Real-world patient characteristics, treatment patterns, and outcomes among patients with advanced cutaneous squamous cell carcinoma treated with cemiplimab at US oncology clinical practices

Wenzhen Ge,[1] Ning Wu,[1] Chieh-I Chen,[1] Timothy J. Inocencio,[1] Patrick R. LaFontaine,[2] Frank Seebach,[1] Matthew Fury,[1] James Harnett,[1] Emily Ruiz[3]

[1]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [2]Sanofi, Cambridge, MA, USA; [3]Department of Dermatology, Dana-Farber Cancer Institute, Boston, MA, USA

Background

- Cutaneous squamous cell carcinoma (CSCC) is the second most common skin cancer in the United States.[1–3]
- Most cases of CSCC are cured by surgery/radiation, but an estimated 1% to 5% of patients will develop advanced disease, which is associated with poor prognosis.[4]
- Cemiplimab was the first treatment approved by the US Food and Drug Administration and European Medicines Agency for the treatment of patients with metastatic or locally advanced CSCC who are not candidates for curative surgery or radiation (i.e., advanced CSCC.[5,6]
- Prior to approval of cemiplimab, median overall survival (OS) for adult patients with advanced CSCC receiving systemic therapy was 8–15 months.[7–15]
- Limited real-world data are available on cemiplimab in the treatment of advanced CSCC in the United States.

Objectives

- To describe patient characteristics, treatment patterns, and outcomes among patients with advanced CSCC treated with cemiplimab monotherapy in largely community oncology clinical practices in the United States.
- To explore potential prognostic factors (demographic and clinical characteristics) associated with OS in this population.

Methods

Study design and data source

- This retrospective cohort study included adult patients with advanced CSCC initiating cemiplimab monotherapy in the United States between 2018 and 2021 in the nationwide de-identified Flatiron Health database.[16]

Study population

- The main study cohort initiated cemiplimab monotherapy (index date: date of first dose of cemiplimab monotherapy) between September 28, 2018, and September 30, 2021, and had ≥2 visits in the Flatiron Health network on or after January 1, 2011, with:
  - Confirmed diagnosis of advanced CSCC (locally advanced CSCC not amenable to curative intent surgery or radiation or metastatic CSCC) on or before index date.
  - First structured electronic health record (EHR) before or within 30 days after advanced CSCC diagnosis date.
  - Excluding patients who initiated cemiplimab with other systemic treatment or participated in a clinical trial on or before index date.
- A trial-like cohort (a sub-cohort of the main cohort) was identified, meeting select inclusion and exclusion criteria of the cemiplimab R2810-ONC-1540 clinical trial.[17–19]
  - Patients with ≥1 Eastern Cooperative Oncology Group (ECOG) performance status (PS) measurement of ≤1 on or within 30 days pre-index.
  - Excluding patients with:
    - Any other malignancy receiving antineoplastic treatment within 3 years before the index date.
    - Any central nervous system metastasis (ICD-10-CM codes C79.3X or C79.4X) on or prior to the index date.
    - Immunocompromised status on or before the index date (≥1 diagnosis of transplant, hematological malignancies, or other conditions using ICD-9/ICD-10 diagnosis or procedure codes and/or abstracted data).
    - Abnormal hepatic, renal, or bone marrow function within 30 days before or on the index date.
- Patients were followed from index date to the end of follow-up (i.e., the date of last structured EHR activity), death, or end of study (December 31, 2021), whichever occurred first.

Outcomes

- Treatment pattern outcomes included the line setting of cemiplimab and type of treatment by line of therapy (LOT).
- Time to treatment discontinuation (TTD): Time from the initiation of a certain LOT until the date of treatment line discontinuation (i.e., having a gap of >90 days with no systemic therapy) or death, whichever occurred first.
- Time to next treatment (TTNT): Time from the initiation of a certain LOT to the date of initiation of a subsequent LOT or death, whichever occurred first.
- Overall survival: Time from index date to date of death.

Statistical analysis

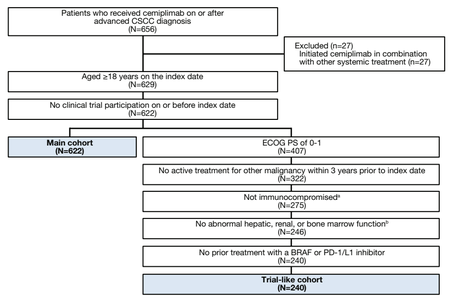
- Baseline characteristics and treatment history for each cohort were summarized using descriptive statistics.
- Median (95% CI) TTD, TTNT, and OS were estimated using the Kaplan–Meier method for each cohort.
- Cox proportional hazard models were used to examine potential prognostic factors associated with OS in the main cohort. Univariate models assessed magnitude/significance of baseline variables, with known prognostic factors and significant variables carried forward to a multivariate model.

Results

Patient selection and characteristics

- In total, 622 patients were included in the main cohort and 240 patients in the trial-like cohort (**Figure 1**).

Figure 1. Study cohort selection



BRAF, B-Raf proto-oncogene, serine/threonine kinase; CSCC, cutaneous squamous cell carcinoma; ECOG, Eastern Cooperative Oncology Group; PD-1/L1, programmed death receptor-1/ligand-1; PS, performance status; ULN, upper limit of normal.
[a]Immunocompromised status defined as having ≥1 of the following on or before the index date: prior transplant (allogenic bone marrow transplant, solid organ transplant), hematological malignancies (leukemia, lymphoma, multiple myeloma), or other conditions (Addison's disease, celiac disease, Grave's disease, Hashimoto's thyroiditis, HIV, inflammatory bowel disease, lupus, multiple sclerosis, myasthenia gravis, pernicious anemia, psoriasis or psoriatic arthritis, rheumatoid arthritis, Sjogren's syndrome, type 1 diabetes, vasculitis). [b]Abnormal hepatic function defined as total bilirubin >1.5 × ULN (or >3 × ULN if liver metastases), transaminases >3 × ULN (or >5 × ULN, if liver metastases), or alkaline phosphatase >2.5 × ULN (or >5 × ULN, if liver or bone metastases). Abnormal renal function defined as serum creatinine >1.5 × ULN or estimated creatinine clearance <30 mL/min. Abnormal bone marrow function defined as hemoglobin <9.0 g/dL, absolute neutrophil count <1.5 × 10⁹/L, or platelet count <75 × 10⁹/L.

- In the main cohort, median age at cemiplimab initiation was 78 years, 77.8% were male, 21.4% were immunocompromised, and 63.8% had metastatic CSCC (**Table 1**).
- Similar patient characteristics were observed in the trial-like cohort except for those that were implemented as inclusion/exclusion criteria by design (**Table 1**).
- Differences in select baseline characteristics were observed for the main cohort when stratified by stage at index (**Supplemental Table; see QR code**).
- Median (95% CI) follow-up was 16.6 (14.9–18.7) months in the main cohort and 15.3 (13.1–18.0) months in the trial-like cohort.

Treatment patterns

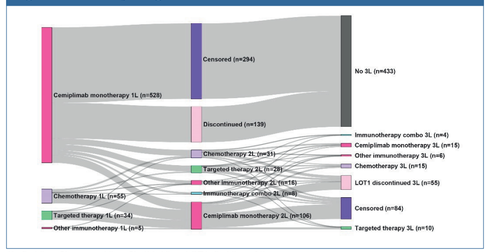
- Most patients (n/N=528/622; 84.9%) in the main cohort initiated cemiplimab monotherapy as the first-line systemic therapy (**Figure 2**).
  - Of those initiating first-line cemiplimab, 95 (18.0%) received second-line systemic therapy whereas 294 (55.7%) were censored.
- For patients who initiated cemiplimab monotherapy in the second line (n/N=76/622; 12.2%), the first-line treatments were mostly chemotherapy (n=40) or targeted therapies (n=32).

Table 1. Baseline demographics and clinical characteristics

	Main cohort (N=622)	Trial-like cohort (N=240)
Age at index, years, median (Q1–Q3)	78 (70–83)	76 (68–83)
Age at index, years, n (%)		
18–59	49 (7.9)	21 (8.8)
60–69	101 (16.2)	45 (18.8)
60–69	201 (32.3)	83 (34.6)
≥80	272 (43.6)	91 (37.9)
Male sex, n (%)	484 (77.8)	178 (74.2)
Race, n (%)		
White	448 (72.0)	174 (72.5)
Other[a]	121 (19.5)	42 (17.5)
Missing	53 (8.5)	24 (10.0)
Ethnicity, n (%)		
Non-Hispanic or Latino	606 (97.4)	231 (96.3)
Hispanic or Latino	16 (2.6)	9 (3.8)
Region, n (%)		
Midwest	50 (8.0)	19 (7.9)
Northeast	42 (6.8)	14 (5.8)
South	300 (48.2)	113 (47.1)
West	64 (10.3)	27 (11.3)
Unknown/other	166 (26.7)	67 (27.9)
Practice type, n (%)		
Academic	128 (20.6)	52 (21.7)
Community	494 (79.4)	188 (78.3)
Insurance type, n (%)		
Commercial	424 (68.2)	164 (68.3)
Medicare or Medicaid	112 (18.0)	44 (18.3)
Other	63 (10.1)	24 (10.0)
Missing	23 (3.7)	8 (3.3)
ECOG performance status, n (%)		
0	167 (26.8)	97 (40.4)
1	240 (38.6)	143 (59.6)
≤2	111 (17.8)	NA
Missing	104 (16.7)	NA
Stage at index, n (%)		
Locally advanced not amenable to curative intent surgery or radiation	225 (36.2)	87 (36.3)
Regional metastatic	274 (44.1)	99 (41.3)
Distant metastatic	123 (19.8)	54 (22.5)
Line setting of cemiplimab, n (%) at index, n (%)		
1	528 (84.9)	209 (87.1)
2+	94 (15.1)	31 (12.9)
Index year		
2018	39 (6.3)	16 (6.7)
2019	212 (34.1)	77 (32.1)
2020	213 (34.2)	90 (37.5)
2021	158 (25.4)	57 (23.8)
Diagnosis to index date, median (IQR), months	1.3 (0.5–6.2)	1.1 (0.5–5.5)
Immunocompromised status, n (%)[b]		
None	489 (78.6)	240 (100.0)
Hematological malignancy	101 (16.2)	NA
Other immunodeficiency	21 (3.4)	NA
Prior transplant	11 (1.8)	NA
Any malignancy diagnosed before index date, n (%)	284 (45.7)	61 (25.4)
Any treatment for other malignancy within 3 years before index date, n (%)	130 (20.9)	0 (0)
Primary location of CSCC, n (%)		
Head and neck only	345 (55.5)	128 (53.3)
Extremities only	91 (14.6)	44 (18.3)
Trunk only	30 (4.8)	10 (4.2)
Other	31 (5.0)	16 (6.7)
Multiple sites	125 (20.1)	42 (17.5)

CSCC, cutaneous squamous cell carcinoma; ECOG, Eastern Cooperative Oncology Group; NA, not applicable.
[a]Other race includes people who selected Asian, Black or African American, or Other race.
[b]Immunocompromised status defined as having 1 or more of the following on or before the index date: prior transplant (allogenic bone marrow transplant, solid organ transplant), hematological malignancies (leukemia, lymphoma, multiple myeloma), or other conditions (Addison's disease, celiac disease, Grave's disease, Hashimoto's thyroiditis, HIV, inflammatory bowel disease, lupus, maultiple sclerosis, myasthenia gravis, pernicious anemia, psoriasis or psoriatic arthritis, rheumatoid arthritis, Sjogren's syndrome, type 1 diabetes, vasculitis).

Figure 2. Sankey diagram[a]

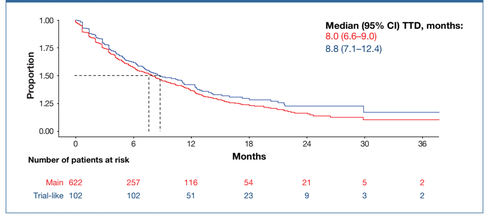


1L, first line; 2L, second line; 3L, third line; LOT1, first line of therapy.
[a]Cemiplimab patients were indexed across first, second, and third lines (most were indexed on LOT1). Targeted therapy included afatinib, cetuximab, erlotinib, gefitinib, lapatinib, panitumumab, dabrafenib, or vemurafenib. Other immunotherapy included atezolizumab, avelumab, durvalumab, nivolumab, pembrolizumab, ipilimumab, cemiplimab, interferon alfa-2a, or pegylated interferon alfa-2a.

Time to treatment discontinuation

- Median (95% CI) TTD was 8.0 (6.6–9.0) months in the main cohort and 8.8 (7.1–12.4) months in the trial-like cohort (**Figure 3**).

Figure 3. Time to treatment discontinuation in main and trial-like cohorts

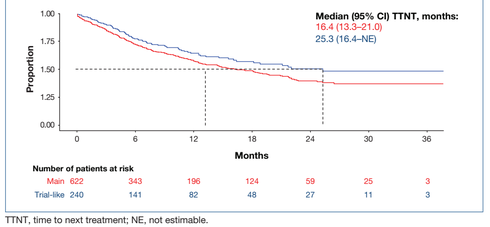


TTD, time to treatment discontinuation.

Time to next treatment

- Median (95% CI) TTNT was 16.4 (13.3–21.0) months in the main cohort and 25.3 months (16.4 months to not estimable [NE]) in the trial-like cohort (**Figure 4**).

Figure 4. Time to next treatment in main and trial-like cohorts

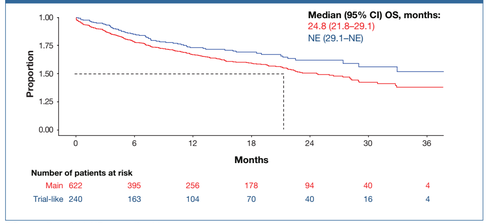


TTNT, time to next treatment; NE, not estimable.

Overall survival

- Median (95% CI) OS was 24.8 (21.8–29.1) months in the main cohort and was not reached in trial-like cohort (**Figure 5**).
- Stratified analysis of OS in the main cohort is shown in the **Supplemental Figure (see QR code)**.

Figure 5. Overall survival in main and trial-like cohorts

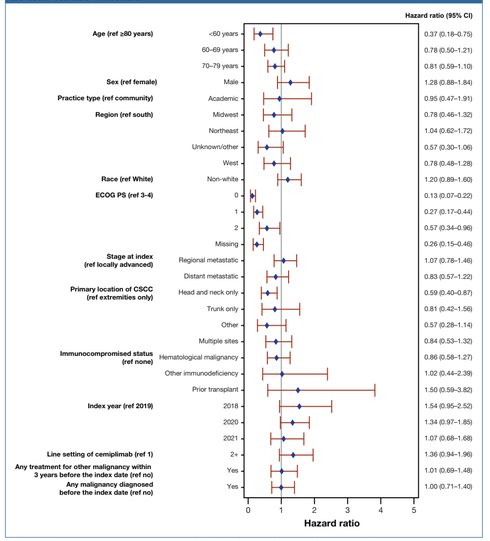


OS, overall survival; NE, not estimable

Prognostic factors for OS

- In multivariable analyses, younger age, lower ECOG PS, and primary CSCC location in the head and neck only (vs extremities) were associated with better OS (**Figure 6**).

Figure 6. Cox results: Prognostic factors for overall survival in the main cohort



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

Conclusions

- In this study, median OS was more than 2 years among patients with advanced CSCC initiating cemiplimab monotherapy in the real-world setting with a study period overlapping with the COVID-19 pandemic.
- Overall survival for patients in our real-world trial-like cohort approached that reported in the phase 2 cemiplimab clinical trial,[20] despite the patients being older and a greater proportion having metastatic disease.
- Our trial-like cohort may not fully resemble patients in the trial as not all inclusion and exclusion criteria were able to be applied and the study population primarily reflects treatment in the community oncology setting.
- These findings confirm the effectiveness of cemiplimab among a heterogenous, real-world population of patients with advanced CSCC and substantiate the clinical activity of cemiplimab as observed in clinical trials.

References

1. Karimkhani C, et al. *J Am Acad Dermatol*. 2015;72:186–187.
2. Rogers HW, et al. *JAMA Dermatol*. 2015;151:1081–1086.
3. Stratigos AJ, et al. *Eur J Cancer*. 2020;128:60–82.
4. Schmults CD, et al. *JAMA Dermatol*. 2013;149:541-547.
5. European Medicines Agency. Libtayo: EPAR - Product information. Available from: https://www.ema.europa.eu/en/documents/productinformation/libtayo-epar-product-information_en.pdf. Accessed March 23, 2023.
6. Regeneron Pharmaceuticals Inc. LIBTAYO® (cemiplimab-rwlc) injection prescribing information. Available from: https://www.regeneron.com/downloads/libtayo_fpi.pdf. Accessed March 23, 2023.
7. Bossi P, et al. *J Clin Oncol*. 2017;35:9543.
8. Foote MC, et al. *Ann Oncol*. 2014;25:2047–2052.
9. Gold KA, et al. *Cancer*. 2018;124:2169–2173.
10. Jarkowski AI, et al. *Am J Clin Oncol*. 2016;39:545–548.
11. Maubec E, et al. *J Clin Oncol*. 2011;29:3419–3426.
12. Picard A, et al. *JAMA Dermatol*. 2017;153:291–298.
13. Sun L, et al. *JAMA Dermatol*. 2019;155:442–447.
14. William WN, Jr., et al. *J Am Acad Dermatol*. 2017;77:1110–1113.e2.
15. Cowey CL, et al. *Cancer Med*. 2020;9:7381–7387.
16. Ma X, et al. *medRxiv*. 2020:2020.03.16.20037143.
17. Migden MR, et al. *Lancet Oncol*. 2020;21:294–305.
18. Migden MR, et al. *N Engl J Med*. 2018;379:341–351.
19. Rischin D, et al. *J Immunother Cancer*. 2020;8:e000775.
20. Rischin D, et al. *J Immunother Cancer*. 2021;9:e002757.

Acknowledgments

The study was funded by Regeneron Pharmaceuticals, Inc. Medical writing support was provided by Prime (Knutsford, UK), funded by Regeneron Pharmaceuticals, Inc.

Scan this QR code for author disclosures and to download a copy of the poster, including supplemental material

Fall Clinical Dermatology Congress, October 19–22, 2023. Encore previously presented at the European Associate of Dermatology (EADO) Congress, April 20–22, 2023.