Poster 399

Cosibelimab, an anti-PD-L1 antibody: Preliminary Safety and Efficacy Results from a Global, Multicohort Phase 1 Clinical Trial

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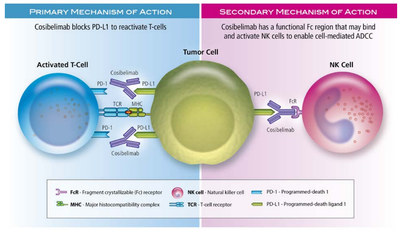
Background

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]

- Study CK-301-101 (NCT03212404) is a global, multicenter, multicohort trial enrolling patients with select advanced cancers, including a cohort with previously untreated high PD-L1 expressing advanced non-small cell lung cancer (NSCLC) and a pivotal cohort with locally advanced or metastatic cutaneous squamous cell carcinoma (cSCC). Here, we present interim safety and efficacy data from these cohorts.

Objectives

Primary

- To evaluate the efficacy of cosibelimab in NSCLC and cSCC by measuring objective response rate (ORR).
- To evaluate the safety and tolerability of cosibelimab in patients with advanced cancers.

Secondary

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

Methods

Key Inclusion Criteria

- Adult patients with Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.
- NSCLC cohort: Stage IV NSCLC with high (tumor proportion score ≥50%) PD-L1 tumor expression as determined by immunohistochemistry, with no prior systemic treatment for advanced/metastatic NSCLC and no EGFR activating mutation or ALK translocation.
- cSCC cohort: unresectable locally advanced or metastatic cSCC not amenable to local therapy.

Key Exclusion Criteria

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

Study Design

- 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 investigator assessment using RECIST 1.1 were conducted every 8 weeks for the initial 32 weeks on study, and every 12 weeks thereafter.

Results

Baseline Characteristics

- As of October 9, 2020, 25 NSCLC patients and 58 cSCC patients were enrolled and treated with cosibelimab.
- Demographic and baseline characteristics are summarized in **Table 1**.

Table 1. Baseline Characteristics

	NSCLC (n=25)	cSCC (n=58)
Median age, years (range)	64 (29–78)	71 (42–95)
≥65 years, n (%)	11 (44.0)	42 (72.4)
Male, n (%)	18 (72.0)	43 (74.1)
ECOG PS 0; 1, n (%)	7 (28.0); 18 (72.0)	13 (22.4); 45 (77.6)
Cancer stage at screening, n (%)		
Metastatic	25 (100.0)	49 (84.5)
Locally advanced	-	9 (15.5)
Prior radiotherapy, n (%)	3 (12.0)	36 (62.1)
Prior systemic therapy, n (%)	-	6 (10.3)

Preliminary Efficacy Results

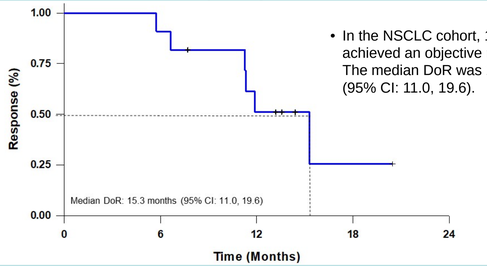
- As of the data cutoff, 25 NSCLC patients and 47 cSCC patients (41 metastatic; 6 locally advanced) were evaluable for response (at least one post-baseline tumor assessment or discontinued prior), respectively.
- In the NSCLC cohort, ORR by investigator assessment was 44.0% (95% CI: 24.4, 65.1). The median duration of response (DoR) and progression-free survival (PFS) were 15.3 and 10.3 months, respectively.
- In the cSCC cohort, ORR by investigator assessment was 51.1% (95% CI: 36.1, 66.0). Of the patients who achieved an objective response, 5 (10.6%) achieved a complete response (all confirmed) and 19 (40.4%) achieved a partial response (12 confirmed and 2 pending). The median duration of response and PFS were not reached.
- Tumor response assessments by cohort are summarized in **Table 2**.

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

	NSCLC (n=25)	cSCC (n=47)
Best overall response, n (%)		
Complete response	-	5 (10.6)
Partial response	11 (44.0)	19 (40.4)
Stable disease	8 (32.0)	8 (17.0)
Progressive disease	2 (8.0)	11 (23.4)
Not evaluated/done[¶]	4 (16.0)	4 (8.5)
Objective response rate (ORR), % (95% CI)	**44.0 (24.4, 65.1)**	**51.1 (36.1, 66.0)**
ORR, Metastatic	44.0 (24.4, 65.1)	51.2 (35.1, 67.1)
ORR, Locally advanced	-	50.0 (11.8, 88.2)
Response ongoing, n (%)	4 (36.4)	20 (83.3)
Median duration of response, months (min, max)	15.3 (5.7, 20.5+)	Not reached (0.8+, 25.8+)

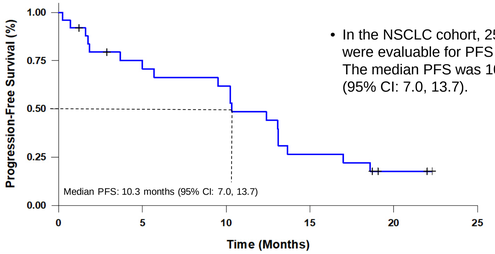
[#]By investigator assessment. [¶]Includes missing and unknown tumor response. ORR = complete response + partial response.

Figure 1. NSCLC Cohort: Duration of Response by RECIST 1.1



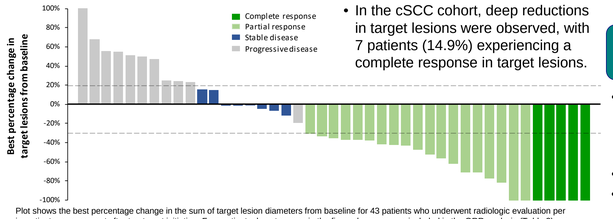
- In the NSCLC cohort, 11 patients achieved an objective response. The median DoR was 15.3 months (95% CI: 11.0, 19.6).

Figure 2. NSCLC Cohort: Progression-Free Survival by RECIST 1.1



- In the NSCLC cohort, 25 patients were evaluable for PFS analysis. The median PFS was 10.3 months (95% CI: 7.0, 13.7).

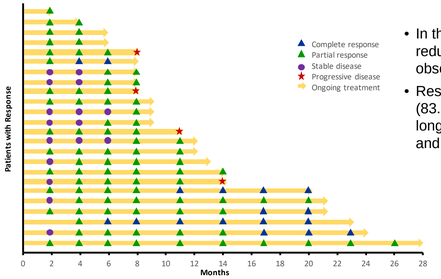
Figure 3. cSCC Cohort: Best Percentage Change in Tumor Lesions by RECIST 1.1



- In the cSCC cohort, deep reductions in target lesions were observed, with 7 patients (14.9%) experiencing a complete response in target lesions.

Plot shows the best percentage change in the sum of target lesion diameters from baseline for 43 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. 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 4. cSCC Cohort: Time to and Duration of Response for Responding Patients by RECIST 1.1



- In the cSCC cohort, rapid and durable reductions in target lesions were observed.
- Responses are ongoing in 20 patients (83.3%) at time of analysis, with the longest response duration at 25.8 months and ongoing.

Preliminary Safety Results

Table 3. Summary of Treatment-Related Adverse Events (n=123)[α]

n (%)	Any grade	Grade ≥3
Any	80 (65.0)	6 (4.9)
Serious	3 (2.4)	1 (0.8)
Led to discontinuation	2 (1.6)	0
Occurred in at least 5% of patients by any grade		
Fatigue	19 (15.4)	2 (1.6)
Rash	17 (13.8)	0
Hypothyroidism	10 (8.1)	0
Infusion-related reaction	10 (8.1)	0
Anemia	7 (5.7)	2 (1.6)
Diarrhea	7 (5.7)	0
Nausea	7 (5.7)	0

[α] Includes all dosed patients with advanced cancers (200 mg q2w [n=1], 400 mg q2w [n=1], 800 mg q2w [n=112], 1200 mg q3w [n=9]).

- One hundred twenty-three 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=19, 15.4%) and rash (n=17, 13.8%). Two patients (1.6%) experienced grade 2 pneumonitis. No reported events of colitis or hepatitis.
- Grade ≥3 TRAEs occurred in six patients (4.9%). Events that occurred in more than one patient were anemia and fatigue (each n=2, 1.6%, grade 3 only).
- Two patients (1.6%) discontinued treatment due to a TRAE.

Conclusions

- Treatment with cosibelimab resulted in robust and durable responses in patients with NSCLC and cSCC.
  - NSCLC: 44.0% ORR (95% CI: 24.4, 65.1). Median DoR and PFS of 15.3 and 10.3 months, respectively.
  - cSCC: 51.1% ORR (95% CI: 36.1, 66.0) in locally advanced and metastatic patients, including 5 complete responses. Median DoR and PFS were not yet reached, with 83.3% 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 locally-advanced or metastatic 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.
Acknowledgements: Study sponsored by Checkpoint Therapeutics, Inc. Disclosures: All authors except JFO are PIs on the CK-301-101 trial supported by Checkpoint Therapeutics.