Phase 2 Study of Cemiplimab in Patients with Advanced Cutaneous Squamous Cell Carcinoma (CSCC): Longer Follow-Up

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Background

- Cutaneous squamous cell carcinoma (CSCC) is the second most common cancer in the US and its incidence is increasing.[1]
- Most cases of CSCC are cured by complete surgical excision.[2,3] However, a small but substantial number of patients present with either metastatic CSCC (mCSCC) or locally advanced CSCC (laCSCC) not amenable to curative surgery or curative radiotherapy (collectively referred to as "advanced CSCC"), both of which have poor prognoses.[4–6]
- Historical data shows median overall survival (OS) of approximately 15 months with conventional chemotherapy or epidermal growth factor receptor inhibitors.[7]
- Cemiplimab is a high-affinity, highly potent human immunoglobulin G4 monoclonal antibody to the programmed cell death (PD)-1 receptor.[8]
- Cemiplimab monotherapy achieved clinically meaningful activity in patients with advanced CSCC and has a safety profile consistent with other anti–PD-1 inhibitors.[9–11]
- Based on initial data (median follow-up of 9.4 months in the pivotal study, NCT02760498), cemiplimab (cemiplimab-rwlc in the US) was approved for the treatment of patients with advanced CSCC.

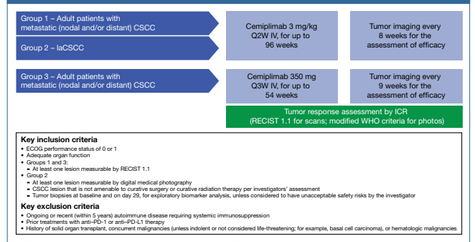
Objective

- The primary objective of the Phase 2 study was to evaluate the objective response rate (ORR) by independent central review (ICR) per Response Evaluation Criteria In Solid Tumors version 1.1 (RECIST 1.1) (for scans)[12] and modified World Health Organization (WHO) criteria (for photos).
- Key secondary objectives included ORR per investigator review (INV), duration of response (DOR) by ICR and INV, progression-free survival (PFS) by ICR and INV, OS, complete response rate by ICR, safety and tolerability, and assessment of health-related quality of life. Durable disease control rate, defined as the proportion of patients with response or stable disease for at least 105 days, was also examined.
  - Please see poster #382 for results on health-related quality of life data from this study.
- Here, we present up to 3-year follow-up (median duration of follow-up for all patients: 15.7 months) from the largest and most mature prospective data set in advanced CSCC.

Methods

- EMPOWER-CSCC-1 is an open-label, non-randomized, multicenter, international Phase 2 study of patients with advanced CSCC.
- Patients received cemiplimab 3 mg/kg every 2 weeks (Q2W) (Group 1; mCSCC; Group 2, laCSCC) or cemiplimab 350 mg every 3 weeks (Q3W) (Group 3, mCSCC) (**Figure 1**).
- The severity of treatment-emergent adverse events (TEAEs) was graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (version 4.03).
- The data cut-off was October 11, 2019.

Figure 1. Study design



ECOG, Eastern Cooperative Oncology Group; IV, intravenously; PD-L1, PD-ligand 1.

Results

Patients

- A total of 193 patients were enrolled (Group 1, n=59; Group 2, n=78; Group 3, n=56) (**Table 1**).

Table 1. Baseline demographics

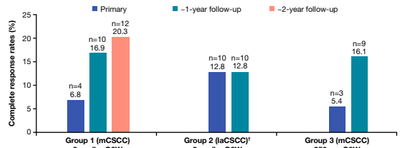
	Advanced CSCC (n=193)
Median age, years (range)	72.0 (38–96)
Male, n (%)	161 (83.4)
ECOG performance status, n (%)	
0	86 (44.6)
1	107 (55.4)
Primary CSCC site: head and neck, n (%)	131 (67.9)
mCSCC, n (%)	115 (59.6)
laCSCC, n (%)	78 (40.4)
Patients with cemiplimab as first-line therapy, n (%)	128 (66.3)
Patients with prior systemic therapy, n (%)[†]	65 (33.7)
Median duration of exposure to cemiplimab, weeks (range)	51.1 (2.0–109.3)
Median number of doses of cemiplimab administered (range)	18.0 (1–48)

[†]Settings for prior lines of therapy included metastatic disease, adjuvant, chemotherapy with concurrent radiation, or other and the most common types of prior systemic therapy were platinum compounds (n=46/65 [70.8%]) and monoclonal antibodies (n=18/65 [27.7%]).

Clinical activity

- Complete response rates at primary analysis, ~1 year follow-up for Groups 1, 2, and 3, and ~2 year follow-up for Group 1 are shown in **Figure 2**.
- Among 89 responders, median time to complete response was 11.2 months (interquartile range [IQR], 7.4–14.8).

Figure 2. Complete response rates per ICR



[†]Among 23 laCSCC patients who were included in the pre-specified Group 2 interim analysis, there were no complete responses.

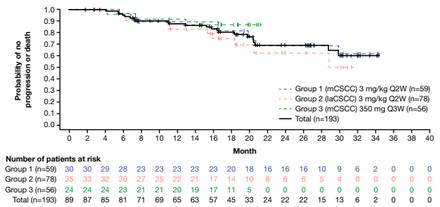
Table 2. Duration of follow-up and tumor response to cemiplimab per ICR

	Group 1 (mCSCC) 3 mg/kg Q2W (n=59)	Group 2 (laCSCC) 3 mg/kg Q2W (n=78)	Group 3 (mCSCC) 350 mg Q3W (n=56)	Total (n=193)
Median duration of follow-up, months (range)	18.5 (1.1–36.1)	15.5 (0.8–35.6)	17.3 (0.6–26.3)	15.7 (0.6–36.1)
ORR, % (95% CI)	50.8 (37.5–64.1)	44.9 (33.6–56.6)	42.9 (29.7–56.8)	46.1 (38.9–53.4)
Complete response, n (%)	12 (20.3)	10 (12.8)	9 (16.1)	31 (16.1)
Partial response, n (%)	18 (30.5)	25 (32.1)	15 (26.8)	58 (30.1)
Stable disease, n (%)	9 (15.3)	27 (34.6)	10 (17.9)	46 (23.8)
Non-complete response/non-progressive disease, n (%)	3 (5.1)	0	2 (3.6)	5 (2.6)
Progressive disease, n (%)	10 (16.9)	10 (12.8)	14 (25.0)	34 (17.6)
Not evaluable, n (%)	7 (11.9)	6 (7.7)	6 (10.7)	19 (9.8)
Disease control rate, % (95% CI)	71.2 (57.9–82.2)	79.5 (68.8–87.8)	64.3 (50.4–76.6)	72.5 (65.7–78.7)
Durable disease control rate,[†] % (95% CI)	61.0 (47.4–73.5)	62.8 (51.1–73.5)	57.1 (43.2–70.3)	60.6 (53.3–67.6)
Median observed time to response, months (IQR)[‡]	1.9 (1.8–2.0)	2.1 (1.9–3.8)	2.1 (2.1–4.2)	2.1 (1.9–3.7)
Median observed time to complete response, months (IQR)	11.1 (7.5–18.4)	10.5 (7.4–12.9)	12.4 (8.2–16.6)	11.2 (7.4–14.8)
Median DOR, months (range)[‡]	NR (20.7, NE)	NR (18.4, NE)	NR (NE, NE)	NR (28.8, NE)
Kaplan–Meier 12-month estimate of patients with ongoing response, % (95% CI)	89.5 (70.9–96.5)	83.2 (64.1–92.7)	91.7 (70.6–97.8)	87.8 (78.5–93.3)
Kaplan–Meier 24-month estimate of patients with ongoing response, % (95% CI)	68.8 (46.9–83.2)	62.5 (38.4–79.4)	NE (NE, NE)	69.4 (55.6–79.6)

[†]Defined as the proportion of patients without progressive disease for at least 105 days.
[‡]Based on number of patients with confirmed complete or partial response.
ORR per INV was 54.4% (95% CI: 47.1–61.6) for all patients; 50.8% (95% CI: 37.5–64.1) for Group 1, 56.4% (95% CI: 44.7–67.6) for Group 2, and 55.4% (95% CI: 41.5–68.7) for Group 3. ORR per INV was 57.8% (95% CI: 48.8–66.5) among treatment-naïve patients and 47.7% (95% CI: 35.1–60.5) among previously treated patients.
CI, confidence interval; NE, not evaluable; NR, not reached.

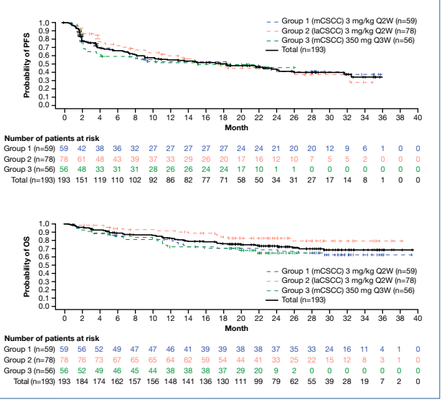
- ORR per ICR was 46.1% (95% CI: 38.9–53.4) among all patients; 50.8% (95% CI: 37.5–64.1) for Group 1, 44.9% (95% CI: 33.6–56.6) for Group 2, and 42.9% (95% CI: 29.7–56.8) for Group 3 (**Table 2**).
- Per ICR, ORR was 48.4% and 41.5% among those who had not received prior anticancer systemic therapy (n=128) and those who had received prior anticancer systemic therapy (n=65), respectively.
- Overall, the observed time to response was 2 months for 41 (46.1%) patients, 2–4 months for 29 (32.6%) patients, 4–6 months for eight (9.0%) patients, and >6 months for 11 (12.4%) patients.
- Median DOR has not been reached (observed DOR range: 1.9–34.3 months). In responding patients, the estimated proportion of patients with ongoing response at 24 months was 69.4% (95% CI: 55.6–79.6) (**Figure 3**).

Figure 3. Kaplan–Meier curves of DOR per ICR



- Estimated median PFS was 18.4 months (95% CI: 10.3–24.3) for all patients. The Kaplan–Meier estimated progression-free probability at 24 months was 44.2% (95% CI: 36.1–52.1) (**Figure 4A**).
- Median OS has not been reached. The Kaplan–Meier estimated probability of OS at 24 months was 73.3% (95% CI: 66.1–79.2) (**Figure 4B**).

Figure 4. Kaplan–Meier curves for A) PFS per ICR and B) OS



Treatment-emergent adverse events

- In total, 192 (99.5%) patients experienced at least one TEAE of any grade regardless of attribution (**Table 3**).
- Overall, the most common TEAEs of any grade were fatigue (n=67, 34.7%), diarrhea (n=53, 27.5%), and nausea (n=46, 23.8%).
- Grade ≥3 TEAEs regardless of attribution occurred in 94 (48.7%) of patients. The most common Grade ≥3 TEAEs were hypertension (n=9; 4.7%) and anemia and cellulitis (each n=8; 4.1%).

Table 3. TEAEs regardless of attribution

n (%)	Advanced CSCC (n=193)	
	Any grade	Grade ≥3
Any	192 (99.5)	94 (48.7)
Led to discontinuation	19 (9.8)	14 (7.3)
Most common[†]		
Fatigue	67 (34.7)	5 (2.6)
Diarrhea	53 (27.5)	2 (1.0)
Nausea	46 (23.8)	0
Pruritus	41 (21.2)	0
Rash	32 (16.6)	1 (0.5)
Cough	32 (16.6)	0
Arthralgia	28 (14.5)	1 (0.5)
Constipation	26 (13.5)	1 (0.5)
Vomiting	24 (12.4)	1 (0.5)
Actinic keratosis	23 (11.9)	0
Maculopapular rash	23 (11.9)	1 (0.5)
Anemia	22 (11.4)	8 (4.1)
Hypothyroidism	22 (11.4)	0
Headache	21 (10.9)	0
Upper respiratory tract infection	20 (10.4)	0

[†]TEAEs reported in ≥10% of patients, ordered by frequency of any grade.

- Grade ≥3 treatment-related adverse events (TRAEs) were reported in 33 (17.1%) patients, with the most common being pneumonitis (n=5, 2.6%), autoimmune hepatitis (n=3; 1.6%), anemia, colitis, and diarrhea (all n=2; 1.0%).
- No new TEAEs resulting in death were reported compared to previous reports.[9–11]

Conclusions

- For patients with advanced CSCC, cemiplimab achieved ORR of 46.1%.
- Patients had deepening responses over time as evidenced by increasing complete response rates.[9–11] Overall, the complete response rate is now 16.1% and median time to complete response was 11.2 months.
- DOR and OS are longer than what has been previously described with other agents.[7]
- With median DOR not reached after an additional 1 year of follow-up, this analysis indicates an increasing, clinically meaningful DOR with cemiplimab.
- The discontinuation rate, regardless of attribution, was low and most TRAEs were Grades 1–2.

See poster #382 reporting post hoc analysis of health-related quality of life in the same patient population presented in this poster. Also see poster #433 that provides the design and rationale of a Phase 3, randomized, double-blind study of adjuvant cemiplimab versus placebo post-surgery and radiation in patients with high-risk CSCC.

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