ASSOCIATION BETWEEN PROGRAMMED-DEATH-LIGAND 1 EXPRESSION AND GENE SIGNATURES OF RESPONSE OR RESISTANCE TO TISLELIZUMAB IN HEPATOCELLULAR CARCINOMA

BACKGROUND

Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer and the second leading cause of cancer death worldwide in 2018, with 841,080 new cases worldwide – hepatocellular carcinoma accounts for 78% of all new liver cancer cases.

- Tislimuzumab as a treatment option for advanced-stage HCC yields moderate survival benefit
- Response or resistance mechanisms are not clear; highlighting an unmet need to identify specific biomarkers to define optimal treatment selection

METHODOLOGY

Study Design

- Paired analysis from two clinical trials were used – BGA-14107 (NCT02845188): French, Korean, multicenter, phase II/III, close-out trial/reduction-intensity expansion study – BGA-13107 (NCT02954051): Chinese, multicenter, phase 12 study
- Samples from both studies were analyzed from patients with previously treated advanced HCC
- A total of 143 samples were collected: 131 of which were used for clinical analysis and 12 for validation
- 18.1 months (18.1, NE)

METHODS

Results

- In sorafenib-exposed samples, immune cell activation signatures were enriched along with the anti-PD-1 signature
- A trend of improved PFS was observed in patients with NR cell-mediated cytotoxicity signature
- No significant association between NR cytotoxicity signature and OS was observed

Table 1: Baseline Characteristics and Clinical Outcome

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<th>Sex</th>
<th>n (% )</th>
<th>Median OS, months (95% CI)</th>
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<tbody>
<tr>
<td>Male</td>
<td>97 (68.2)</td>
<td>13.3 (11.13, NE)</td>
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<tr>
<td>Female</td>
<td>44 (31.8)</td>
<td>12.97 (11.13, NE)</td>
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Figure 1A: Sorafenib Exposure May Affect PD-L1 Expression as Well as Tumor Microenvironmental Related Gene Signature

Figure 1B: Sorafenib-Exposed, Novel Killer Cell-Mediated Cytotoxicity Is Associated With Clinical Outcomes in Tislimuzumab-Monotherapy

CONCLUSIONS

- Tislimuzumab is associated with the predictive potential of PD-L1 expression and tumor microenvironmenet-related gene signatures to anti-PD-1 therapy
- In sorafenib-exposed patients, there was an association of PD-L1 expression and NR cell-mediated cytotoxicity signatures with clinical outcomes from tislimuzumab monotherapy
- Elevated immune, immune checkpoint expression, and cell cycle signatures were observed in both nonresponders and responders of tislimuzumab monotherapy, which may indicate resistance to single-agent PD-1 inhibitors and may potentially benefit from combination therapies
- These findings increase our understanding of PD-L1 expression levels and tumor microenvironment profiles in HCC that are associated with the clinical efficacy of anti-PD-1 strategies

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REFERENCES


