Cemiplimab (cemiplimab-rwlc in the US) is the only therapy approved by the US Food and Drug Administration and the European Commission for treatment of patients with metastatic or locally advanced CSCC who are not candidates for curative surgery or radiation.

While the clinical activity of cemiplimab as monotherapy has been established in patients with advanced CSCC who are not candidates for curative surgery or radiation, this study aims to evaluate its role as an adjuvant therapy.

The exploratory objectives of the study are to:

- Evaluate the clinical activity of cemiplimab versus placebo after surgery and post-operative radiation.
- Compare health-related quality of life in patients treated with cemiplimab or placebo.
- Assess the safety and tolerability of cemiplimab versus placebo.
- Evaluate the association between clinical activity of cemiplimab and molecular features in pre-treatment tumor samples.

Table 1. Key inclusion criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>18 years or older (in Japan: only ≥21 years)</td>
</tr>
<tr>
<td>Prior malignancies</td>
<td>None</td>
</tr>
<tr>
<td>Target lesion</td>
<td>High-risk CSCC defined as one of the following: poorly differentiated histology and recurrent lesion of ≥20 mm; primary CSCC with nodal involvement; or CSCC nodal metastasis with nominal ≥T3 (recurrent lesion of ≥4 cm in diameter, minor bone involvement, or ≥2 cm in diameter without bone involvement); history of immune-related pneumonitis within 5 years; or history of solid organ transplant except corneal transplant</td>
</tr>
<tr>
<td>Prior systemic anti-cancer immunotherapy for CSCC</td>
<td>None</td>
</tr>
<tr>
<td>Concurrent malignancy other than localized CSCC within 3 years of study entry</td>
<td>None</td>
</tr>
<tr>
<td>Prior systemic anti-cancer immunotherapy for other malignancy (except localized CSCC) within 3 years of study entry</td>
<td>None</td>
</tr>
<tr>
<td>Prior radiation treatment of the known primary CSCC lesion previously treated within the draining lymph node basin</td>
<td>None</td>
</tr>
<tr>
<td>History of immunosuppressive medications and/or use of immunosuppressive corticosteroids &gt;10 mg prednisone daily or equivalent within 4 weeks prior to the first dose of cemiplimab</td>
<td>None</td>
</tr>
<tr>
<td>Prior history of any other major medical condition not adequately treated</td>
<td>None</td>
</tr>
<tr>
<td>Adequate hepatic and renal functions</td>
<td>None</td>
</tr>
</tbody>
</table>

Methods

Study design

This randomized, placebo-controlled, double-blind, multicenter Phase III trial (C-POST) is evaluating the clinical activity of adjuvant cemiplimab versus placebo in patients with high-risk CSCC, after surgery and post-operative radiation.

The study consists of two parts:

- Part 1: Double-blind, randomized, placebo-controlled study. Inclusion criteria: patients with high-risk CSCC confined to single site or single draining lymph node basin within 4 weeks of definitive treatment (surgery, radiation, or combined modality therapy). Exclusion criteria: history of any other malignancy, prior radiation treatment of the known primary lesion, and any other major medical condition that would prevent safe administration of the study drugs. Duration: A single period of up to 28 days for randomization, a treatment period of up to 48 weeks, and a follow-up period of up to disease recurrence or end of study (Figure 1).

- Part 2: Open-label study. Inclusion criteria: patients with high-risk CSCC, after surgery and post-operative radiation. Exclusion criteria: history of any other malignancy, prior radiation treatment of the known primary lesion, and any other major medical condition that would prevent safe administration of the study drugs. Duration: A period of up to 48 weeks for treatment, and a follow-up period of up to 48 weeks or until disease recurrence or end of study (Figure 1).

Table 2. Key exclusion criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of immune-related pneumonitis within 5 years</td>
<td>None</td>
</tr>
<tr>
<td>History of any other malignancy other than localized CSCC within 3 years of study entry</td>
<td>None</td>
</tr>
<tr>
<td>Prior radiation treatment of the known primary CSCC lesion previously treated within the draining lymph node basin</td>
<td>None</td>
</tr>
<tr>
<td>Any infection requiring hospitalization and/or intravenous antibiotic therapy</td>
<td>None</td>
</tr>
<tr>
<td>Prior history of any other major medical condition not adequately treated</td>
<td>None</td>
</tr>
<tr>
<td>Use of immunosuppressive medications and/or use of immunosuppressive corticosteroids &gt;10 mg prednisone daily or equivalent within 4 weeks prior to the first dose of cemiplimab</td>
<td>None</td>
</tr>
</tbody>
</table>

A Phase 3, Randomized, Double-Blind Study of Adjuvant Cemiplimab Versus Placebo Post-Surgery and Radiation in Patients with High-Risk Cutaneous Squamous Cell Carcinoma (CSCC)

Danny Rischin, Matthew G. Burns, Israel Lowy, Elizabeth Stankievich, Siyu Li, Huy-Nam Han, Sandro V. Porceddu

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Background

Cutaneous squamous cell carcinoma (CSCC) is the second most common skin cancer with an estimated incidence of around 1 million cases per year in the US. While surgical resection is the current standard of care for primary CSCC, locoregional recurrence, distant metastasis, and disease-related death may still occur in some patients. While the clinical activity of cemiplimab as monotherapy has been established in patients with advanced CSCC who are not candidates for curative surgery or radiation, this study aims to evaluate its role as an adjuvant therapy.

The exploratory objectives of the study are to:

- Evaluate the clinical activity of cemiplimab versus placebo after surgery and post-operative radiation.
- Compare health-related quality of life in patients treated with cemiplimab or placebo.
- Assess the safety and tolerability of cemiplimab versus placebo.
- Evaluate the association between clinical activity of cemiplimab and molecular features in pre-treatment tumor samples.

Summary

Patients with high-risk CSCC often experience relapse with locoregional recurrence or distant metastasis despite initial treatment with surgery and post-operative radiation.

Cemiplimab, a PD-1 monoclonal antibody, has demonstrated clinical activity with a safety profile comparable to those of other anti-PD-1 agents in advanced malignancies, including CSCC.

Cemiplimab (cemiplimab-rwlc) is the only therapy approved by the US Food and Drug Administration and the European Commission for treatment of patients with metastatic or locally advanced CSCC who are not candidates for curative surgery or curative radiation.

This study will provide insight into the clinical activity of cemiplimab versus placebo as an adjuvant treatment in patients with CSCC at high risk for recurrence, after surgery and post-operative radiation.

This study is ongoing and is actively enrolling patients.

References


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