# Efficacy and safety of LM-108, an anti-CCR8 monoclonal antibody, in combination with an anti-PD-1 antibody in patients with gastric cancer: Results from phase 1/2 studies

Jifang Gong, Chang Liu, Jun Yao, Junli Xue, Jing Dai, Yinghua Ji, Ben Markman, Alison Hiong, Xiuli Yang, Rusen Zhao, Yi Zheng, Qingshan Li, Jun Wu, Minal A. Barve, Mihitha Hashara Ariyapperuma, Gary Edward Richardson, Xia Qin, Crystal Ying Qin, Lin Shen

## Background

Targeting tumour-infiltrating regulatory T cells (Tregs) is a potential approach to overcome immunotherapy resistance in the treatment of cancers. LM-108 is a novel Fc-optimized, anti-CCR8 monoclonal antibody that selectively depletes tumour-infiltrating Tregs. Here we report a pooled analysis of results from 3 phase 1/2 studies (NCT05199753; NCT05255484; NCT05518045) to evaluate the efficacy and safety of LM-108 in combination with anti-PD-1 therapy in patients with gastric cancer.

## Aim

Primary objective: • To assess the safety and tolerability, obtain the recommended phase 2 dose (RP2D)/optimal biologic dose (OBD) and/or Maximum Tolerated Dose (MTD) for LM-108 as a single agent or in combination with an anti-PD-1 antibody in subjects with advanced solid tumours. Secondary objectives: • To assess the pharmacokinetic (PK) characteristics of LM-108 as a single agent or in combination with an anti-PD-1 antibody. • To assess the immunogenicity of LM-108. • To assess preliminary anti-tumour activity of LM-108 as a single agent or in combination with an anti-PD-1 antibody in subjects with advanced solid tumours. Exploratory objective: • To assess potential biomarkers for the anti-tumour activity of LM-108 as a single agent or in combination with an anti-PD-1 antibody.

## Method

Eligible patients with gastric cancer treated with LM-108 in combination with an anti-PD-1 antibody were included in the analysis. Patients received intravenous LM-108 at dose levels of 3 mg/kg Q2W, 6 mg/kg Q3W, or 10 mg/kg Q3W plus an anti-PD-1 antibody (intravenous pembrolizumab 200 mg Q3W or 400 mg Q6W or toripalimab 240 mg Q3W). The primary endpoint was investigator-assessed ORR per RECIST v1.1. The secondary endpoints included safety, other efficacy outcomes, and biomarkers analysis. Data cut-off date for the pooled analysis was December 25, 2023.

## Results

Forty-eight patients with gastric cancer (median age: 60.5 years; male: 72.9%) from China, USA, and Australia were treated ≥ 1 dose of LM-108 in combination with pembrolizumab or toripalimab. Most (n = 47, 97.9%) patients had received at least 1 prior anticancer treatment, and 43 (89.6%) had received prior anti-PD-1 therapy. Treatment-related adverse events (TRAEs) occurred in 39 (81.3%) patients, in which the most common events (≥15%) were alanine transaminase increased (25.0%), aspartate transaminase increased (22.9%), white blood cell decreased (22.9%), anaemia (16.7%). Grade ≥ 3 TRAEs occurred in 18 (37.5%) patients, the most common events (≥ 4%) were aanemia (8.3%), lipase increased (4.2%), rash (4.2%), and lymphocyte count decreased (4.2%). Among 36 efficacy-evaluable patients across all regimens, ORR was 36.1% (95% CI 20.8%–53.8%) and DCR was 72.2% (95% CI 54.8%–85.8%). The median PFS was 6.53 months (95% CI 2.96–NA). Among 11 patients whose disease had progressed on first-line treatment, ORR was 63.6% (95% CI 30.8%–89.1%) and DCR was 81.8% (95% CI 48.2%–97.7%). Of the 11 patients who progressed on first-line treatment, 8 had high CCR8 expression. Among these 8 patients, ORR was 87.5% and DCR was 100%, with 1 CR, 6 PR, and 1 SD observed.

## Conclusion

LM-108 in combination with an anti-PD-1 antibody showed promising antitumor activity in patients with gastric cancer that was resistance to anti-PD-1 therapy. The combination therapy was well tolerated. These results support further evaluation of LM-108 in CCR8 positive gastric cancer.

## References

Journal of Clinical Oncology
Volume 42, Number 16_suppl
https://doi.org/10.1200/JCO.2024.42.16_suppl.2504