A phase 2 study of sintilimab plus IBI310 for Epstein-Barr virus (EBV)-associated gastric cancer (FPN: 1032P)


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Background

• EBV is associated with about 5% of gastric cancers. Preliminary data has indicated that patients (pts) with EBV-associated gastric cancer (EBVaGC) could benefit from immunotherapy.

• The purpose of this study is to evaluate safety and efficacy of sintilimab (anti-PD-1) plus IBI310 (anti-CTLA-4) for EBVaGC in first-line (cohort B, 1L) and ≥2 lines (cohort C, ≥2L) settings.

Methods

• This phase 2 study (NCT04202601) enrolled adult pts with EBV+ gastric cancer (GC) or gastroesophageal junction cancer (GEJC).

Inclusion criteria: EBV+ (in situ hybridization, ISH), unresectable locally advanced or metastatic, histopathologically confirmed GC/GEJC.

Cohort B: pts with treatment-naïve (1L)

Cohort C: pts failed at least one standard treatment regimen (≥2L)

Treatment: sintilimab 3mg/kg (200mg for weight>60kg) IV Q3W plus IBI310 1mg/kg IV Q6W combination regimen for 1-3 cycles

Maintenance: sintilimab monotherapy until disease progression, unacceptable toxicity or for up to 24 months.

• The endpoints include objective response rate (ORR) per RECIST v1.1 by investigator, other efficacy measures and safety profile in both cohorts.

Results

• Baseline: As of July 18, 2023, 52 pts were enrolled including 30 pts in cohort B (median age 61.5 years, range 26-82) and 22 pts in cohort C (median age 53.5 years, range 28-68). All pts had ECOG score of 0 or 1. The efficacy (confirmed) and safety of sintilimab plus IBI310 in two cohorts were summarized in Table 1.

Table 1

<table>
<thead>
<tr>
<th>Treatment</th>
<th>ORR, % (95% CI)</th>
<th>DCR, % (95% CI)</th>
<th>DoR, months (median (95% CI))</th>
<th>PFS, months (median (95% CI))</th>
<th>OS, months (median (95% CI))</th>
<th>TRAE, n(%)</th>
<th>irAE, n(%)</th>
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<tbody>
<tr>
<td><strong>Cohort B, 1L</strong></td>
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<tr>
<td>(n=30)</td>
<td>60.0 (40.6-77.3)</td>
<td>76.7 (57.7-90.1)</td>
<td>8.3 (4.1-15.1)</td>
<td>7.1 (4.2-10.9)</td>
<td>25.3 (15.6-28.8)</td>
<td>25 (83.3)</td>
<td>7 (23.3)</td>
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<tr>
<td><strong>Cohort C, ≥2L</strong></td>
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<tr>
<td>(n=22)</td>
<td>36.4 (17.2-59.3)</td>
<td>68.2 (45.1-86.1)</td>
<td>17.6 (4.1-NR)</td>
<td>5.4 (2.7-8.4)</td>
<td>12.8 (4.3-NR)</td>
<td>19 (86.4)</td>
<td>6 (27.3)</td>
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</table>

*Abbreviations: Disease control rate (DCR), Duration of Response (DoR), Progression-Free Survival (PFS), Overall Survival (OS), Treatment-Related Adverse Event (TRA), immune-related Adverse Event (irAE).

• **Efficacy:** In cohort B, 18 pts had confirmed partial response (PR, 60%), 5 pts had stable disease (SD, 16.7%) and 5 pts had progressive disease (PD, 16.7%). In cohort C, 8 pts had confirmed PR (36.4%), 7 pts had SD (31.8%) and 4 pts had PD (18.2%).

• **Safety:** Treatment-related serious adverse events (TRAE) occurred in 2 (6.7%) pts in cohort B and 3 (13.6%) pts in cohort C. TRAEs leading to dose interruption occurred in 8 (26.7%) pts in cohort B and 7 (31.8%) pts in cohort C. No TRAE leading to treatment discontinuation or death occurred in two cohorts.

Conclusion

Sintilimab in combination with IBI310 were well tolerated, and shown promising anti-tumor efficacy both in first-line and ≥2 line locally advanced or metastatic EBV-associated gastric cancer.

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