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

Guilherme Rabinowits,¹ Jade Homsi,² Soo J Park,³ Nikhil Khushalani,⁴ Timothy Panella,⁵ David M Ellison,⁶ Rhonda W Gentry,⁷ Suraj S Venna,⁸ John Strasswimmer,⁹ Richard Zuniga,¹⁰ Sunandana Chandra,¹¹ Emily S Ruiz,¹² Michael R Migden,¹³ Sherrif F Ibrahim,¹⁴ Nikita Mehta,¹⁵ Timothy Inocencio,¹⁶ Xuanyao He,¹⁶ Haixin R Zhang,¹⁶ Kathryn Gillis,¹⁶ Jean-Francois Pouliot¹⁶

¹Department of Hematology and Oncology, Miami Cancer Institute/Baptist Health South Florida, Miami, FL, USA; ⁴Moffitt Cancer Center, Tampa, FL, USA; ¹Division of Hematology and Oncology, University of California San Diego, CA, USA; ⁴Moffitt Cancer Center, Tampa, FL, USA; ¹Division of Hematology and Oncology, University of California San Diego, San Diego, CA, USA; ⁴Moffitt Cancer Center, Tampa, FL, USA; ¹Division of Hematology and Oncology, University of California San Diego, San Diego, CA, USA; ⁴Moffitt Cancer Center, Tampa, FL, USA; ¹Division of Hematology and Oncology, University of California San Diego, San Diego, San Diego, CA, USA; ⁴Moffitt Cancer Center, Tampa, FL, USA; ¹Division of Hematology and Oncology, University of California San Diego, ⁵University of Tennessee Medical Center, Knoxville, TN, USA; ⁸College of Medicine (Dermatology) and College of Sciences (Biochemistry), Florida Atlantic University, Boca Raton, FL, USA; ¹⁰New York Cancer and Blood Specialists, Port Jefferson, NY, USA; ¹¹Division of Hematology and Oncology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA; ¹²Brigham and Women's Hospital, Boston, MA, USA; ¹³University of Texas MD Anderson Cancer Center, Houston, TX, USA; ¹⁴Rochester Dermatologic Surgery, PC, Victor, NY, USA; ¹⁵Sanofi, Cambridge, MA, USA; ¹⁶Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA

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-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 \geq 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



- Adult patients (aged \geq 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.



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
- Chronic obstructive pulmonary disease
- with prednisone
- Myeloproliferative disorder
- Undergone allogenic bone marrow or solid organ transplantation

Iable 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 G	Group.			

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



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). 			Total (N=196)
		Treatment ongoing, n (%) Treatment discontinued, n (%) Primary reason for treatment discontinuation, n (%) [†]	85 (43.4) 111 (56.6)
Table 2. Tumor response to cemiplima	ab	Adverse event	13 (11.7)
	Patients who enrolled prior to Cycle 3 (N=174)	Complete response Death Disease progression	6 (5.4) 4 (3.6) 17 (15.3)
ORR, % (95% CI)	37.4 (30.2–45.0)	Lost to follow-up	1 (0.9)
Best overall response, n (%)		Non-compliance	2 (1.8)
Complete response	17 (9.8)	Other	16 (14.4)
Partial response	48 (27.6)	Patient initiated CSCC-related drug treatment	3 (2.7)
Stable disease	30 (17.2)	Patient initiated CSCC-related surgery	3 (2.7)
Progressive disease	13 (7.5)	Patient withdrawal Physician decision	19 (17.1) 27 (24 3)
Mixed response	4 (2.3)	Primary reason for follow-up discontinuation. n (%) [‡]	
Unable to evaluate	3 (1.7)	Completed	1 (1.6)
Not applicable	7 (4.0)	Death	29 (46.8)
DCR. % (95% CI)	54.6 (46.9–62.1)	Disease progression	4 (6.5)
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.		Lost to follow-up Patient withdrawal	3 (4.8) 18 (29.0)
Safety data		Physician decision	3 (4.8)
		Other	4 (6.5)
 Safety was evaluated in all patients included in the study (n=196). Ning (4.6%) patients experienced a treatment related pariaus adverse event (Table 2) 		[†] Percentages are calculated from the number of patients who discontinued treatment (n=111).	62)

- Nine (4.6%) patients experienced a treatment-related serious adverse event (laple 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
- Decreased lymphocyte count

Increased blood creatinine

- Hypothyroidism
- Maculo-papular rash Acute kidney injury Fatigue

Table 3. Safety data

– Pruritus

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, immu	une-related adverse event; SAR, serious ad	dverse reaction.

Table 4. Treatment discontinuation

rencentages 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.

References

- 1. de Jong E et al. J Eur Acad Derm Venereol. 2021;36(Suppl. 1):6-10.
- 2. Burova E et al. Mol Cancer Ther. 2017;16:861–870.
- Regeneron Pharmaceuticals, Inc. LIBTAYO® [cemiplimab-rwlc] injection full US prescribing information.
- Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761097s007lbl.pdf [Accessed Jul 9, 2022].
- European Medicines Agency. LIBTAYO[®] EPAR. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/libtayo [Accessed Jul 25, 2022].

Acknowledgments

The authors thank the patients, their families, all other investigators, and all investigational site members involved in this study. The study was funded by Regeneron Pharmaceuticals, Inc., and Sanofi. Medical writing support and typesetting was provided by Jenna Lee, MSc, of Prime, Knutsford, UK, funded by Regeneron Pharmaceuticals, Inc., and Sanofi.

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. Additional author disclosures are available in the supplementary material.



