ASSOCIATION BETWEEN IMMUNE AND TUMOR GENE SIGNATURES WITH RESPONSE OR RESISTANCE TO TISLELIZUMAB MONOTHERAPY

or in combination with chemotherapy in Gastroesophageal Adenocarcinoma

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BACKGROUND

Gastroesophageal adenocarcinoma (GEA), including gastro-esophageal junction (GEJ), cardia, and esophagus, is an increasing global threat with rising morbidity and mortality. Indeed, a large number of patients die from GEA with high mortality and has a low 5-year overall survival rate when diagnosed at an advanced stage.

- While recently approved PD-1 inhibitors have shown moderate clinical benefit, identification of biomarkers that may predict clinical outcomes in patients with GECA is urgently needed.
- Exploring immune and tumor transcriptional features and their association with clinical outcomes may improve the understanding of the tumor microenvironment and help understanding the effect of pembrolizumab in patients with advanced GEA.

METHODS

Study Design

Classical Hodgkin’s lymphoma and for patients with locally advanced or metastatic GEA.

The study population included patients with classical Hodgkin’s lymphoma and for patients with locally advanced or metastatic GEA.

Statistical significance was tested using a two-sided Wilcoxon test—

RESULTS

Table 1: Characteristics of Patients at Baseline

<table>
<thead>
<tr>
<th>Tumor Signature</th>
<th>n</th>
<th>%</th>
<th>ORR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFN-γ-high</td>
<td>38</td>
<td>54.7</td>
<td>0.041</td>
<td>0.000</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>IFN-γ-low</td>
<td>37</td>
<td>52.4</td>
<td>0.041</td>
<td>0.000</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Signet ring cell carcinoma</td>
<td>10</td>
<td>13.3</td>
<td>0.743</td>
<td>0.000</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>EAC</td>
<td>65</td>
<td>25 (47.2)</td>
<td>0.743</td>
<td>0.000</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>unknown</td>
<td>10</td>
<td>2 (16.7)</td>
<td>0.743</td>
<td>0.000</td>
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Table 2: Association of IFN-γ Signature With Clinical Outcomes of Tislelizumab Monotherapy

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CONCLUSIONS

- These findings increase the understanding of tumor immune profiles in GEA and their potential association with clinical efficacy of IFN-γ monotherapy.
- IFN-γ signature as a potential biomarker of response and multiple gene signatures that may influence resistance.
- Higher IFN-γ signatures were associated with favorable clinical benefit in IFN-γ patients receiving tislelizumab monotherapy.
- Compared with responders, elevated angiogenesis, macrophage, cell cycle, or ERBB4 signature were observed in either non-responder subpopulation.
- The association between tumor immune signatures and clinical efficacy of pembrolizumab plus chemotherapy or monotherapy is promising.
- Further validation will be considered in an ongoing phase 3 study designed to compare pembrolizumab plus chemotherapy or pembrolizumab monotherapy in patients with advanced GECA (NCT03467187).

- Unlike patients receiving monotherapy, responders to combination therapy showed high cell cycle gene expression signature (Figure 4A).
- Non-responders had no substantial correlation between IFN-γ signature and response or resistance to pembrolizumab.
- Single gene DEG analyses showed FCDEG was highly expressed in responders, respectively.
- Transcriptional profiles of patients with IFN-γ signature could be clustered into four distinct GEA subgroups according to tumor immune signatures and clinical outcomes.

REFERENCES


RESULTS

Patient Characteristics

Of 120 enrolled patients, 87 had samples evaluable for GEP analysis (Table 1).