Safety, Efficacy, and Pharmacokinetic Profile of Cosibelimab, an Anti-PD-L1 Antibody, in Patients with Advanced Cancers

Poster 469P

Philip R. Clingan[1], Andrew Mant[2], Gary Richardson[3], Dariusz M. Kowalski[4], Piotr Koralewski[5], Iwona Lugowska[4], Arunee Dechaphunkul[6], Chaiyut Charoentum[7], Aumkhae Sookprasert[8], Virote Sriuranpong[9], Andrey Akopov[10], Vadim Kozlov[11], Natalia Fadeeva[12], Boris Kasparov[13], Nadezhda V. Kovalenko[14], Vasiliy Oschepkov[15], Leonid Gorelik[16], Yune Kunes[16], James F. Oliviero[16], Dean L. Harris[17]

[1]Medical Oncology, Southern Medical Day Care Centre, Wollongong, NSW, Australia, [2]Medical Oncology Unit, Eastern Health, Box Hill, VIC, Australia, [3]Oncology Research, Cabrini Hospital, Malvern, VIC, Australia, [4]Medical Oncology, Maria Sklodowska-Curie Memorial Cancer Centre-Institute of Oncology, Warsaw, Poland, [5]Medical Oncology, Szpital Specjalistyczny Ludwika Rydygiera, Krakow, Poland, [6]Division of Medical Oncology, Prince of Songkla University, Songkhla, Thailand, [7]Division of Oncology, Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, Thailand, [8]Division of Medical Oncology, Srinagarind Hospital, Khon Kaen, Thailand, [9]Medical Oncology Unit, King Chulalongkorn Memorial Hospital, Bangkok, Thailand, [10]Medical Oncology, First St. Petersburg State Medical University n.a. I.P. Pavlov, Saint-Petersburg, Russian Federation, [11]Medical Oncology, Novosibirsk Regional Clinical Oncology Dispensary, Novosibirsk, Russian Federation, [12]Medical Oncology, Chelyabinsk Regional Clinical Oncology Center, Chelyabinsk, Russian Federation, [13]Medical Oncology, NMRC of Oncology n.a. N.N. Petrov, Saint-Petersburg, Russian Federation, [14]Medical Oncology, Volgograd Regional Clinical Oncology Dispensary, Volgograd, Russian Federation, [15]Medical Oncology, Multidisciplinary Clinical Medical Center "Medical City", Tyumen, Russian Federation, [16]R&D, Checkpoint Therapeutics, Inc., New York, NY, United States of America, [17]Medical Oncology, Christchurch Hospital, Christchurch, New Zealand

Background

- Cosibelimab (a/k/a CK-301) is a high affinity, fully-human IgG1 monoclonal antibody (mAb) that directly binds to programmed death ligand-1 (PD-L1) and blocks the PD-L1 interaction with the programmed death receptor-1 (PD-1) and B7.1 receptors.[1]
- Cosibelimab also has a functional Fc domain capable of inducing antibody-dependent cell-mediated cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC) against PD-L1 expressing tumor cells.[1]
- Here, we present interim safety, efficacy and pharmacokinetic data from a multicenter, open-label, phase 1 dose escalation study (NCT03212404) with ongoing expansion cohorts in patients with advanced/metastatic cancers, including cutaneous squamous cell carcinoma (cSCC) and non-small cell lung cancer (NSCLC).

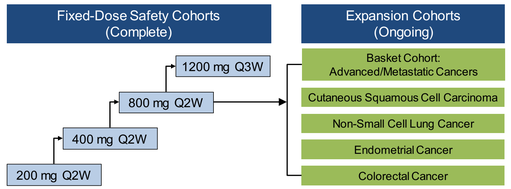
Primary objectives

- Assess the safety and tolerability of cosibelimab when administered every 14-21 days to subjects with selected recurrent or metastatic cancers.
- Evaluate the efficacy of cosibelimab by measuring overall response rate (ORR).

Secondary objectives

- Characterize pharmacokinetics and immunogenicity of cosibelimab.

Study Design



Select Inclusion Criteria

- Adult patients with advanced/metastatic cancers; measurable disease by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1; Eastern Cooperative Oncology Group (ECOG) performance status of 0-1; brain metastases without evidence of progression; adequate organ function.
- cSCC cohort: unresectable or metastatic cSCC not amenable to local therapy.
- NSCLC cohort: Stage IV NSCLC with high (>50%) PD-L1 tumor expression as determined by immunohistochemistry, with no prior systemic treatment for metastatic NSCLC and no EGFR sensitizing (activating) mutation or ALK translocation.
- Endometrial cohort: Endometrial cancer with disease progression on or after at least 1 line of anti-cancer therapy, but received no more than 2 lines of anti-cancer therapy.
- Colorectal cohort: Colorectal cancer assessed as microsatellite instability-high or mismatch repair deficient that has progressed on or after, or been intolerant of, previous treatments including a fluoropyrimidine- and oxaliplatin- and irinotecan-based chemotherapy.

Select Exclusion Criteria

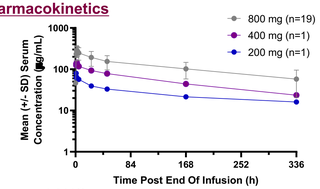
- Prior immune checkpoint inhibitor therapy; any anti-cancer therapy within 4 weeks of initial dose; active or suspected autoimmune disease.

Results

Demographic and Baseline Characteristics

Characteristics (all dosed patients)	n=81
Age, median, years	64
Gender, male/female, %	62/38
Race, white/Asian/other, %	72/27/1
Tumor Types, n (%)	
- Colorectal cancer	10 (12.4)
- Cutaneous squamous cell carcinoma	21 (25.9)
- Endometrial cancer	7 (8.6)
- Head/neck squamous cell carcinoma	1 (1.2)
- Hodgkin's lymphoma	1 (1.2)
- Melanoma	10 (12.4)
- Mesothelioma	2 (2.5)
- Non-small cell lung cancer	27 (33.3)
- Urothelial carcinoma	2 (2.5)

Pharmacokinetics



- C_{max} and AUC_{inf} are dose proportional.

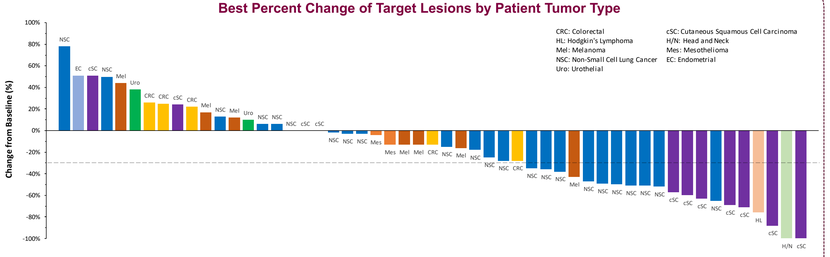
Preliminary Efficacy Results

At the August 5, 2019 cutoff date, 68 patients had at least two tumor assessments or discontinued treatment prior. Tumor assessments by RECIST v1.1 were conducted every 8 weeks for the initial 32 weeks on study, and every 12 weeks thereafter. The best overall tumor response is shown below for all tumor types, and the subgroup cohorts of cSCC and first-line NSCLC.

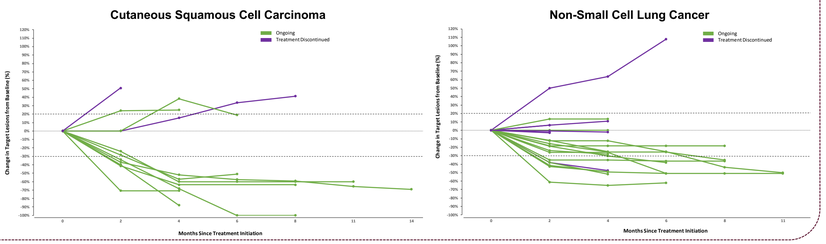
Best Overall Tumor Response by RECIST v1.1	All Tumor Types (n=68)	cSCC (n=14)	NSCLC (n=25)
Complete response, n (%)	1 (1.5)	1 (7.1)	0 (0.0)
Partial response, n (%)	18 (26.4)	6 (42.9)	10 (40.0)
Stable disease, n (%)	20 (29.4)	2 (14.3)	9 (36.0)
Progressive disease, n (%)	14 (20.6)	2 (14.3)	2 (8.0)
Not evaluated/done, n (%)	15 (22.1)	3 (21.4)	4 (16.0)
Overall response rate, % (95% CI)	**27.9 (17.7, 40.1)**	**50.0 (23.0, 77.0)**	**40.0 (21.1, 61.3)**
Response ongoing, n (%)	17/19 (89.5)	7/7 (100.0)	9/10 (90.0)
Median duration of response, months (min, max)	Not reached (0.1, 11.4)	Not reached (2.5, 11.4)	Not reached (0.1, 11.0)
Disease control rate, %	57.3	64.2	76.0
Reductions in sum of target lesions, n (%)	34 (50.0)	7 (50.0)	16 (64.0)

- ORR for cSCC cohort was 50.0%. One patient achieved a complete response and 6 patients achieved partial responses. All 7 responses (100.0%) are confirmed and ongoing with the longest duration at 11.4 months (ongoing) at time of analysis.
- ORR for NSCLC cohort was 40.0%. Ten patients achieved partial responses (8 confirmed and 2 pending confirmation). Nine of 10 responses (90.0%) are ongoing with the longest duration at 11.0 months (ongoing) at time of analysis.

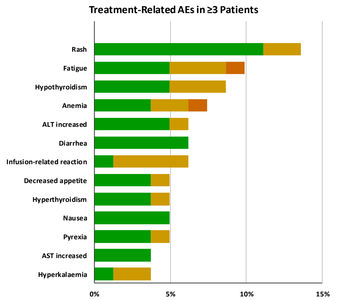
Best Percent Change of Target Lesions by Patient Tumor Type



Relative Percent Change in Total Tumor Burden in cSCC and NSCLC Cohorts



Preliminary Safety Results



Summary of Treatment-Emergent Adverse Events (AEs)	
n (%)	n=81[a]
AE (all grade, related and unrelated)	69 (85.2)
Treatment-related AE (TRAE)	48 (59.3)
AE grade ≥3 (related and unrelated)	27 (33.3)
Treatment-related grade ≥3	5 (6.2)
Serious AE (all grade, related and unrelated)	18 (22.2)
Serious treatment-related AEs	2 (2.5)
Treatment-related AEs leading to discontinuation	2 (2.5)

- Most common TRAEs include rash (n=11, 13.6%), fatigue (n=8, 9.9%), hypothyroidism (n=7, 8.6%), anemia (n=6, 7.4%), alanine aminotransferase increased, diarrhea, and infusion-related reaction (n=5, 6.2% each).
- Grade ≥3 TRAEs occurred in 5/81 (6.2%) patients, including single grade 3 events of anemia, asthenia, blood creatinine increased, confusional state, fatigue, and hypertension (n=1 each), and one death due to colon cancer.

[a] Includes all dosed patients. 200 mg q2w (n=1), 400 mg q2w (n=1), 800 mg q2w (n=74), 1200 mg q3w (n=5).

Conclusions

- Cosibelimab, a high affinity, fully-human, anti-PD-L1 mAb with functional Fc domain, demonstrated a safe and well-tolerated safety profile in patients with advanced/metastatic cancers, with dose proportional PK at fixed doses of 200, 400 and 800 mg.
- Preliminary efficacy data indicates confirmed and durable RECIST v1.1 responses in multiple tumor types, with robust activity in cutaneous squamous cell carcinoma (cSCC) and non-small cell lung cancer (NSCLC):
  - 50.0% ORR in cSCC with 100.0% of responses ongoing (max: 11.4 months)
  - 40.0% ORR in NSCLC with 90.0% of responses ongoing (max: 11.0 months)
- Enrollment in expansion cohorts ongoing evaluating the safety and efficacy of the 800 mg q2w fixed dosing regimen.

References: 1. Gorelik L, et al. *Cancer Research* 2017; 77(13 Suppl):Abstract nr 4606.

Acknowledgements: Study sponsored by Checkpoint Therapeutics, Inc.

Disclosures: All authors except LG, YK and JFO are PIs on the CK-301-101 trial supported by Checkpoint Therapeutics, Inc. PRC is a PI on trials supported by Merck Sharp & Dohme, AbbVie, Eli Lilly, and Bristol-Myers Squibb. AM has no disclosures to declare. GR has received research funding through his institution from Novotech, Roche, AstraZeneca, Pfizer and Alphapharm. DMK has no disclosures to declare. PK has no disclosures to declare. IL has received honoraria from Bristol-Myers Squibb, Merck, Roche, Amgen, Janssen and Novartis; and received research funding from Novartis, Roche and Bristol-Myers Squibb. AD has served on the speaker bureau for Roche and received expenses paid or reimbursed by Eisai. CC has received research funding from Roche and AstraZeneca. AS has received honoraria from Roche, Novartis, Eisai and Pfizer; and served as a consultant and on the speaker bureaus for Roche, Novartis and Pfizer. VS has received honoraria from AstraZeneca, Novartis, Roche, Pfizer, Sanofi, Eisai, Boehringer, Taiho, Merck Sharp & Dohme and Bristol-Myers Squibb; served as a consultant for Merck Sharp & Dohme, Novartis, Pfizer, Roche, Eisai, and Amgen; and received research funding through his institution from AstraZeneca, Novartis, Roche, Pfizer, Boehringer, Eisai, Taiho, Eli Lilly, and Merck Sharp & Dohme. AA, VK, NF, BK, NVK and VO have no disclosures to declare. LG owns stock or other ownership interests in Checkpoint Therapeutics, Inc. YK owns stock or other ownership interests in Checkpoint Therapeutics, Inc. JFO is a paid employee and stockholder at Checkpoint Therapeutics, Inc. DLH has received research funding from Merck, Roche and Targovax.

Presenting author email address: Philip R. Clingan, philipclingan.smdcctrials@live.com.au