Official Title: A Phase 2 Study of INCB086550 (Oral PD-L1 Inhibitor) in Participants Who Are Immune Checkpoint Inhibitor–Naïve With Selected Solid Tumors

NCT Number: NCT04629339

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Statistical Analysis Plan

INCB 86550-203

A Phase 2 Study of INCB086550 (Oral PD-L1 Inhibitor) in Participants Who Are Immune Checkpoint Inhibitor–Naïve With Selected Solid Tumors

IND Number:	**139,900 (NCT04629339)**
EudraCT Number:	**2020-000157-27**
Sponsor:	**Incyte Corporation** **1801 Augustine Cut-Off** **Wilmington, DE 19803** **United States**
Protocol Version:	**Protocol Amendment 1 dated 08 MAR 2021**
CRF Approval Date:	**30 MAR 2022**
SAP Version:	**Amendment 1**
SAP Author:	[redacted]**, PhD** [redacted]**, Biostatistics**
Date of Plan:	**01 DEC 2023**

This study is being conducted in compliance with Good Clinical Practice, including the archiving of essential documents.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

Abbreviation	Term
AE	adverse event
ALK	anaplastic lymphoma kinase
[redacted]	
BID	twice daily
CI	confidence interval
[redacted]	
CNS	central nervous system
COVID-19	coronavirus disease 2019
CPS	composite performance score
CR	complete response
CRF	Case Report Form
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
DCR	disease control rate
DOR	duration of response
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	electronic Case Report Form
EGFR	epidermal growth factor receptor
FAS	full analysis set
FDA	Food and Drug Administration
HCC	hepatocellular carcinoma
irAE	immune-related adverse event
KM	Kaplan Meier
MedDRA	Medical Dictionary for Regulatory Activities
NE	not evaluable
NSCLC	non–small cell lung cancer
ORR	objective response rate
[redacted]	

Abbreviation	Term
PD	progressive disease
PD-1	programmed death 1
PD-L1	programmed death-ligand 1
[redacted]	
PR	partial response
PS	performance score
PT	preferred term
QT	QT interval in electrocardiogram tracings
QTc	corrected QT interval
RECIST	Response Evaluation Criteria in Solid Tumors
RCC	renal cell carcinoma
ROS	reactive oxygen species
SAP	Statistical Analysis Plan
SD	stable disease
SOC	system organ class
[redacted]	
TEAE	treatment-emergent adverse event
[redacted]	
TPS	tumor proportion score
UC	urothelial carcinoma
ULN	upper limit of normal
[redacted]	

1. INTRODUCTION

This open-label, global, nonrandomized, multicohort trial is designed to provide a benchmark of efficacy for INCB086550 in key indications in which other PD-(L)1 inhibitors have already demonstrated efficacy.

Section 2 of the Protocol provides a detailed description of the investigational product, rationale for doses to be examined, and potential risks and benefits of treatment with INCB086550.

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in INCB 86550-203 Protocol Amendment 1. The scope of this plan includes the analyses that are planned and will be executed by the Department of Biostatistics or designee. Pharmacokinetic analysis will not be performed for this study. This study was terminated early.

[redacted]

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 86550-203 Protocol Amendment 1 dated 08 MAR 2021 and CRFs approved 30 MAR 2022. Unless superseded by an amendment, this SAP will be effective for all subsequent Protocol amendments and eCRF versions.

2.2. Study Objectives and Endpoints

Table 1 presents the objectives and endpoints.

Table 1: Objectives and Endpoints

Objectives	Endpoints
Primary	
To determine the ORR of participants treated with INCB086550.	ORR, defined as the percentage of participants with a best overall response of CR or PR confirmed by at least 1 repeat assessment ≥ 28 days later according to RECIST v1.1 as determined by the investigator.
Secondary	
To determine the efficacy of INCB086550 in participants with advanced solid tumors in respect to DCR.	DCR, defined as the percentage of participants with a best overall response of CR or PR confirmed by at least 1 repeat assessment ≥ 28 days later, or SD for ≥ 12 weeks, by investigator assessment per RECIST v1.1.
To determine the efficacy of INCB086550 in participants with advanced solid tumors in respect to DOR.	DOR, defined as the time from the earliest date of CR or PR confirmed by at least 1 repeat assessment ≥ 28 days later until the earliest date of disease progression by investigator assessment per RECIST v1.1, or death due to any cause, if occurring sooner than progression.
To evaluate the safety of INCB086550 in participants with advanced solid tumors.	Safety is determined by monitoring the frequency and severity of AEs, including the evaluation of laboratory tests, vital signs, and ECGs.
[redacted]	

3. STUDY DESIGN

This study is a Phase 2, open-label, global, multicenter study designed to assess the clinical activity and safety of INCB086550 as initial immune checkpoint inhibitor therapy in participants with advanced selected solid tumors in which the efficacy of PD-(L)1 inhibitors has previously been established. Participants will be enrolled at 1 or more dose levels into disease-specific cohorts (see Figure 1), with a safety/efficacy run-in analysis in up to 15 participants and a nonbinding interim futility analysis planned after approximately 50% of the participants in each cohort are evaluable for response using the RECIST evaluable population. This study was terminated early.

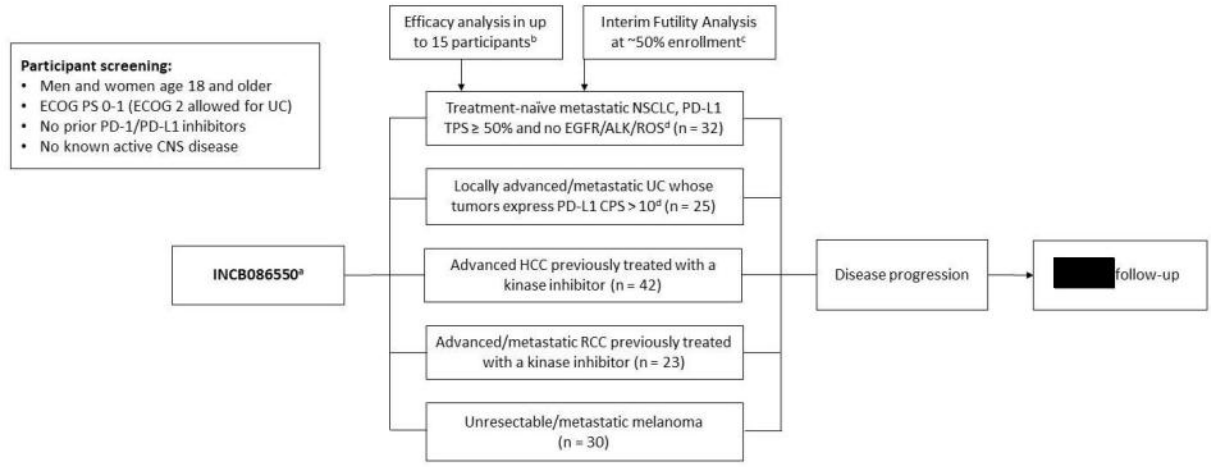
The primary endpoint is confirmed ORR as determined by the investigator using RECIST v1.1.

The study consists of 3 periods: screening, study drug treatment, and follow-up.

A maximum study treatment duration of 2 years is allowed. Participants who achieve a CR may discontinue INCB086550 after 4 additional cycles (with a minimum of 1 year of treatment) upon consultation with the medical monitor.

The follow-up period will begin once a participant has completed 2 years of study treatment or has met criteria for discontinuation from study drug. Participants will be evaluated for AEs (including irAEs) for 90 days after the last dose of study drug.

Figure 1: Study Design Schema



[a] Information on dosing is included in Protocol Section 2.2.2.
[b] Nonbinding efficacy run-in is planned after enrollment of up to 15 participants in select disease-specific cohorts are evaluable for response using the RECIST evaluable population.
[c] Nonbinding interim futility analyses are planned after approximately 50% of the participants in each disease-specific cohort are evaluable for response using the RECIST evaluable population.
[d] PD-L1 staining assessed using the Dako PD-L1 IHC 22C3 pharmDx assay.

3.1. Randomization

Not applicable.

3.2. Control of Type I Error

Not applicable.

3.3. Sample Size Considerations

The number of participants based on a group sequential design with 1 interim per cohort at approximately 50% information using a Hwang-Shih-DeCani (1990) spending function has been determined independently for each disease-specific cohort (irrespective of dose level) and can be found in Table 2. The target ORR (p_1) for each cohort is based on published clinical experience with a reference PD-1 inhibitor (El-Khoueiry et al 2017, Keytruda 2018, Mok et al 2019, Motzer et al 2015, Reck et al 2016, Robert et al 2015). The target ORR (p_1) for the NSCLC cohort was calculated by combining 2 different studies (Mok et al 2019, Reck et al 2016). The null ORR (p_0) for the melanoma and RCC cohorts is based on the control arm ORRs in the reference studies. For the NSCLC, UC, and HCC cohorts, the null ORR (p_0) was selected to be the p_0 that creates a test with a rejection region that begins with the lower CI bound of the reference PD-1 inhibitors. The sample size for each cohort provides approximately 80% power and 5% 1-sided Type I error.

Table 2: Sample Size per Cohort

Tumor Type (Cohort)	ORR		Sample Size
	p_0	p_1	
NSCLC	18.0%	41.1%	32
UC	20.0%	47.0%	25
HCC	6.0%	20.0%	42
RCC	5.0%	25.0%	23
Melanoma	11.9%	32.9%	30

3.4. Schedule of Assessments

Refer to Protocol Amendment 1 dated 08 MAR 2021 for a full description of all study procedures and assessment schedules for this study.

4. DATA HANDLING DEFINITIONS AND CONVENTIONS

4.1. Scheduled Study Evaluations and Study Periods

4.1.1. Day 1

Day 1 is the date that the first dose of study drug (INCB086550) is administered to the participants.

4.1.2. Study Day

If a visit/reporting date is on or after Day 1, then the study day at the visit/reporting date will be calculated as

Day # = (visit/reporting date – Day 1 date + 1).

If the visit/reporting date is before Day 1, then the study day at the visit/reporting date will be calculated as

Day # = (visit/reporting date – Day 1 date).

A study day of –1 indicates 1 day before Day 1.

4.1.3. Baseline Value

Baseline is the last nonmissing measurement obtained before the first administration of INCB086550.

When scheduled assessments and unscheduled assessments occur on the same day and the time of the assessment or time of first dose is not available, use the following convention to determine baseline:

- If both a scheduled and an unscheduled visit are available on the day of the first dose and the time is missing, use the scheduled assessment as baseline.
- If all scheduled assessments are missing on the day of the first dose and an unscheduled assessment is available, use the unscheduled assessment as baseline.

4.1.4. Handling of Missing and Incomplete Dates

In general, values for missing dates will not be handled unless methods for handling missing dates are specified in this section or relevant sections. The original reported dates collected on the eCRF should be used in all relevant listings. The following rules will be used for handling partial dates for analyses requiring dates.

When calculating the time since diagnosis of cancer, a partial cancer diagnosis date will be handled as follows in the calculation:

- If only the day is missing, then the first day of the month will be used.
- If both the month and day are missing, then 01 JAN of the year will be used.
- If the diagnosis date is completely missing, then the time since diagnosis will not be calculated.

When the date of the last dose is used in deriving variables such as duration of treatment or TEAE flag, a missing or partial date of the last dose will be handled as follows:

- If only the day is missing, then the earlier date of the last day of the month or the date that the participant discontinued treatment will be used.
- If both the month and day are missing, then the earlier date of 31 DEC of the year or the date that the participant discontinued treatment will be used.
- Otherwise, the date that the participant discontinued treatment will be used as the date of the last dose.

For DOR, [redacted], a partial date of the death date will be handled as follows in the calculation:

- If mmyyyy for the last known alive date = mmyyyy for the death date, then the death date will be set to the day after the last known alive date.
- If mmyyyy for the last known alive date < mmyyyy for the death date, then the death date will be set to the first day of the death month.
- Otherwise, the partial death date will not be imputed.

4.1.5. Cycle Length and Duration

Cycle 1 Day 1 is the day that the first dose of study drug is administered. The scheduled cycle length is either 21 or 28 days (Protocol Tables 3-6). The actual Day 1 of subsequent cycles will correspond with the first day of administration of INCB086550 in that cycle; thus, treatment cycles may become out of sync with the originally planned schedule, and the cycle length may be different from 21 or 28 days. The date of the Day 1 of subsequent cycles recorded on the eCRF will be used as the Day 1 of the subsequent cycles.

4.2. Variable Definitions

4.2.1. Prior and Concomitant Medication

Prior medication is defined as any nonstudy medication started before the first dose of INCB086550.

Concomitant medication is defined as any nonstudy medication that is started accordingly:

- Before the date of first administration of INCB086550 and is ongoing throughout the study or ends on/after the date of first study drug administration.
- On/after the date of first administration of INCB086550 and is ongoing or ends during the course of the study.

A prior medication could also be classified as "both prior and concomitant medication" if the end date is on or after the first dose of INCB086550. In the listing, it will be indicated whether a medication is only prior, only concomitant, or both prior and concomitant.

For the purposes of analysis, all medications will be considered concomitant medications unless the medications can unequivocally be defined as not concomitant.

5. STATISTICAL METHODOLOGY

5.1. General Methodology

Unless otherwise noted, SAS® software (SAS Institute Inc, Cary, NC; v9.4 or later) will be used for the generation of all tables, graphs, and statistical analyses. Descriptive summaries for continuous variables will include but not be limited to the number of observations, mean, standard deviation, median, minimum, and maximum. Descriptive summaries for categorical variables will include the number and percentage of participants in each category.

Interim analyses are planned for this study as defined in Section 10; however, the study was terminated early, and no interim analyses will be performed.

5.2. Treatment Groups

Participants will be enrolled at 1 or more dose levels into disease-specific cohorts, with a safety/efficacy run-in analysis in up to 15 participants. The study was terminated prior to completion of the safety/efficacy run-in analysis. Data will be summarized separately for each cohort and dose level and may be summarized in total, as appropriate depending on enrollment.

5.3. Analysis Populations

Table 3 presents the populations for analysis. Table 4 presents the analysis populations by endpoint.

Table 3: Populations for Analysis

Population	Description
FAS	The FAS includes all study participants who received at least 1 dose of study drug. The FAS will be used for the summary of demographics, baseline characteristics, participant disposition, and all efficacy analyses. Participants will be analyzed according to the treatment group/dose to which they have been assigned.
Safety evaluable	The safety evaluable population includes all participants who received at least 1 dose of study drug. All safety analyses will be conducted using the safety evaluable population. Treatment groups for this population will be determined according to the actual treatment group/dose the participant received regardless of assigned study drug treatment.

Table 4: Analysis Populations by Endpoint

Endpoint	Analysis Population
ORR, defined as the percentage of participants with a best overall response of CR or PR confirmed by at least 1 repeat assessment ≥ 28 days later according to RECIST v1.1 as determined by the investigator.	FAS
DCR, defined as the percentage of participants with a best overall response of CR or PR confirmed by at least 1 repeat assessment ≥ 28 days later, or SD for ≥ 12 weeks, by investigator assessment per RECIST v1.1.	FAS
DOR, defined as the time from the earliest date of CR or PR confirmed by at least 1 repeat assessment ≥ 28 days later until the earliest date of disease progression by investigator assessment per RECIST v1.1, or death due to any cause, if occurring sooner than progression.	FAS
Safety is determined by monitoring the frequency and severity of AEs, including the evaluation of laboratory tests, vital signs, and ECGs.	Safety evaluable

6. BASELINE, EXPOSURE, AND DISPOSITION

Appendix A provides a list of data displays. Sample data displays are included in a separate document.

6.1. Demographics, Baseline Characteristics, and Disease History

6.1.1. Demographics and Baseline Characteristics

The following demographics and baseline characteristics will be summarized for the FAS: age, sex, race, ethnicity, weight, and height.

6.1.2. Baseline Disease Characteristics and Disease History

The following baseline disease characteristics and disease history will be summarized for the FAS: ECOG PS, cancer type, current stage, current sites of metastatic disease, and PD-L1 TPS for participants with NSCLC and participants with UC. Relevant [redacted]

6.1.3. Prior Anticancer Therapy

Prior anticancer therapy will be listed.

6.1.4. Medical History

Medical history will be listed.

6.2. Disposition of Participants

The number and percentage of participants who were treated, who were ongoing with study treatment, who completed study treatment, who discontinued study treatment with a primary reason for discontinuation, who were still in the study, who completed the study, and who withdrew from the study with a primary reason for withdrawal will be summarized for the FAS. The number of participants enrolled by country and/or site will also be provided by cohort and dose level.

6.3. Protocol Deviations

Important Protocol deviations will be summarized and listed for the FAS.

6.4. Exposure

For participants in the safety evaluable population, exposure will be summarized as follows:

- **Duration of treatment with INCB086550 days:** (date of last dose of INCB086550 – date of first dose of INCB086550 + 1) (including scheduled dose holds [days] for intermittent schedule).
- **Average daily dose of INCB086550 (mg/day):** total actual INCB086550 dose taken (mg) / duration of treatment with INCB086550 (days).

Total actual dose taken will be calculated based on the information entered on the Dosing eCRF.

6.5. Study Drug Compliance

For participants in the safety evaluable population, overall compliance (%) for INCB086550 will be calculated for all participants as follows:

compliance (%) = 100 × [total dose actually taken] / [total prescribed dose].

The total prescribed dose is defined as the sum of the doses prescribed by the investigator accounting for dose modifications.

The total actual dose taken will be calculated based on information entered on the Dosing eCRF.

6.6. Prior and Concomitant Medications

Prior medications and concomitant medications will be listed.

7. EFFICACY

Appendix A provides a list of data displays. Sample data displays are included in a separate document.

7.1. Efficacy Hypotheses

Not applicable.

7.2. Analysis of the Primary Efficacy Parameters

7.2.1. Response Criteria

Overall disease status will be categorized using RECIST v1.1 (Eisenhauer et al 2009). Participants will have their overall response evaluated as CR, PR, SD, PD, or NE at each postbaseline radiologic assessment based on changes in target lesions, nontarget lesions, and appearance of new lesions.

7.2.2. Best Overall Response

In general, under RECIST v1.1, best overall response is the best response recorded postbaseline prior to and including the first PD, in the order of CR, PR, SD, PD, and NE. The best overall response will be determined from response assessments prior to or on the same day as new anticancer therapy. If any alternative cancer therapy is taken while on study, any subsequent assessments will be excluded from the best overall response determination.

In the case of SD, measurements must meet the SD criteria at least once after the date of first dose at a minimum interval of 12 weeks. Participants who fail to meet this criterion will have best overall response of PD if the next available assessment indicates PD or NE if there is no additional assessment available.

The participant's best overall response assessment will depend on the achievement of both measurement and confirmation criteria in Table 5, with confirmation assessment occurring after a gap of ≥ 28 days.

Table 5: Confirmed Response Based on Subsequent Assessments

First Timepoint Response	Second Timepoint Response	Confirmed Response
CR	CR	CR or SD or NE[a]
CR	PR[b]	SD or NE[c]
CR	PR[b]	SD or NE[c]
CR	PD	SD or NE[c]
CR	NE	SD or NE[c]
CR	No further evaluation	SD or NE[c]
PR	CR	PR or SD or NE[d]
PR	PR	PR or SD or NE[e]
PR	SD	SD or NE[c]
PR	NE	SD or NE[c]
PR	PD	SD or NE[c]
PR	No further evaluation	SD or NE[c]
SD	CR	SD or NE[c]
SD	PR	SD or NE[c]
SD	SD	SD or NE[c]
SD	PD	SD or NE[c]
SD	NE	SD or NE[c]
SD	No further evaluation	SD or NE[c]
PD	No further evaluation	PD
NE	CR	NE
NE	PR	NE
NE	SD	NE
NE	PD	NE
NE	NE	NE
NE	No further evaluation	NE

Note: A confirmed response of SD can only be made after the participant is on study for a minimum of 12 weeks according to the study Protocol or SAP. If the participant is on study less than 12 weeks, any tumor assessment indicating SD before this time period will have a confirmed response of NE. NE is not required to be confirmed according to the table.

Note: Subsequent documentation of CR may provide confirmation of a previously identified CR for participants where the second integrated response was NE. Subsequent documentation of PR may provide confirmation of a previously identified PR for participants where the second integrated response was NE or SD. If the third tumor assessment confirms the CR (or PR), then the confirmed response will be CR (or PR). Only 1 intervening NE is allowed between CRs/PRs. For example: CR NE CR = CR; PR NE PR/CR = PR. Additionally, 1 SD (≥ 25% reduction in target lesions comparing with baseline) is allowed between PRs (eg, PR SD PR/CR = PR). Note: in the scenario of PR SD NE PR, this is not a confirmed PR.

[a] Confirmed response is CR if 28-day gap is met. Otherwise, confirmed response is SD if at least 12 weeks on study or NE if within 12 weeks on study.

[b] Special case programming: assign PR or SD following CR as PD in confirmed response.

[c] Confirmed response will be SD if the first tumor assessment is at least 12 weeks on study. Otherwise, the confirmed response will be NE.

[d] Confirmed response is PR if 28-day gap is met. Otherwise, confirmed response is SD if at least 12 weeks on study or NE if within 12 weeks on study.

7.2.3. Objective Response Rate

A participant is considered an objective responder if they have a best overall response of CR or PR confirmed by at least 1 repeat assessment ≥ 28 days later according to RECIST v1.1 as determined by the investigator. The ORR will be calculated separately for each cohort and dose level.

7.3. Analysis of the Secondary Efficacy Parameters

7.3.1. Duration of Response

Duration of response is defined as the time from the earliest date of CR or PR confirmed by at least 1 repeat assessment ≥ 28 days later until the earliest date of disease progression by investigator assessment per RECIST v1.1, or death due to any cause, if occurring sooner than progression. Partial death dates will be handled using the rules described in Section 4.1.4.

For participants who have not had disease progression and are still alive at the time of the analysis, DOR will be censored on the day of last evaluable disease assessment. For participants who have discontinued the study or have started other anticancer treatment, DOR will be censored on the day of last evaluable disease assessment documenting absence of PD before the discontinuation or the start of the new anticancer treatment. The KM estimate of median DOR and its 95% CI will be calculated using the KM method if the number of responders is ≥ 5. Duration of response will be listed for each responder.

7.3.2. Disease Control Rate

Disease control rate is defined as the percentage of participants with a best overall response of CR or PR confirmed by at least 1 repeat assessment ≥ 28 days later, or SD for ≥ 12 weeks, by investigator assessment per RECIST v1.1. The DCR will be summarized separately for each cohort and dose level.

[redacted]

[redacted]

[redacted]

[redacted].

[redacted]

9. SAFETY AND TOLERABILITY

Appendix A provides a list of data displays. Sample data displays are included in a separate document.

9.1. General Considerations

The clinical safety data (ie, routine laboratory tests and AEs) will be summarized using descriptive statistics (eg, mean, frequency) using the safety evaluable population.

9.2. Adverse Events

9.2.1. Adverse Event Definitions

A TEAE is any AE either reported for the first time or worsening of a pre-existing event after the first dose of study drug up to 90 days after the last dose of study drug or until the start of new anticancer therapy, whichever occurs first. Analysis of AEs (as discussed below) will be limited to TEAEs, but data listings will include all AEs regardless of their timing in relation to study drug administration. For purposes of analysis, all AEs will be considered TEAEs unless the AE can unequivocally be defined as not treatment-emergent.

Adverse events will be tabulated by MedDRA SOC and PT. Severity of AEs will be graded using the National Cancer Institute CTCAE v5 using Grades 1 through 5. The CTCAE reporting guidelines and grading details are available on the Cancer Therapy Evaluation Program website.

The subset of AEs considered by the investigator to be related to study drug will be considered to be treatment-related AEs. If the investigator does not specify the relationship of the AE to study drug, the AE will be considered to be treatment-related.

Any missing onset date, causality, or severity must be queried for resolution. Unresolved missing causality and severity will be handled according to the following rules:

- An unresolved missing causality will be considered treatment-related.
- An unresolved missing severity will be identified as an unknown severity.

9.2.2. Immune-Related Adverse Events

Number (%) of participants reporting any irAEs will be tabulated by immune-related category and PT. Potential irAEs will be identified according to a sponsor-defined list of terms. Final clinical irAE review details will be outlined in the CSR.

9.2.3. Adverse Event Summaries

Overall summaries of AEs and irAEs by cohort, dose, and total will include the following:

- Participants who had a TEAE/irAE
- Participants who had a serious TEAE/irAE
- Participants who had a Grade 3 or higher TEAE/irAE
- Participants who had a treatment-related TEAE

- Participants who had a serious treatment-related TEAE
- Participants who had a Grade 3 or higher treatment-related TEAE
- Participants who had a fatal TEAE/irAE
- Participants who had a TEAE/irAE leading to dose reduction
- Participants who had a TEAE/irAE leading to dose interruption
- Participants who had a TEAE/irAE leading to discontinuation of INCB086550
- Participants who had a TEAE/irAE leading to dose reduction, interruption, or discontinuation of INCB086550

The following summaries will be produced by MedDRA SOC and/or PT or irAE category:

- Summary of TEAEs by SOC and PT
- Summary of TEAEs by PT in decreasing order of frequency
- Summary of serious TEAEs by SOC and PT
- Summary of serious treatment-related TEAEs by PT in decreasing order of frequency
- Summary of TEAEs with a fatal outcome by SOC and PT
- Summary of TEAEs leading to dose modification of INCB086550 by SOC and PT
- Summary of TEAEs leading to discontinuation of INCB086550 by SOC and PT
- Summary of sponsor-defined irAEs by category and PT

9.3. Clinical Laboratory Tests

9.3.1. Laboratory Value Definitions

Laboratory values and change from baseline values will be summarized descriptively by visit. Baseline will be determined according to Section 4.1.3. If there are multiple values that meet the criteria for baseline, additional rules may be provided after consultation with the medical monitor to delineate which value will be defined as baseline. Laboratory test values will be assessed for severity using Grades 1 through 4 using CTCAE v5 when applicable.

9.3.2. Laboratory Value Summaries

A certified laboratory local to the investigative site will perform all clinical laboratory assessments for safety (ie, blood chemistries, hematology assessments, coagulation tests, endocrine function, and urinalysis).

Any laboratory test results and associated normal ranges from local laboratories will be converted to SI units.

Shift tables will be presented showing change in CTCAE grade from baseline to worst grade postbaseline for hematology and chemistry laboratory assessments. Separate summaries for abnormally high and abnormally low laboratory values will be provided when the laboratory

parameter has both high and low grading criteria. The denominator for the percentage calculation will be the number of participants in the baseline category.

9.3.3. Potential Drug-Induced Liver Injuries

Participants with elevated alanine aminotransferase or aspartate aminotransferase ≥ 3 × ULN and alkaline phosphatase < 2 × ULN accompanied by total bilirubin ≥ 2 × ULN within ± 7 days will be listed by cohort and dose.

10. INTERIM ANALYSES

An interim analysis was planned per Protocol Section 10.5, but due to early study termination, the interim analysis was not conducted.

11. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 6.

Table 6: Statistical Analysis Plan Versions

SAP Version	Date
Original	09 FEB 2022
Amendment 1	01 DEC 2023

11.1. Changes to Protocol-Defined Analyses

The analysis of potential Hy's law events has been changed from the Protocol version to a newly created company standard of assessing potential drug-induced liver injuries.

[redacted]

The ECG variable QTcF was updated to QTc to correct a typo in the statistics section of the Protocol. RR was also removed since it was not mentioned in Protocol Section 8.3.5.

The number of responses needed at the final analysis was increased by 1 for the HCC and RCC cohorts in order to make the number higher than the number required for the interim.

[redacted]

11.2. Changes to the Statistical Analysis Plan

11.2.1. Original to Amendment 1

Modifications were made to the original SAP to streamline analyses for a synoptic CSR, as this study was terminated early with minimal enrollment.

12. REFERENCES

Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumors: revised RECIST guideline (version 1.1). Eur J Cancer 2009;45:228-247.

El-Khoueiry AB, Sangro B, Yau T, et al. Nivolumab in patients with advanced hepatocellular carcinoma (CheckMate 040): an open-label, non-comparative, phase 1/2 dose escalation and expansion trial. Lancet 2017;389:2492-2502.

Hwang IK, Shih WJ, De Cani JS. Group sequential designs using a family of Type I error probability spending functions. Stat Med 1990;9:1439-1445.

Keytruda (pembrolizumab) [prescribing information]. Merck & Co, Inc; June 2018.

Mok TSK, Wu YL, Kudaba I, et al. Pembrolizumab versus chemotherapy for previously untreated, PD-L1-expressing, locally advanced or metastatic non-small-cell lung cancer (KEYNOTE-042): a randomised, open-label, controlled, phase 3 trial. Lancet 2019;393:1819-1830.

Motzer R, Escudier B, McDermott D, et al. Nivolumab versus everolimus in advanced renal-cell carcinoma. N Engl J Med 2015;373:1803-1813.

Reck M, Rodríguez-Abreu D, Robinson AG, et al. Pembrolizumab versus chemotherapy for PD-L1-positive non-small-cell lung cancer. N Engl J Med 2016;375:1823-1833.

Robert C, Schachter J, Long GV, et al. Pembrolizumab versus ipilimumab in advanced melanoma. N Engl J Med 2015;372:2521-2532.

APPENDIX A. PLANNED TABLES AND LISTINGS

This appendix provides a list of the planned tables and listings for the CSR. Standard tables will follow the conventions in the standard safety tables. Shells are provided for nonstandard tables in a separate document. In-text tables are identical in structure and content as appendix tables but follow a rich text format.

The list of tables and listings and the shells are to be used as guidelines. Modifications of the list or shells that do not otherwise affect the nature of the analysis will not warrant an amendment to the SAP.

Tables

Table No.	Title	Population	Standard
Baseline and Demographic Characteristics			
1.1.1	Analysis Populations	FAS	X
1.1.2	Summary of Participant Disposition	FAS	X
1.1.3	Summary of Number of Participants Enrolled by Country and Site	FAS	X
1.1.4	Summary of Important Protocol Deviations	FAS	X
1.2.1	Summary of Demographics and Baseline Characteristics	FAS	X
1.3.1	Summary of Baseline Disease Characteristics	FAS	X
Efficacy			
2.3.1	Summary of Best Overall Response per RECIST v1.1	FAS	
Safety			
3.1.1	Summary of Exposure and Duration of Exposure to INCB086550	Safety	X
3.1.2	Summary of Study Drug Compliance	Safety	X
3.2.1	Overall Summary of Treatment-Emergent Adverse Events	Safety	X
3.2.1.1	Overall Summary of Sponsor-Defined Immune-Related Adverse Events	Safety	X
3.2.2	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.3	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X
3.2.4	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.5	Summary of Serious Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X
3.2.6	Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.7	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of INCB086550 by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.8	Summary of Sponsor-Defined Immune-Related Adverse Events by Category and MedDRA Preferred Term	Safety	X
3.2.9	Summary of Treatment-Emergent Adverse Events Leading to Dose Modification of INCB086550 by MedDRA System Organ Class and Preferred Term	Safety	
3.3.3.1	Shift Summary of Hematology Laboratory Values in CTCAE Grade – to the Worst Abnormal Value	Safety	X
3.3.3.2	Shift Summary of Chemistry Laboratory Values in CTCAE Grade – to the Worst Abnormal Value	Safety	X

Listings

Listing No.	Title
2.1.1	Participant Enrollment and Disposition Status
2.1.1.1	Deaths
2.1.2	Participant Inclusion and Exclusion Criteria Violations
2.2.1	Important Protocol Deviations
2.3.1	Analysis Populations
2.4.1	Demographic and Baseline Characteristics
2.4.2	Disease History
2.4.3	Prior Anticancer Radiation Treatment
2.4.4	Prior Systemic Anticancer Therapy
2.4.5	Prior Anticancer Surgery or Surgical Procedure
2.4.6	Medical History
2.4.7	Prior and Concomitant Medication
2.4.8	ECOG Performance Status
2.5.1	Study Drug Compliance
2.5.2	Study Drug Administration
2.6.1	Investigator-Reported Response Assessment per RECIST v1.1
2.6.2	Duration of Response per RECIST v1.1
2.6.3	Response Assessment: Target Lesions
2.6.4	Response Assessment: Nontarget Lesions
2.6.5	Response Assessment: New Lesions
2.6.6	Bone Scan Results
2.7.1	Adverse Events
2.7.2	Serious Adverse Events
2.7.3	Fatal Adverse Events
2.7.4	Adverse Events Leading to Interruption, Reduction, or Discontinuation of INCB086550
2.7.5	Sponsor-Defined Immune-Related Adverse Events
2.8.1.1	Clinical Laboratory Values – Hematology
2.8.1.2	Clinical Laboratory Values – Chemistry
2.8.1.3	Clinical Laboratory Values – Endocrine Function
2.8.1.4	Potential Drug-Induced Liver Injuries