NK cells may express PD-1, and PD-1/PD-L1 interaction can impair NK activity. Preliminary data indicates that Fc-modified antibodies (including margetuximab) can enhance the activity of innate and adaptive immune cells. Margetuximab is a next generation anti-HER2 monoclonal antibody featuring an optimized Fc domain designed to enhance its Fc-dependent functions, including antibody-dependent cell cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC). Loss of HER2 expression after trastuzumab has been reported in up to 70% of patients with HER2+ GEA. This study was sponsored by MacroGenics, Inc. Copies of this poster obtained at SITC 2018, P338.

**Background**

- Trastuzumab: chemotherapy is standard treatment in 1st line advanced HER2+ gastric adenocarcinoma (GA).
- margetuximab: anti-HER2 monoclonal antibody targeting non-mutated extracellular HER2.
- Data indicates that Fc-modified antibodies (including margetuximab) can enhance the activity of innate and adaptive immune cells.
- It is well-tolerated and has activity in both HER2+ and HER2- patients when combined with pembrolizumab.

**Methods**

- **Efficacy**
  - Anti-PD-1 antibody (pembrolizumab), 200 mg q3w: Safety, tolerability, overall response rate (ORR), progression-free survival (PFS), overall survival (OS)
  - Patients: HER2+ IHC3+/PD-L1+ GEA patients post-trastuzumab, who have failed a HER2-targeted agent

- **Overall Response Rates and Biomarker Incidence (IVBO Cohorts)**
  - HER2+ IHC3+/PD-L1+ GEA patients post-trastuzumab
  - Treatment: margetuximab 10 mg/kg q3w + pembrolizumab 200 mg q3w

**Results**

- **Objective Response Observed Irrespective of Fc Receptor Genotype**
  - 15 confirmed/5 unconfirmed responses, 15 patients ongoing
  - Partial response (PR) + stable disease (SD) = 22.4% (19/85)
  - Median PFS: 2.7 months (95% CI: 21.6, 4.7)

**Conclusions**

- Margetuximab + pembrolizumab is a chemotherapy free combination, designed to coordinate innate and adaptive immune activity for treatment of GEA.
- The therapeutic combination demonstrated an acceptable safety profile that benchmarked favorably to historical experience with SoC with similar treatment-related adverse events.
- Enhanced immune cell infiltrate following treatment with Margetuximab/Pembrolizumab in a patient with subsequent complete response to therapy.