Neoadjuvant chemotherapy plus Tislelizumab followed by adjuvant Tislelizumab for locoregionally advanced nasopharyngeal carcinoma (NPC): A single-arm, phase II trial (NCT05448885)

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Introduction

- Nasopharyngeal carcinoma is an epithelial malignancy originating from the mucosal lining of the nasopharynx, with a peak annual incidence approaching 35 per 100,000 persons in southern China, southeast Asia, and northern Africa.
- Prognosis of NPC with T4 or N3 remains unsatisfactory due to high-risk of distant metastasis. More effective treatment strategies are needed for these patients.
- Tislelizumab is a humanized IgG4 anti–PD-1 monoclonal antibody specifically designed to minimize binding to FcγR on macrophages. Tislelizumab plus GP has been shown to improve the survival in recurrent or metastatic NPC.

Objective

Explore the efficacy and safety of Tislelizumab combined with induction chemotherapy and maintenance therapy after concurrent chemoradiotherapy for stage IVA nasopharyngeal carcinoma.

Methods

Patients

- Adult pts with Locally advanced non-keratinizing nasopharyngeal squamous cell carcinoma diagnosed as T4 or N3 stage according to AJCC 8th are eligible for inclusion.

Study design

- Single group assignment, Open label, phase 2 study (Figure 1)

Results

A total of 27 pts were enrolled from Sep. 2021 to Sep. 2022. Response rate to neoadjuvant therapy were evaluable for these pts.

Tumor response to neoadjuvant therapy

Data cut-off on November 7, 2022

<table>
<thead>
<tr>
<th>BOR, n(%)</th>
<th>Total (N=27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>3 (11.1%)</td>
</tr>
<tr>
<td>PR</td>
<td>21 (77.8%)</td>
</tr>
<tr>
<td>SDa*</td>
<td>3 (11.1%)</td>
</tr>
<tr>
<td>ORR</td>
<td>24 (88.9%)</td>
</tr>
<tr>
<td>DCR</td>
<td>27 (100%)</td>
</tr>
</tbody>
</table>

Figure 2: Maximum tumor reduction in evaluable pts (n=27)

Safety and tolerability

Table 3: TEAEs (N=27)

- Leukopenia 1 (40.0%) 4 (14.8%)
- Neutropenia 10 (37.0%) 3 (11.1%)
- Thrombocytopenia 6 (22.2%) 2 (7.4%)
- Anemia 12 (44.4%) 1 (3.7%)
- Hepatotoxicity 11 (40.7%) 4 (14.8%)
- Myocarditis 1 (3.7%)
- Hypothyroidism 2 (7.4%)
- Nausea 16 (59.3%) 7 (25.9%)
- Vomiting 3 (11.1%)
- Rash 9 (33.3%)
- Fatigue 20 (74.1%)
- Diarrhea 3 (11.1%)
- Weight loss 4 (14.8%)

Figure 3: A case of CR to neoadjuvant therapy

Conclusions

- Tislelizumab plus chemotherapy has preliminarily shown a promising anti-tumor efficacy and manageable safety profile for stage IVA NPC.
- Among 27 evaluable patients, ORR was 88.9% and DCR was 100%.
- Further follow-up is needed to confirm the long-term efficacy of this strategy.

Before Neoadjuvant therapy

After Neoadjuvant therapy

*SDa is defined of tumor shrinkage occurred and below a 30% decrease in the sum of diameters of target lesions, taking the baseline sum diameters as reference.

Key inclusion criteria: (N=50)
- T4 or N3 LA NPC
- ECOG PS 0-1
- No prior anti-tumor treatment

Neoadjuvant therapy

- Tislelizumab (200mg)
- Gemcitabine (1000 mg/m² on day 1, 8)
- Cisplatin (25 mg/m² on day 1-3) Q3W for 2 cycles

concurent CRT

- IMRT concurrently with cisplatin 100 mg/m² Q3W

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