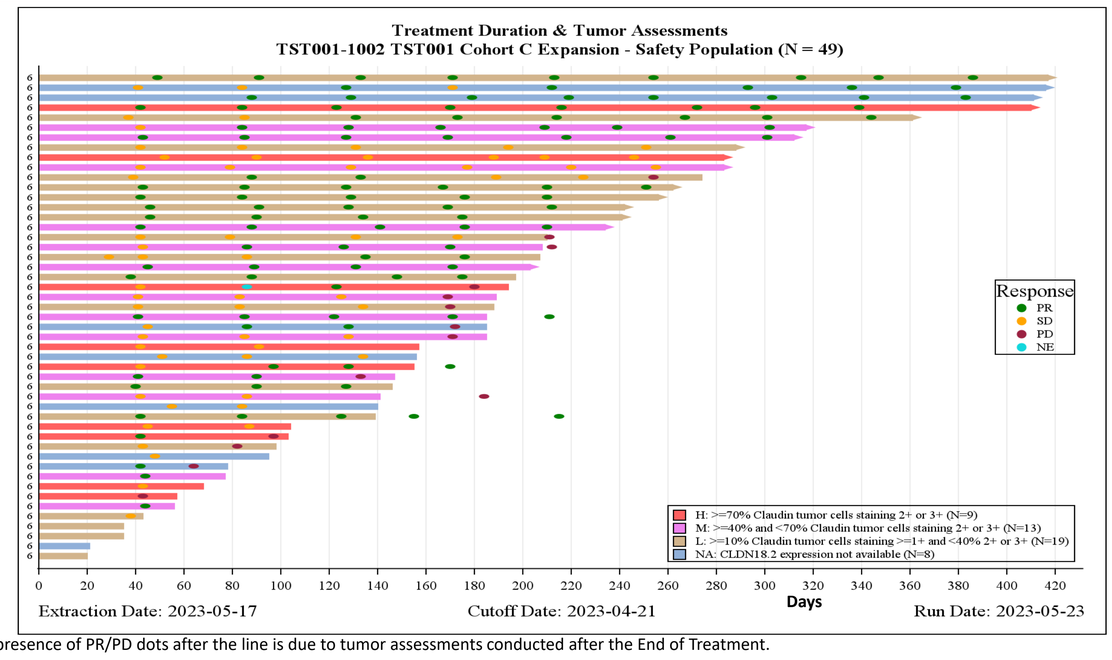
- As of Apr. 21, 2023, a total of 64 patients were dosed with osemitamab in combination with CAPOX, 15 patients received osemitamab at doses ranging from 1 to 8 mg/kg Q3W in the dose escalation and 49 patients at 6 mg/kg in the dose expansion. The median follow-up was 195 days.
- 41 out of 49 patients in the dose expansion at 6mg/kg had CLDN18.2 positive tumor (see below for definitions, High: n=9, Medium: n=13, Low: n=19), 8 patients didn't get their tumor tested (unknown CLDN18.2 expression). The baseline demographics of this dose expansion are similar to the overall population published on 2023 ASCO (abstract 4046*) and there are no clinically significant differences in baseline characteristics across different CLDN18.2 expression levels.
- The safety profile of osemitamab is mainly characterized by manageable on-target off-tumor effects and has been presented during 2023 ASCO (abstract 4046*). Most of these AEs are of grade 1 or 2 and occurring during the first 2 cycles.
- As of April 21, 2023, among the 49 patients at 6mg/kg from dose expansion, 42 patients had measurable lesions and at least one post treatment tumor assessment, 28 (66.7%) achieved partial response. Best overall response assessment by CLDN18.2 expressions levels at 6mg/kg in the dose expansion are presented in Table 1. The response rate appears similar regardless of the CLDN18.2 expression levels.

Table 1: Best Overall Response of Patient at Dose of 6mg/kg in Expansion Cohort

	CLDN18.2 High-Medium#	CLDN18.2 Low#	CLDN18.2 Unknown	Overall (N=49)
Patient dosed at 6mg/kg, n (%)	**22**	**19**	**8**	**49**
Subjects with measurable lesions at baseline	22	19	4	45
Subjects with measurable lesions at baseline and at least one post-baseline tumor evaluation	22	16	4	42
Best Overall Response, n (%)				
CR	0	0	0	0
PR	13 (59.1)	11 (68.8)	4 (100)	28 (66.7)
Confirmed PR	9 (41)	11 (68.8)	3 (75)	23 (54.8)
SD	8 (36.4)	5 (31.2)	0	13 (31)
PD	1 (4.5)	0	0	1 (2.4)

 # 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+

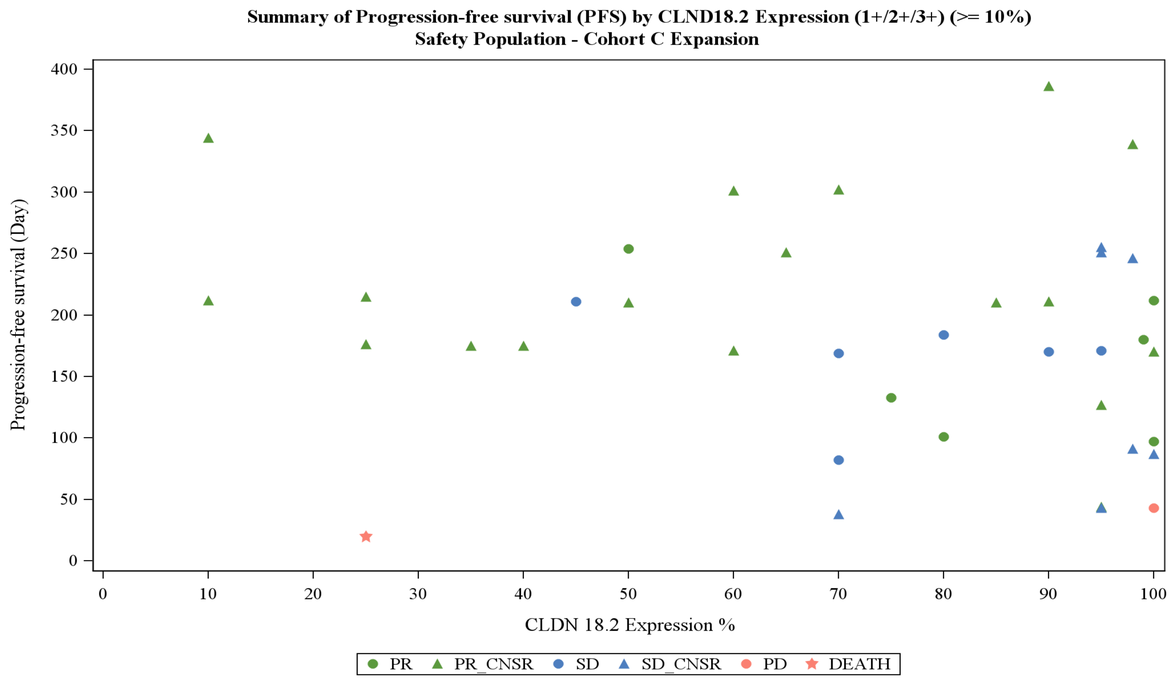
Figure 3. Treatment Duration and Tumor Assessments– Cohort C, 6mg/kg in Dose Expansion



The presence of PR/PD dots after the line is due to tumor assessments conducted after the End of Treatment.

- As of the cut-off date, there is no clear trend between progression-free survival and the total (1+/2+/3+ combined) CLDN18.2 expression levels (Figure 4). The same trend was observed whether CLDN18.2 expression was assessed by 2+/3+ combined or 3+ only (data not shown).

Figure 4. Summary of PFS by CLDN18.2 Expression (1+/2+/3+)(≥10%)-Expansion Population

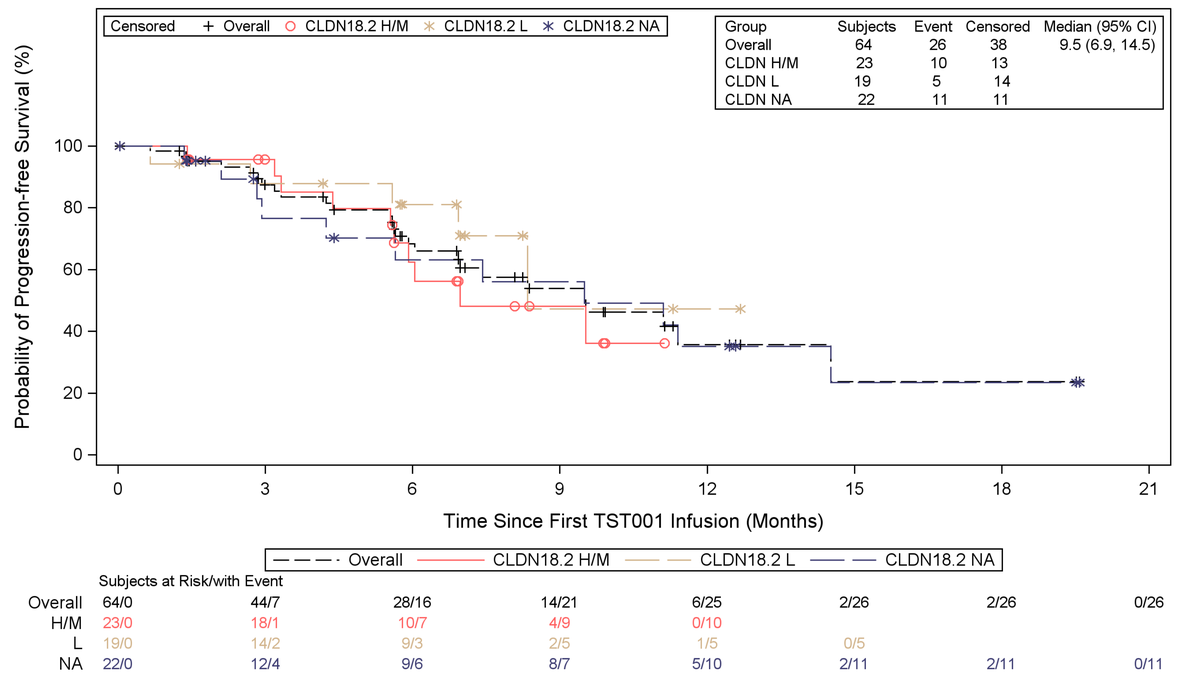


* Claudin 18.2 expression is sum of percentages of 1+/2+/3+.
* The PFS are presented by BOR (Best Overall Response) if having post-baseline tumor assessment(s), or Death if subject died before first tumor assessment.

CNSR: Censor. If a patient didn't experience PFS event by cut-off date, one was censored at the last tumor assessment date.
Population: patients at dose of 6mg/kg in dose expansion and had PFS survival longer than 1 days.

- As of cut-off date, 26 out of 64 patients had progression disease or death, with an estimated median progression-free survival (PFS) 9.5 months, median PFS stratified according to CLDN18.2 was immature and need long term follow-up (Figure 5).

Figure 5. Progression-Free Survival – Safety Population (all doses, including 49 patients from the expansion at 6mg/kg)



CONCLUSION

- Osemitamab plus CAPOX as first-line treatment for patients with G/GEJ cancer demonstrated good safety and tolerability.
- Encouraging and durable anti-tumor activities also have been observed regardless of the CLDN18.2 expression levels above 10%, 1+ per central LDT assay.
- Osemitamab potentially provides benefit for CLDN18.2 low to medium expression patients, in addition to the CLDN18.2 high expression patients, and therefore osemitamab may provide benefit for a broader patient population.

***Lin Shen et al.** Osemitamab 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).J Clin Oncol 41, 2023 (suppl 16; abstr 4046)

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