Efficacy and Safety of Cosibelimab, an Anti–PD-L1 Antibody, in Patients With Metastatic Cutaneous Squamous Cell Carcinoma: Results From Pivotal Cohort

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OBJECTIVE

- To present efficacy and safety data from a metastatic cutaneous squamous cell carcinoma (mCSCC) registration-enabling expansion cohort from a phase 1, open-label, global, multicenter trial of cosibelimab in patients with advanced cancers (NCT03212404)

CONCLUSIONS

- Treatment with cosibelimab once every 2 weeks (Q2W) resulted in a robust objective response rate (ORR) with durable responses and demonstrated a predictable and manageable safety profile in patients with mCSCC, supporting its use in the treatment of this cancer
- NCT03212404 is continuing enrollment of a registration-enabling cohort of patients with locally advanced cutaneous squamous cell carcinoma and a cohort of mCSCC patients treated with a dosing regimen of 1200 mg cosibelimab every 3 weeks

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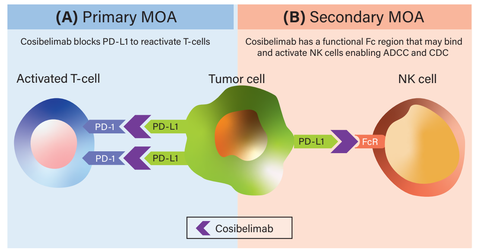
INTRODUCTION

- Cutaneous squamous cell carcinoma is one of the most common human cancers in the United States, and advanced or metastatic disease is associated with substantial morbidity and mortality[1]
- Programmed death receptor-1 (PD-1)–blocking antibodies are approved as monotherapy for patients with mCSCC who are not candidates for surgery or radiation[2]
- Cosibelimab is a high-affinity, fully human programmed death-ligand 1 (PD-L1)–blocking monoclonal antibody with a functional fragment crystallizable (Fc) domain capable of inducing antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC) against tumor cells, supporting its use for cancer immunotherapy (**Figure 1**)[3,4]

Figure 1. Cosibelimab dual mechanisms of action. (A) Modeling predicts that cosibelimab sustains a >99% tumor target occupancy to block PD-L1 interaction with PD-1 and reactivate T cells.[3,4] (B) Cosibelimab contains a functional Fc domain capable of inducing ADCC and CDC against tumor cells.[4]



ADCC, antibody-dependent cellular cytotoxicity; CDC, complement-dependent cytotoxicity; Fc, fragment crystallizable; FcR, Fc receptor; MOA, mechanism of action; NK, natural killer; PD-1, programmed death receptor-1; PD-L1, programmed death-ligand 1.

METHODS

PATIENT POPULATION

- Key eligibility criteria for patients included in the study are shown in **Table 1**

Table 1. Key Eligibility Criteria

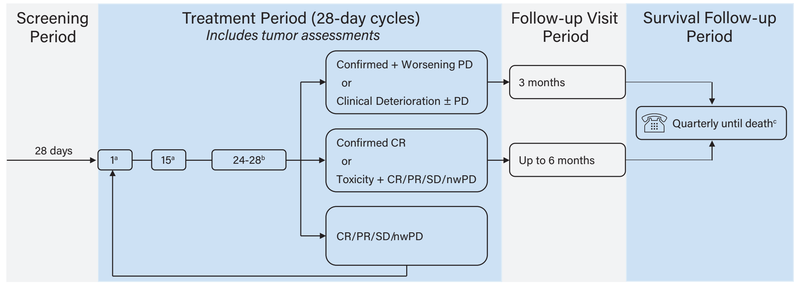
Inclusion	Exclusion
≥18 years of age	Prior immune checkpoint inhibitor therapy
ECOG PS of 0 or 1 and life expectancy of ≥3 months	Active, suspected, or documented history of autoimmune disease
Histologically confirmed diagnosis of mCSCC (nodal and/or distant) not amenable to local therapy	Concurrent immunosuppressive doses of steroids (>10 mg/day prednisone or equivalent)

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

STUDY DESIGN

- Patients with mCSCC received cosibelimab 800 mg administered intravenously Q2W until confirmed complete response (CR), worsening disease progression, toxicity, or clinical deterioration followed by posttreatment follow-up (**Figure 2**)
- After patients stopped treatment and completed the necessary follow-up visits, they were contacted by telephone quarterly for survival and tumor status until death

Figure 2. Study design for patients with mCSCC who received cosibelimab 800 mg Q2W.



CR, complete response; mCSCC, metastatic cutaneous squamous cell carcinoma; nwPD, nonworsening progressive disease; PD, progressive disease; PR, partial response; Q2W, every 2 weeks; SD, stable disease. [a]Patients received cosibelimab 800 mg intravenously on days 1 and 15 of each 28-day treatment cycle. [b]End-of-cycle tumor assessments occurred between days 24 and 28 in cycles 2, 4, 6, and 8 and every 3 cycles thereafter and informed the decision to treat patients with additional cycles or begin follow-up visits. [c]After patients stop treatment and complete the necessary follow-up visits, they are contacted by telephone quarterly for survival and tumor treatment status, if available, until death.

OUTCOME MEASURES

- Key endpoints assessed in the study are shown in **Table 2**

Table 2. Key Study Endpoints

Primary	Secondary
ORR (No. of patients with CR or PR/No. of enrolled patients) assessed by independent central review (ICR) according to RECIST v1.1[a]	DOR for patients with CR or PR assessed by ICR according to RECIST v1.1
	Incidence and severity of treatment-emergent AEs according to the NCI-CTCAE Version 5.0
	Clinical laboratory data, vital signs, ECGs, ECOG PS evaluations, physical exams

AE, adverse event; CR, complete response; DOR, duration of response; ECG, electrocardiogram; ECOG PS, Eastern Cooperative Oncology Group performance status; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; ORR, objective response rate; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1. Deaths due to COVID-19 that occurred before a post-baseline response assessment were excluded from ORR calculations in the modified ITT population.

RESULTS

PATIENT POPULATION

- Overall, 78 patients with mCSCC received cosibelimab 800 mg Q2W and comprised the safety and intent-to-treat (ITT) populations
  - 2 of the 78 patients died because of coronavirus disease 2019 (COVID-19) before conduct of a post-baseline response assessment and were excluded from the modified ITT population (n=76)
- Patients were predominantly male (75.6%), aged ≥65 years (71.8%), with distant mCSCC (66.7%) and Eastern Cooperative Oncology Group performance status (ECOG PS) of 1 (70.5%; **Table 3**)
- This multiregional clinical trial enrolled patients at 24 sites in 8 countries, grouped as Australia/New Zealand (57.7%), Europe (24.4%), South Africa (10.3%), and Thailand (7.7%; **Table 3**)

EFFICACY

- As of November 18, 2021, confirmed ORR by ICR in the modified ITT population was 48.7% (95% CI, 37.0-60.4; **Table 4**)
- Robust and durable reductions in target lesions were observed (**Table 4**; **Figures 3 and 4**)
  - 13.2% of patients achieved a CR in target lesions
  - 75.7% of responses were ongoing (range, 1.4 to ≥31.8 months)
  - Median duration of follow-up was 15.2 months
  - Kaplan-Meier -estimated probability of maintaining a response at 6 and 24 months was 88.1% and 72.5%, respectively

SAFETY

- Treatment-related adverse events (TRAEs) were reported in 55 patients (70.5%; **Table 5**)
  - 7 patients (9.0%) experienced ≥1 TRAE grade ≥3; no grade 4 or 5 TRAEs were reported
  - 3 patients (3.8%) experienced treatment-related serious adverse events (SAEs); no treatment-related SAEs occurred in >1 patient
  - 1 patient discontinued cosibelimab because of pemphigoid, which was deemed possibly related to study drug
- AEs led to death in 3 patients (3.8%) and were COVID-19 (2 patients) and cardiac arrest (1 patient); none were considered to be related to treatment

Table 3. Patient Demographics and Baseline Characteristics

Demographic	mCSCC (n=78)
Age, median (range), y	71.6 (37-91)
<65 y, n (%)	22 (28.2)
≥65 y, n (%)	56 (71.8)
Female, n (%)	19 (24.4)
Male, n (%)	59 (75.6)
Race, n (%)	
Asian	6 (7.7)
Black or African American	1 (1.3)
White	69 (88.5)
Unknown	2 (2.6)
Ethnicity, n (%)	
Hispanic or Latino	3 (3.8)
Not Hispanic or Latino	73 (93.6)
Unknown	2 (2.6)
Country/Region, n (%)	
Australia/New Zealand	45 (57.7)
Europe	19 (24.4)
South Africa	8 (10.3)
Thailand	6 (7.7)
ECOG PS, n (%)	
0	23 (29.5)
1	55 (70.5)
Primary CSCC site, n (%)	
Head/Neck	46 (59.0)
Extremity	19 (24.4)
Trunk	9 (11.5)
Other	4 (5.1)
Type of metastatic disease, n (%)	
Distant	52 (66.7)
Nodal	26 (33.3)
Prior cancer-related radiotherapy, n (%)	51 (65.4)
Prior cancer-related systemic therapy, n (%)	7 (9.0)

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

Table 4. Tumor Response by ICR According to RECIST v1.1

Parameter	mCSCC (n=78)
Best overall response, n (%)	
CR	6 (7.7)
PR	31 (39.7)
Stable disease	12 (15.4)
Progressive disease	21 (26.9)
Not evaluable	8 (10.3)
ORR in ITT population, % (95% CI)	47.4 (36.0-59.1)
ORR in modified ITT population, % (95% CI)	48.7 (37.0-60.4)[a]
Response ongoing, n (%)	28 (75.7)
Median duration of response, months (min, max)	NR (1.4, 31.8)
Kaplan-Meier–estimated 6-month DOR probability, % (95% CI)	88.1 (71.3-95.4)
Kaplan-Meier–estimated 24-month DOR probability, % (95% CI)	72.5 (51.6-85.5)
Median duration of follow-up, months (95% CI)	15.2 (12.0-20.5)

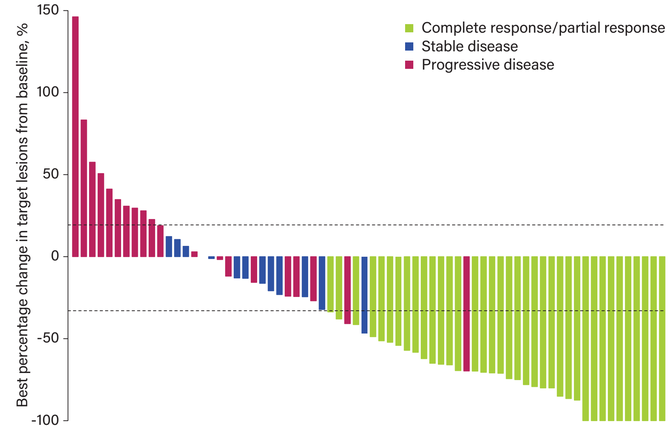
CI, confidence interval; CR, complete response; DOR, duration of response; ITT, intent to treat; mCSCC, metastatic cutaneous squamous cell carcinoma; NR, not reached; ORR, objective response rate; PR, partial response. [a]Deaths due to COVID-19 that occurred before a post-baseline response assessment were excluded from ORR calculations in the modified ITT population.

Table 5. Summary of TRAEs

TRAEs, n (%)	mCSCC (n=78)
Any	55 (70.5)
Grade ≥3	7 (9.0)
Grade ≥3 immune-related	1 (1.3)
Serious	3 (3.8)
Leading to discontinuation	1 (1.3)
Occurring in ≥5% of patients	
Fatigue	9 (11.5)
Rash	8 (10.3)
Diarrhea	5 (6.4)
Pruritis	5 (6.4)
Infusion-related reaction	4 (5.1)
Lipase increased	4 (5.1)

mCSCC, metastatic cutaneous squamous cell carcinoma; TRAE, treatment-related adverse event.

Figure 3. Best percentage change in the sum of target lesion diameters from baseline for patients who underwent tumor assessment by ICR according to RECIST v1.1 after treatment initiation.



Horizontal dashed lines indicate RECIST v1.1 criteria for partial response (≥30% decrease in the sum of target lesion diameters) and progressive disease (≥20% increase in target lesion diameters). ICR, independent central review.

Figure 4. Time to and duration of response in responding patients who underwent tumor assessment by ICR according to RECIST v1.1 after treatment initiation.