Cosibelimab, an Anti-PD-L1 Antibody, in Metastatic Cutaneous Squamous Cell Carcinoma (mCSCC): Preliminary Safety and Efficacy Results from a Phase 1 Clinical Trial

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Background

Cosibelimab: Anti-PD-L1 with Dual Mechanism of Action

• High affinity, fully-human IgG1 monoclonal antibody (mAb) that binds to programmed death-ligand 1 (PD-L1) to restore adaptive immunity and engage innate immunity.
• Sustained >99% tumor target occupancy and B7.1 receptors.
• A functional Fc domain capable of inducing antigen-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC) against tumor cells.

Objectives

Primary

• To evaluate the efficacy of cosibelimab in metastatic cutaneous squamous cell carcinoma (mCSCC) by measuring the rate of objective response (ORR: complete response + partial response) per Response Evaluation Criteria in Tumors (RECIST) 1.1.
• To evaluate the safety and tolerability of cosibelimab in patients with advanced cancers.

Secondary

• To evaluate additional efficacy parameters, including duration of response, progression-free survival and overall survival.

Study Design

• Study QK-201-101 (NCT03212340) is a global, multicenter, phase II trial enrolling patients with select advanced cancers, including a registration-enabling cohort of mCSCC patients.
• mCSCC patients received cosibelimab administered as a fixed dose of 800 mg every two weeks (Q2W) or 1200 mg Q3W until confirmed and worsening disease progression or clinical deterioration, followed by post-treatment follow-up.
• Tumor assessments by RECIST 1.1 were conducted every 6 weeks for the initial 32 weeks on study, and every 12 weeks thereafter.
• The data cutoff date for this analysis was August 14, 2020.

Key Inclusion Criteria

• Adults with mCSCC (nodal and/or distant).
• Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.
• At least 3 months from prior systemic treatment.
• Adequate organ function.
• At least one measurable lesion by RECIST 1.1.

Key Exclusion Criteria

• Prior immune checkpoint inhibitor therapy.
• Active autoimmune disease.
• Immune-associated disorders such as Sjogren's syndrome, sarcoidosis, or psoriasis.
• Current or prior infection with Hepatitis B or C virus.
• Chemotherapy, radiation therapy, or biological therapy within 4 weeks of screening.
• More than 12 weeks since previous cytokine therapy.
• Known human immunodeficiency virus (HIV) infection.

Methods

Demographic and Baseline Characteristics

• Forty-one mCSCC patients were enrolled and treated with cosibelimab administered 800 mg Q2W or 1200 mg Q3W (n=1).
• Demographic and baseline characteristics are summarized in Table 1.

Table 1. Demographic and Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number (Percent)</th>
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<tbody>
<tr>
<td>Sex: Male (n=29, 70.7%)</td>
<td></td>
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<tr>
<td>Age, years (median)</td>
<td>53 (range: 19-80)</td>
</tr>
<tr>
<td>ECOG performance status</td>
<td>0 (n=20, 48.8%)</td>
</tr>
<tr>
<td>Prior immune checkpoint therapy</td>
<td>0 (n=20, 48.8%)</td>
</tr>
<tr>
<td>Immunosuppressive doses</td>
<td>0 (n=20, 48.8%)</td>
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Response Evaluation Criteria in Tumors (RECIST) 1.1

• Complete response: no evidence of disease.
• Partial response: ≥30% decrease in the sum of target lesion diameters.
• Stable disease: no progression or response.
• Progressive disease: ≥20% increase in the sum of target lesion diameters.

Results

Tumor Response by RECIST v1.1

• ORR: 51.4% (95% CI: 34.4, 68.1), including five (13.5%) complete responses.
• Seven patients (17.1%) achieved a complete response and 14 (37.8%) achieved a partial response.
• Complete responders included one patient with mCSCC metastatic to lung and one patient with cervical mCSCC.

Table 2. Tumor Response by RECIST v1.1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number (Percent)</th>
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<tbody>
<tr>
<td>Complete response</td>
<td>5 (12.2%)</td>
</tr>
<tr>
<td>Partial response</td>
<td>14 (34.1%)</td>
</tr>
<tr>
<td>Stable disease</td>
<td>21 (51.2%)</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>1 (2.4%)</td>
</tr>
</tbody>
</table>

Median duration of response has not been reached, with 84.2% of responses ongoing. Median duration of response has not been reached, with 84.2% of responses ongoing.

In patients with mCSCC metastatic to lung:

• One hundred fourteen patients with advanced cancers have been enrolled and treated with cosibelimab.
• Treatment-related adverse events (TRAEs) are summarized in Table 3.
• The most common TRAEs included fatigue (17/4, 14.9%) and rash (16, 14.9%). Two patients (1.9%) experienced grade 2 pneumonitis. No reported events of colitis or hepatitis.
•-grade 3 TRAEs occurred in six patients (5.3%). Events occurred in more than one patient were anemia and fatigue (each 2/18, grade 3).
• Three patients (2.5%) discontinued treatment due to a TRAE.

Conclusion

• Treatment with cosibelimab resulted in robust and durable responses, including complete responses, in patients with mCSCC.
• ORR: 51.4% (95% CI: 34.4, 68.1), including five (12.2%) complete responses.
• Median duration of response has not been reached, with 84.2% of responses ongoing.

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