Evaluating Tumor Microenvironment Identifies Immune Correlates of Response to Combination Immunotherapy with Metargximab (M) and Pembrolizumab (P) in HER2+ Gastroesophageal Adenocarcinoma (GEA)


Background

- Gastric cancer is the fifth most common cancer and the third most common cause of cancer deaths worldwide.
- Despite improvements in treatment, the 5-year survival of patients with GEA is disappointing.
- Individual molecular subtypes of GEA display preferential responses to PD-1 blockade.

Materials and Methods

- 92 patients with advanced, relapsed/refractory HER2+ gastric cancer (GC) and gastroesophageal junction (GEJ) cancer were treated with metargximab + pembrolizumab in the CP-MAUH2-05 study.
- Pre-treatment tumor samples were assessed by NanoString's PanCancer IO360™.

Results

- **ERBB2/HER2 Expression Is Associated with Response**
  - **HER2 (IHC3+)** gastric cancer: Increased response rate in patients with HER2 IHC PFS HER2 IHC3+ compared with HER2 IHC PFS HER2 IHC2+ tumors.

- **Differential Gene Expression Associated with Anti-Tumor Activity**
  - **PD-L1-positive tumors had higher expression of PD-L1, IFN-γ signaling, LAG3, IDO1, compared with IHC2+ tumors**

- **PD-L1 IHC Is Associated with Interferon-related Signatures**
  - **PD-L1-positive tumors had higher expression of PD-L1, IFNγ signaling, LAG3, IDO1, inflammatory chemokine and tumor inflammation signature (TIS) scores**

Discussion

- **GEA tumors expressed higher levels of ERBB2 (5.25 FC, p=0.001) compared with GC tumors**
- **PD-L1+ tumors had lower expression of ERBB2 and higher expression of RTM1, MHC and STAT3, and less clinical responses**

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