CemiplimAb-rwlc Survivorship and Epidemiology (CASE): A prospective study of the safety and efficacy of cemiplimab in patients with advanced cutaneous squamous cell carcinoma (CSCC) in a real-world setting

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Background

- CSCC is one of the most commonly diagnosed cancers worldwide, but epidemiologic information of the condition is very limited.
- Patient survival rates after early diagnosis of CSCC are good, but morbidity and mortality rates in patients with advanced CSCC not amenable to curative surgery or curative radiotherapy remain high, leaving a significant unmet need.[1]
- Cemiplimab is a high-affinity, highly potent, fully human, immunoglobulin G4 monoclonal antibody to the programmed cell death (PD)-1 receptor, derived using VelocImmune technology.[2]
- Cemiplimab (cemiplimab-rwlc in the USA) is approved by the European Medicines Agency and the US Food and Drug Administration for the treatment of adult patients with locally advanced or metastatic CSCC who are not candidates for curative surgery or curative radiation; adult patients with locally advanced or metastatic basal cell carcinoma (BCC) previously treated with (US prescribing information [USPI])[3]/progressed on (Summary of Product Characteristics [SmPC])[4] a hedgehog pathway inhibitor, or for whom a hedgehog pathway inhibitor is not appropriate (USPI)[3]/intolerant (SmPC),[4] and for first-line treatment of patients with locally advanced or metastatic non-small cell lung cancer who are not candidates for surgery or definitive chemoradiation and whose tumors have a tumor proportion score of ≥50% and with no *EGFR*, *ALK*, or *ROS1* aberrations.[3,4]
- Limited data exist on the clinical characteristics, management, disease progression, and survivorship of patients with advanced CSCC in real-world clinical practice.
- Here, we describe the demographics, effectiveness, and safety of an initial cohort of patients with advanced CSCC treated with cemiplimab in real-world clinical practice and enrolled in the CASE study (NCT03836105).

Objectives

- The objectives of the CASE study are to, in patients with advanced CSCC or BCC in real-world clinical settings who received cemiplimab 350 mg administered intravenously (IV) every 3 weeks (Q3W):
  - Describe effectiveness based on objective response rate (ORR) and disease control rate (DCR).
  - Evaluate the safety of cemiplimab based on incidence of treatment-related immune-related adverse events (irAEs), infusion-related reactions, and treatment-related serious adverse reactions.
  - Investigate long-term effectiveness and quality of life (QoL).

Methods

- CASE is a prospective, non-interventional, multi-center, real-world, longitudinal study evaluating effectiveness, safety, QoL, and survivorship in patients with advanced CSCC treated with cemiplimab (**Figure 1**).

Figure 1. Study schema

CSCC, cutaneous squamous cell carcinoma; DCR, disease control rate; irAE, immune-related adverse event; IRR, infusion-related reaction; ORR, objective response rate; TSAR, treatment-related serious adverse reaction.

- Adult patients (aged ≥18 years) who had recently started or planned to start treatment of CSCC or BCC with commercially available cemiplimab 350 mg IV Q3W per the approved indication and routine standard of care at one of 43 US academic and community centers were eligible to be enrolled.
- Patients were excluded if they were receiving cemiplimab for indications other than CSCC or advanced BCC, or if they had any condition that might interfere with participation in the study, restrict compliance with the treatment plan, or prevent completion of QoL assessments.
- Tumors were assessed by computed tomography or magnetic resonance imaging, and response assessments were performed according to Response Evaluation Criteria in Solid Tumours version 1.1.
- The data cut-off was February 9, 2022.

Results

Baseline demographics and disease characteristics

- As of February 9, 2022, 198 patients were enrolled in the CASE study CSCC cohort, 37 (18.7%) of whom were immunocompromised/immunosuppressed (IC/IS).
- Of the total enrolled patient population,196 patients (including 36 who were IC/IS) received at least one dose of cemiplimab (full analysis set).
- Demographics and safety data presented here are from the full analysis set; response assessment data is shown for patients who enrolled prior to starting cycle 3 of cemiplimab treatment.
- Median age was 76.0 years (range: 33.0–98.0), 75.5% of patients were male, and 90.3% were White (**Table 1**).
- IC/IS patients were investigator reported and identified as having one or more of the following diagnoses in medical history:
  - Inflammatory bowel diseases
  - Leukemia
  - Lupus
  - Lymphoma
  - Multiple myeloma
  - Multiple sclerosis
  - Rheumatoid arthritis
  - Polycythemia vera
  - Myeloproliferative disorder
  - Chronic obstructive pulmonary disease with prednisone
  - Undergone allogenic bone marrow or solid organ transplantation

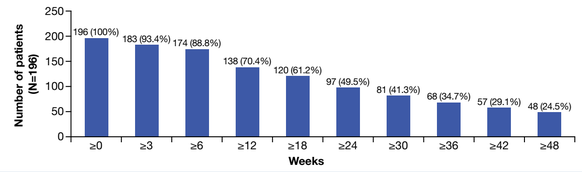
Table 1. Baseline demographics and tumor characteristics

Characteristic	Total (N=196)
Age, median (range), years	76.0 (33–98)
Male, n (%)	148 (75.5)
White, n (%)	177 (90.3)
ECOG performance status, n (%)	
0	43 (21.9)
1	89 (45.4)
2	18 (9.2)
3	2 (1.0)
Missing	44 (22.4)
Metastatic CSCC, n (%)	72 (36.7)
Locally advanced CSCC, n (%)	124 (63.3)
Current skin lesion locations, n (%)	
Head and neck	136 (69.4)
Thorax and abdomen	18 (9.2)
Upper and lower extremities	54 (27.6)
Not known	9 (4.6)
Missing	3 (1.5)
Patients with prior radiation therapy, n (%)	84 (42.9)
Patients with prior surgery, n (%)	147 (75.0)
Patients with prior systemic therapy, n (%)	89 (45.4)
Multidisciplinary input, n (%)	85 (43.4)

CSCC, cutaneous squamous cell carcinoma; ECOG, Eastern Cooperative Oncology Group.

- The median duration of cemiplimab exposure was 23.3 weeks (interquartile range: 9.1–47.1) (**Figure 2**).

Figure 2. Duration of treatment exposure



Tumor response

- Efficacy was evaluated in patients who were enrolled prior to starting cycle 3 of cemiplimab treatment (n=174).
  - Twenty-two patients were not included in the analysis, as informed consent and study enrollment were on or after the third dose of cemiplimab.
- The ORR as assessed and reported by the investigator for these patients was 37.4% (95% confidence interval [CI]: 30.2–45.0%; **Table 2**).
  - Seventeen (9.8%) patients had a complete response, and 48 (27.6%) patients had a partial response.
- The ORR for the IC/IS population of patients who were enrolled prior to starting cycle 3 (n=28) was 42.9% (95% CI: 24.5–62.8%).
- The DCR per investigator assessment was 54.6% (95% CI: 46.9–62.1%; **Table 2**).

Table 2. Tumor response to cemiplimab

	Patients who enrolled prior to Cycle 3 (N=174)
ORR, % (95% CI)	37.4 (30.2–45.0)
Best overall response, n (%)	
Complete response	17 (9.8)
Partial response	48 (27.6)
Stable disease	30 (17.2)
Progressive disease	13 (7.5)
Mixed response	4 (2.3)
Unable to evaluate	3 (1.7)
Not applicable	7 (4.0)
DCR, % (95% CI)	54.6 (46.9–62.1)

Most mixed responses were evaluated by physician visual assessment and were not included in the calculation of ORR or DCR.
CI, confidence interval; DCR, disease control rate; ORR, objective response rate.

Safety data

- Safety was evaluated in all patients included in the study (n=196).
- Nine (4.6%) patients experienced a treatment-related serious adverse event (**Table 3**).
- Forty-nine (25.0%) patients experienced a treatment-related irAE, with the most common being hypothyroidism in 15 (7.7%) patients (**Table 3**).
- There was one event of death attributed to a treatment-related serious adverse event of pneumonitis (**Table 3**).
- Thirteen (11.7%) patients discontinued due to an adverse event (**Table 4**).
- In general, cemiplimab was well-tolerated in IC/IS patients:
  - One (2.8%) patient experienced a treatment-related serious adverse event of acute kidney injury (**Table 3**).
  - Seven (19.4%) patients experienced a treatment-related irAE (**Table 3**), including:
    - Increased alanine aminotransferase
    - Increased aspartate aminotransferase
    - Pruritus
    - Hypothyroidism
    - Increased blood creatinine
    - Decreased lymphocyte count
    - Maculo-papular rash
    - Acute kidney injury
    - Fatigue

Table 3. Safety data

n (%)	Total (N=196)	IC/IS (n=36)
Any treatment-related SAR	9 (4.6)	1 (2.8)
Led to discontinuation	5 (2.6)	0
Led to death	1 (0.5)	0
Colitis	2 (1.0)	0
Adrenal insufficiency	1 (0.5)	0
Autoimmune hepatitis	1 (0.5)	0
Encephalitis	1 (0.5)	0
Pneumonia	1 (0.5)	0
Urosepsis	1 (0.5)	0
Hyperglycemia	1 (0.5)	0
Acute kidney injury	1 (0.5)	1 (2.8)
Pneumonitis	1 (0.5)	0
Any treatment-related irAE	49 (25.0)	7 (19.4)
Any infusion-related reaction	1 (0.5)	0

IC/IS, immunocompromised/immunosuppressed; irAE, immune-related adverse event; SAR, serious adverse reaction.

Table 4. Treatment discontinuation

	Total (N=196)
Treatment ongoing, n (%)	85 (43.4)
Treatment discontinued, n (%)	111 (56.6)
Primary reason for treatment discontinuation, n (%)†	
Adverse event	13 (11.7)
Complete response	6 (5.4)
Death	4 (3.6)
Disease progression	17 (15.3)
Lost to follow-up	1 (0.9)
Non-compliance	2 (1.8)
Other	16 (14.4)
Patient initiated CSCC-related drug treatment	3 (2.7)
Patient initiated CSCC-related surgery	3 (2.7)
Patient withdrawal	19 (17.1)
Physician decision	27 (24.3)
Primary reason for follow-up discontinuation, n (%)‡	
Completed	1 (1.6)
Death	29 (46.8)
Disease progression	4 (6.5)
Lost to follow-up	3 (4.8)
Patient withdrawal	18 (29.0)
Physician decision	3 (4.8)
Other	4 (6.5)

†Percentages are calculated from the number of patients who discontinued treatment (n=111). ‡Percentages are calculated from the number of patients who discontinued from follow-up (n=62).
CSCC, cutaneous squamous cell carcinoma.

Limitations

- Not all patients were enrolled and followed within the study from the time of treatment, and there is inherent bias associated with observational studies versus a prospective interventional study.

Conclusions

- Observational studies such as CASE enroll a broader, real-world patient population that is not limited by stricter eligibility criteria.
- The safety, tolerability, and effectiveness of cemiplimab in this initial cohort of patients with advanced CSCC was generally consistent with that observed in clinical trials (NCT02383212, NCT02760498), considering real-world practice setting and a broader patient population.
- In this initial cohort of patients who were identified as IC/IS, the safety, tolerability, and effectiveness of cemiplimab was consistent with the overall patient population.
- Further follow-up and future analyses will provide additional outcomes measures and understanding of cemiplimab in the real-world setting (and during the COVID-19 pandemic), in patients with advanced CSCC and the subset of those who are IC/IS.

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Disclosures

Guilherme Rabinowits reports consulting/advisory roles for EMD Serono, Pfizer, Sanofi, Regeneron Pharmaceuticals, Inc., and Merck and Castle; and stock/other ownership interests from Syros Pharmaceuticals and Regeneron Pharmaceuticals, Inc.

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