Trial in Progress: A phase 3 randomized study of low-dose intralesional cemiplimab versus primary surgery for patients with early-stage cutaneous squamous cell carcinoma (CLEAR CSCC)

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OBJECTIVES & CONCLUSIONS

- **There is an unmet need for non-surgical management of early-stage CSCC.**
- **Cemiplimab (350 mg IV Q3W), a high-affinity, fully human programed cell death-1–blocking monoclonal antibody, is approved by many health authorities globally and is a widely accepted standard of care for the treatment of advanced CSCC.**
- **The purpose of this study (NCT06585410) is to determine the non-inferiority of cemiplimab (5 mg IL QW for 6 weeks) versus primary surgery, along with its safety, tolerability, and efficacy, in patients with early-stage CSCC.**
- **This study will help establish the potential clinical utility and broader applicability of low-dose IL cemiplimab in early-stage CSCC.**

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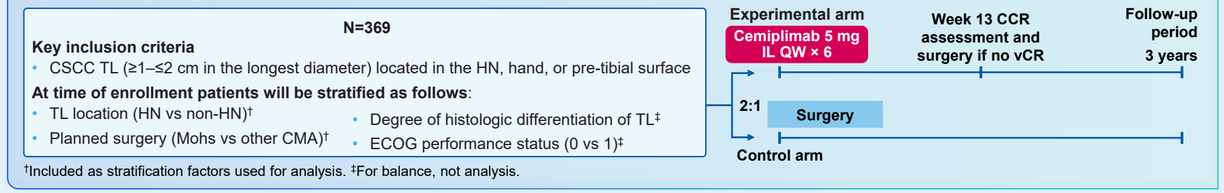
SYNOPSIS

- CSCC is a malignant proliferation of epidermal keratinocytes with invasion of the dermis. Risk factors include ultraviolet skin damage due to chronic sun exposure, advanced age, light-colored skin, and immunosuppression.
- Cemiplimab (350 mg IV Q3W) is approved for the treatment of patients with advanced CSCC who are not candidates for curative surgery or radiation.[1,2]
- Surgery is the standard of care for early-stage CSCC; however, it can result in detrimental impacts such as scars, infection, and pain.[3]
- For patients who prefer non-surgical management of early-stage CSCC, low-dose IL cemiplimab demonstrated promising clinical activity in a pilot study (NCT03889912).[4]

Figure 1. Study design



†Included as stratification factors used for analysis. ‡For balance, not analysis.

METHODS

Study design

- In this phase 3, randomized, open-label multicenter study (NCT06585410), approximately 369 patients with early-stage CSCC will be randomized 2:1 to either cemiplimab (5 mg IL QW for 6 weeks) or primary surgery. The study design is shown in **Figure 1**.
- Enrollment will be completed approximately 1.5 years after the study start. The study duration is expected to be 4.5 years.
- For patients in the experimental arm (treated with IL cemiplimab): TL treatment will be assessed at Week 13. Patients with a vCR will undergo biopsies to evaluate the pathologic response. If there has not been a vCR at Week 13, the residual area of the TL abnormality will undergo surgery (Mohs or equivalent method of CMA).
- For patients in the control arm: 1 day for surgery, with post-surgical visits at Week 3 and Week 13.
- All patients will be followed for a total of 3 years after randomization: every 3 months for Years 1 and 2; and every 4 months for Year 3.

Study objectives and endpoints

- Study objectives and endpoints are provided in **Tables 1** and **2**.

Table 1. Study objectives

Primary objective

- The primary objective is to evaluate the efficacy of IL cemiplimab versus surgery in early-stage CSCC, based on event-free survival in both study arms.

Secondary objective

- Evaluate the efficacy of IL cemiplimab in early-stage CSCC TLs based on composite complete response.
- Evaluate the efficacy of cemiplimab in non-TLs.
- Evaluate the safety and tolerability of cemiplimab and primary surgery.
- Evaluate the size of the surgical defect after TL resection.

Table 2. Study endpoints

Primary endpoint

- Event-free survival in patients who received cemiplimab or surgery, from randomization until 1 year and 3 years, per investigator assessment.

Secondary endpoint

Experimental arm (cemiplimab):
- Composite clinical response rate for TLs, defined as visual plus pathologic clearance.
- Presence or absence of non-TLs in the region of the TL at baseline compared with Week 13.

Both arms (cemiplimab or surgery):
- Incidence and severity of treatment-emergent adverse events in all participants through the end of the study.
- The product of the longest diameters of the surgical defect after resection of the TL (prior to closure) for all participants who undergo surgery.

Patient eligibility

- Key inclusion and exclusion criteria are provided in **Tables 3** and **4**.

Table 3. Key inclusion criteria

- ≥18 years of age.
- TL ≥1.0–≤2.0 cm in the maximum diameter in the HN, hand, or pre-tibial surface.
- Patients eligible for surgical resection of their CSCC TL, and the method of planned surgical resection is Mohs surgery or other surgical method of CMA.
- ECOG performance status ≤1.
- Adequate hepatic function: total bilirubin ≤1.5 × ULN; alanine aminotransferase and aspartate aminotransferase both ≤3 × ULN; and alkaline phosphatase ≤2.5 × ULN.†
- Adequate renal function: serum creatinine ≤1.5 × ULN or estimated creatinine clearance >30 mL/min according to the Cockcroft and Gault method.†
- Adequate bone marrow function: hemoglobin ≥9.0 g/dL; absolute neutrophil count ≥1.5 × 10^9/L; and platelet count ≥100 × 10^9/L.†

Table 4. Key exclusion criteria

- TL is a keratoacanthoma, adenosquamous carcinoma, desmoplastic carcinoma, basal cell carcinoma, basosquamous carcinoma, Bowen's disease, or CSCC in situ without an invasive component.
- Ongoing or recent evidence of significant autoimmune disease that required treatment with systemic immunosuppressive treatments.
- Concurrent or prior solid tumor or hematologic malignancy (except for protocol-allowed exceptions).
- A history of solid organ transplant.
- Prior systemic therapy for CSCC (systemic chemotherapy, systemic immunotherapy, systemic targeted therapy), investigational or standard of care.

†Testing may be repeated once during the screening period.

RESULTS

- The study is currently recruiting patients.
- Enrollment is planned at study sites across North America and Australia.

REFERENCES

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DISCLOSURES

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ABBREVIATIONS

CCR, composite clinical response; CMA, complete margin assessment; CSCC, cutaneous squamous cell carcinoma; ECOG, Eastern Cooperative Oncology Group; HN, head and neck; IL, intralesional; IV, intravenous; Q3W, every 3 weeks; QW, weekly; TL, target lesion; ULN, upper limit of normal; vCR, visual complete response.

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