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A Phase 1 Study Exploring the Safety and Tolerability of the Small-Molecule PD-L1 Inhibitor, INCB099318, in Patients With Select Advanced Solid Tumors

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Introduction

- Programmed cell death protein 1 (PD-1)/programmed cell death ligand 1 (PD-L1) pathway blockade, and subsequent T-cell activation, provides therapeutic benefit for many tumor types[1]
- Overall survival benefit has been demonstrated with intravenous monoclonal antibodies targeting PD-1/PD-L1 in a variety of cancers
- INCB099318 is a novel, orally administered small-molecule inhibitor of PD-L1, disrupting the PD-1/PD-L1 interaction
- We report here results from the ongoing phase 1 INCB099318 study

Objective

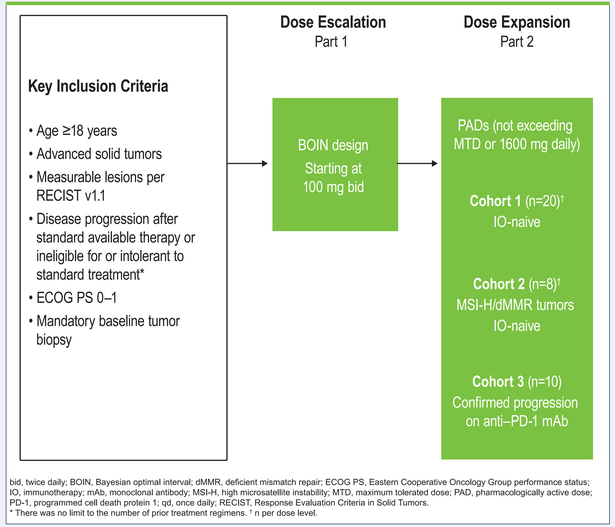
- This ongoing phase 1 study (NCT04272034) evaluates the safety, tolerability, and preliminary efficacy of INCB099318 in advanced solid tumors and aims to identify a pharmacologically active dose or maximum tolerated dose, whichever is lower

Methods

Patients and Study Design

- This phase 1, open-label, dose-finding study is evaluating INCB099318 in adults whose disease had previously progressed on available therapy
- Part 1 uses a Bayesian optimal interval dose escalation design (**Figure 1**)
- In part 2, doses will be expanded for patients with various tumor types (**Figure 1**)

Figure 1. Study Design



bid, twice daily; BOIN, Bayesian optimal interval; dMMR, deficient mismatch repair; ECOG PS, Eastern Cooperative Oncology Group performance status; IO, immunotherapy; mAb, monoclonal antibody; MSI-H, high microsatellite instability; MTD, maximum tolerated dose; PAD, pharmacologically active dose; PD-1, programmed cell death protein 1; qd, once daily; RECIST, Response Evaluation Criteria in Solid Tumors.
* There was no limit to the number of prior treatment regimens. † n per dose level.

Endpoints

- The primary endpoints were safety and tolerability of INCB099318, measured by monitoring frequency and severity of adverse events
- Exploratory endpoints included the objective response rate, defined as the percentage of patients with a best overall response of complete response or partial response per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1

Statistical Analyses

- Descriptive statistics were used for all analyses in this exploratory study

Results

Patient Characteristics and Disposition

- A total of 42 patients were treated before data cutoff on July 8, 2022; all 42 patients (100%) were enrolled in dose escalation (part 1); no patients had been treated in dose expansion at time of data cutoff (part 2; **Table 1**)
- The majority previously received 1–2 lines of anticancer therapy for advanced or metastatic disease (**Table 2**)
- 21 patients (50.0%) discontinued treatment, 18 due to disease progression

Table 1. Number of Patients per Dose Level*

	Dose escalation	
	Dose Level	Number of Patients (N=42)
Part 1	100 mg bid	3
	200 mg bid	8
	300 mg bid	5
	400 mg bid	10
	600 mg qd	4
	600 mg bid	12

bid, twice daily; qd, once daily.
* Cancer types for patients enrolled in dose levels ≥200 mg bid were: cervical (n=10); esophageal (n=4); basal cell carcinoma, cancer of unknown primary (n=3); ovarian, squamous cell carcinoma of the head and neck (including nasopharyngeal), pancreatic (n=2); endometrial, hepatocellular carcinoma, colorectal, mesothelioma, breast, urothelial carcinoma, anal carcinoma, squamous cell penile carcinoma, cholangiocarcinoma, prostate, sarcoma, testicular, parotid (n=1).

Table 2. Patient Demographics

	Total (N=42)
Age, median (range), y	61.5 (34–78)
Female, n (%)	23 (54.8)
Race, n (%)	
White	36 (85.7)
Black	1 (2.4)
Asian	2 (4.8)
Other	1 (2.4)
Not reported	2 (4.8)
ECOG status, n (%)	
0	15 (35.7)
1	27 (64.3)
Prior IO treatment, n (%)	6 (14.3)
Previous lines of therapy, n (%)	
0	3 (7.1)
1	15 (35.7)
2	11 (26.2)
≥3	13 (31.0)

ECOG, Eastern Cooperative Oncology Group; IO, immunotherapy.

Safety

- 37 patients (88.1%) experienced a treatment-emergent adverse event (TEAE; **Table 3**); the most frequent TEAEs and treatment-related TEAEs included nausea and fatigue (**Tables 4** and **5**)
  - No patients experienced treatment-related serious TEAEs
- Unlike with the oral PD-L1 inhibitor INCB086550 **[SITC 2022 Poster 774]**, no dose-limiting immune-mediated peripheral neuropathy has occurred to date with INCB099318

Table 3. Safety

n (%)	Total (N=42)
Any-grade TEAE	37 (88.1)
Treatment-related TEAE	26 (61.9)
Grade ≥3 treatment-related TEAE	1 (2.4)
Treatment-related serious TEAE	0
Treatment-related death	0

TEAE, treatment-emergent adverse event.

Table 4. Very Common TEAEs (≥15% [n≥7] Patients) by MedDRA Preferred Term

n (%)	Total (N=42)	
	Any Grade	Grade ≥3
Nausea	10 (23.8)	1 (2.4)
Fatigue	9 (21.4)	2 (4.8)
Constipation	8 (19.0)	0

MedDRA, Medical Dictionary for Regulatory Activities (v24.0); TEAE, treatment-emergent adverse event.

Table 5. Common TRAEs (≥5% [n≥3] Patients) by MedDRA Preferred Term

n (%)	Total (N=42)	
	Any Grade	Grade ≥3
Nausea	6 (14.3)	0
Aspartate aminotransferase increased	5 (11.9)	0
Fatigue	5 (11.9)	1 (2.4)
Pruritus	5 (11.9)	0
Alanine aminotransferase increased	4 (9.5)	0
Diarrhea	3 (7.1)	0

MedDRA, Medical Dictionary for Regulatory Activities (v24.0); TRAE, treatment-related treatment-emergent adverse event.

- Sponsor-defined immune-related TEAEs (irTEAEs) occurred in 2 patients (4.8%); the most common irTEAEs, including their management, are presented in **Table 6**
  - The 2 patients who experienced irTEAEs received INCB099318 300 mg twice daily (bid) and 600 mg bid; only 1 case (pruritus) was considered related to treatment, whereas the other case was hypothyroidism biochemically detected in a patient with a history of hypothyroidism
  - Neither irTEAE resulted in INCB099318 interruption, reduction, or discontinuation

Table 6. Summary of Sponsor-Defined irTEAEs and Their Management

irTEAE, n (%)	Any Grade (N=42)	Grade ≥3 (N=42)	Management (N=42)			
			Dose Reduction	Dose Interruption	Discontinuation	Corticosteroid Treatment
Any	2 (4.8)	0	0	0	0	0
Most common*						
Hypothyroidism	1 (2.4)	0	0	0	0	0
Pruritus	1 (2.4)	0	0	0	0	0

irTEAE, immune-related treatment-emergent adverse event.
*Includes all irTEAEs.

Efficacy

- Responses were seen at or above 200 mg bid in tumor types such as clear cell ovarian cancer (200 mg bid), squamous cell carcinoma of the cervix (300 mg bid), and adenosquamous carcinoma of the cervix (400 mg bid)

Conclusions

- **INCB099318 was generally well tolerated at total daily doses up to 1200 mg**
- **Preliminary efficacy results indicate antitumor activity, supporting the continued clinical investigation of INCB099318**
- **Further dose escalation and dose expansion are ongoing**

Disclosures

HP has received honoraria from Amgen, AstraZeneca, Bayer, Roche, and Sanofi.

AS and MH have no disclosures to declare. DJP, RP, MG, JY, KBS, WE, LN, AA, NK, SS, and UB have declared no disclosures.

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References

1. Ai L, et al. *Drug Des Devel Ther.* 2020;14:3625-3649.

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