# Interim Analysis of Phase 2 Results for Cemiplimab, a Human Monoclonal Antibody to Programmed Death-1, in Patients with Locally Advanced Cutaneous Squamous Cell Carcinoma


**Michael R. Migden,**[1] Carola Berking,[2] Anne Lynn S. Chang,[3] Thomas K. Eigentler,[4] Axel Hauschild,[5] Leonel Hernandez-Aya,[6] Nikhil I. Khushalani,[7] Karl D. Lewis,[8] Friedegund Meier,[9] Badri Modi,[10] Danny Rischin,[11] Dirk Schadendorf,[12] Chrysalyne D. Schmults,[13] Claas Ulrich,[14] Jocelyn Booth,[15] Siyu Li,[15] Kosalai Mohan,[16] Elizabeth Stankevich,[15] Israel Lowy,[16] Matthew G. Fury[16]

[1]Departments of Dermatology and Head and Neck Surgery, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Department of Dermatology and Allergy, Munich University Hospital (LMU), Munich, Germany; [3]Department of Dermatology, Stanford University School of Medicine, Redwood City, CA, USA; [4]Department of Dermatology, University Medical Center Tübingen, Tübingen, Germany; [5]Schleswig-Holstein University Hospital, Kiel, Germany; [6]Division of Medical Oncology, Department of Medicine, Washington University School of Medicine, St Louis, MO, USA; [7]Department of Cutaneous Oncology, Moffitt Cancer Center, Tampa, FL, USA; [8]University of Colorado Denver, School of Medicine, Aurora, CO, USA; [9]Department of Dermatology, University Hospital Dresden, Dresden, Germany; [10]Division of Dermatology, City of Hope, Duarte, CA, USA; [11]Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia; [12]University Hospital Essen, Essen and German Cancer Consortium, Essen, Germany; [13]Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA; [14]Department of Dermatology, Venereology and Allergology, Skin Cancer Center Charité, Berlin, Germany; [15]Regeneron Pharmaceuticals, Inc., Basking Ridge, NJ, USA; [16]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA.


## Background

- Cutaneous squamous cell carcinoma (CSCC) is the second most common skin cancer, after basal cell carcinoma.[1]
- Surgical cure rate for CSCC is high in early stage disease.[2]
- There is no approved systemic therapy for patients with advanced CSCC (locally advanced CSCC that is no longer amenable to surgery or radiation therapy, or metastatic CSCC).
- Cemiplimab (REGN2810) is a high-affinity, highly potent human monoclonal antibody directed against programmed death-1 (PD-1).[3,4]
- Cemiplimab demonstrated substantial activity and durable response with a safety profile comparable with other anti-PD-1 agents, in patients with advanced CSCC from Phase 1 expansion cohorts and patients with metastatic CSCC from primary analysis of the Phase 2 study.[4]
- Here, we present a prespecified interim analysis of the locally advanced CSCC cohort from the pivotal Phase 2 study (NCT02760498).

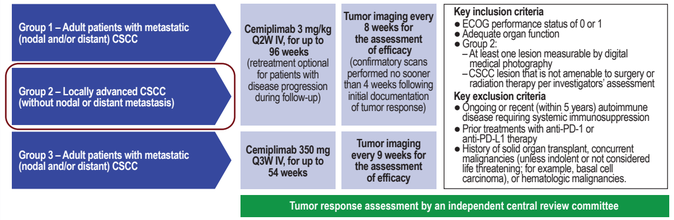
## Objectives

- The primary objective was to evaluate overall response rate according to independent central review per Response Evaluation Criteria In Solid Tumors (RECIST) 1.1[5] (for scans) and modified World Health Organization criteria (WHO; for photos).
- Secondary objectives include:
  - Estimation of duration of response (durable disease control rate was also analyzed)
  - Assessment of safety and tolerability of cemiplimab.

## Methods

- Adult patients with locally advanced CSCC (without nodal or distant metastasis), who were not candidates for surgery or radiation therapy, from Group 2 of the Phase 2, non-randomized, global, pivotal trial of cemiplimab in patients with advanced CSCC are included in this analysis (Figure 1).
- Severity of treatment-emergent adverse events (TEAEs) was graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (version 4.03).
- This interim analysis was prespecified and includes patients who started study treatment at least 9 months prior to the data cut-off date (October 27, 2017).

**Figure 1.** Study design




ECOG, Eastern Cooperative Oncology Group; IV, intravenously; PD-L1, programmed death-ligand 1; Q2W, every 2 weeks; Q3W, every 3 weeks.

## Results

### Baseline characteristics, disposition, and treatment exposure

- As of the data cut-off date, 23 patients were eligible for inclusion in this analysis (Table 1).
  - Thirteen patients (56.5%) remained on treatment and 10 (43.5%) have discontinued treatment (the most common reason for discontinuation was disease progression [n=3; 13.0%]).
  - The median duration of follow-up at the time of data cut-off was 9.7 months (range: 0.8–15.9).

**Table 1.** Patient demographics, baseline characteristics, and exposure to cemiplimab

| | Locally advanced CSCC (N=23) |
|---|---|
| Median age, years (range) | 67 (47–96) |
| ≥ 65 years, n (%) | 13 (56.5) |
| Male, n (%) | 17 (73.9) |
| ECOG performance status score, n (%) | |
| 0 | 13 (56.5) |
| 1 | 10 (43.5) |
| Primary CSCC site, n (%) | |
| Head/neck | 17 (73.9) |
| Extremity | 5 (21.7) |
| Trunk | 1 (4.3) |
| Prior systemic therapy for CSCC, n (%) | 6 (26.1) |
| Prior radiotherapy for CSCC, n (%) | 14 (60.9) |
| Median duration of cemiplimab exposure (range), weeks | 43.3 (2.0–68.0) |
| Median number of cemiplimab doses administered (range) | 22 (1–31) |

### Clinical efficacy

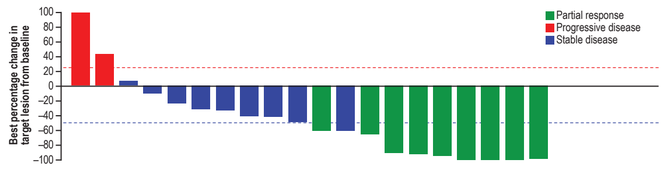
- Tumor response assessment, characteristics of tumor response, and examples of reductions in visible lesions following cemiplimab treatment are shown in Table 2 and Figures 2–4.
- Median duration of response has not been reached. The longest duration of response at the time of data cut-off is 12.9+ months.

**Table 2.** Tumor response assessment by independent central review

| | Locally advanced CSCC (N=23) |
|---|---|
| Best overall response, n (%) | |
| Complete response | 0 |
| Partial response | 10 (43.5) |
| Stable disease | 9 (39.1) |
| Progressive disease | 2 (8.7) |
| Not evaluable† | 2 (8.7) |
| Overall response rate, % (95% CI) | 43.5 (23.2–65.5) |
| Durable disease control rate, % (95% CI)‡ | 69.6 (47.1–86.8) |
| Median observed time to response, months (range)§ | 2.8 (1.9–7.6) |

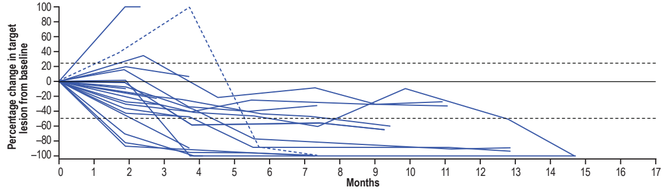
†Includes missing and unknown tumor response. ‡Defined as the proportion of patients without progressive disease for at least 105 days. §Data shown are from patients with confirmed responses.
CI, confidence interval.

**Figure 2.** Clinical activity of tumor response to cemiplimab in patients who underwent photo evaluation per WHO criteria by independent central review



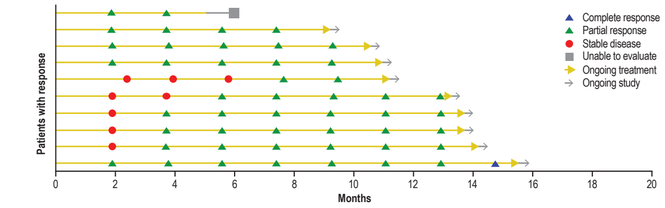

Plot shows the best percentage change in the sum of target lesion diameters from baseline for 20 patients who underwent photo evaluation per independent central review after treatment initiation. Lesion measurements after progression were excluded. Blue and red dotted lines indicate WHO criteria for partial response (≥50% decrease in the sum of target lesion diameters) and progressive disease (≥25% increase in the target lesion diameters). Three patients that do not appear in the figure (but are included in the overall response analysis [Table 2], per intention-to-treat) are: two patients with no evaluable post-treatment tumor assessment and one patient who did not have a measurable skin disease.

**Figure 3.** Change in target lesion per WHO criteria over time




Plot shows the percentage change in target lesion diameters from baseline over time. Patients shown in this figure are the same as those in Figure 2. Horizontal dotted lines indicate criteria for partial response (≥50% decrease in the sum of target lesion diameters) and progressive disease (≥25% increase in the target lesion diameters). One patient (dashed blue line) had increased target lesion measurements at week 8 and week 16 that met criteria for progressive disease (by independent central review), followed by complete resolution of target lesions. This suggests that patients with locally advanced CSCC may occasionally experience an increase in target lesions, followed by subsequent durable response.

**Figure 4.** Time to response and duration of response in responding patients




Plot shows time to response and duration of response in the 10 responding patients. Each horizontal line represents one patient. Nine of the 10 patients remain in response and on study at time of data cut-off. One patient was censored (top line) after missing treatments due to co-morbidities and withdrawing consent from study; therefore, they no longer met the dual criteria of ongoing response per independent central review and ongoing study treatment.

- Neither median overall survival nor median progression-free survival had been reached at the time of data cut-off.
  - The estimated probability of survival at 12 months was 91.1% (95% CI: 68.8–97.7).
  - The estimated progression-free probability at 12 months was 65.6% (95% CI: 37.6–83.4).

### Treatment-emergent adverse events

- TEAEs regardless of attribution are summarized in Table 3.
- Investigator-assessed treatment-related TEAEs are summarized in Table 4.

**Table 3.** TEAEs regardless of attribution

| TEAEs | Locally advanced CSCC (N=23) | |
|---|---|---|
| n (%) | Any grade | Grade ≥3 |
| Any | 23 (100.0) | 8 (34.8) |
| Serious | 5 (21.7) | 4 (17.4) |
| Led to discontinuation | 1 (4.3) | 1 (4.3) |
| With an outcome of death† | 2 (8.7) | 2 (8.7) |
| Occurred in at least four patients‡ | | |
| Fatigue | 9 (39.1) | 1 (4.3) |
| Diarrhea | 7 (30.4) | 0 |
| Nausea | 6 (26.1) | 0 |
| Pruritus | 5 (21.7) | 0 |
| Hypothyroidism | 5 (21.7) | 0 |
| Arthralgia | 4 (17.4) | 1 (4.3) |
| Decreased appetite | 4 (17.4) | 0 |
| Dry skin | 4 (17.4) | 0 |
| Pneumonia | 4 (17.4) | 3 (13.0) |

†One death was considered unrelated to study treatment: the patient was hospitalized on study day 134 with pneumonia and placed on a ventilator for support. The patient was also found to have evidence of heart failure, considered secondary to septic shock. The patient was extubated and died on study day 136. Details of the death that was considered related to treatment can be found in Table 4. ‡Events are listed as indicated on the case report form. Adverse events were coded according to Preferred Terms (MedDRA version 20.0). Included in this table are TEAEs of any grade that occurred in ≥4 patients. Events are listed in decreasing order of frequency by any grade.

**Table 4.** Investigator-assessed treatment-related TEAEs

| TEAEs | Locally advanced CSCC (N=23) | |
|---|---|---|
| n (%) | Any grade | Grade ≥3 |
| Any | 20 (87.0) | 3 (13.0) |
| Serious | 1 (4.3) | 1 (4.3) |
| Led to discontinuation | 1 (4.3) | 1 (4.3) |
| With an outcome of death† | 1 (4.3) | 1 (4.3) |
| Occurred in at least four patients‡ | | |
| Fatigue | 7 (30.4) | 0 |
| Nausea | 5 (21.7) | 0 |
| Diarrhea | 4 (17.4) | 0 |
| Hypothyroidism | 4 (17.4) | 0 |

†Patient developed hyponatraemia on study day 13 and pneumonia on study day 14; both TEAEs were assessed as unrelated to treatment. The patient died on study day 24 due to unknown cause that was assessed as treatment-related. ‡Events are listed as indicated on the case report form. Adverse events were coded according to Preferred Terms (MedDRA version 20.0). Included in this table are investigator-assessed treatment-related TEAEs of any grade that occurred in ≥4 patients. Events are listed in decreasing order of frequency by any grade. Grade ≥3 treatment-related TEAEs reported were dizziness (n=1) and increased aspartate aminotransferase (n=1).

## Conclusions

- The results of the prespecified interim analysis of patients with locally advanced CSCC from this Phase 2 prospective study show that treatment with cemiplimab 3 mg/kg Q2W is associated with substantial activity and durable responses. The safety profile is comparable with other anti-PD-1 agents.
- Combined with recently published data,[4] this analysis further demonstrates that advanced CSCC, whether metastatic or locally advanced, is responsive to cemiplimab.

**The locally advanced CSCC cohort (Group 2) of the Phase 2 study is now fully enrolled; the primary analysis of the results is pending.**


### References

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