RATIONALE-309: Effects of Tislelizumab on Health-Related Quality of Life (HRQoL) in Patients with Recurrent or Metastatic Nasopharyngeal Cancer (R/M NPC)

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DECLARATION OF INTERESTS

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Patients with nasopharyngeal cancer (NPC) suffer from significant declines in health-related quality of life (HRQoL)\(^1\)-\(^6\)

- HRQoL is an important patient-reported outcome (PRO) that may impact the mortality risk for patients with NPC\(^7\)

Liver metastases (LM) in NPC patients is considered as a significant negative prognostic factor for overall survival and cancer-specific survival for patients with NPC\(^8\)-\(^{11}\)

- The presence of liver metastasis in patients with NPC is significantly associated with poor response to chemotherapy\(^1\),\(^2\)

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Background (2 of 2)

- RATIONALE-309 (NCT03924986) - double-blinded, randomized, phase 3 study
  - Tislelizumab + gemcitabine and cisplatin (tisle + chemo) vs placebo + gemcitabine and cisplatin (placebo + chemo) as first-line treatment for recurrent or metastatic (R/M) NPC
  - Significant improvement in progression-free survival for Tisle + chemo compared to placebo + chemo (median progression free survival (PFS): 9.6 vs 7.4 months, respectively; hazard ratio [HR]=0.50, 95% confidence interval [CI]: 0.37, 0.68)
  - mPFS2 was not reached for the tisle + chemo arm and was 13.9 months for the placebo + chemo arm (HR=0.38, 95% CI: 0.25, 0.58)
- The objective of this analysis was to evaluate the impact of tisle + chemo on patients’ HRQoL and NPC-related symptoms
  - Post-hoc analysis also explored HRQoL and NPC-related symptoms in patients with LM
Study Design: Randomized, Double-Blind, Phase 3 Trial

**Method (1 of 2)**

**Key eligibility criteria:**
- Histologically or cytologically confirmed R/M NPC
- Treatment-naïve*
- Age 18–75 years
- ≥ 1 measurable lesion (RECIST v1.1)
- ECOG PS ≤ 1

**Stratification factors:**
- Gender (male vs female)
- Liver metastases (yes vs no)

**PRO endpoints:**
- The European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 items (QLQ-C30): global health status/quality of life (GHS/QoL), physical functioning, and fatigue
- EORTC Head and Neck Module (QLQ-H&N35): symptom index, pain, senses, and speech problems scales

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**Randomized, Double-Blind, Phase 3 Trial**

- **Tisle + chemo**
  - Tislelizumab 200 mg IV D1 (Q3W)
  - Gemcitabine 1 g/m² IV D1, D8 + cisplatin 80 mg/m² IV D1(Q3W, 4–6 cycles)

- **Placebo + chemo**
  - Placebo 200 mg IV D1 (Q3W)
  - Gemcitabine 1 g/m² IV D1, D8 + cisplatin 80 mg/m² IV D1(Q3W, 4–6 cycles)

Until disease progression, intolerable toxicity, death, or withdrawal of consent

**Crossover to tislelizumab monotherapy (200 mg IV Q3W) only if progressive disease and investigator considers clinically beneficial (not all patients)**

**Tislelizumab monotherapy (200 mg IV Q3W) if investigator considers clinically beneficial**
Method (2 of 2)

- The key clinical cycles were cycle 4 and cycle 8 and were selected to measure change in PRO endpoints representing during chemotherapy (cycle 4) as well as after chemotherapy (cycle 8).
- Two sets of analyses were conducted for the PRO endpoints: intent-to-treat (or, ITT) population and intent-to-treat (or, ITT) population with liver metastasis (or the LM subgroup) were conducted.
- Change from baseline in each key PRO endpoint to cycle 4 and cycle 8 was analyzed using the linear mixed effect model for repeated measures.
- Time to deterioration (TTD) for each key PRO endpoint was assessed in both the full ITT population and the LM subgroup.
  - TTD was defined as the time from randomization to first onset time at which deterioration is as defined by ≥10-point change from baseline in the direction of worsening for two consecutive assessments or 1 assessment followed by death from any cause within 3 weeks.
## Results

### Patients Demographics

<table>
<thead>
<tr>
<th></th>
<th>Tisle + chemo (N = 131)</th>
<th>Placebo + chemo (N = 132)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>50.0</td>
<td>50.0</td>
</tr>
<tr>
<td>Min, Max</td>
<td>26, 74</td>
<td>23, 73</td>
</tr>
<tr>
<td><strong>Age Group, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 65 years</td>
<td>121 (92.4)</td>
<td>120 (90.9)</td>
</tr>
<tr>
<td>≥ 65 years</td>
<td>10 (7.6)</td>
<td>12 (9.1)</td>
</tr>
<tr>
<td><strong>Sex, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>103 (78.6)</td>
<td>103 (78.0)</td>
</tr>
<tr>
<td>Female</td>
<td>28 (21.4)</td>
<td>29 (22.0)</td>
</tr>
<tr>
<td><strong>Ethnicity, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not Hispanic or Latino</td>
<td>131 (100.0)</td>
<td>132 (100.0)</td>
</tr>
<tr>
<td><strong>Race, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>131 (100.0)</td>
<td>132 (100.0)</td>
</tr>
<tr>
<td><strong>Region, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>122 (93.1)</td>
<td>126 (95.5)</td>
</tr>
<tr>
<td>Thailand</td>
<td>5 (3.8)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Taiwan, China</td>
<td>4 (3.1)</td>
<td>5 (3.8)</td>
</tr>
<tr>
<td><strong>Liver Metastases, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>56 (42.7)</td>
<td>57 (43.2)</td>
<td></td>
</tr>
<tr>
<td><strong>ECOG Performance Status, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>51 (38.9)</td>
<td>46 (34.8)</td>
</tr>
<tr>
<td>1</td>
<td>80 (61.1)</td>
<td>86 (65.2)</td>
</tr>
</tbody>
</table>

- All 263 randomized patients (tisle + chemo n=131; placebo + chemo n=132) comprised the ITT population
- 43% of the 263 patients (n=113; tisle + chemo n=56; placebo + chemo n=57) were diagnosed with liver metastases
- Demographics and clinical characteristics of the ITT population were generally balanced across the two treatment arms and were representative of the target patient population
## Results

### Completion Rates

<table>
<thead>
<tr>
<th></th>
<th>Tisle + chemo (n=131)</th>
<th>Placebo + chemo (n=132)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completion rate(^a) (%)</td>
<td>100/100 (100.0)</td>
<td>100/100 (100.0)</td>
</tr>
<tr>
<td>Adjusted completion rate(^b) (%)</td>
<td>100/100 (100.0)</td>
<td>100/100 (100.0)</td>
</tr>
<tr>
<td><strong>Cycle 4</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completion rate(^a) (%)</td>
<td>109/131 (83.2)</td>
<td>117/132 (88.6)</td>
</tr>
<tr>
<td>Adjusted completion rate(^b) (%)</td>
<td>109/110 (99.1)</td>
<td>117/117 (100.0)</td>
</tr>
<tr>
<td><strong>Cycle 8</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completion rate(^a) (%)</td>
<td>98/131 (74.8)</td>
<td>88/132 (66.7)</td>
</tr>
<tr>
<td>Adjusted completion rate(^b) (%)</td>
<td>98/98 (100.0)</td>
<td>88/88 (100.0)</td>
</tr>
</tbody>
</table>

\(^a\) Completion rate = number of patients completed questionnaire / total number of patients in relevant treatment arm. \(^b\) Adjusted completion rate = number of patients completed questionnaire / total number of patients in study at relevant visits in relevant treatment arm.

- For the two PRO questionnaires QLQ-C30 and QLQ-H&N35, the completion rate was 100% at baseline.
- At cycle 4, the completion rate was 83% or higher.
- At cycle 8, the completion rate decreased to 74.8% in the tisle + chemo arm and 66.7% in the placebo + chemo arm.
- The adjusted completion rates remained over 99% for both arms at cycle 4 and cycle 8.
Results

EORTC QLQ-C30 Change from Baseline

- No differences in change from baseline to cycles 4 or 8 between the arms were observed for the ITT population or LM subgroup for the QLQ-C30 scales.

Note: Higher scores represent better outcomes on the GHS/QoL scale and physical functioning scale but worse outcome on the fatigue scale.
Results

EORTC QLQ-H&N35 Change from Baseline to Cycle 4

- No differences between the arms emerged at cycle 4

Note. Higher scores indicating worse outcomes
Results

EORTC QLQ-H&N35 Change from Baseline to Cycle 8

- There was a greater reduction from baseline in the tisle + chemo arm vs the placebo + chemo for the **pain score** (ITT: -2.37 [95% CI: -4.21, -0.53], P=0.0117; LM: -3.79 [95% CI: -6.62, -0.97], P=0.0092)

- In the LM subgroup, there was a greater improvement from baseline in the tisle + chemo arm vs the placebo + chemo arm for **senses problems** (LM -5.13 [95% CI: -9.86, -0.40], P=0.0338)

- In the LM subgroup, improvements from baseline in the tisle + chemo arm vs the placebo + chemo were observed for
  - Symptoms index (-2.22 [95% CI: -4.51, 0.08], P=0.0580).
  - Speech problems (-2.85 [95% CI: -5.92, 0.23], P=0.0694)

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Results

Time to deterioration

- There were no significant differences between the two arms in the risk of deterioration for all the key PRO endpoints in either the ITT population or LM subgroup
Discussion

• The findings of current investigation suggest that HRQoL and NPC associated symptoms remained relatively stable in NPC patients treated with tislelizumab + chemo in the ITT population through cycle 8.

• In addition, the subgroup patients clinically diagnosed with LM experienced reductions in overall NPC symptoms as well as reductions in individual symptoms.

• These results, along with improved survival and favorable safety profile, suggest tislelizumab + chemo represents a potential first line treatment option for patients with R/M NPC.
Acknowledgments

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References


