Neoadjuvant Therapy with Tislelizumab plus Chemotherapy followed by Concurrent Chemoradiotherapy in Patients with Stage IVa Nasopharyngeal Carcinoma: A Single-arm, Phase II trial

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BACKGROUND

➢ The effect of comprehensive treatment for locally advanced nasopharyngeal carcinoma (LANPC) is still unsatisfied, especially for stage IVa NPC.
➢ Prognosis of nasopharyngeal carcinoma with T4 or N3 remains poor after neoadjuvant therapy. Therefore 3 cycles of neoadjuvant chemotherapy may not be enough for these patients. Immunochemistry has been reported to benefit patients with LANPC.
➢ Therefore, this study investigated the efficacy and safety of four cycles tislelizumab combined with neoadjuvant chemotherapy in treating stage IVa NPC.

METHODS

Study design: phase II, open-label, single-armed, Simon two-stage

Key eligibility criteria:(N=25)
• Histologically confirmed nasopharyngeal carcinoma
• Age 18-70
• Adequate organ functions

Neoadjuvant therapy:
• cCRT
  ➢ Tislelizumab 10mg/D1
  ➢ Cisplatin 80mg/m2 D1
  ➢ QIN907600mg/D1
  ➢ QIN907600mg,D1 4 cycles
• GTVnx: 70Gy/33f, GTVnd: 66Gy/33f, CTV: 54Gy/33f, CTV2: 45Gy/33f, DDP 40mg/m2 as D1, 8, 15, 22, 29, 36 f RT for 4 cycles

Endpoint:
➢ Primary endpoint: Complete response (CR) rate after neoadjuvant treatment(RECIST v1.1)
➢ Secondary endpoints: ORR(after neoadjuvant treatment), ORR(after cCRT), 1-y DFS, 2-y DFS, 1-y OS, 2-y OS, tolerance.

All patient will be followed up after concurrent chemoradiotherapy. Clinical trial information: ChiCTR2200056941

RESULTS

Data Cut-off date: Sep 15th, 2022

Some patients are still undertaking IMRT until data cut-off. So the efficacy of chemoradiotherapy is not reported.

Efficacy:
➢ 12 patients (50%) achieved CR after neoadjuvant chemotherapy.
➢ A higher CR rate of PD-L1+ (TC≥1%) patients than PD-L1-(TC<1%) patients (61.1% vs 0) was observed. But the ORRs were 94.4% and 100% in PD-L1+ and PD-L1- patients, respectively.
➢ The ORR of all evaluable patients was 95.8%.

Table 1. Baseline demographics and disease characteristics (n=24)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients(n=24)</th>
</tr>
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<tbody>
<tr>
<td>Age (median-yr)</td>
<td>49</td>
</tr>
<tr>
<td>Male, n(%)</td>
<td>15(62.5)</td>
</tr>
<tr>
<td>Stage , n (%)</td>
<td>T2-3N3M0 7(29.2) T4N1-2M0 7(29.2) T4N3M0 10(41.6)</td>
</tr>
<tr>
<td>PD-L1 expression , n (%)</td>
<td>TC≥1% 18(75) TC&lt;1% 4(16.7) Not evaluable 2(8.3)</td>
</tr>
</tbody>
</table>

Table 2. Response of evaluated patients (n=24)

<table>
<thead>
<tr>
<th></th>
<th>RECIST LI</th>
<th>CR (n %)</th>
<th>PR (n %)</th>
<th>SD (n %)</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>8 (53.3%)</td>
<td>6 (40%)</td>
<td>1 (6.7%)</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Stage 2</td>
<td>4 (44.4%)</td>
<td>5 (55.6%)</td>
<td>0</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>12 (50%)</td>
<td>11 (45.8%)</td>
<td>1 (4.2%)</td>
<td>24</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. The change of neoadjuvant therapy

CONCLUSION

➢ Four cycles tislelizumab in combination with neoadjuvant chemotherapy demonstrated a manageable safety profile and improved clinical response in high-risk LANPC patients.
➢ Patients with PD-L1 positive may be associated with favorable response. All the patients with PD-L1 negative still achieved partial response although limitation number.
➢ Long-term survival benefit will be followed continuously in this ongoing trial.