# First-line Osemitamab (TST001) plus Nivolumab and CAPOX for Advanced G/GEJ Cancer (TranStar102) - Results of Cohort G from a Phase I/IIa Study

Xiaotian Zhang[1], Zengqing Guo[2], Jingdong Zhang[3], Weijian Guo[4], Meili Sun[5], Nong Xu[6], Charlie Qi[7], Xuelian Zhu[7], Lijuan Zhang[7], Xueming Qian[7], Caroline Germa[8], Lin Shen[1]
1. Peking University Cancer Hospital; 2. Fujian Cancer Hospital; 3. Liaoning Cancer Hospital; 4. Fudan University Shanghai Cancer Center; 5. Jinan Central Hospital; 6. Affiliated Hospital Zhejiang University; 7. Suzhou Transcenta Therapeutics Co, Ltd.; 8. Transcenta Therapeutics, INC. USA.
E-mail: zhangxiaotian@bjmu.edu.cn

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**Abstract 4048**

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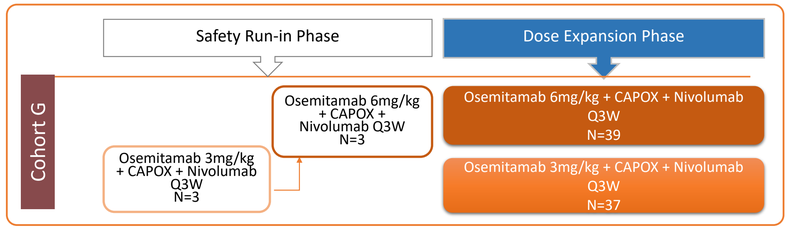
## BACKGROUND

- Osemitamab (TST001) is a potential best-in-class antibody with improved claudin 18.2 (CLDN18.2) affinity and enhanced antibody-dependent cell-mediated cytotoxicity effect, leading to anti-tumor activity in CLDN18.2 positive gastric cancer animal models, including those with low to medium levels of expression.
- Animal models have demonstrated strong synergistic anti-cancer activities among osemitamab, anti-PD-1 antibodies and chemotherapies, regardless of the PD-L1 CPS levels.
- Promising efficacy of osemitamab plus CAPOX chemotherapy as first-line treatment for G/GEJ cancer has been observed in cohort C of TranStar102, which was reported previously at ASCO and ESMO-GI.

## 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 alternatively 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 Claudin 18.2 IHC 14G11 LDT assay.
- Comparisons were made across the subsets by CLDN18.2 expression levels as an alternative approach to estimate the possible effect size due to lack of “real” control.

### Figure 1. Study Design




## RESULTS

- As of April 18, 2024, 82 patients have been dosed with a median follow-up of 12.6 months, 40 patients at 3mg/kg, 42 patients at 6mg/kg. The study is still ongoing.
- 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.
- The baseline demographics of patients across CLDN18.2 expression are generally similar (Table 1).
- The safety profile of the triplet is generally consistent with the safety data of osemitamab plus CAPOX combination in first-line G/GEJ cancer patients presented previously (*J Clin Oncol 41, 2023 , suppl 16; abstr 4046*), which was mainly characterized by manageable on-target-off-tumor effects, including nausea, hypoalbuminaemia, and vomiting, and most of them were of grade 1 or 2 (Table 2).

### 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 | 27 (84.4) | 16 (72.7) | 21 (75.0) | 64 (78.0) |
| | Missing | 1 (3.1) | 0 | 0 | 1 (1.2) |
| 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) | 14 (50.0) | 55 (67.1) |
| | Partial or total | 5 (15.6) | 6(27.3) | 13(46.4) | 24 (29.3) |
| | 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 | 2 (6.3) | 1 (4.5) | 0 | 3 (3.7) |
| | M1 | 30 (93.8) | 21 (95.5) | 28 ( 100) | 79 (96.3) |
| No. of Metastasis sites, n (%) | 0-2 | 21 (65.6) | 15 (68.2) | 19 (67.9) | 55 (67.1) |
| | ≥3 | 9 (28.1) | 6 (27.3) | 9 (32.1) | 24 (29.3) |
| | Missing | 2 (6.3) | 1 (4.5) | 0 | 3 (3.7) |
| Sites of Metastasis, n (%) | Hepatic | 10 (31.3) | 9 ( 40.9) | 18 ( 64.3) | 37 (45.1) |
| | Peritoneum | 10 (31.3) | 3 ( 13.6) | 3 ( 10.7) | 16 (19.5) |
| | Pulmonary | 2 (6.3) | 5 ( 22.7) | 7 ( 25.0) | 14 (17.1) |

### Table 2. Adverse Events in Safety Analysis Set

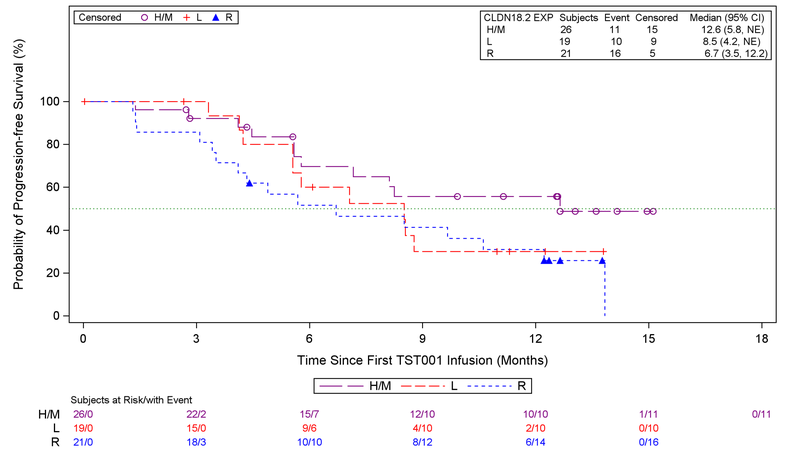
| | TEAE, incidence ≥20%, regardless of grade | | TRAE | |
|---|---|---|---|---|
| By Preferred Term | All Grade | Grade≥3 | All Grade | Grade≥3 |
| Subjects with at least one adverse event | 82 (100) | 56 (68.3) | 82 (100) | 43 (52.4) |
| Nausea | 56 (68.3) | 3 (3.7) | 55 (67.1) | 3 (3.7) |
| Vomiting | 49 (59.8) | 2 (2.4) | 49 (59.8) | 2 (2.4) |
| Diarrhoea | 20 (24.4) | 4 (4.9) | 13 (15.9) | 2 (2.4) |
| Hypoalbuminaemia/Hypoproteinaemia | 64 (78.0) | 0 | 56 (68.3) | 0 |
| Hyponatraemia | 37 (45.1) | 2 (2.4) | 25 (30.5) | 1 (1.2) |
| Decreased appetite | 36 (43.9) | 4 (4.9) | 35 (42.7) | 4 (4.9) |
| Hypokalaemia | 28 (34.1) | 10 (12.2) | 18 (22.0) | 7 (8.5) |
| Hypocalcaemia | 18 (22.0) | 1 (1.2) | 9 (11.0) | 0 |
| Hyperglycaemia | 17 (20.7) | 0 | 7 (8.5) | 0 |
| Aspartate aminotransferase increased | 49 (59.8) | 4 (4.9) | 36 (43.9) | 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 | 39 (47.6) | 3 (3.7) | 26 (31.7) | 1 (1.2) |
| Weight decreased | 40 (48.8) | 3 (3.7) | 33 (40.2) | 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) | 22 (26.8) | 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) | 36 (43.9) | 4 (4.9) |
| Proteinuria | 22 (26.8) | 0 | 18 (22.0) | 0 |

- Here we report the efficacy data in the 66 patients with known PD-L1 & CLDN18.2 expression status. As of the cut-off date, 37 patients had progression disease or death. There was a clear trend between anti-tumor efficacy and CLDN18.2 expression, with a median progression-free survival of 12.6 months for the patients with H/M expression. The mPFS was 12.6 months in the patients with H/M CLDN18.2 and PD-L1 CPS<5 (n=22) .

### Table 3. Tumor Response and Durable Anti-tumor Effect

| PD-L1 CPS & CLDN18.2 Status Known N=66 | H/M N=26 | L N=19 | R N=21 |
|---|---|---|---|
| ORR (confirmed) | 68.0% | 61.1% | 50.0% |
| mPFS | 12.6m (95% CI: 5.8, NE) | 8.5m (95% CI: 4.2, NE) | 6.7m (95% CI: 3.5, 12.2) |

### Figure 2. Progression-Free Survival of Cohort G by CLDN18.2 level




| Overall (N=66) PFS | Hazard Ratio (HR) point estimate | 95% CIs for HR | |
|---|---|---|---|
| CLDN 18.2 (H/M vs R), R as reference | 0.443 | 0.205 | 0.958 |
| CLDN 18.2 (H/M /L vs R), R as reference | 0.560 | 0.292 | 1.074 |

## CONCLUSION

- The combination of osemitamab plus CAPOX and nivolumab as first-line treatment for patients with G/GEJ cancer is safe and well tolerated. The triple combination didn’t increase the safety risk compared with osemitamab combination with CAPOX.
- Preliminary efficacy data indicate that the combination of osemitamab plus CAPOX and nivolumab as first-line treatment for patients with G/GEJ cancer had very encouraging anti-tumor activities regardless of PD-L1 expression, especially for the patients with H/M CLDN18.2 expression compared with the historical data of existing or emerging therapies.