Background Claudin18.2 (CLDN18.2), a tight junction protein highly specific to gastric mucosa, is a promising target for gastric cancer (GC) treatment. Immunotherapy targeting PD-1 combined with chemotherapy has been approved as the first line treatment of GC. Understanding the expression profiles of CLDN18.2 and PD-L1 could offer guidance for the development of combination therapies that maximize the benefits of both agents. This study investigated the prevalence of CLDN18.2 expression in gastric/gastroesophageal junction (GC/GEJ) adenocarcinoma and its correlation with PD-L1 expression in Chinese patients.

Methods Expression of CLDN18.2 in formalin-fixed, paraffin-embedded (FFPE) GC/GEJ tissue samples was detected by immunohistochemistry (IHC) using an in-house anti-CLDN18.2 antibody (Clone14G11) on the Leica Bond III IHC stainer. Both the staining intensity (0, 1+, 2+, 3+) and the percentage of positive tumor cells were evaluated. CLDN18.2 positivity was defined as expression of CLDN18.2 in ≥10% tumor cells with intensity ≥1+. Samples with moderate-to-strong CLDN18.2 membrane staining (intensity ≥2+) in ≥40% tumor cells were also analyzed. PD-L1 expression was assessed based on combined positive score (CPS) using Agilent’s PD-L1 IHC 28-8 pharmDx.

Results A total of 300 GC/GEJ resected tissue samples were assessed, 89 (30%) were histologically classified as intestinal, 158 (52%) diffuse, 33 (11%) mixed, and 20 (7%) others. 295 (98%, 286 GC, 9 GEJ) samples were from primary site, 5 (2%) samples were from metastatic site (ovary, lymph node, omentum or left adnexa). CLDN18.2 staining was positive in 216 (72%), and negative in 84 (28%) of the tissue samples. 136 (45%) samples showed moderate-to-strong CLDN18.2 membrane staining in ≥40% tumor cells. CLDN18.2 positivity prevalence was 75% (n = 119/158) in diffuse and 61% (n=54/89) in intestinal subtypes. Moderate-to-strong CLDN18.2 membrane staining in ≥40% tumor cells was observed in 48% (n=76/158) diffuse subtypes, and in 39% (n=35/89) intestinal subtypes. For PD-L1 expression, 51 (17%) had PD-L1 CPS ≥5. 19% (n=41/216) of the CLDN18.2 positive samples also showed PD-L1 CPS ≥ 5. In the CLDN18.2 subgroup with moderate-to-strong CLDN18.2 membrane staining in ≥40% tumor cells, 21% (n=28/136) had PD-L1 CPS≥5. It appears that the distribution of CLDN18.2 expression is independent of PD-L1 status.

Conclusions High prevalence of CLDN18.2 expression in Chinese patients with GC/GEJ adenocarcinoma was observed. About 80% CLDN18.2 positive tumors had PD-L1 CPS < 5. These results support the value of CLDN18.2-targeted therapy in gastric cancer, especially for those patients who may not benefit from anti-PD-1/PD-L1 immuno-checkpoint therapy.

REFERENCES