Background
The programmed cell death protein 1 (PD-1) inhibitor pembrolizumab was approved as first-line treatment for recurrent or metastatic (M1) head and neck squamous cell carcinoma (HNSCC) alone or in combination with the chemotherapy regimen 5-fluorouracil plus platinum agent (5-FU/platinum)-based in results from the INDUCE Phase 1 study. In some patients, inhibition of immune checkpoint pathways alone may not be enough to control HNSCC, therefore combining agents with immunomodulatory properties (including chimeric antibodies that target different aspects of the immune system) may result in improved antitumor responses and overall survival.

Methods
Study design
INDUCE (NCT02752888) is a Phase 1 study with two parts: Part 1: GS-3359609 monotherapy and Part 2: GS-3359609 combination therapy with each part consisting of a dose escalation phase followed by a cohort expansion phase (Figure 1).

- Dose escalation phases (Parts 1A and 2A): Patients were treated with GS-3359609 in a standard 3+3 cohort schedule using a modified q28. Patients were enrolled on a 1:1:1 randomization ratio in cohorts defined by a recorded objective response (OR), which was categorized as objective response (OR), unconfirmed objective response (uOR), or no response (NR). The starting dose was 10 mg/kg and escalated in 10 mg/kg dose increments. Patients were treated in 28-day cycles.

- Expansion phases (Parts 1B and 2B): Treatment was continued in all patients who showed objective response or unconfirmed OR until disease progression or unacceptable toxicity.

Key inclusion criteria
Patients were selected for treatment with pembrolizumab (HNSCC) in the following categories: OR, uOR, or NR.

- Dose levels and maximum tolerated doses: Dose levels and maximum tolerated doses were determined in the dose escalation phase.

- Dose selection: The dose selection was made based on the following criteria: OR, uOR, or NR.

- Toxicity: Patients were treated with pembrolizumab in the following categories: OR, uOR, or NR.

- Dose selection: The dose selection was made based on the following criteria: OR, uOR, or NR.

Results
Patient characteristics
As of data cut-off of March 20, 2020, a total of 20 patients were evaluable in these 3 INDUCE safety cohorts.

- Patients in the GS-3359609 plus 5-FU/platinum cohort and 19 in the GS-3359609 plus 5-FU/platinum cohort (Part 1).

- All patients received at least one dose of study treatment and were evaluated for safety; data cut-off was March 16, 2020.

Table 1: Patient characteristics (n=20)

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Prior systemic treatment</th>
<th>Primary site (HNSCC)</th>
<th>CPS, combined positive score (CPS)</th>
<th>OS, median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Part 1A</td>
<td>57 (21)</td>
<td>Female</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Part 1B</td>
<td>57 (21)</td>
<td>Male</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2: Treatment-related adverse events (n=20)

<table>
<thead>
<tr>
<th>Event</th>
<th>Grade 1-2</th>
<th>Grade 3-4</th>
<th>Grade 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>8 (40)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>9 (45)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>11 (55)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>9 (45)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2 (10)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mucositis</td>
<td>14 (70)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Oral herpes</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Figure 2: Dose expansion phase for pembrolizumab (HNSCC) (n=9). This is a Case study 1: 62.

Case study 1: 62

1. **Patient demographics:**
   - Age: 62 years
   - Sex: Male
   - Prior treatment: 3 cycles of neoadjuvant chemotherapy

2. **Diagnosis:**
   - Primary site: HNSCC
   - CPS, combined positive score: 100

3. **Treatment:**
   - Induction: Pembrolizumab (HNSCC) plus 5-FU/platinum

4. **Results:**
   - OR: Yes
   - OS: 100
   - Treatment delay or dose reduction: No

5. **Safety:**
   - Anemia: Grade 1-2
   - Diarrhea: Grade 1-2
   - Nausea: Grade 1-2
   - Fatigue: Grade 1-2
   - Hypertension: Grade 1-2
   - Mucositis: Grade 1-2
   - Oral herpes: Grade 1-2
   - Thrombocytopenia: Grade 1-2

Conclusion
INDUCE: Report on Safety Run-in Cohorts Combining Inducible T-cell Co-stimulatory Receptor Agonist GSK3359609 With 5-Fluorouracil/Platinum Chemotherapy, With or Without Pembrolizumab, for the Treatment of Advanced Solid Tumors

Poster No. 205

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Disclosures
No disclosures were reported for this activity.

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References