Phase 2 ILUSTRO trial of 1L zolbetuximab plus mFOLFOX6 and nivolumab in patients with CLDN18.2+ locally advanced (LA) unresectable or metastatic gastric or gastroesophageal junction (mG/GEJ) adenocarcinoma

Kohei Shitara, Hirokazu Shoji, Nicola Fazio, Sara Lonardi, Keun-Wook Lee, Li-Yuan Bai, Kensei Yamaguchi, Jean-Philippe Metges, Gianluca Masi, Denis Smith, Tae-Yong Kim, Maria Matsangou, Archita Shrivastava, Miaomai Zhou, Aziz Zaanan, Samuel J. Klempner

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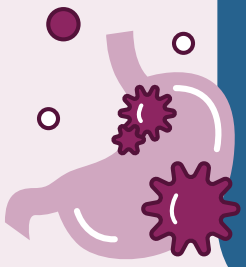


Key Summary

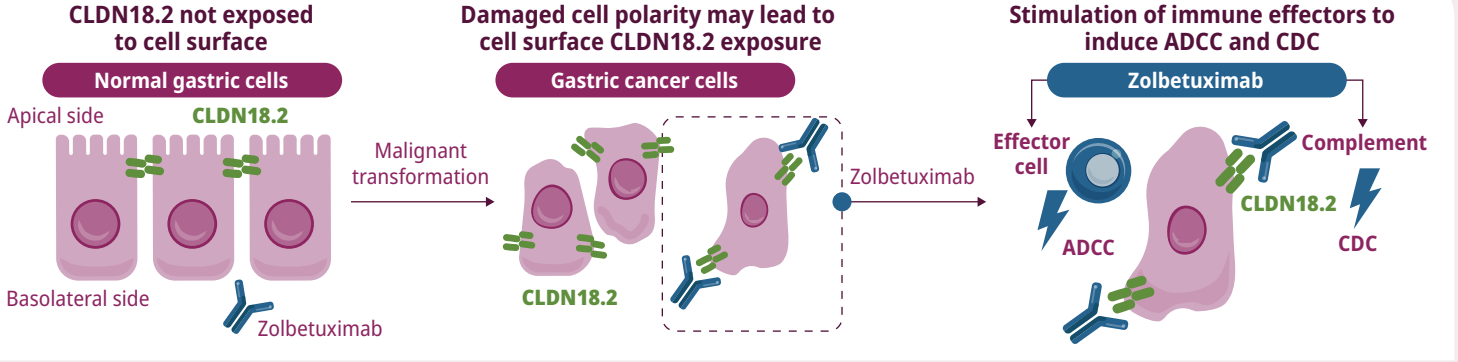
The triplet therapeutic combination of zolbetuximab + chemotherapy + immunotherapy showed promising antitumor activity and improved survival for patients with HER2-, LA unresectable or mG/GEJ adenocarcinoma whose tumors were CLDN18.2+

Unmet need:

Patients with LA mG/GEJ adenocarcinoma have a poor prognosis: survival in clinical trials of chemotherapy in Western countries has historically been < 1 year. While checkpoint inhibitors plus chemotherapy have improved outcomes, new treatment approaches targeting other biomarkers are needed[1,2]

Proposed mechanism of action of zolbetuximab:

CLDN18.2 is a tight junction protein targeted by zolbetuximab, a first-in-class monoclonal antibody[3-7]



ILUSTRO trial overview:

The ILUSTRO trial evaluated first-line triplet therapy of zolbetuximab plus mFOLFOX6 and nivolumab in patients with previously untreated LA unresectable or mG/GEJ adenocarcinoma whose tumors were HER2– and CLDN18.2+[a]. Exploratory analyses were conducted between PD-L1 CPS

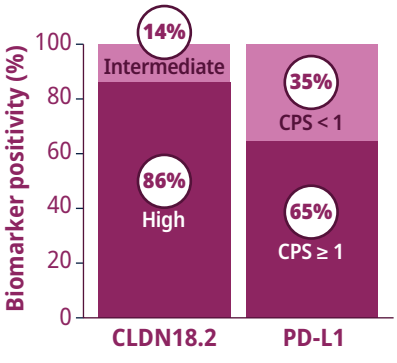
Cohort 4A: Safety lead-in phase (*n* = 12)[b]

Cycles 1–4	Cycles 5+
Zolbetuximab[b] + nivolumab 240 mg + mFOLFOX6 Q2W	Zolbetuximab 400 mg/m^2 + nivolumab 240 mg + 5-FU/FA[d] Q2W

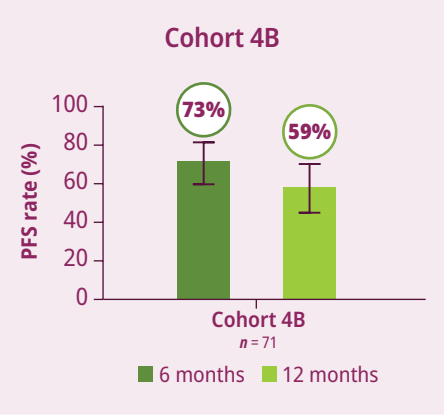
Cohort 4B: Expansion phase (*n* = 71)

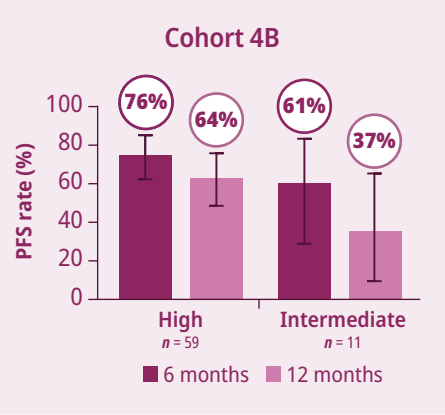
Cycles 1–4	Cycles 5+
Zolbetuximab 800/400[c] mg/m^2 + nivolumab 240 mg + mFOLFOX6 Q2W	Zolbetuximab 400 mg/m^2 + nivolumab 240 mg + 5-FU/FA[d] Q2W

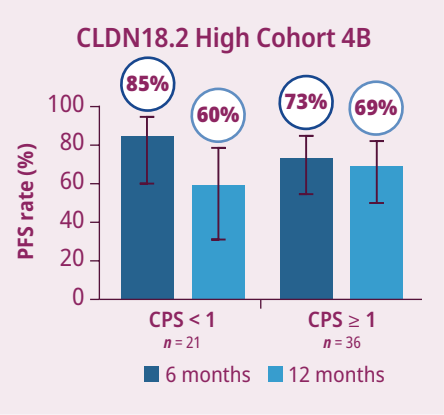
Tumor biomarker expression in Cohorts 4A + 4B



PFS results were most favorable in patients exhibiting high CLDN18.2 expression coupled with PD-L1 CPS ≥ 1

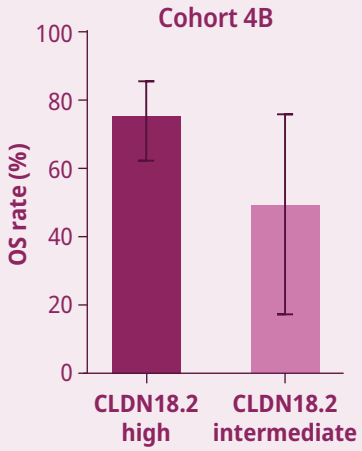






Preliminary analysis showed that overall survival at 12 months was greater in patients with high CLDN18.2 expression

versus those with intermediate CLDN18.2 expression

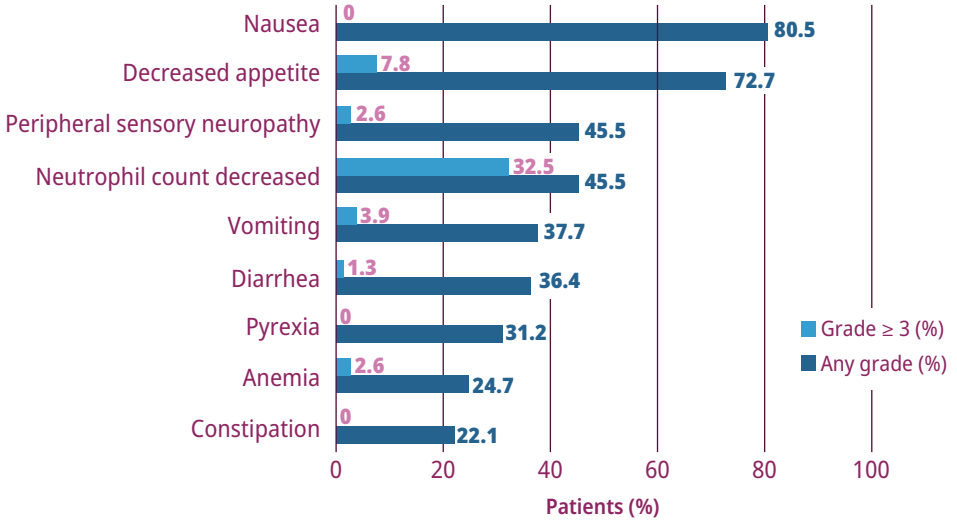


Median PFS in Cohort 4B was 14.8 months, and was 18.0 months in the CLDN18.2-high population

Triplet therapy including zolbetuximab demonstrated **an objective response rate of 62% in Cohort 4B**

Safety: The inclusion of zolbetuximab in the triplet regimen was well tolerated,

and side effects were consistent with each medication alone



[a] CLDN18.2 positivity was defined as moderate-to-strong membranous CLDN18 staining in ≥ 50% to < 75% of tumor cells (intermediate) and ≥ 75% of tumor cells (high); [b] The tolerability and safety of zolbetuximab + mFOLFOX6 + nivolumab were evaluated during a 2-week DLT assessment period; cycle 1 day 1 doses of zolbetuximab in Cohort 4A were 600 mg/m^2 (n = 6) or 800 mg/m^2 (n = 6), both followed by subsequent doses of 400 mg/m^2;
[c] 800 mg/m^2 at cycle 1 day 1 followed by subsequent doses of 400 mg/m^2; [d] At the discretion of the investigator.

References: 1. Lordick F, et al. *Ann Oncol*. 2022;33(10):1005-20; **2.** Sundar R, et al. *Lancet.* 2025;405:2087-102; **3.** Nakayama I, et al. *Nat Rev Clin Oncol*. 2024;21(5):354-69; **4.** Pellino A, et al. *J Pers Med*. 2021;11(11);1095; **5.** Sahin U, et al. *Clin Cancer Res*. 2008;14(23):7624-34; **6.** Sahin U, et al. *Eur J Cancer*. 2018;100:17-26; **7.** Tureci O, et al. *Ann Oncol*. 2019;30(9):1487-95.

Abbreviations: 5-FU/FA, fluorouracil/folinic acid; ADCC, antibody-dependent cellular cytotoxicity; CDC, complement-dependent cytotoxicity; CLDN18.2, claudin 18 isoform 2; CPS, combined positive score; DLT, dose-limiting toxicity; HER2, human epidermal growth factor receptor 2; LA, locally advanced; mG/GEJ, metastatic gastric or gastroesophageal junction; mFOLFOX6, modified folinic acid, 5-fluorouracil, and oxaliplatin regimen; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; Q2W, every 2 weeks.