Poster 1084P

Cosibelimab, an Anti-PD-L1 Antibody, in Metastatic Cutaneous Squamous Cell Carcinoma (CSCC): Preliminary Safety and Efficacy Results from a Phase 1 Clinical Trial

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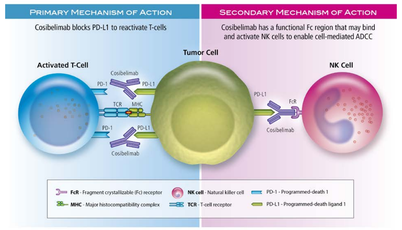
Background

Cosibelimab: Anti-PD-L1 with Dual Mechanism of Action



- High affinity, fully-human IgG1 monoclonal antibody (mAb) that binds to programmed death ligand-1 (PD-L1) to restore adaptive immunity and engage innate immunity through:
  - sustained >99% tumor target occupancy to block PD-L1 interaction with the programmed death receptor-1 (PD-1) and B7.1 receptors.[1,2]
  - a functional Fc domain capable of inducing antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC) against tumor cells.[1]

Objectives

Primary

- To evaluate the efficacy of cosibelimab in metastatic cutaneous squamous cell carcinoma (mCSCC) by measuring the rate of objective response (ORR; complete response + partial response) per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1.
- To evaluate the safety and tolerability of cosibelimab in patients with advanced cancers.

Secondary

- To evaluate additional efficacy parameters, including duration of response, progression-free survival and overall survival.

Methods

Study Design

- Study CK-301-101 (NCT03212404) is a global, multicenter, multicohort trial enrolling patients with select advanced cancers, including a registration-enabling cohort of mCSCC patients.
- mCSCC patients received cosibelimab administered as a fixed dose of 800 mg every two weeks (Q2W) or 1200 mg every three weeks (Q3W) until confirmed and worsening disease progression or clinical deterioration, followed by post-treatment follow-up.
- Tumor assessments by RECIST 1.1 were conducted every 8 weeks for the initial 32 weeks on study, and every 12 weeks thereafter.
- The data cutoff date for this analysis was August 14, 2020.

Key Inclusion Criteria

- Adult patients with mCSCC (nodal and/or distant).
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.
- Adequate organ function.
- At least one measurable lesion by RECIST 1.1.

Key Exclusion Criteria

- Prior immune checkpoint inhibitor therapy.
- Active or suspected autoimmune disease.
- Immunosuppressive doses of steroids (>10 mg/day prednisone or equivalent).

Results

Demographic and Baseline Characteristics

- Forty-one mCSCC patients were enrolled and treated with cosibelimab administered 800 mg Q2W (n=40) or 1200 mg Q3W (n=1).
- Demographic and baseline characteristics are summarized in **Table 1**.

Table 1.
Demographic and Baseline Characteristics

	mCSCC (n=41)
Median age, years (range)	69 (42–91)
≥65 years, n (%)	28 (68.3)
Male, n (%)	29 (70.7)
ECOG performance status, n (%)	
0	9 (22.0)
1	32 (78.0)
Primary CSCC site, n (%)	
Head/neck	20 (48.8)
Trunk	10 (24.4)
Extremity	7 (17.1)
Other	4 (9.7)
Prior cancer-related radiotherapy, n (%)	27 (65.9)
Prior cancer-related systemic therapy, n (%)	5 (12.2)

Preliminary Efficacy Results

- Thirty-seven enrolled mCSCC patients had at least one post-baseline tumor assessment or discontinued prior.
- ORR by investigator assessment was 51.4% (95% CI: 34.4, 68.1). Of the patients who achieved an objective response, 5 (13.5%) achieved a complete response (all confirmed) and 14 (37.8%) achieved a partial response (12 confirmed and 2 pending).
- Tumor response assessments are summarized in **Table 2**.

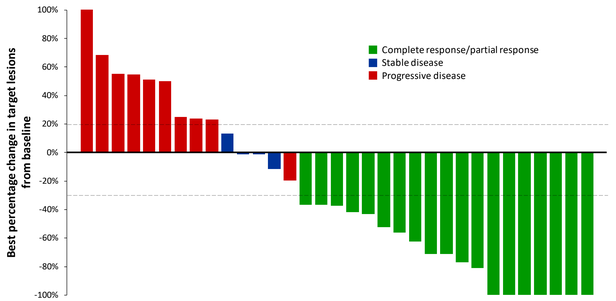
Table 2.
Tumor Response by RECIST v1.1[#]

	mCSCC (n=37)
Best overall response, n (%)	
Complete response	5 (13.5)
Partial response	14 (37.8)
Stable disease	4 (10.8)
Progressive disease	10 (27.0)
Not evaluated/done[¶]	4 (10.8)
Objective response rate, % (95% CI)	**51.4 (34.4, 68.1)**
Response ongoing, n (%)	16 (84.2)
Median duration of response, months (min, max)	Not reached (0.3, 24.0)
Patients with duration of response ≥6 months, n (%)*	11 (91.7)
Median observed time to response, months (range)	1.8 (1.6, 7.7)

[#]By investigator assessment. Two objective responses pending confirmation at next scan. [¶]Includes missing and unknown tumor response. *Proportion excludes 7 patients with ongoing response duration <6 months at data cutoff.

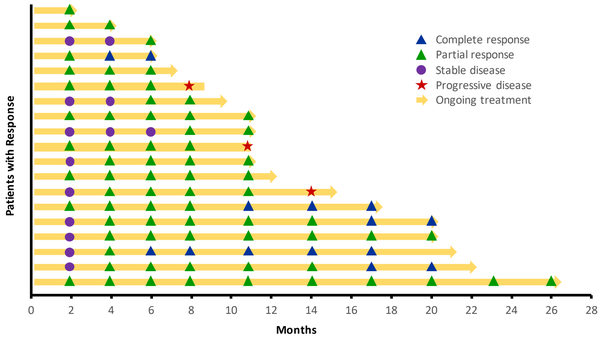
- Rapid, deep, and durable reductions in target lesions were observed (**Figures 1 and 2**).
- Seven patients (18.9%) achieved a complete response in target lesions (**Figure 1**).
- Responses are ongoing in 16 patients (84.2%) at time of analysis, with the longest response duration at 24 months (**Figure 2**).

Figure 1.
Best Percentage Change in Tumor Lesions



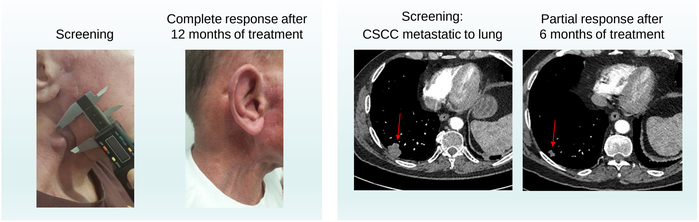
Plot shows the best percentage change in the sum of target lesion diameters from baseline for 33 patients who underwent radiologic evaluation per investigator assessment after treatment initiation. Four patients do not appear in the figure, however, are included in the ORR analysis (Table 2) per intention-to-treat, as they did not have an evaluable post-baseline assessment. Lesion measurements after progression were excluded. Horizontal dashed lines indicate RECIST 1.1 criteria for partial response (≥30% decrease in the sum of target lesion diameters) and progressive disease (≥20% increase in target lesion diameters). Two partial responses are pending confirmation. Two patients with complete responses in target lesions are classified as partial responses in ORR analysis (table 2) due to presence of non-target lesions.

Figure 2.
Time to and Duration of Response and Responding Patients



- Two mCSCC patients with robust and durable responses to cosibelimab treatment are shown in **Figure 3**.

Figure 3.
Complete and Partial Responses in Two Patients with mCSCC Treated with Cosibelimab



Preliminary Safety Results

Table 3.
Summary of Treatment-Related Adverse Events (n=114)[a]

n (%)	Any grade	Grade ≥3
Any	74 (64.9)	6 (5.3)
Serious	3 (2.6)	1 (0.9)
Led to discontinuation	3 (2.6)	1 (0.9)
Occurred in at least 5% of patients by any grade		
Fatigue	17 (14.9)	2 (1.8)
Rash	16 (14.0)	0
Hypothyroidism	10 (8.8)	0
Anemia	8 (7.0)	2 (1.8)
Infusion-related reaction	8 (7.0)	0
Nausea	8 (7.0)	0
Diarrhea	7 (6.1)	0

[a]Includes all dosed patients with advanced cancers (200 mg q2w [n=1], 400 mg q2w [n=1], 800 mg q2w [n=103], 1200 mg q3w [n=9]).

- One hundred fourteen patients with advanced cancers have been enrolled and treated with cosibelimab.
- Treatment-related adverse events (TRAEs) are summarized in **Table 3**.
- The most common TRAEs included fatigue (n=17, 14.9%) and rash (n=16, 14.0%). Two patients (1.8%) experienced grade 2 pneumonitis. No reported events of colitis or hepatitis.
- Grade ≥3 TRAEs occurred in six patients (5.3%). Events that occurred in more than one patient were anemia and fatigue (each n=2, 1.8%, grade 3 only).
- Three patients (2.6%) discontinued treatment due to a TRAE.

Conclusions

- Treatment with cosibelimab resulted in robust and durable responses, including complete responses, in patients with mCSCC.
  - ORR: 51.4% (95% CI: 34.4, 68.1), including five (13.5%) complete responses.
  - Median duration of response has not been reached, with 84.2% of responses ongoing.
- Cosibelimab has a predictable and manageable safety profile in patients with advanced cancers.
- A registration-enabling trial is ongoing in patients with metastatic and locally-advanced CSCC evaluating the safety and efficacy of the 800 mg Q2W and 1200 mg Q3W fixed dosing regimens.

References: [1]Gorelik L, et al. *Cancer Research* 2017; 77(13 Suppl):Abstract 4606. [2]Lin, L., et al. *Society for Immunotherapy of Cancer 34th Annual Meeting;* Abstract P431.

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