529 PHASE 1 STUDY OF INCB086550, AN ORAL PD-L1 INHIBITOR, IN IMMUNE-CHECKPOINT NAIVE PATIENTS WITH ADVANCED SOLID TUMORS

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Background INCB086550 is an orally administered small molecule that binds PD-L1 and inhibits PD-1/PD-L1 interaction. Translational data demonstrating markers of immune activation in patients following INCB086550 were previously reported.[1] Preliminary clinical data from this phase 1 study are presented below.

Methods Adult patients (≥18 years) with advanced solid tumors were enrolled into this open-label study. Patients had disease progression after standard available therapy or were intolerant of or ineligible for standard treatment. Measurable disease was required. A modified 3+3 dose-escalation design was employed, followed by dose expansions. The primary endpoints were safety and tolerability of INCB086550, identification of a pharmacologically active dose and/or MTD, and confirmation of the RP2D. Secondary endpoints included PK, pharmacodynamics, and efficacy as assessed by investigator-determined ORR and DCR (CR, PR, or SD ≥12 weeks).

Results As of 9Apr2021, 79 patients received treatment (**Table 1**); 57.0% were female, 62.0% had ≥2 prior lines of therapy, and 16% received prior IO treatment. Forty-six (58.2%) patients had treatment-related TEAEs; those occurring in ≥5% of patients are presented in **Table 2**. Ten patients (12.7%) had grade ≥3 treatment-related TEAEs. Immune-related TEAEs occurred in 15 patients (19.0%); the most common (>1 patient) included peripheral sensory neuropathy (n=5), pruritus (n=3), immune-mediated neuropathy (n=2), and peripheral motor neuropathy (n=2). In total, 10 (12.7%) patients had TEAEs of peripheral neuropathy; all were grade ≤3. All grade 2 or 3 TEAEs of peripheral neuropathy resolved or improved with either study drug continuation without dose modification, dose reduction, or drug interruption/discontinuation. Patients with TEAEs leading to treatment interruption were 21 (26.6%), dose reduction 5 (6.3%), and discontinuation 13 (16.5%). Five patients (6.3%) died of a TEAE (cerebrovascular accident, dyspnea, general physical health deterioration, intestinal obstruction, intracranial hemorrhage [each n=1]); all fatal TEAEs were considered unrelated to study drug. The efficacy-evaluable population included 68 patients; ORR was 11.8% (95%CI, 5.2%–21.9%; CR, 1.5%; PR, 10.3%), and DCR was 19.1% (95%CI, 10.6%–30.5%; **Table 3**). Eight objective responses were observed at doses ≥400 mg BID (**Table 4**); 3 of these were noted among the 5 IO treatment-naive patients with MSI-H tumors who received 400 mg BID.

Conclusions Immune-related AEs observed in this ongoing phase 1 study are consistent with those seen with antibody immune checkpoint inhibitors, with the exception of peripheral neuropathy. Preliminary efficacy of INCB086550 in tumor types known to be responsive to anti-PD-(L)1 therapy is encouraging and warrants further investigation.

Abstract 529 Table 1 Number of patients per dose level

Dose Level	Number of Patients
100 mg QD	6
200 mg QD	3
200 mg BID	24
400 mg QD	4
400 mg BID	32
800 mg QD	1
800 mg BID	6
400 mg BID 1 week; 100 mg QD 1 week; repeat	1
400 mg BID 2 weeks; 100 mg QD 2 weeks; repeat	2
Total	79

BID, twice daily; QD, once daily.
The tumor types in the study included breast, cervical, colorectal, endometrial, esophageal, gastric, hepatocellular, melanoma, mesothelioma, ovarian, small cell lung cancer, squamous cell carcinoma of the head and neck, renal cell, urothelial, adrenal, anal, cholangiocarcinoma, gall bladder, pancreatic, penile, salivary gland, sarcoma, vaginal, prostate, basal cell, pleomorphic sarcoma, fallopian, carcinoma of parotid gland, well-differentiated liposarcoma, myoepithelial, castrate-resistant prostate cancer, cancer of unknown primary, neuroendocrine, prostate adenocarcinoma with neuroendocrine differentiation, glioblastoma, anal canal, angiosarcoma, and gastroesophageal junction.

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Abstract 529 Table 2 Treatment-related TEAEs reported by ≥5% of patients (N=79)

Preferred Term, n (%)	Any Related TEAE	Grade ≥3 Related TEAE
Nausea	13 (16.5)	0
Fatigue	8 (10.1)	1 (1.3)
Decreased appetite	7 (8.9)	0
Vomiting	7 (8.9)	1 (1.3)
Diarrhea	6 (7.6)	0
Lipase increased	6 (7.6)	0
Headache	5 (6.3)	0
Peripheral sensory neuropathy	5 (6.3)	2 (2.5)
Pruritus	5 (6.3)	1 (1.3)
Rash	5 (6.3)	1 (1.3)

TEAE, treatment-emergent adverse event.

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Abstract 529 Table 3 Summary of best overall response by RECIST v1.1 or RANO*

Response, n (%)	Efficacy-Evaluable Population† (N=68)
ORR (CR+PR)	8 (11.8)
CR	1 (1.5)
PR	7 (10.3)
DCR (CR+PR+SD ≥12 weeks)	13 (19.1)
SD (SD ≥12 weeks)	5 (7.4)
Progressive disease	39 (57.4)
Not evaluable‡	8 (11.8)
Not assessed§	8 (11.8)

CR, complete response; DCR, disease control rate; GBM, glioblastoma; ORR, objective response rate; PR, partial response; RANO, Response Assessment of Neuro-Oncology; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.
* 1 patient with GBM was assessed by RANO and had best overall response of progressive disease.
† The efficacy-evaluable population included all solid tumor participants enrolled in the study who received at least 1 dose of INCB086550, completed a baseline scan, and met at least 1 of the following criteria: ≥1 postbaseline scan, participant had been on the study for a minimum of 63 days of follow-up, or participant had discontinued from treatment.
‡ "Not evaluable" indicates participants in the efficacy-evaluable population that did not have valid postbaseline overall response assessments by RECIST or RANO.
§ "Not assessed" indicates participants in the efficacy-evaluable population that did not have any postbaseline overall response assessments by RECIST or RANO.

Abstract 529 Table 4 Tumor types with investigator-assessed objective response per RECIST v1.1 (n=8)

Tumor Type	IO Treatment -Naive	Dose	Best Overall Response	Duration of Response (Months)
Squamous cell anal cancer	Yes	800 mg BID	Partial Response	4.17
Squamous cell anal cancer	Yes	400 mg BID	Complete Response	5.78
MSI-H colon adenocarcinoma	No	400 mg BID	Partial Response	5.78+
Clear cell ovarian cancer	Yes	400 mg BID	Partial Response	3.35+
MSI-H colon adenocarcinoma	Yes	400 mg BID	Partial Response	3.71+
dMMR gastric cancer	Yes	400 mg BID	Partial Response	1.87+
MSI-H neuroendocrine colon cancer	Yes	400 mg BID	Partial Response	1.87
Squamous cell vaginal cancer	Yes	400 mg BID	Partial Response	0.03+

BID, twice daily; dMMR, deficient mismatch repair; IO, immuno-oncology; MSI-H, high microsatellite instability; RECIST, Response Evaluation Criteria in Solid Tumors.
+Ongoing response.

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Trial Registration ClinicalTrials.gov identifier NCT03762447

REFERENCES

1. Piha-Paul S, et al. J Immunother Cancer. 2020;8(suppl 3):A255.

Ethics Approval The study protocol was approved by institutional review boards (IRB) or independent ethics committees at participating centers. All study participants gave informed consent before taking part. The approval numbers were: Integ Review IRB (Austin, TX), RM 598; MD Anderson Cancer Center Office of Human Subject Protection (Houston, TX), IRB ID 2018-0765; ADVARRA (Columbia, MD), IRB# 00000971; Ethisch Comité/Comité d' Ethique Hospital (Brussels, Belgium), A2021/085; Hôpital Saint-Louis (Paris, France), Prof Le Tourneau – 2020-118/Ref. of the Promoter 0.09.22.72214; NHS Health Research Authority London - City & East Research Ethics Committee (Bristol, UK), IRAS project ID:282291/REC reference: 20/LO/1001; Comitato Etico IRCCS Pascale (Milan, Italy), ISS Validation Protocol Number 29111(2020)-PRE21-1835; Comitato Etico Della Fondazione IRCCS "Istituto Nazionale Dei Tumori"- Milano CE150053 (Milan, Italy), INT 230/20; Comitato Etico Regione Toscana - Area Vasta Sud Est CE150047, 18064; Comitato Etico Indipendente Istituto Clinico Humanitas CE150081, 940/20; Regulatory Pharma Net (Pisa, Italy), IEC 1393.

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