**Background**

The development and progression of cancers are frequently promoted by immunosuppressive cells, such as regulatory T cells (Tregs) and myeloid-derived suppressor cells (MDSCs) mediated by various immune checkpoint molecules. Recently, the immune checkpoint inhibitor anti-PD-1 neutralizing antibody has become available for the first-line treatment of gastric cancer (GC) in Japan. However, there is no correlation between PD-1 or PD-L1 expression in Tregs or GC tissues and clinical responses to anti-PD-1 antibody. MDSCs are immature myeloid cells thought to suppress immune cell action, but the functional cell surface markers that define MDSCs correlated with cancer progression have not yet been clarified well. In this study, we identified a new subset of potential diagnostic and therapeutic targets for MDSCs in GC patients.

**Methods**

A total of 71 patients with GC who visited Juntendo University Hospital were included in the study. The study protocol was approved by the ethical committee of Juntendo University and written informed consent was obtained from all participants prior to enrolment. Flow cytometry was performed on fresh peripheral blood, using flow cytometer/cell sorter. For identification of circulating MDSCs, various fluorochrome-labeled antibodies to CD11b, CD14, CD33, HLA-DR, CD66b, PD-1 and PD-L1, and for T cell activation, antibodies to CD3, CD28, CD69, CD134 and CD137 were used.

**Results**

A significantly higher number of circulating monocytic-MDSCs and granulocytic-MDSCs (G-MDSCs) with CCR2 was detected in advanced GC patients (n=29, Stage III and IV) compared to early stage of GC donors (n=42, Stage I and II). We also found that significantly higher levels of PD-1 and PD-L1 were expressed on G-MDSCs (Lin-/HLA-DR-/CD33+/CD66b++) from advanced than early-stage of GC patients.

With the intent to identify the immunosuppressive function of PD-1 on G-MDSCs, isolated G-MDSCs pretreated with anti-PD-1 were mixed with CD3/CD28-activated T cells in vitro. Interestingly, both CD4 and CD8 T cell responses were ameliorated only in the pretreatment of G-MDSCs but not to T cells. We also found that immunosuppressive potential of G-MDSCs in GC patients was attenuated 3 weeks after anti-PD-1 Ab therapy.

**Conclusions**

The result of this pilot study, limited by the patient number, shows a clear increase in peripheral G-MDSCs expressing functional PD-1 in advanced GC patients. Although needed to be confirmed in the relationship between PD-1 on G-MDSCs and the duration of time of anti-PD-1 Ab therapy, these data suggest a novel subset of G-MDSCs expressing PD-1 found in advanced GC could be diagnostic and therapeutic targets.

**Ethics Approval**

Patients with gastric cancer who visited Juntendo University Hospital (Tokyo, Japan) were included in the study. The study protocol was approved by the ethical committee of Juntendo University and written informed consent was obtained from all participants prior to enrolment.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.1040-C