1419P Osemitamab (TST001) plus Nivolumab and CAPOX as the First-line Therapy for the Patients with Advanced G/GEJ Cancer (TranStar102)

Lin Shen[1], Zengqing Guo[2], Jingdong Zhang[3], Weijian Guo[4], Meili Sun[5], Nong Xu[6], Chuan Qi[7], Xuelian Zhu[7], Lijuan Zhang[7], Li Xu[8], Caroline Germa[8].
1. Peking University Cancer Hospital; 2. Fujian Cancer Hospital; 3. Liaoning Cancer Hospital; 4. Fudan University Shanghai Cancer Center; 5. Jinan Central Hospital Affiliated to Shandong University ; 6. The First Affiliated Hospital of Medical School of Zhejiang University; 7. Suzhou Transcenta Therapeutics Co, Ltd. 8. Transcenta Therapeutics, Inc.

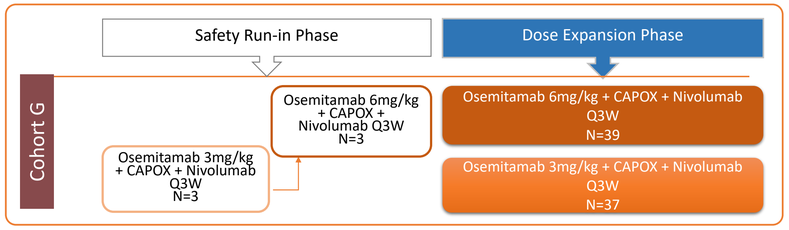
BACKGROUND

- Osemitamab , a humanized monoclonal antibody with improved affinity to claudin (CLDN) 18.2 and enhanced antibody-dependent cell-mediated cytotoxicity, has demonstrated great synergistic effect with anti-PD-1 antibody and chemotherapy in pre-clinical research.
- As checkpoint inhibitor plus chemotherapy is the current standard of care (SOC), we explored the combination of CLDN18.2 antibody osemitamab with this SOC in CLDN18.2 positive 1L G/GEJ (gastric/gastroesophageal junction) cancer.

METHODS

- Cohort G from Transtar102 study (NCT04495296) was designed to explore the safety and efficacy of osemitamab plus CAPOX and nivolumab as first-line treatment for advanced G/GEJ cancer (Figure 1), with a safety lead-in and expansion phase. Patients were alternately allocated to 3 or 6mg/kg at expansion phase. Eligible patients include HER2 negative or unknown, unresectable locally advanced or metastatic G/GEJ cancer, regardless of CLDN18.2 or PD-L1 expression. CLDN18.2 and PD-L1 status were analyzed retrospectively using IHC 14G11 LDT assay and PD-L1 IHC 28-8 pharmDx at a central laboratory. The CLDN18.2 expression was divided into three subgroups: H/M (high/medium), L (low) and R (rest) according to the tumor cells showing membranous CLDN18.2 staining per CLDN18.2 IHC 14G11 LDT assay.
- Comparisons were made across the subsets by CLDN18.2 expression level as an alternative approach to estimate the possible effect size due to lack of “real” control.

Figure 1. Study Design



RESULTS

- As of Jul 17, 2024, a total of 82 patients had been dosed with TST001 plus CAPOX and nivolumab (40 at 3 mg/kg, 42 at 6mg/kg) with median follow-up 15.2 months. Of the 82 patients, 32 were with CLDN18.2 H/M expression, 22 with L expression, and 28 were in the Rest subgroup with CLDN18.2 expression lower than L (n=7), negative (n=19) or unknown (n=2). 66 patients had PD-L1 test results, and 56 were CPS< 5.
- All patients experienced treatment-related adverse events (TRAE). The most common TRAEs were hypoalbuminaemia, nausea and vomiting, most of them were of CTC AE grade 1 or 2 and manageable. The safety profile was similar to TST001 in combination with CAPOX which was presented previously (*J Clin Oncol 41, 2023 , suppl 16; abstr 4046*). The administration of the backbone therapy wasn’t compromised by the addition of osemitamab (data not shown).

Table 1. Demographic and Baseline Characteristics

		CLDN18.2 H/M (N=32)	CLDN18.2 L (N=22)	CLDN18.2 R (N=28)	Overall (N=82)
Age at Consent (years)	Median	56.5	62.5	60	58.5
	Min, Max	27, 72	41, 76	45, 71	27, 76
Sex, n (%)	Male	21 (65.6)	17 (77.3)	23 (82.1)	61 (74.4)
ECOG Status, n (%)	0	4 (12.5)	6 (27.3)	7 (25.0)	17 (20.7)
	1	28 (87.5)	16 (72.7)	21 (75.0)	65 (79.3)
Cancer Type, n (%)	Gastric Cancer	31 (96.9)	18 (81.8)	24 (85.7)	73 (89.0)
	GEJ Cancer	1 (3.1)	4 (18.2)	4 (14.3)	9 (11.0)
Gastrectomy, n (%)	None	25 (78.1)	16 (72.7)	13 (46.4)	54 (65.9)
	Partial or total	5 (15.6)	6 (27.3)	14 (50.0)	25 (30.5)
	Other	2 (6.3)	0	1 (3.6)	3 (3.7)
PD-L1 CPS-Central Result, n (%)	< 5	22 (68.8)	16 (72.7)	18 (64.3)	56 (68.3)
	≥5	4 (12.5)	3 (13.6)	3 (10.7)	10 (12.2)
	Missing	6 (18.8)	3 (13.6)	7 (25.0)	16 (19.5)
Metastasis status at study entry, n (%)	M0	1 (3.1)	1 (4.5)	0	2 (2.4)
	M1	31 (96.9)	21 (95.5)	28 (100)	80 (97.6)
No. of Metastasis sites, n (%)	0-2	22 (68.8)	16 (72.7)	19 (67.9)	57 (69.5)
	≥3	9 (28.1)	5 (22.7)	9 (32.1)	23 (28.0)
	Missing	1 (3.1)	1 (4.5)	0	2 (2.4)
Sites of Metastasis, n (%)	Hepatic	10 (31.3)	9 (40.9)	18 (64.3)	37 (45.1)
	Peritoneum	12 (37.5)	3 (13.6)	3 (10.7)	18 (22.0)
	Pulmonary	2 (6.3)	5 (22.7)	7 (25.0)	14 (17.1)

Table 2. Adverse Events in Safety Analysis Set

	TEAE, incidence ≥20%, regardless of grade		TRAE	
By Preferred Term	All Grade	Grade≥3	All Grade	Grade≥3
Subjects with at least one adverse event	82 (100)	56 (68.3)	82 (100)	44 (53.7)
Nausea	56 (68.3)	3 (3.7)	55 (67.1)	3 (3.7)
Vomiting	49 (59.8)	2 (2.4)	49 (59.8)	2 (2.4)
Constipation	18 (22.0)	0	5 (6.1)	0
Diarrhoea	20 (24.4)	4 (4.9)	13 (15.9)	2 (2.4)
Hypoalbuminaemia/Hypoproteinaemia	65 (79.3)	0	57 (69.5)	0
Hyponatraemia	38 (46.3)	3 (3.7)	26 (31.7)	2 (2.4)
Decreased appetite	38 (46.3)	4 (4.9)	37 (45.1)	4 (4.9)
Hypokalaemia	28 (34.1)	11 (13.4)	19 (23.2)	8 (9.8)
Hypocalcaemia	17 (20.7)	1 (1.2)	7 (8.5)	0
Hyperglycaemia	17 (20.7)	0	7 (8.5)	0
Aspartate aminotransferase increased	51 (62.2)	4 (4.9)	38 (46.3)	3 (3.7)
Neutrophil count decreased	52 (63.4)	16 (19.5)	36 (43.9)	10 (12.2)
Platelet count decreased	49 (59.8)	10 (12.2)	38 (46.3)	8 (9.8)
White blood cell count decreased	40 (48.8)	3 (3.7)	27 (32.9)	1 (1.2)
Weight decreased	41 (50.0)	3 (3.7)	34 (41.5)	2 (2.4)
Alanine aminotransferase increased	31 (37.8)	3 (3.7)	19 (23.2)	3 (3.7)
Lipase increased	25 (30.5)	5 (6.1)	21 (25.6)	4 (4.9)
Lymphocyte count decreased	17 (20.7)	5 (6.1)	13 (15.9)	3 (3.7)
Amylase increased	19 (23.2)	1 (1.2)	16 (19.5)	1 (1.2)
Anaemia	57 (69.5)	8 (9.8)	35 (42.7)	4 (4.9)
Proteinuria	22 (26.8)	0	17 (20.7)	0

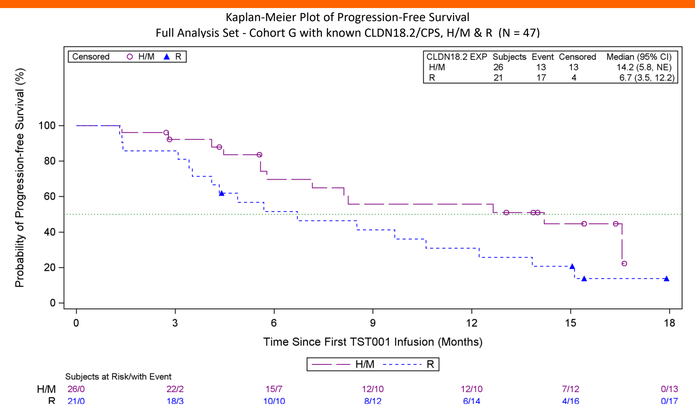
- Here we reported the exploratory analysis of the subgroup efficacy of patients with H/M CLDN18.2 expression group in overall (n=32) and in subgroup with PD-L1 CPS<5 (n=22). (Table 3).

Table 3. Tumor Response and Durable Anti-tumor Effect

	Overall#			Overall with/ known CLDN18.2 / PD-L1			PD-L1 CPS<5		
	H/M N=32	L N=22	R N=28	H/M N=26	L N=19	R N=21	H/M N=22	L N=16	R N=18
ORR* (confirmed)	58.1%	52.4%	55.6%	68.0%	61.1%	50.0%	71.4%	60.0%	47.1%
mPFS	12.6 m (95% CI: 5.8-16.6)	7.1 m (95% CI: 4.2-8.8)	8.5 m (95% CI: 4.3-12.2)	14.2m (95% CI: 5.8-NE)	8.5 m (95% CI: 4.2-NE)	6.7m (95% CI: 3.5-12.2)	16.6 m (95% CI: 5.6-NE)	7.1 m (95% CI: 4.2-NE)	5.7 m (95% CI: 3.5-13.8)

- *In patients with measurable disease at baseline; # including patients with unknown CLDN18.2 or PD-L1.
- Note: The Rest (“control arm”) all patients outperformed significantly low CLDN18.2 expression subgroup in overall probably because more PDL1 unknown patients (25%) from “Rest”.

Figure 2. Progression-Free Survival of Cohort G for the Patients, by CLDN18.2



Overall with known CLDN18.2/PD-L1 (N=66) PFS	Hazard Ratio (HR) point estimate	95% CIs for HR	
CLDN 18.2 (H/M vs R), R as reference	0.505	0.244	1.045

- 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 (82 patients) in this cohort was 73.8% (95% CI: 62.0-82.4%).

CONCLUSION

- Updated data indicated that the combination of osemitamab plus nivolumab and CAPOX as first-line treatment for patients with G/GEJ cancer was safe and well tolerated.
- The addition of osemitamab to CAPOX and nivolumab as first-line treatment for patients with advanced or metastatic G/GEJ cancer leads to encouraging and durable anti-tumor activities, especially for patients with high/medium CLDN18.2 expression regardless of PD-L1 CPS when cross comparing to historical controls.

The study sponsored by Suzhou Transcenta Therapeutics Co, Ltd.
E-mail address:linshenpku@163.com
The first author is the scientific advisor of Suzhou Transcenta Therapeutics Co, Ltd.