Phase 1 Study of Cemiplimab, a Human Monoclonal Anti-PD-1 Antibody, in Patients with Unresectable Locally Advanced or Metastatic Cutaneous Squamous Cell Carcinoma (CSCC): Longer Follow-up Efficacy and Safety Data

Taofeek K. Owonikoko,[1] Kyriakos P. Papadopoulos,[2] Melissa L. Johnson,[3] Marta Gil-Martin,[4] Victor Moreno,[5] April K. Salama,[6] Emiliano Calvo,[7] Nelson S. Yee,[8] Howard Safran,[9] Raid Aljumaily,[10] Daruka Mahadevan,[11] Jiaxin Niu,[12] Kosalai Kal Mohan,[13] Jingjin Li,[14] Elizabeth Stankevich,[14] Melissa Mathias,[13] Israel Lowy,[13] Matthew G. Fury,[13] Hani M. Babiker[15]

[1]*Department of Hematology and Medical Oncology, Winship Cancer Institute, Emory University, Atlanta, GA, USA;* [2]*START, San Antonio, TX, USA;* [3]*Sarah Cannon Research Institute, Nashville, TN, USA;* [4]*Institut Català D'Oncologia-IDIBELL, L'Hospitalet de Llobregat, Barcelona, Spain;* [5]*START Madrid FJD, Hospital Fundación Jiménez Diaz, Madrid, Spain;* [6]*Duke University, Durham, NC, USA;* [7]*START Madrid, Centro Integral Oncológico Clara Campal, Madrid, Spain;* [8]*Hematology/Oncology Division and Penn State Cancer Institute, Hershey, PA, USA;* [9]*Brown University, Providence, RI, USA;* [10]*Oklahoma University Medical Center, Oklahoma City, OK, USA;* [11]*The University of Arizona Cancer Center, Tucson, AZ, USA. Formerly of The University of Tennessee Health Science Center and West Cancer Center, Memphis, TN, USA;* [12]*Department of Medical Oncology, Banner MD Anderson Cancer Center, Gilbert, AZ, USA;* [13]*Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA;* [14]*Regeneron Pharmaceuticals, Inc., Basking Ridge, NJ, USA;* [15]*The University of Arizona Cancer Center, Tuscon, AZ, USA.*

Background

- Cutaneous squamous cell carcinoma (CSCC) is the second most common skin cancer after basal cell carcinoma.[1]
- Although CSCC has a surgical cure rate of >95%, an estimated 3,932–8,791 patients died from CSCC in 2012 in the United States (US).[2,3]
- Cemiplimab (REGN2810) is a high-affinity, highly potent human monoclonal antibody directed against programmed death-1 (PD-1).[4,5]
- Cemiplimab is the only Food and Drug Administration (FDA)-approved treatment for patients with metastatic or locally advanced CSCC who are not candidates for curative surgery or curative radiation in the US.[6]
- In the primary analysis (data cut-off October 2, 2017), by independent central review, of Phase 1 CSCC expansion cohorts, cemiplimab demonstrated encouraging efficacy results with acceptable safety profile in patients with advanced CSCC.[5]
- Here, we report longer follow-up data, per investigator assessment, from the CSCC expansion cohorts of the Phase 1 study (NCT02383212).

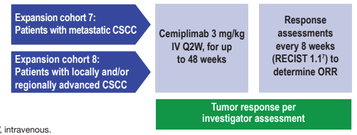
Objectives

- The co-primary objectives of the CSCC expansion cohorts were to:
  - Characterize the safety and tolerability of cemiplimab 3 mg/kg every two weeks (Q2W)
  - Evaluate the efficacy of cemiplimab 3 mg/kg Q2W by measuring overall response rate (ORR).

Methods

- Adult patients with metastatic CSCC or locally and/or regionally advanced CSCC who were not candidates for surgery were enrolled (**Figure 1**).
- Acceptable reasons for surgery to be deemed inappropriate for patients with locally/regionally advanced CSCC were:
  - Recurrence of CSCC after two or more surgical procedures and an expectation that curative resection would be unlikely, and/or;
  - Substantial morbidity or deformity anticipated from surgery.
- Key inclusion criteria included Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, adequate organ function, and at least one lesion measurable by Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1.[7]
- Patients were excluded if they had any ongoing or recent (within 5 years) autoimmune disease requiring systemic immunosuppression; active brain metastases; or invasive malignancy within 5 years.

Figure 1. Study design: CSCC expansion cohorts



IV, intravenous.

- Other selected exclusion criteria were treatment with immunosuppressive doses of steroids (>10 mg prednisone daily or equivalent); systemic antitumor treatment within 4 weeks of initial dose of cemiplimab; history of solid organ transplant; or primary tumors of lip or eyelid.
- Severity of adverse events was graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (version 4.03).
- The data cut-off date was January 20, 2018.

Results

Baseline characteristics, disposition, and treatment exposure

- Twenty-six patients (median age, 73 years; 10 metastatic and 16 locally/regionally advanced CSCC) were enrolled.
- Patient baseline characteristics are summarized in **Table 1**.

Table 1. Patient demographics and baseline characteristics

	Metastatic CSCC (n=10)	Locally/ regionally advanced CSCC (n=16)	Total (N=26)
Median age (range), year	71 (55–85)	73 (56–88)	73 (55–88)
≥65 years old, n (%)	7 (70.0)	14 (87.5)	21 (80.8)
Male, n (%)	8 (80.0)	13 (81.3)	21 (80.8)
ECOG performance status score, n (%)			
0	4 (40.0)	6 (37.5)	10 (38.5)
1	6 (60.0)	10 (62.5)	16 (61.5)
Primary CSCC site, n (%)			
Head/neck†	5 (50.0)	13 (81.3)	18 (69.2)
Extremity‡	3 (30.0)	2 (12.5)	5 (19.2)
Trunk	1 (10.0)	1 (6.3)	2 (7.7)
Penis	1 (10.0)	0	1 (3.8)
Prior systemic therapy for CSCC, n (%)	9 (90.0)	6 (37.5)	15 (57.7)
Prior radiotherapy for CSCC, n (%)	6 (60.0)	14 (87.5)	20 (76.9)

†Includes ear and temple. ‡Includes arms/hands and leg/feet.

- At the time of data cut-off (January 20, 2018), 12 patients (46.2%) had completed the planned treatment and 14 (53.8%) had discontinued treatment, mainly due to disease progression (n=7).
- The median number of administered doses of cemiplimab was 16 (range: 2–44) and the median duration of exposure was 36.0 weeks (range: 4.0–86.7).
  - At the time of data cut-off, two patients had entered the retreatment phase.
  - One of these patients had an extended retreatment phase with an overall 86.7 weeks of continued cemiplimab exposure (beyond the planned 48-week treatment duration) as it was considered, by the investigator, to be in the best interest of the patient.
- The median duration of follow-up at the time of data cut-off was 11.9 months (range: 1.1–18.2).

Treatment-emergent adverse events (TEAEs)

- TEAEs of any grade, regardless of attribution, were reported in all patients (**Table 2**).

Table 2. Summary of TEAEs, regardless of attribution, in the combined CSCC expansion cohorts

TEAEs	N=26	
n (%)	Any grade	Grade ≥3†
Any	26 (100.0)	12 (46.2)
Serious	7 (26.9)	6 (23.1)
Led to discontinuation	2 (7.7)	1 (3.8)
With an outcome of death‡	1 (3.8)	1 (3.8)
Occurred in at least four patients		
Fatigue	7 (26.9)	0
Decreased appetite	4 (15.4)	0
Diarrhea	4 (15.4)	0
Hypercalcemia	4 (15.4)	2 (7.7)
Hypophosphatemia	4 (15.4)	0
Nausea	4 (15.4)	0
Urinary tract infection	4 (15.4)	1 (3.8)

†The only TEAEs of grade ≥3 that occurred in more than one patient were hypercalcemia and skin infection (each 7.7%). ‡The fatal TEAE occurred in an 81-year-old man with baseline congestive heart failure and renal insufficiency who later had a TEAE of urinary tract infection and became anuric. The fatal renal failure was considered unrelated to study treatment.

- Investigator-assessed treatment-related TEAEs of any grade occurred in 16 patients (61.5%), with four patients (15.4%) experiencing the following five grade ≥3 treatment-related TEAEs:
  - Adrenal insufficiency, asthenia, increased alanine aminotransferase, increased aspartate aminotransferase, and maculo-papular rash.
- The most common investigator-assessed treatment-related TEAEs of any grade were fatigue (26.9%), arthralgia, diarrhea, hypothyroidism, muscle weakness, and maculo-papular rash (each 7.7%).
- Two patients discontinued treatment due to treatment-related TEAEs:
  - An 86-year-old female discontinued treatment after three doses of cemiplimab due to grade 3 rash and grade 2 cough. The patient completed 6 months post-treatment follow-up and had a partial response during the last post-treatment assessment by the investigator
  - A 58-year old male developed grade 2 muscular weakness after five doses of cemiplimab; patient continued treatment for an additional five doses, after disease progression, before treatment was permanently discontinued due to this TEAE.

Clinical efficacy

- ORR by investigator assessment was 50.0% (13/26 patients: 95% confidence interval [CI]: 29.9–70.1; **Table 3**).
- Durable disease control rate was 57.7% (95% CI: 36.9–76.6).

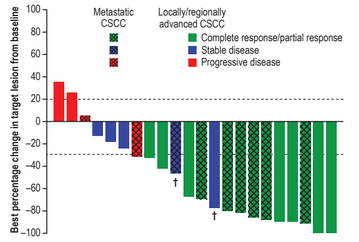
Table 3. Tumor response by investigator assessment

	Metastatic CSCC (n=10)	Locally/ regionally advanced CSCC (n=16)	Total (N=26)
Best overall response, n (%)			
Complete response	0	2 (12.5)	2 (7.7)
Partial response	6 (60.0)	5 (31.3)	11 (42.3)
Stable disease	1 (10.0)	4 (25.0)	5 (19.2)
Progressive disease	2 (20.0)	4 (25.0)	6 (23.1)
Not evaluable†	1 (10.0)	1 (6.3)	2 (7.7)
Overall response rate, % (95% CI)	60.0 (26.2–87.8)	43.8 (19.8–70.1)	50.0 (29.9–70.1)
Durable disease control rate, % (95% CI)‡	60.0 (26.2–87.8)	56.3 (29.9–80.2)	57.7 (36.9–76.6)
Median observed time to response, months (range)§	2.7 (1.7–5.5)	1.9 (1.7–7.5)	1.9 (1.7–7.5)
Observed duration of response of ≥6 months, n (%)§	4 (66.7)	5 (71.4)	9 (69.2)

†Include missing and unknown tumor response. ‡Defined as the proportion of patients without progressive disease for at least 105 days. §Data shown are for patients with confirmed complete or partial response.

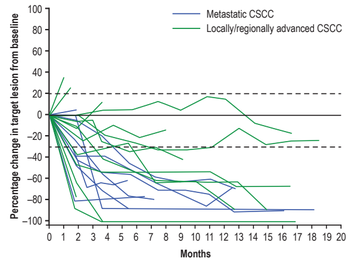
- Rapid, deep, and durable target lesion reductions were observed in most patients who had at least one tumor assessment on treatment (**Figures 2–4**).
- Median duration of response had not been reached at data cut-off.

Figure 2. Clinical activity of tumor response to cemiplimab per investigator assessment



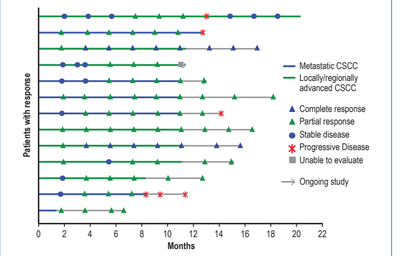
Plot shows the best percentage change in the sum of target lesion diameters from baseline for 22 patients from both CSCC expansion cohorts who underwent radiologic evaluation per investigator assessment. Lesion measurements after progression were excluded. The horizontal dashed lines indicate criteria for partial response (≥30% decrease in the sum of target lesion diameters) and progressive disease (≥20% increase in the target lesion diameters), respectively. Two patients (with cross symbols under bar) had tumor lesion reduction of >30% from baseline; however, best overall response was stable disease as the tumor lesion reduction had not been confirmed. The following four patients do not appear in the figure (but are included in the ORR analysis [Table 3], per intention-to-treat): one patient with locally advanced CSCC who had missing target lesion measurements and three patients (one with metastatic, and two with locally advanced, CSCC) with no evaluable post-treatment tumor assessment.

Figure 3. Change in target lesion over time



Plot shows the percent change in target lesion diameters from baseline over time. Patients shown in this figure are the same as those in Figure 2. The horizontal dashed lines indicate criteria for partial response (≥30% decrease in the sum of target lesion diameters) and progressive disease (≥20% increase in the target lesion diameters).

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



Plot shows time to response and duration of response in the 13 patients with complete or partial response at the time of data cut-off. Each horizontal bar represents one patient.

Conclusions

- In this analysis of longer follow-up data from CSCC expansion cohorts of the Phase 1 study, cemiplimab continued to show substantial antitumor activity and a durable response with a safety profile comparable with other anti-PD-1 agents; there were no new safety concerns compared with previous analyses.
- Primary analysis of the metastatic CSCC cohort and prespecified interim analysis of the locally advanced CSCC cohort from the Phase 2 study (NCT02760498) provides further evidence of substantial antitumor activity and durable response with cemiplimab treatment in advanced CSCC.[5,8]

References

1. Rogers HW et al. *JAMA Dermatol.* 2015;151:1081–1086.
2. Kauvar AN et al. *Dermatol Surg.* 2015;41:1214–1240.
3. Karia PS et al. *J Am Acad Dermatol.* 2013;68:957–966.
4. Burova E et al. *Mol Cancer Ther.* 2017;16:861–870.
5. Migden MR et al. *N Engl J Med.* 2018;379:341–351.
6. Regeneron. Libtayo® (cemiplimab-rwlc) prescribing information. Available at https://www.regeneron.com/sites/default/files/Libtayo_FPI.pdf, accessed November 9, 2018.
7. Eisenhauer EA et al. *Eur J Cancer.* 2009;45:228–247.
8. Migden MR et al. Poster presentation at EADV 2018 (abstract #2551).

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Disclosures

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