STATISTICAL ANALYSIS PLAN

INCB 24360-203

A Phase 1/2 Study Exploring the Safety, Tolerability, and Efficacy of INCB024360 in Combination With MEDI4736 in Subjects With Selected Advanced Solid Tumors

IND Number: [redacted]

Date of Plan: 26 NOV 2014

Based on: Protocol Amendment 1 dated 29 SEP 2014

CRF version approved 08 SEP 2014

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This study is being conducted in compliance with good clinical practice, including the archiving of essential documents.

STATISTICAL ANALYSIS PLAN APPROVAL

SAP:	INCB 24360-203 SAP
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☒ Approval of Initial SAP	☐ Approval of Amendment of SAP

NOTE:

1. An amendment made before the release of unblinded data (eg, treatment assignment received by each subject) for a blinded study or database release for an open-label study must be included in an updated SAP.
2. An amendment made to the statistical analyses defined in the SAP that occurs after unblinding or database release must be documented in the final Clinical Study Report.
3. The approvers must ensure that all relevant functions are in agreement with the final SAP.

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LIST OF ABBREVIATIONS

Abbreviation	Term
AE	adverse event
ADA	antidrug antibody
ALT	alanine aminotransferase
aPTT	activated partial thromboplastin time
AST	aspartate aminotransferase
AUC	area under the concentration-time curve
AUC_{0-12h}	AUC from hour 0 to 12
$AUC_{0-\tau}$	AUC from time zero (predose) to time of last observed quantifiable concentration within a subject across all treatments
BID	twice daily
CI	confidence intervals
CL/F	apparent oral dose clearance
C_{max}	maximum observed concentration
CR	complete response
CRF	case report form
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
DLCO	diffusing capacity of the lung for carbon monoxide
DLT	dose-limiting toxicity
DoR	duration of response
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
EOT	end of treatment
FDA	Food and Drug Administration
FEF	forced expiratory flow
FEV_1	forced expiratory volume in 1 second
FVC	forced vital capacity
GGT	gamma-glutamyl transferase
HBV-DNA	hepatitis B virus deoxyribonucleic acid
HCV-RNA	hepatitis C virus ribonucleic acid
IDO	indoleamine 2,3–dioxygenase
IgG1κ	human immunoglobulin G1 kappa
INR	international normalized ratio
ITT	intent to treat
IV	intravenously
LFT	liver function tests
LLN	lower limit of normal
MedDRA	Medical Dictionary for Regulatory Activities

Abbreviation	Term
mRECIST v1.1	modified Response Evaluation Criteria in Solid Tumors version 1.1
MTD	maximum tolerated dose
NE	not evaluable
NSCLC	non–small cell lung cancer
ORR	objective response rate
PAD	pharmacologically active dose
PD	[redacted] progressive disease
PD-L1	programmed cell-death ligand 1
PFS	progression-free survival
PK	pharmacokinetics
PR	partial response
PT	prothrombin time
RECIST	Response Evaluation Criteria in Solid Tumors
RR	ribonucleotide reductase
SCCHN	squamous cell carcinoma of the head and neck
SD	stable disease
SAE	serious adverse event
SAP	statistical analysis plan
SI	International System of Units
$t_{½}$	terminal phase half-life
T_{max}	time of occurrence of C_{max}
TEAE	treatment-emergent adverse event
ULN	upper limit of normal
VA	alveolar volume
WHO	World Health Organization

1. INTRODUCTION

INCB 24360-203 is a Phase 1/2 study of INCB024360 administered in combination with MEDI4736 in subjects with advanced melanoma, non–small cell lung cancer (NSCLC), pancreatic cancer, or squamous cell carcinoma of the head and neck (SCCHN). Phase 1 will be an open-label dose escalation to identify the maximum tolerated dose (MTD) or pharmacologically active dose (PAD) of INCB024360 in combination with MEDI4736. Phase 2 will further explore the safety and efficacy of the MTD or PAD of INCB024360 in combination with MEDI4736 determined in Phase 1. INCB024360 represents a novel, potent, and selective inhibitor of the enzyme indoleamine 2,3–dioxygenase 1 (IDO1) in both human tumor cells and human dendritic cells.

MEDI4736 is a human immunoglobulin G1 kappa (IgG1κ) monoclonal antibody directed against human programmed cell-death ligand 1 (PD-L1). The antibody is composed of 2 identical heavy chains of approximately 49,670 Da each and 2 identical light chains of approximately 23,390 Da each. The fragment crystallizable domain of MEDI4736 contains a triple mutation in the constant domain of the IgG1 heavy chain that reduces binding to the complement component C1q and the fragment crystallizable gamma receptors responsible for mediating antibody-dependent cell-mediated cytotoxicity.

A detailed description of the investigational product, target patient population, rationale for doses to be examined, and potential risks and benefits of treatment with INCB024360 and MEDI4736 is provided in the Protocol, Section 1. The purpose of this Statistical Analysis Plan (SAP) is to define the methodology for analyzing and summarizing the data collected during the conduct of Study INCB 24360-203.

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 24360-203 Protocol Amendment 1 dated 29 SEP 2014 and case report form (CRF) approved on 08 SEP 2014. Unless superseded by an amendment, this SAP will be effective for all subsequent Protocol amendments and CRF versions.

2.2. Study Objectives

2.2.1. Primary Objectives

The primary objectives of the study are:

- Phase 1: To evaluate the safety and tolerability, and define the MTD or a PAD of INCB024360 administered in combination with MEDI4736 in subjects with select advanced solid tumors.
- Phase 2: To evaluate the efficacy of INCB024360 administered in combination with MEDI4736 in subjects with select advanced solid tumors by assessing the objective response rate (ORR) per modified RECIST version 1.1 (mRECIST v1.1) at the MTD or PAD.

2.2.2. Secondary Objectives

The secondary objectives of the study are:

- Phase 1: To evaluate the efficacy of INCB024360 administered in combination with MEDI4736 in subjects with select advanced solid tumors by assessing the ORR per mRECIST v1.1.
- Phase 2: To evaluate the safety and tolerability of the MTD or PAD of INCB024360 administered in combination with MEDI4736 in subjects with select advanced solid tumors.
- Phases 1 and 2: To evaluate the efficacy of INCB024360 administered in combination with MEDI4736 in subjects with select advanced solid tumors by assessing duration of response (DoR) and progression-free survival (PFS).
- Phases 1 and 2: To evaluate the pharmacokinetics (PK) of INCB024360 and MEDI4736 when administered in combination.
- Phases 1 and 2: To determine the immunogenicity of MEDI4736 when administered with INCB024360.

[redacted]

2.3. Study Endpoints

2.3.1. Primary Endpoints

- Phase 1: MTD or PAD. The MTD is defined by the highest dose cohort where no more than 1 of 6 subjects experience a dose-limiting toxicity (DLT), or the highest Protocol-defined dose for each agent in the absence of exceeding the MTD. Alternatively, the PAD is defined as a tolerated dose of INCB024360 (in combination with MEDI4736) that produces substantial pharmacological target inhibition. Safety and tolerability will be assessed by monitoring the frequency, duration, and severity of adverse events (AEs), through physical examinations, by evaluating changes in vital signs and electrocardiograms (ECGs), and through clinical laboratory blood and urine sample evaluations.
- Phase 2: ORR determined by radiographic disease assessments per mRECIST v1.1.

2.3.2. Secondary Endpoints

- Phase 1: ORR determined by radiographic disease assessments per mRECIST v1.1.
- Phase 2: Safety and tolerability of the combination as assessed by monitoring the frequency, duration, and severity of AEs, through physical examinations, by evaluating changes in vital signs and ECGs, and through clinical laboratory blood and urine sample evaluations.
- Phases 1 and 2: Durability of response determined by radiographic disease assessment defined as the time from earliest date of disease response until earliest date of disease progression.
- Phases 1 and 2: PFS determined from the date of randomization until disease progression or death.
- Phases 1 and 2: The endpoints for assessment of PK of MEDI4736 and INCB024360 include individual MEDI4736 and INCB024360 concentrations and PK parameters.
- Phases 1 and 2: The endpoints for assessment of immunogenicity of MEDI4736 include the number and percentage of subjects who develop detectable antidrug antibodies (ADAs).

3. STUDY DESIGN

This is a Phase 1/2 open-label study of INCB024360 administered in combination with MEDI4736 in subjects with advanced melanoma, NSCLC, pancreatic cancer or SCCHN. The dose-escalation part of the study (Phase 1) uses a 3 + 3 design to identify the MTD or PAD of INCB024360 in combination with MEDI4736. Phase 2 will further explore the safety and efficacy of the MTD or PAD of INCB024360 in combination with MEDI4736 determined in Phase 1.

3.1. Phase 1 Dose-Escalation Design

Phase 1 is the dose-escalation phase, which will include up to 7 cohorts of subjects treated with INCB024360 at doses of 25 mg twice daily (BID), 50 mg BID, 75 mg BID, 100 mg BID, 200 mg BID, and 300 mg BID in combination with MEDI4736 3mg/kg or 10 mg/kg given on Day 1 of each 14-day cycle.

A minimum of 3 subjects will be enrolled and treated in each cohort, and all 3 subjects will be observed for a minimum of 42 days before the subsequent cohort begins enrollment. In Phase 1, only 2 subjects may be enrolled within a week. A 1-week interval will be required between subjects in successive weeks.

Subjects must have received the cohort-specific dose of INCB024360 for at least 75% of the doses (63 doses) and have received at least 3 doses of MEDI4736 during the 42-day DLT observation period, or have reported a DLT to be evaluable for dose tolerability. Additional subjects will be enrolled in a cohort to achieve the minimum of 3 evaluable subjects if dropouts or dose interruptions/reductions occur that result in a subject being nonevaluable for DLTs. Alternative intermediate doses (eg, 75 mg once daily) or schedules (eg, 1 week on, 1 week off)

of INCB024360 may be evaluated based on emerging safety, PK, and PD observations. If an alternate schedule is tested and determined to be safe, re-escalation of INCB024360 according to Table 1 will proceed.

The dose of INCB024360 will be escalated if 0 of the first 3 evaluable subjects enrolled report a DLT. If 1 of the first 3 evaluable subjects enrolled report a DLT, the cohort will be expanded to include 3 additional evaluable subjects. If 2 or more of either 3 or 6 subjects enrolled report a DLT, the prior dose level will be considered the MTD. If only 3 subjects were treated at this dose level, the dose will be confirmed as the MTD by evaluation of an additional 3 subjects before this dose is recommended for Phase 2 testing.

Alternative schedules of INCB024360 (ie, 25 mg BID 1 week on/1 week off) may be evaluated if 25 mg BID continuous treatment cannot be safely combined with MEDI4736 3 mg/kg. The cohorts and dose levels are shown in Table 1. If cohort de-escalation is required and Cohort -1 is tested and determined to be safe, re-escalation of INCB024360 according to Table 1 will proceed with the alternative treatment schedule of INCB024360. Intrasubject dose escalation is not permitted.

Table 1: Treatment Cohorts

Cohort	Maximum Daily Dose of INCB024360	Dose of MEDI4736 (Once Every 14 Days)
-1	Alternative treatment schedule of 25 mg BID orally[a]	3 mg/kg IV
1	**25 mg BID orally**	**3 mg/kg IV**
2	25 mg BID orally	10 mg/kg IV
3	50 mg BID orally	10 mg/kg IV
4	75 mg BID orally	10 mg/kg IV
5	100 mg BID orally	10 mg/kg IV
6	200 mg BID orally	10 mg/kg IV
7	300 mg BID orally	10 mg/kg IV

IV = intravenously.
[a] An alternative treatment schedule (ie, 25 mg BID 1 week on/1 week off) may be evaluated if 25 mg BID continuous treatment cannot be safely combined with MEDI4736.

3.1.1. Phase 2

Approximately 68 to 157 subjects with advanced melanoma, NSCLC, pancreatic cancer, or SCCHN will be enrolled at the MTD or PAD of INCB024360 in combination with MEDI4736. The approximate number of subjects needed for each tumor type will be determined using the Simon 2-stage design: Stage 1 will be the initial number of subjects per tumor type, and the decision to proceed with Stage 2 will be determined by the response rate observed in Stage 1 (further described in Section 3.3.2). To allow the combination therapy to be explored in subjects with PD-L1–positive tumors, at least 5 subjects with PD-L1–positive tumor samples may be required in each stage of the tumor-specific expansion cohorts. If this is not met, additional subjects may be enrolled into these cohorts until 5 PD-L1–positive subjects are enrolled.

The number of subjects to be enrolled in each stage per tumor type is detailed in Table 2.

Table 2: Approximate Number of Subjects by Tumor Type and Stage of Study

Tumor Type	Number of Subjects Enrolled		
	Stage 1	Stage 2 (If Study Proceeds to Stage 2)	Total (Stage 1 + 2)
Melanoma	15	25	40
NSCLC	16	22	38
Pancreatic cancer	21	20	41
SCCHN	16	22	38

3.2. Control of Type I Error

Not applicable. No formal efficacy hypotheses will be tested. All confidence intervals (CIs) will be 95%.

3.3. Sample Size Considerations

3.3.1. Sample Size in Phase 1

The primary objective of the open-label Phase 1 portion of the study is to determine the MTD or PAD and DLT of INCB024360 in combination with MEDI4736. The total number of subjects will depend on the number of dose levels tested before the MTD or PAD is established. Up to 42 subjects (6 subjects per dose level for 7 dose levels) will be included based on the dose escalation. Dose escalation will follow the 3 + 3 design algorithm as defined in Section 3.1. Based on this algorithm, which enrolls 3 evaluable subjects in each cohort with a maximum of 6 subjects at any dose level, the probabilities of dose de-escalation from a given dose level for the various DLT rates are provided in Table 3.

Table 3: Probability of Dose De-Escalation for Various Dose-Limiting Toxicity Rates

True DLT Rate	Probability of Dose De-Escalation
20%	23.6%
30%	47.2%
40%	68.3%
50%	83.4%
60%	92.4%

For example, if the true DLT rate is 50% at a given dose level, there is a 17% chance that the dose would be escalated. Further, if the true DLT rate is 20%, there is a 76% chance that the dose would be escalated.

3.3.2. Sample Size in Phase 2

The sample size for each group will be guided by the optimal Simon 2-stage design (Simon 1989). Let P_0 denote a clinically uninteresting response rate (eg, for melanoma P_0 = 30%). In order to determine whether a target response rate (eg, 55%) is likely, an initial number of subjects (eg, 15 subjects) will be treated at first in a cohort (Stage 1). In a group in which ≤ 5 subjects have responses (suggest the first scheduled Week 8 visit be the tumor assessment), it

will be concluded that the true response rate is unlikely to be greater than or equal to the target rate and no more subjects will be enrolled in that group in Stage 2. Otherwise, in the groups in which at least 6 responses among the Stage 1 subjects are observed, 25 additional subjects will be treated in Stage 2 to estimate the response rate. At the end of Stage 2, if ≤ 16 subjects have responded (suggest the first scheduled Week 8 visit be the tumor assessment) among a total of 40 subjects, the drug will be declared nonpromising. The response does not need to be confirmed. In other words, after the study is finished, if there is a sufficient number of responses in the 2 stages combined, the study compound is considered promising; otherwise it is considered nonpromising. The detail is displayed in Table 4 using a Type I error of 0.05 and power of 90% for estimation.

Table 4: Details of Simon 2-Stage Optimal Design by Tumor Type

	Pancreatic (P_0 = 5%, Target RR = 20%)	**Melanoma (P_0 = 30%, Target RR = 55%)**	**NSCLC (P_0 = 17%, Target RR = 40%)**	**SCCHN (P_0 = 17%, Target RR = 40%)**
Drug is not promising if Stage 1 responder number ≤	1	5	3	3
Sample size for Stage 1	21	15	16	16
Drug is not promising if total responder number ≤	4	16	10	10
Sample size total	41	40	38	38

RR = ribonucleotide reductase.

3.4. Schedule of Assessments

All study assessments will be performed as indicated in the schedule of assessments (Table 5) and laboratory assessments (Table 6). The required analytes for the each laboratory test as well as the assessments to be performed as part of the pulmonary function tests are shown in Appendix A. The order of assessments is suggested by the order of mention within the schedule of assessments.

Table 5: Schedule of Assessments

Visit (Range)	Screening	Treatment Cycles						EOT	Follow-Up			
		C1D1	C1D8	C2D1	C2D8	Day 1 All Subsequent Cycles	Every 8 Weeks	Discon	Safety Follow-Up Visit 1	Safety Follow-Up Visit 2	Follow-Up	Survival Follow-Up
	Day -28 to -1	± 3 Days	± 3 Days	± 3 Days	± 3 Days	± 3 Days	± 5 Days	Time of Discon ± 5 Days	42 Days After EOT or Last Dose ± 7 Days	90 Days After EOT or Last Dose ±7 Days	Every 8 Weeks After Discon	Every 3 Months After Discon
Administrative procedures												
Informed consent	X											
Inclusion/exclusion criteria	X	X										
Medical and cancer history	X											
Smoking history	X											
Prior/concomitant medications review	X	X		X		X						
Administer INCB024360 at clinic		X	X	X								
Administer MEDI4736		X		X		X						
Poststudy anticancer therapy status									X	X	X	
Survival status											X	X
Clinical procedures and assessments												
Comprehensive physical examination	X							X	X	X		
Targeted physical examination		X		X		X						
ECOG performance status	X	X		X		X		X				
Assess for serotonin syndrome		X[a]		X		X		X				
Vital signs and weight (height at screening only)	X	X		X		X		X				

Table 5: Schedule of Assessments (Continued)

Visit (Range)	Screening	Treatment Cycles						EOT	Follow-Up			
		C1D1	C1D8	C2D1	C2D8	Day 1 All Subsequent Cycles	Every 8 Weeks	Discon	Safety Follow-Up Visit 1	Safety Follow-Up Visit 2	Follow-Up	Survival Follow-Up
	Day -28 to -1	± 3 Days	± 3 Days	± 3 Days	± 3 Days	± 3 Days	± 5 Days	Time of Discon ± 5 Days	42 Days After EOT or Last Dose ± 7 Days	90 Days After EOT or Last Dose ±7 Days	Every 8 Weeks After Discon	Every 3 Months After Discon
Postinfusion observation[b]		X										
12-lead ECG	X	X[c]		X[c]				X	X	X		
Adverse event assessment[d]	X	X		X		X		X	X	X		
Laboratory assessments	X	X	X[e]	X	X[f]	X	X	X	X	X		
Pulmonary function testing	X											
Chest radiograph	X											
Tumor tissue collection[g]	X	X[h]										
Tumor imaging	X						X[i]	X[j, k]			X[j]	

C1D1 = Cycle 1 Day 1; C1D8 = Cycle 1 Day 8; C2D1 = Cycle 2 Day 1; C2D8 = Cycle 2 Day 8; Discon = discontinuation; EOT = end of treatment; LFT = liver function test; PD = progressive disease.

[a] Assessment should occur approximately 6 hours postdose on Day 1. An information sheet will also be provided to subjects describing the signs and symptoms of serotonin syndrome instructing them to seek immediate care if any of these symptoms are observed.

[b] Subjects will be observed in clinic for 3 hours after the first infusion of MEDI4736 is administered.

[c] ECG should be performed prior to INCBC024360 and MEDI4736 administration at Cycle 2 Day 1 and 60 to 90 minutes after administration of INCB024360 at Cycle 1 Day 1 and Cycle 2 Day 1.

[d] Subjects need to be followed for AEs for 90 days after the last dose of study treatment.

[e] Liver function tests, PK, and [redacted] are performed on Cycle 1 Day 8 as described in Table 6.

[f] Liver function tests are performed weekly for the first 8 weeks on study treatment. If LFTs are abnormal, then LFT monitoring should increase to twice per week until resolved to baseline.

[g] If the subjects agrees to such in the informed consent form, any leftover tissue will be stored for future biomedical research.

[h] Optional and can be obtained anytime for safety or with confirmed response or progression.

[i] Imaging will be performed every 8 weeks for the first 12 months and then may be done every 12 weeks thereafter. Per the mRECIST v1.1 criteria used in this Protocol, if imaging shows PD, the imaging assessment should be performed at a minimum of 4 weeks later in order to confirm PD as described in the Protocol.

[j] Subjects who discontinue treatment for reasons other than disease progression, every effort should be made to continue monitoring their disease status by imaging every 8 weeks for 1 year and then every 12 weeks thereafter until the start of new anticancer therapy, documented disease progression, death, or the end of the study, whichever occurs first.

[k] If a scan was obtained within 4 weeks prior to the date of discontinuation, then a scan at treatment discontinuation isn't mandatory. In subjects who discontinue study therapy without confirmed disease progression, a radiologic evaluation should be repeated at the time of treatment discontinuation (ie, date of discontinuation ± 4 week window).

Table 6: Laboratory Assessments

Visit (Range)	Screening Day -28 to -1	Treatment Cycles[a] C1D1 ± 3 Days	 C1D8 ± 3 Days	 C2D1 ± 3 Days	 C2D8 ± 3 Days	Day 1 All Subsequent Cycles ± 3 Days	Every 8 Weeks[b] ± 5 Days	EOT Discon Time of Discon ± 5 Days	Safety Follow-Up Visit 1 42 Days After EOT or Last Dose ± 7 Days	Safety Follow-Up Visit 2 90 Days After EOT or Last Dose ± 7 Days
Safety and eligibility[c]										
Chemistry panel	X	X[d]		X		X		X	X	X
Liver function tests[e]	X	X	X	X	X	X[e]		X	X	X
Hematology with differential	X	X[d]		X		X		X	X	X
Coagulation panel (PT, INR, aPTT)[f]	X									
Endocrine function testing	X	X[d]					X	X		
Urinalysis	X						X	X		
Serum pregnancy or urine[g]	X									
Hepatitis B and C	X									
Pharmacokinetics										
Blood sample for INCB24360 PK		X[h]	X[h]	X[h]						
Blood sample for MEDI4736 PK		X[i]	X	X		X[i]		X		X
Immunogenicity										
Immunogenicity assessment		X				X[j]		X		X
[redacted]										

aPTT = activated partial thromboplastin time; C1D1 = Cycle 1 Day 1; C1D8 = Cycle 1 Day 8; C2D1 = Cycle 2 Day 1; C2D8 = Cycle 2 Day 8; Discon = discontinuation; EOT = end of treatment; INR = international normalized ratio; PT = prothrombin time.

[a] All assessments may not be required for subjects continuing on monotherapy treatment.
[b] Sample will be drawn at Cycle 5 and every 4 cycles thereafter.
[c] All safety laboratory tests will be performed locally.
[redacted]
[e] Liver function tests should be performed at screening, weekly for the first 8 weeks of study treatment, and then at Day 1 of each subsequent cycle. If LFTs are abnormal, then LFT monitoring should increase to twice per week until resolved to baseline.
[f] Subjects on anticoagulation treatment should have parameters monitored throughout the study as clinically indicated.
[g] For women of childbearing potential, a serum pregnancy test is required at screening. Pregnancy tests (serum or urine) should be repeated if required by local regulations.
[h] See Section 7.5 for detailed timing and information for PK sample collection.
[i] Pharmacokinetic samples should be collected predose and end of infusion on Cycle 1 Day 1 and Cycle 13 Day 1. For all other timepoints drawn at dosing visits, PK samples should be collected predose. For subjects in Phase 1 of the study, PK sampling should occur at Cycle 5 and every 8 weeks thereafter. For subjects in Phase 2 of the study, PK sampling should occur only at Cycles 7, 13, and 25.
[redacted]
[k] Whole blood sample for INCB024360 PD will be collected in concert with the INCB024360 PK sample on the designated visits only at selected sites for subjects in Phase 1 of the study only.
[redacted]

4. DATA HANDLING DEFINITIONS AND CONVENTIONS

4.1. Scheduled Study Evaluations and Study Periods

4.1.1. Day 1

Day 1 is the date of first dose of INCB024360 or MEDI4736.

4.1.2. Study Day

The study day at a visit or reporting date will be calculated by the visit or reporting date minus the Day 1 date plus 1 (visit date - Day 1 date + 1). This study day will be subtracted by 1 if it is ≤ 0, so that a study day of 0 will never occur. A study day of -1 indicates 1 day before Day 1.

4.1.3. Scheduled Visits

Study evaluations in weeks or days from Day 1 are presented in the Schedule of Assessments (Table 5).

4.1.4. Baseline Assessments

Baseline is defined as the last nonmissing measurement obtained before the first dose of INCB024360 or MEDI4736 is administered.

4.1.5. Last Available Value

The last available value is the last nonmissing measurement obtained after starting INCB024360 or MEDI4736 and within 90 days after the last dose of INCB024360 or MEDI4736.

4.1.6. Cycle Length and Duration

Cycle 1 Day 1 is defined as the day of the first dose of INCB024360 or MEDI4736. One treatment cycle consists of 14 days. The first cycle of therapy is defined as the period beginning with the first dose of INCB024360 or MEDI4736 and ending the earlier of: (1) 14 calendar days (inclusive) later; or (2) permanent discontinuation of INCB024360. Subsequent cycles have Day 1 as the corresponding visit date associated with the corresponding cycle.

4.2. Variable Definitions

4.2.1. Age

Subject age will be calculated as the integer part of the number of years from date of birth to the date of signing the informed consent form, using the following formula:

Age = integer part of (date of informed consent - date of birth + 1)/365.25

If date of birth is missing, then the age entered in the Demography section of the CRF will be used instead.

4.2.2. Prior and Concomitant Medication

Prior medication is defined as any nonstudy drug started before the first dose of INCB024360 or MEDI4736.

Concomitant medication is defined as any nonstudy drug that is taken as follows:

- Started before the date of first administration of INCB024360 or MEDI4736 and is ongoing throughout the study or ends on/after the date of first study drug administration
- Started on/after the date of first administration of INCB024360 or MEDI4736 and is ongoing or ends during the course of study drug administration

Note: A prior medication could also be classified as "both prior and concomitant medication" if the end date is on or after first dose of INCB024360 or MEDI4736. In the listing, it will be indicated whether a medication is prior only, concomitant only, or both prior and concomitant medication.

The start/stop dates recorded in the CRF by the investigator and his or her research staff will be used to identify when a concomitant medication was taken during the study. Any missing start date must be queried for resolution. Unresolved missing start dates will be handled as follows:

- If the date is completely missing, the medication will be considered both prior and concomitant.
- If only the day is missing, and the last day of the month is before the first dose date on Day 1, then the concomitant medication will be considered as starting before Day 1, and the incomplete date will be imputed as the last day of the month.
- If only the day is missing, and the first day of the month is after the first dose date on Day 1, then the concomitant medication will be considered as starting after Day 1, and the incomplete date will be imputed as the first day of the month.
- If only the day is missing, and the month is equal to the month of the first dose date on Day 1, then the incomplete date will be imputed as the first day of the month.
- If both the month and day are missing, and the last day of the year is before the first dose date on Day 1, then the concomitant medication will be considered as starting before Day 1, and the incomplete date will be imputed as if it is the last day of the year. Otherwise, the incomplete date will be imputed as if it is the first day of the year.

5. STATISTICAL METHODOLOGY

5.1. General Methodology

Unless otherwise noted, SAS® software (SAS Institute Inc, Cary, NC; version 9.1 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 subjects in each category.

For the dose-escalation portion of the study, the Phase 1 safety population (defined in Section 5.3.2) will be used for all safety analyses, and the Phase 1 intent-to-treat (ITT) population will be used for all efficacy analyses. For the expansion portion of the study, the Phase 2 safety population will be used for all safety analyses, and the Phase 2 ITT population will be used for all efficacy analyses. Analyses of PK endpoints are described in Section 7.5 and will be performed by the Incyte and MedImmune pharmacokineticist, respectively.

Interim safety analyses are planned for this study as defined in Section 9.

5.2. Treatment Groups

Subjects will be summarized overall and based on the dose regimen initially assigned:

- 3 mg/kg IV MEDI4736 once every 14 days + 25 mg BID INCB024360 (Phase 1)
- 10 mg/kg IV MEDI4736 once every 14 days + 25 mg BID INCB024360 (Phase 1)
- 10 mg/kg IV MEDI4736 once every 14 days + 50 mg BID INCB024360 (Phase 1)
- 10mg/kg IV MEDI4736 once every 14 days + 75 mg BID INCB024360 (Phase 1)
- 10 mg/kg IV MEDI4736 once every 14 days + 100 mg BID INCB024360 (Phase 1)
- 10 mg/kg IV MEDI4736 once every 14 days + 200 mg BID INCB024360 (Phase 1)
- 10 mg/kg IV MEDI4736 once every 14 days + 300 mg BID INCB024360 (Phase 1)
- 3 mg/kg or 10 mg/kg IV MEDI4736 once Every 14 Days + selected MTD/PAD of INCB024360 (Phase 2: Melanoma)
- 3 mg/kg or 10 mg/kg IV MEDI4736 once every 14 days + selected MTD/PAD of INCB024360 (Phase 2: NSCLC)
- 3 mg/kg or 10 mg/kg IV MEDI4736 once every 14 days + selected MTD/PAD of INCB024360 (Phase 2: Pancreatic Cancer)
- 3 mg/kg or 10 mg/kg IV MEDI4736 once every 14 days + selected MTD/PAD of INCB024360 (Phase 2: SCCHN)

Table summaries, unless otherwise indicated, will be provided by treatment group. Note that separate summaries will be provided for the Phase 1 and Phase 2 portions of the study.

5.3. Analysis Populations

5.3.1. Phase 1 Intent-to-Treat Population

The Phase 1 ITT population will include all subjects who are enrolled in the Phase 1 portion of the study. Treatment groups for this population will be defined according to the treatment assignment at the time of enrollment on Day 1 regardless of the actual study drug the subject might receive during his/her continued participation in the study. This population will be used for analyses of all efficacy data for Phase 1.

5.3.2. Phase 1 Safety Population

The Phase 1 safety population includes all subjects enrolled in the Phase 1 portion of the study who received at least 1 dose of INCB024360 or MEDI4736. Treatment groups for this population will be determined according to the actual treatment the subject received on Day 1 regardless of the actual study drug the subject might receive during his/her continued participation in the study. All Phase 1 safety analyses will be conducted using the Phase 1 safety population.

5.3.3. Phase 2 ITT Population

The Phase 2 ITT population will include all subjects who are enrolled in the Phase 2 portion of the study. Treatment groups for this population will be defined according to the tumor type at the time of enrollment on Day 1. This population will be used for analyses of all efficacy data for Phase 2.

5.3.4. Phase 2 Safety Population

The Phase 2 safety population includes all subjects enrolled in the Phase 2 portion of the study who received at least 1 dose of INCB024360 or MEDI4736. Treatment groups for this population will be determined according to the tumor type at the time of enrollment on Day 1. All Phase 2 safety analyses will be conducted using the Phase 2 safety population.

5.3.5. Pharmacokinetic [redacted] Evaluable Population

The PK[redacted] evaluable population will include all subjects who received at least 1 dose of INCB024360 and provided at least 1 postdose plasma sample (1 PK[redacted] measurement). The study pharmacokineticist will review data listings of subject dose administration and sample records to identify subjects to be excluded from analyses of PK data. [redacted]

6. BASELINE, EXPOSURE, AND DISPOSITION VARIABLES AND ANALYSES

Sample data displays are provided in Appendix C. Data from Phase 1 and 2 portions will be summarized separately where appropriate.

6.1. Baseline and Demographics, Physical Characteristics, and Disease History

The following demographic and baseline characteristics will be summarized for the ITT population: age, sex, race, ethnicity, weight, height, ECOG performance status, staging, prior radiation (yes/no), prior surgery (yes/no), prior systemic therapy other than radiation (yes/no), date of diagnosis, and primary tumor histology.

6.2. Disposition of Subjects

The number and percentage of subjects who were enrolled and who were withdrawn from the study (with a primary reason for withdrawal) will be summarized for the ITT and safety populations.

6.3. Protocol Deviations

Protocol deviations captured on the Protocol Deviation Log will be presented in the subject data listings.

6.4. Exposure

For subjects in the ITT and safety populations, descriptive statistics will be provided by cohort; number of cycles; duration of treatment; average daily dose (mg) and total dose (mg) of INCB024360; and number of doses, relative dose intensity (mg/kg), and average dose (mg/kg) of MEDI4736.

- **Number of Cycles:** Number of cycles for INCB024360 will be the number of cycles with a nonzero dose of INCB024360.
- **Duration of Treatment:** The number of study days between Day 1 and the last nonzero dose administration record of INCB024360 or MEDI4736 taken by the subject.
- **Number of Doses of MEDI4736:** Number of doses of MEDI4736 for a subject will be the number of administered, scheduled infusions of MEDI4736 recorded on the MEDI4736 Dosing CRF.
- **Average Doses of MEDI4736 (mg/kg):** The average dose of MEDI4736 (in mg/kg) will be the sum of the doses of MEDI4736 recorded on the MEDI4736 Dosing CRF divided by the number of doses of MEDI4736.

Treatment with MEDI4736 will be discontinued after 12 months of treatment. Discontinuation of MEDI4736 treatment may also be considered for subjects who have attained a confirmed complete response (CR). Subjects may continue on INCB024360 monotherapy at this time.

Subjects who then report radiographic disease progression will be eligible for re-treatment with MEDI4736 at the discretion of the investigator if no cancer treatment was administered other than INCB024360 and the subject meets the safety parameters listed in the inclusion/exclusion criteria. Subjects will resume therapy at the same dose and schedule at the time of initial discontinuation. Number of does, average doses, and dose intensity for MEDI4736 in this re-treatment phase will be summarized separately and then combined with all previous doses.

6.5. Study Drug Compliance

For subjects in the ITT and safety populations, overall compliance (%) for INCB024360 will be calculated for all subjects as follows:

$$\text{Overall Compliance (\%)} = 100 \times [\text{total dose taken}] / [\text{intended dose}]$$

The intended dose will be determined up to the earliest study day of permanent discontinuation of INCB024360 (ie, AE discontinuation is the first AE with action taken being "drug withdrawn"), last study drug record in the database, or subject death. Intended dose is defined as the sum of the doses prescribed by the investigator accounting both for planned dose reductions as well as those reductions or increases mandated by the investigator.

6.6. Medical History

For subjects in the ITT and safety population, medical history will be summarized by assigned treatment group. This summation will include the number and percentage of subjects with significant medical history for each body system/organ class and documented on the Medical History CRF.

6.7. Prior and Concomitant Medication

For subjects in the safety population, prior medications and concomitant medications will be coded using the WHO Drug Dictionary and summarized by WHO drug class and WHO drug term. In the data listing, each medication will be recorded as prior, concomitant, or both prior and concomitant. Results will be summarized as number and percentage of subjects with prior and concomitant medications by preferred term and WHO drug class.

Prior medication information will also be used to identify anticancer medication received by subjects before enrollment into the study. Prior anticancer medication data will be summarized and presented by treatment group as well as listed.

7. EFFICACY

Sample data displays are provided in Appendix C.

7.1. General Considerations

Not applicable.

7.2. Efficacy Hypotheses

Not applicable.

7.3. Analysis of the Primary Efficacy Parameter

7.3.1. Objective Response Rate

The primary variable for the Phase 2 portion of the study is ORR. Objective disease status will be categorized using mRECIST v1.1. Subjects' objective response will be evaluated as CR, partial response (PR), stable disease (SD), progressive disease (PD), or not evaluable (NE) at each postbaseline radiological assessment based on changes in target lesions, nontarget lesions, and appearance of new lesions.

For subjects with measurable disease at baseline, the mRECIST v1.1 assessment criteria presented in Table 7 can be used to determine the overall response at a given timepoint based on the target lesion, nontarget lesion, and new lesion assessment.

Table 7: RECIST Evaluation Criteria for Objective Response: Measurable Disease at Baseline

Target Lesions	Nontarget Lesions	New Lesions	Overall Response
CR	CR (or no nontarget lesion)	No	CR
CR	Non-CR/non-PD	No	PR
CR	NE	No	PR
PR	Non-PD and NE (or no nontarget lesion)	No	PR
SD	Non-PD and NE (or no nontarget lesion)	No	SD
Not all evaluated	Non-PD	No	NE
PD	Any	Yes or No	PD
Any	PD	Yes or No	PD
Any	Any	Yes	PD

PR = partial response.

A subject is considered an objective responder as assessed by mRECIST if they have an overall response of CR or PR at any postbaseline visit. The proportion of responders within each treatment group will be estimated with 95% CIs by treatment group. Confidence intervals will be calculated based on the exact method for binomial distributions.

In general, best response is determined on subject level using the highest overall response achieved postbaseline. In the case of SD, measurements must meet the SD criteria at least once after study entry at a minimum interval of 56 (± 7) days. Subjects who fail to meet these criteria will have best response of PD if the next available RECIST evaluation after the initial scan indicates PD or NE if there are no additional RECIST evaluations are available.

A sensitivity analysis for the primary endpoint will be performed in response evaluable population.

7.4. Analysis of Secondary Efficacy Parameters

7.4.1. Objective Response Rate

One of the secondary variables for the Phase 1 portion of the study is ORR. The definition and analysis for this variable is same as Section 7.3.1.

7.4.2. Durability of Response

For objective responders, the DoR is the time from the first overall response contributing to an objective response (CR or PR) to the earlier of the subject's death or first assessment of PD (for mRECIST v1.1) occurring after the first objective response contributing to the objective response. Median DoR will be estimated using the Kaplan-Meier method. Confidence intervals for median survival time will be calculated using the method of Brookmeyer and Crawley (1982), which is the default method within SAS v9.1. Subjects who are still responding (no PD or death) at the time of database freeze or discontinuation will be right censored at the time of last valid RECIST assessment. The DoR evaluation will be performed separately for each treatment arm and no statistical comparison will be made.

7.4.3. Progression-Free Survival

Progression-free survival is defined as the number of days from enrollment to the earlier of death or disease progression by mRECIST v1.1. Date of death will be determined using the Death Report, the Survival Follow-Up, and the Subject Status CRFs. Censoring for PFS will follow the algorithm outlined in Table 8, which is based on FDA guidance (FDA 2007). Of note, the Protocol mandates radiological evaluation of subjects every 8 weeks after the first dose of study treatment for 12 months (and then every 12 weeks thereafter until disease progression), and radiological evaluation should follow calendar days and not be adjusted for delays in cycle starts or extension of combination treatment cycle frequencies. The analyses will be based on the ITT population, according to treatment group assignment. Time-to-event data will be analyzed by the Kaplan-Meier method. The Kaplan-Meier curve for PFS will be provided.

Table 8: Evaluation and Censoring of Progression-Free Survival

Situation	Outcome	Date of Progression or Censoring
No baseline tumor assessments	Censored	Date of randomization
Progression documented between scheduled visits	Progressed	Earliest of: • Date of radiological assessment showing new lesion (if progression is based on new lesion); or • Date of last radiological assessment of measured lesions (if progression is based on increase in sum of measured lesions)
No progression	Censored	Date of last valid radiologic assessment (not NE and not missing)
Treatment discontinuation for undocumented progression	Censored	Date of last valid radiologic assessment (not NE and not missing)
Treatment discontinuation for toxicity or other reason	Censored	Date of last valid radiologic assessment (not NE and not missing)
New anticancer treatment started	Censored	Date of last valid radiologic assessment (not NE and not missing)
Death before first PD assessment	Progressed	Date of death
Death between adequate assessment visits	Progressed	Date of death
Death or progression after more than 1 missed consecutive assessment	Censored	Date of last valid radiologic assessment (not NE and not missing)

7.4.4. Largest Percent Reduction in Sum of Diameters of Target Lesions

For each subject, the percentage change from baseline in sum of the diameters (shortest diameter is used for lymph nodes, longest diameter for all other target lesions per RECIST v1.1) of target lesions will be derived for each postbaseline period at which a valid target lesion assessment is provided. The best percentage change for each subject will be derived for waterfall plots [redacted]

Per RECIST criteria, target lesions considered "too small to measure" will be assigned a default value of 5 mm for purposes of this analysis. Likewise, target lesions identified as "not present" at postbaseline assessments will be assigned 0 mm for this analysis. In the event a target lesion is unaccounted for in a particular postbaseline timepoint, that is, assessment missing or NE, then the overall sum of target lesions will not be evaluable for that postbaseline timepoint.

7.4.5. Other Efficacy Analyses

7.4.5.1. Eastern Cooperative Oncology Group Performance Status

Subjects' ECOG performance status at scheduled assessment times (see Table 5) will be summarized in the listings.

7.4.5.2. Weight

Subjects' body weight at scheduled assessment times (see Table 5) will be summarized in the listings.

7.5. Pharmacokinetic Analyses

INCB024360 PK in this subject population will be evaluated using noncompartmental analysis and/or population PK modeling.

7.5.1. Pharmacokinetic Data

Subject will withhold morning dose of INCB024360 during INCB024360 PK days. The time of last dose of INCB024360 and prior meal will be recorded in the CRF. Pharmacokinetic samples will be obtained at the visits indicated in Table 6. After the predose PK sample is drawn (predose is defined as within 24 hours before administration of MEDI4736 and before administration of INCB024360), subjects will take INCB024360 and then begin infusion of MEDI4736. The exact date and time of the PK blood draws will be recorded in the CRF along with the date and time of the last dose of study drug preceding the blood draw. Sample collection times for INCB024360 are shown in Table 9.

Table 9: Sample Collection Windows for Pharmacokinetic Assessments for INCB024360

Study Visit	Timing of Sample Relative to INCB024360 Administration						
Cycle 1 Day 1	Predose	0.5 h ± 10 min	1 h ± 10 min	2 h ± 30 min	4 h ± 30 min	6 h ± 30 min	OPTIONAL 8 to 10 h ± 30 min
Cycle 1 Day 8	Predose	0.5 h ± 10 min	1 h ± 10 min	2 h ± 30 min	4 h ± 30 min	6 h ± 30 min	OPTIONAL 8 to 10 h ± 30 min
Cycle 2 Day 1	Predose	Anytime (required)					

Measurement of MEDI4736 concentrations in serum will be performed using validated immunoassays. Only subjects who receive at least 1 dose of MEDI4736 and provide at least 1 post-treatment sample will be evaluated. Individual MEDI4736 will be tabulated by dose cohort along with descriptive statistics. The following PK parameters after the first and steady-state dose will be estimated (as data allow): peak concentration (C_{max}), trough concentration (C_{min}), time to maximum observed concentration (t_{max}), and AUC. Accumulation to steady state will be assessed as the ratio of $C_{max,ss}$:C_{max} and $C_{min,ss}$:C_{min}. All PK parameters will be estimated by noncompartmental analysis. Descriptive statistics of noncompartmental PK parameters will be provided.

7.5.2. Subject Demographic, Clinical Laboratory, Disease-Related, and Pharmacogenomic Variables and Concomitant Medications

Subject demographic assessments (age, weight, BMI, gender, and race), clinical laboratory measurements (eg, creatinine clearance, serum albumin, total bilirubin, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase), and the baseline polymorphism of

UGT1A9 may be explored as time-independent predictors of PK variability. Concomitant medications may be explored as covariates in the population PK analysis.

7.5.3. INCB024360 Pharmacokinetic Analyses

The noncompartmental analysis for INCB024360 PK will be performed using commercial software such as Phoenix WinNonlin version 6.0 or later (Pharsight Corporation, Mountain View, CA). Nominal times may be used in all cases except when the difference between the actual collection time and the nominal collection time is greater than 15 minutes for samples collected up to 4 hours after administration and greater than 30 minutes for samples collected more than 4 hours after administration. The following 6 PK parameters will be estimated where possible: C_{max}, T_{max}, $AUC_{0\text{-}t}$, $AUC_{0\text{-}12h}$, $t_{½}$, and CL/F (the latter 3 parameters will only be assessed on C1D8).

For the optional population PK analysis for INCB024360, the data preparation will be performed using SAS version 9.1. [redacted] Compartment models with first-order absorption and linear elimination will be tested for their ability to characterize the PK of INCB024360. Interindividual variability will be modeled using an exponential error model and explored for each PK parameter. Proportional error, additive error, and mixed additive plus proportional error models will be individually evaluated for their ability to describe the magnitude of residual variability. The first-order conditional estimation method with the interaction option will be used.

After a final base model is identified, covariates will be tested as predictors of PK variability. A generalized additive model analysis will be used as a screening tool to initially identify covariates to be formally tested for statistical significance in NONMEM. The candidate covariates will be incorporated into the PK model as fixed-effect parameters by making the typical values of the structural PK parameters a function of the covariate. NONMEM regression analysis will be performed on the model, with covariate parameters being added in a stepwise univariate fashion during the forward selection process and removed in the model reduction (backward elimination) process. The likelihood ratio test will be used to evaluate the significance of incorporating parameters into or removing parameters from the population model. The accuracy and robustness of the final population PK model will be investigated using a visual predictive check method.

7.5.4. Immunogenicity for MEDI4736

Validated assays will be used for the determination of ADAs to MEDI4736 in human serum.

Only subjects who receive at least 1 dose of MEDI4736 and provide at least 1 post-treatment sample will be evaluated. Immunogenicity results will be analyzed descriptively by summarizing the number and percentage of subjects who develop detectable anti-MEDI4736 antibodies. Samples confirmed positive may also be evaluated for neutralizing antibody activity.

7.5.5. Report

A PK report will be prepared to include listings of observed INCB024360 plasma concentration data and estimated PK parameters in accordance with guidance of both US and EU regulatory authorities.

[redacted]

8. SAFETY AND TOLERABILITY

Sample data displays are provided in Appendix C.

8.1. General Considerations

The analyses for this section will be provided for Phase 1 and 2 portion using Phase 1 and Phase 2 safety evaluable population, respectively. Summary tables may be replaced with listings when appropriate. For instance, an AE frequency table may be replaced with a listing if it only contains a few unique preferred terms reported on relatively few subjects. Additional summaries for specific subgroups may be included on an ad hoc basis.

8.2. Adverse Events

8.2.1. Adverse Event Definitions

A treatment-emergent adverse event (TEAE) is any AE either reported for the first time or worsening of a pre-existing event after first dose of study drug. Analysis of AEs (as discussed below) will be limited to TEAEs, but data listings will include all AEs regardless of their timing to study drug administration.

Adverse Events will be tabulated by the MedDRA preferred term and system organ class. Severity of AEs will be described and graded using the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v4.03. The CTCAE reporting guidelines and grading details are available on the Cancer Therapy Evaluation Program website.

A grading (severity) scale is provided for each AE term. If the toxicity is not included in the CTCAE v4.03 criteria, it will be rated on a scale of 1 to 4 as follows: 1 = mild, 2 = moderate, 3 = severe, and 4 = life threatening. All toxicities will be graded based on the worst level reached, not the level they may have reached if they had not been treated. When the intensity of

an AE changes over time for a reporting period (eg, between visits), each change in intensity will be reported as an AE until the event resolves.

The subset of AEs considered by the investigator to be related to INCB024360 or MEDI4736 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. The incidence of AEs and treatment-related AEs will be tabulated. Serious adverse events (SAEs) will also be tabulated.

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

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

For purposes of analysis, all AEs will be considered TEAEs unless the AE can unequivocally be defined as not treatment emergent. Therefore, an unsolved missing onset date will be considered treatment emergent, with the following exceptions:

- If the stop/resolution date is before the first dose administration date on Day 1, then the AE will be considered as not being treatment emergent.
- If both the month and day are missing, and the last day of the year is before the first dose administration date on Day 1, then the AE will not be considered treatment emergent.
- If only the day is missing, and the last day of the month is before the first dose administration date on Day 1, then the AE will not be considered treatment emergent.
- If only the day is missing, and the first day of the month is after the first dose administration date on Day 1, then the AE will be considered treatment emergent.

8.2.2. Adverse Event Summaries

An overall summary of AEs by treatment group will include:

- Number (%) of subjects reporting any TEAEs
- Number (%) of subjects reporting any treatment-related TEAEs
- Number (%) of subjects reporting any SAEs
- Number (%) of subjects reporting any Grade 3 or 4 TEAEs
- Number (%) of subjects who temporarily interrupted study drug because of TEAEs
- Number (%) of subjects who permanently discontinued study drug because of TEAEs
- Number (%) of subjects who withdrew from study because of a TEAE
- Number (%) of subjects with INCB024360 dose reductions because of TEAEs
- Number (%) of subjects who had a fatal TEAE

The following summaries will be produced by MedDRA term (if ≤ 10 subjects appear in a table, a listing may be appropriate):

- Number (%) of subjects reporting TEAEs by system organ class and preferred term
- Number (%) of subjects reporting TEAEs by preferred term in decreasing order of frequency
- Number (%) of subjects reporting TEAEs by system organ class, preferred term, and highest CTCAE grade
- Number (%) of subjects reporting any Grade 3 or 4 TEAEs by system organ class and preferred term
- Number (%) of subjects reporting treatment-related AEs by system organ class and preferred term
- Number (%) of subjects reporting treatment-related AEs by preferred term in decreasing order of frequency
- Number (%) of subjects reporting treatment-related AEs by system organ class, preferred term, and highest CTCAE grade
- Number (%) of subjects reporting any Grade 3 or 4 treatment-related AEs by system organ class and preferred term
- Number (%) of subjects reporting TEAEs leading to death by system organ class and preferred term
- Number (%) of subjects reporting treatment emergent SAEs by system organ class and preferred term
- Number (%) of subjects reporting treatment-related SAEs by system organ class and preferred term
- Number (%) of subjects reporting TEAEs leading to withdrawal from the study by system organ class and preferred term
- Number (%) of subjects reporting TEAEs leading to dose reduction of INCB024360 by system organ class and preferred term
- Number (%) of subjects reporting TEAEs leading to discontinuation of medication by system organ class and preferred term
- Number (%) of subjects reporting TEAEs requiring concomitant medications by system organ class and preferred term
- Number (%) of subjects reporting treatment-emergent non-SAE by system organ class and preferred term
- Number (%) of subjects reporting events of special interest by system organ class and preferred term
- Number (%) of subjects reporting treatment-emergent immune-related AEs by system organ class and preferred term
- Number (%) of subjects reporting Grade 3 or higher treatment-emergent immune-related AEs by system organ class and preferred term

For the last 2 items above, Table 10 includes the full list of preferred terms that should be considered as the immune-related AEs. Pneumonitis, hypersensitivity reactions, hepatic function abnormalities (hepatotoxicity), and serotonin syndrome should be considered as the events of special interest.

Table 10: Immune-Related Adverse Events (Preferred Terms)

Pneumonitis		
Acute interstitial pneumonitis	Interstitial lung disease	Pneumonitis
Colitis		
Intestinal obstruction	Colitis	Colitis microscopic
Enterocolitis	Enterocolitis hemorrhagic	Gastrointestinal perforation
Necrotizing colitis	Diarrhea	
Endocrine		
Adrenal insufficiency	Hyperthyroidism	Hypophysitis
Hypopituitarism	Hypothyroidism	Thyroid disorder
Thyroiditis		
Hematologic		
Autoimmune hemolytic anemia	Aplastic anemia	Thrombotic thrombocytopenic purpura
Idiopathic (or immune) thrombocytopenia purpura	Disseminated intravascular coagulation	Hemolytic uremic syndrome
Any Grade 4 anemia regardless of underlying mechanism		
Hepatic		
Hepatitis	Autoimmune hepatitis	Transaminase elevations
Infusion Reactions		
Allergic reaction	Anaphylaxis	Cytokine release syndrome
Serum sickness	Infusion reactions	Infusion-like reactions
Neurologic		
Autoimmune neuropathy	Guillain-Barre syndrome	Demyelinating polyneuropathy
Myasthenic syndrome		
Ocular		
Uveitis	Iritis	
Renal		
Nephritis	Nephritis autoimmune	Renal failure
Renal failure acute	Creatinine elevations (report as event of clinical interest if ≥ Grade 3 or any grade resulting in dose modification or use of systemic steroids to treat the AE)	
Skin		
Dermatitis exfoliative	Erythema multiforme	Pruritus
Rash	Rash generalized	Rash maculo-papular
Stevens-Johnson syndrome	Toxic epidermal necrolysis	
Any rash considered clinically significant in the physician's judgment		
Other		
Myocarditis	Pancreatitis	Pericarditis
Any other Grade 3 event which is considered immune-related by the physician		

8.3. Clinical Laboratory Tests

8.3.1. Laboratory Value Definitions

Laboratory values and change from baseline values will be summarized descriptively by visit. The baseline value will be determined using the last nonmissing values collected prior the first dose. For baseline laboratory candidates with the same date and time, additional rules may be provided after consultation with the medical monitor to delineate which value will be defined as baseline.

Laboratory test values outside the normal range will be assessed for severity based on CTCAE grade or similar criteria where clinical intervention is required for CTCAE grading. See Appendix B for laboratory grading criteria. The incidence of abnormal laboratory values and shift tables relative to baseline will be tabulated.

8.3.2. Laboratory Value Summaries

Clinical laboratory tests, including hematology and serum chemistry (see Appendix A), will be performed for each subject during the study in accordance with Table 6.

If specific safety issues arise, additional unscheduled laboratory tests/analyses may be performed at the discretion of the investigator.

All test results and associated normal ranges from central laboratories will be reported in International System of Units (SI). All tests with numeric values will have a unique unit per test. Any laboratory test results and associated normal ranges from local laboratories will be converted to SI units. For the limited number of cases where the associated normal ranges from a local laboratory cannot be obtained despite due diligence, a set of standard normal ranges based on documented reference ranges will be applied to facilitate reporting the test results.

When there are multiple nonmissing laboratory values for a subject's particular test within a visit window, the convention shown in Table 11 will be used to determine the record used for by-visit tabulations and summaries.

Table 11: Identification of Records for By-Visit Summaries

Priority	Laboratory Visit	Proximity to Visit Window	Tiebreaker
1	Scheduled	In-window	Use smallest laboratory sequence number
2	Unscheduled	In-window	
3	Scheduled	Out-of-window	

Laboratory parameters identified in Appendix A will be summarized. Shift tables based on worst postbaseline value recorded will use all postbaseline values. Other laboratory parameters collected will only be listed in an appendix to the Clinical Study Report (CSR) in their original units without SI conversions.

Numeric laboratory values will be summarized descriptively, and non-numeric test values will be tabulated. In addition, line graph and box-and-whisker plots will be provided for prespecified laboratory parameters.

For test results that will be summarized with available normal ranges, the number and percentage of subjects with the laboratory values being low (but never high), normal, high (but never low), and both low and high will be calculated for each test.

This shift summary will be produced for each test for the safety population as well as the subset of subjects treated at the MTD. The denominator for the percentage calculation will use the number of subjects in the baseline category (ie, low, high, normal, missing) as the denominator for the percentage in each of the categories during the treatment period.

For all gradable laboratory parameters identified in Appendix A, the values will be classified into grade levels corresponding to CTCAE v4.03 criteria. For specific laboratory values requiring clinical intervention to grade, the classification according to the quantitative component will be provided. See Appendix B for laboratory grading criteria.

The number and percentage of subjects with the laboratory values of Grade 1, 2, 3, or 4 will be calculated for each treatment according to the largest treatment-emergent worsening of laboratory grade. Separate summaries for abnormally high and abnormally low laboratory values will be provided when the laboratory in question has both high and low grading criteria. For instance, if a subject has a baseline fasting glucose of 210 mg/dL, maximum fasting glucose after starting treatment of 245 mg/dL, and minimum fasting glucose after starting treatment of 52 mg/dL, then the subject should be reported as follows:

- The subject will be counted as a Grade 2 "Glucose decreased" in summaries of hypoglycemia because the subject was not hypoglycemic at study entry but became hypoglycemic after treatment.
- The subject will not count as a "Glucose increased" in summaries of hyperglycemia because the subject met the numeric requirements for Grade 2 hyperglycemia at baseline (fasting glucose value > 160 to 250 mg/dL) and did not increase in grade after starting treatment.

In cases where differentials of hematology parameters are obtained without corresponding absolute count data, efforts will be made to investigate if the conversion to an absolute value will lead to additional abnormalities. This will be discussed with the clinical team regarding appropriate documentation and action.

8.4. Vital Signs

Vital signs, including systolic blood pressure, diastolic blood pressure, heart rate, respiration rate, and body temperature, will be taken with subjects in the seated position during the study in accordance with Table 5. Change and percentage change from baseline will be calculated using the last nonmissing value before first dose of study drug (Day 1) as the baseline value.

Incidences of clinically notable vital sign abnormalities are defined in Table 12. The abnormal values for subjects exhibiting clinically notable vital sign abnormalities will be listed along with their assigned treatment group. Alert vital signs are defined as an absolute value outside the defined range and percentage change greater than 25%.

Table 12: Criteria for Clinically Notable Vital Sign Abnormalities

Parameter	High Threshold	Low Threshold
Systolic blood pressure	> 155 mmHg	< 85 mmHg
Diastolic blood pressure	> 100 mmHg	< 40 mmHg
Heart rate	> 100 bpm	< 45 bpm
Temperature	> 38ºC	< 35.5ºC
Respiratory rate	> 24/min	< 8/min

8.5. Electrocardiograms

Twelve-lead ECGs will be obtained for each subject during the study in accordance with Table 5. Electrocardiogram results will be reviewed for clinically notable abnormalities according to predefined criteria (see Table 13). Electrocardiogram abnormalities, both at baseline and postbaseline visits, will be tabulated by treatment group. Incidences of abnormalities will be listed with study visit, assigned treatment group, and a description of the abnormality.

Table 13: Criteria for Clinically Notable ECG Abnormalities

Parameter	High Threshold	Low Threshold
QTcF[a]	> 460 ms	< 295 ms
PR	> 220 ms	< 75 ms
QRS	> 120 ms	< 50 ms
QT	> 500 ms	< 300 ms
RR	> 1500 ms	< 600 ms

[a] QTcF (Fridericia correction).

9. INTERIM ANALYSES

9.1. Overview of Interim Analysis

No interim analysis for efficacy or futility will be conducted in this study. As this Phase 1/2 study is intended to support a Phase 3 development decision, the selected Type I and Type II error rates lead to a relatively small sample size in this Protocol. As such, the level of uncertainty for point estimates at an interim analysis limits the value of such an interim analysis. The safety of subject participants will be assessed through regular meetings between investigators and sponsors who will monitor for critical safety signals.

9.2. Guidelines for Decision Rules

An interim safety analysis is planned for Phase 2 after 16 subjects have been enrolled and treated for 8 weeks, and then every 3 months thereafter. If either of the following is reported during

these reviews, enrollment of subjects would be suspended until the sponsor determined the appropriate course of action and notified IRBs and regulatory authorities:

- ≥ 40% of subjects report a DLT or
- ≥ 20% of subjects have had a nondermatologic immune-related AE ≥ Grade 3 that was attributable to the investigational agent.

Based on these rules, the probabilities of stopping a treatment group for safety is provided in Table 14.

Table 14: Probability of Early Termination for Various Safety Event Rates

Proportion of Subjects Having DLT	Probability of Early Termination Based Upon DLT Rule[a]	Proportion of Subjects Having Immune Event	Probability of Early Termination Based on Immune-Related Toxicity[a]
5%	0.0%	5%	6.4%
10%	0.5%	10%	24.6%
15%	2.3%	15%	50.4%
20%	7.0%	20%	74.4%
25%	16.4%	25%	89.8%
30%	32.0%	30%	97.1%
40%	72.5%	40%	99.9%

[a] Assumes the interim safety analyses occur when enrollment in the active treatment arm are 8, 19, 30, and 41 subjects. Probability estimated via simulation with 100,000 replications.

10. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

Dates for the SAP, including any amendments, are included in Table 15.

Table 15: Dates for SAP Amendments

SAP Version	Date
Original	26 NOV 2014

10.1. Changes to Protocol-Defined Analyses

Not applicable.

10.2. Changes to the Statistical Analysis Plan

Not applicable.

11. REFERENCES

Brookmeyer R, Crowley J. A confidence interval for the median survival time. Biometrics 1982;38:29-41.

Food and Drug Administration (FDA). Guidance for Industry: Clinical trial endpoints for the approval of cancer drugs and biologics. 2007. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm071590.pdf. Accessed November 25, 2014.

Simon R. Optimal two-stage designs for phase II clinical trials. Control Clin Trials 1989;10:1-10.

APPENDIX A. LABORATORY TESTS: REQUIRED ANALYTES AND PULMONARY FUNCTION TESTS

Comprehensive Chemistry Panel	Hematology	Other
Albumin Alkaline phosphatase ALT AST Amylase Bicarbonate Blood urea nitrogen Calcium Chloride Creatinine Glucose Iron Lactate dehydrogenase Lipase Phosphorus Potassium Sodium Total bilirubin Direct bilirubin (if total bilirubin is elevated above ULN) Total protein Uric acid	Complete blood count including: Hemoglobin Hematocrit Platelet count Red blood cell count White blood cell count Differential count including: • Basophils • Eosinophils • Lymphocytes • Monocytes • Neutrophils	**Serology:** Hepatitis B surface antigen Hepatitis B surface antigen antibody Hepatitis B core antibody Hepatitis C virus antibody HCV-RNA HBV-DNA **Pregnancy test:** Female subjects of childbearing potential only require a serum test at screening. Pregnancy tests (serum or urine) should be repeated if required by local regulations. **Urinalysis with microscopic examination:** Color and appearance pH and specific gravity Bilirubin Glucose Ketones Leukocytes Nitrite Occult blood Protein Urobilinogen **Coagulation:** PT aPTT INR
Endocrine Monitoring	**Standard LFT Monitoring**	[redacted]
Adrenocorticotropic hormone Serum cortisol (9 AM) Luteinizing hormone[a] Prolactin Thyroid stimulating hormone Free tyroxine (T4) Total triiodothyronine (T3) Serum testosterone (9 AM)[b]	Alkaline phosphatase ALT AST Total bilirubin	
Pulmonary Function Tests		
Largest FVC FVC % Predicted Largest FEV_1 FEV_1 % predicted FEV_1/FVC $FEF_{25-75\%}$ $FEF_{25-75\%}$ Predicted Peak expiratory flow	**Pulse Oximetry** Oxygen saturation Pulse rate	**DLCO** DLCO DLCO % predicted DLCO/VA DLCO/VA % predicted DLCO corrected for Hb DLCO corrected % predicted DLCO/VA corrected for Hgb DLCO/VA corrected % predicted

ALT = alanine aminotransferase; aPTT = activated partial thromboplastin time; AST = aspartate aminotransferase; DLCO = diffusing capacity of the lung for carbon monoxide; FEF = forced expiratory flow; FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; HBV-DNA = hepatitis B virus deoxyribonucleic acid; HCV-RNA = hepatitis C virus ribonucleic acid; INR = international normalized ratio; LFT = liver function test; PT = prothrombin time; ULN = upper limit of normal; VA = alveolar volume.

a Not needed in subjects taking thyroid hormone replacement therapy.

b Not needed in women, surgically castrated men, or men taking luteinizing hormone-releasing hormone agonist therapy.

APPENDIX B. LABORATORY GRADING

Laboratory	Grade 1	Grade 2	Grade 3	Grade 4
Haptoglobin decreased	< LLN	–	–	–
Hemoglobin decreased	< LLN - 100 g/L	< 100 – 80 g/L	< 80 g/L	–
Hemoglobin increased	Increase in > 0 – 2 g/dL above ULN or above baseline if baseline is above ULN	Increase in > 2 – 4 g/dL above ULN or above baseline if baseline is above ULN	Increase in > 4 g/dL above ULN or above baseline if baseline is above ULN	–
Lymphocyte count decreased	< LLN – 0.8 × 10^9 /L	< 0.8 - 0.5 × 10^9 /L	< 0.5 - 0.2 × 10^9 /L	< 0.2 × 10^9 /L
Lymphocyte count increased	-	> 4000/mm^3 - 20,000/mm^3	> 20,000/mm^3	–
Neutrophil count decreased	< LLN – 1.5 × 10^9 /L	< 1.5 - 1.0 × 10^9 /L	< 1.0 - 0.5 × 10^9 /L	< 0.5 × 10^9 /L
Platelet count decreased	< LLN - 75.0 × 10^9 /L	< 75.0 - 50.0 × 10^9 /L	< 50.0 - 25.0 × 10^9 /L	< 25.0 × 10^9/L
White blood cell decreased	< LLN – 3.0 × 10^9 /L	< 3.0 - 2.0 × 10^9 /L	< 2.0 - 1.0 × 10^9 /L	< 1.0 × 10^9 /L
Activated partial thromboplastin time prolonged	> ULN – 1.5 × ULN	> 1.5 - 2.5 × ULN	> 2.5 × ULN	–
INR increased	> 1 - 1.5 × ULN	> 1.5 - 2.5 × ULN	> 2.5 × ULN;	–
Alanine aminotransferase increased	> ULN – 3.0 × ULN	> 3.0 - 5.0 × ULN	> 5.0 - 20.0 × ULN	> 20.0 × ULN
Alkaline phosphatase increased	> ULN – 2.5 × ULN	> 2.5 - 5.0 × ULN	> 5.0 - 20.0 × ULN	> 20.0 × ULN
Aspartate aminotransferase increased	> ULN – 3.0 × ULN	> 3.0 - 5.0 × ULN	> 5.0 - 20.0 × ULN	> 20.0 × ULN
Blood bilirubin increased	> ULN - 1.5 × ULN	> 1.5 - 3.0 × ULN	> 3.0 - 10.0 × ULN	> 10.0 × ULN
CD4 lymphocytes decreased	< LLN - 0.5 × 10^9 /L	< 0.5 - 0.2 × 10^9 /L	< 0.2 - 0.05 × 10^9 /L	< 0.05 × 10^9 /L
Cholesterol high	> ULN - 7.75 mmol/L	> 7.75 - 10.34 mmol/L	> 10.34 - 12.92 mmol/L	> 12.92 mmol/L
CPK increased	> ULN - 2.5 × ULN	> 2.5 × ULN - 5 × ULN	> 5 × ULN - 10 × ULN	> 10 × ULN
Creatinine increased	> 1 - 1.5 × baseline; >ULN - 1.5 × ULN	> 1.5 - 3.0 × baseline; >1.5 - 3.0 × ULN	> 3.0 baseline; >3.0 - 6.0 × ULN	> 6.0 × ULN

Laboratory	Grade 1	Grade 2	Grade 3	Grade 4
Fibrinogen decreased	< 1.0 - 0.75 × LLN or < 25% decrease from baseline	< 0.75 - 0.5 × LLN or 25 - < 50% decrease from baseline	< 0.5 - 0.25 × LLN or 50 - < 75% decrease from baseline	< 0.25 × LLN or 75% decrease from baseline or absolute value < 50 mg/dL
GGT increased	> ULN - 2.5 × ULN	> 2.5 - 5.0 × ULN	> 5.0 - 20.0 × ULN	> 20.0 × ULN
Lipase increased	> ULN - 1.5 × ULN	> 1.5 - 2.0 × ULN	> 2.0 - 5.0 × ULN	> 5.0 × ULN
Serum amylase increased	> ULN - 1.5 × ULN	> 1.5 - 2.0 × ULN	> 2.0 - 5.0 × ULN	> 5.0 × ULN
Serum albumin decreased	< LLN - 30 g/L	< 30 - 20 g/L	< 20 g/L	–
Serum calcium decreased	< LLN - 2.0 mmol/L	< 2.0 - 1.75 mmol/L	< 1.75 - 1.5 mmol/L	< 1.5 mmol/L
Serum calcium increased	> ULN - 2.9 mmol/L	> 2.9 - 3.1 mmol/L	> 3.1 - 3.4 mmol/L	> 3.4 mmol/L
Serum glucose decreased (fasting)	< LLN - 3.0 mmol/L	< 3.0 - 2.2 mmol/L	< 2.2 - 1.7 mmol/L	< 1.7 mmol/L
Serum glucose increased (fasting)	> ULN - 8.9 mmol/L	> 8.9 - 13.9 mmol/L	> 13.9 - 27.8 mmol/L	> 27.8 mmol/L
Serum magnesium decreased	< LLN - 0.5 mmol/L	< 0.5 - 0.4 mmol/L	< 0.4 - 0.3 mmol/L	< 0.3 mmol/L
Serum magnesium increased	> ULN - 1.23 mmol/L	–	> 1.23 - 3.30 mmol/L	> 3.30 mmol/L
Serum phosphate decreased	< LLN - 0.8 mmol/L	< 0.8 - 0.6 mmol/L	< 0.6 - 0.3 mmol/L	< 0.3 mmol/L
Serum potassium decreased	< LLN - 3.0 mmol/L	–	< 3.0 - 2.5 mmol/L	< 2.5 mmol/L
Serum potassium increased	> ULN - 5.5 mmol/L	> 5.5 - 6.0 mmol/L	> 6.0 - 7.0 mmol/L	> 7.0 mmol/L
Serum sodium decreased	< LLN - 130 mmol/L	–	< 130 - 120 mmol/L	< 120 mmol/L
Serum sodium increased	> ULN - 150 mmol/L	> 150 - 155 mmol/L	> 155 - 160 mmol/L	> 160 mmol/L
Serum triglycerides increased	1.71 - 3.42 mmol/L	> 3.42 - 5.7 mmol/L	> 5.7 - 11.4 mmol/L	> 11.4 mmol/L
Serum uric acid increased	> ULN - 0.59 mmol/L	–	> ULN - 0.59 mmol/L	> 0.59 mmol/L;

APPENDIX C. PLANNED TABLES, FIGURES, AND LISTINGS

This appendix provides a list of the planned tables, figures, and listings for the CSR. Standard tables will follow the conventions in the Standard Safety Tables initial version. Shells are provided for nonstandard, in-text CSR tables. In-text tables are identical in structure and content as appendix tables, but follow a Rich Text Format.

Tables

Table No.	Title	Population	Standard	In-Text
Baseline and Demographic Characteristics				
1.1.1	Analysis Populations		X	X
1.1.2.1	Summary of Subject Disposition	Phase 1 ITT	X	X
1.1.2.2	Summary of Subject Disposition	Phase 2 ITT	X	X
1.2.1.1	Summary of Demographics	Phase 1 ITT	X	X
1.2.1.2	Summary of Demographics	Phase 2 ITT	X	X
1.3.1.1	Summary of Baseline Disease Characteristics	Phase 1 ITT		X
1.3.1.2	Summary of Baseline Disease Characteristics	Phase 2 ITT		X
1.3.2.1	Summary of General Medical History	Phase 1 ITT		
1.3.2.2	Summary of General Medical History	Phase 2 ITT		
1.4.1.1	Summary of Prior Medications	Phase 1 ITT		
1.4.1.2	Summary of Prior Medications	Phase 2 ITT		
1.4.2.1	Summary of Concomitant Medications	Phase 1 ITT		
1.4.2.2	Summary of Concomitant Medications	Phase 2 ITT		
1.4.3.1	Summary of Prior Medications for Cancer	Phase 1 ITT		X
1.4.3.2	Summary of Prior Medications for Cancer	Phase 2 ITT		X
1.5.1	Summary of Study Medication Compliance	Phase 1 Safety		X
1.5.2	Summary of Study Medication Compliance	Phase 2 Safety		X
Efficacy				
2.1.1	Kaplan-Meier Analysis of Progression-Free Survival by RECIST Criteria	Phase 1 ITT		X
2.1.2	Kaplan-Meier Analysis of Progression-Free Survival by RECIST Criteria	Phase 2 ITT		X
2.2.1.1	Summary of Best Response by RECIST Criteria	Phase 1 ITT		X
2.2.1.2	Summary of Best Response by RECIST Criteria	Phase 2 ITT		X
2.2.4.1	Summary of Duration of Response	Phase 1 ITT		X
2.2.4.2	Summary of Duration of Response	Phase 2 ITT		X
Safety				
3.1.1.1	Summary of Exposure and Duration of Exposure to INCB024360 and MEDI4736	Phase 1 ITT		X
3.1.1.2	Summary of Exposure and Duration of Exposure to INCB024360 and MEDI4736	Phase 2 ITT		X
3.2.1.1	Overall Summary of Treatment-Emergent Adverse Events	Phase 1 Safety	X	X
3.2.1.2	Overall Summary of Treatment-Emergent Adverse Events	Phase 2 Safety	X	X
3.2.2.1	Summary of Treatment-Emergent Adverse Events By MedDRA System Organ Class and Preferred Term	Phase 1 Safety	X	

Table No.	Title	Population	Standard	In-Text
3.2.2.2	Summary of Treatment-Emergent Adverse Events By MedDRA System Organ Class and Preferred Term	Phase 2 Safety	X	
3.2.3.1	Summary of Treatment-Emergent Adverse Events By MedDRA Preferred Term in Decreasing Order of Frequency	Phase 1 Safety	X	X
3.2.3.2	Summary of Treatment-Emergent Adverse Events By MedDRA Preferred Term in Decreasing Order of Frequency	Phase 2 Safety	X	X
3.2.4.1	Summary of Treatment-Emergent Adverse Events By MedDRA System Organ Class, Preferred Term, and Maximum Severity	Phase 1 Safety	X	
3.2.4.2	Summary of Treatment-Emergent Adverse Events By MedDRA System Organ Class, Preferred Term, and Maximum Severity	Phase 2 Safety	X	
3.2.7.1	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events By MedDRA System Organ Class and Preferred Term	Phase 1 Safety	X	X
3.2.7.2	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events By MedDRA System Organ Class and Preferred Term	Phase 2 Safety	X	X
3.2.11.1	Summary of Treatment-Related Adverse Events By MedDRA System Organ Class and Preferred Term	Phase 1 Safety	X	
3.2.11.2	Summary of Treatment-Related Adverse Events By MedDRA System Organ Class and Preferred Term	Phase 2 Safety	X	
3.2.12.1	Summary of Treatment-Related Adverse Events By MedDRA Preferred Term in Decreasing Order of Frequency	Phase 1 Safety	X	
3.2.12.2	Summary of Treatment-Related Adverse Events By MedDRA Preferred Term in Decreasing Order of Frequency	Phase 2 Safety	X	
3.2.13.1	Summary of Treatment-Related Adverse Events By MedDRA System Organ Class, Preferred Term, and Maximum Severity	Phase 1 Safety	X	
3.2.13.2	Summary of Treatment-Related Adverse Events By MedDRA System Organ Class, Preferred Term, and Maximum Severity	Phase 2 Safety	X	
3.2.16.1	Summary of Grade 3 or Higher Treatment-Related Adverse Events By MedDRA System Organ Class and Preferred Term	Phase 1 Safety	X	
3.2.16.2	Summary of Grade 3 or Higher Treatment-Related Adverse Events By MedDRA System Organ Class and Preferred Term	Phase 2 Safety	X	
3.2.17.1	Summary of Treatment-Emergent Adverse Events Leading to Death By MedDRA System Organ Class and Preferred Term	Phase 1 Safety	X	X
3.2.17.2	Summary of Treatment-Emergent Adverse Events Leading to Death By MedDRA System Organ Class and Preferred Term	Phase 2 Safety	X	X
3.2.18.1	Summary of Serious Treatment-Emergent Adverse Events By MedDRA System Organ Class and Preferred Term	Phase 1 Safety	X	X
3.2.18.2	Summary of Serious Treatment-Emergent Adverse Events By MedDRA System Organ Class and Preferred Term	Phase 2 Safety	X	X

Table No.	Title	Population	Standard	In-Text
3.2.19.1	Summary of Non-Serious Treatment-Emergent Adverse Events By MedDRA System Organ Class and Preferred Term	Phase 1 Safety	X	
3.2.19.2	Summary of Non-Serious Treatment-Emergent Adverse Events By MedDRA System Organ Class and Preferred Term	Phase 2 Safety	X	
3.2.20.1	Summary of Treatment-Related Serious Adverse Events By MedDRA System Organ Class and Preferred Term	Phase 1 Safety	X	
3.2.20.2	Summary of Treatment-Related Serious Adverse Events By MedDRA System Organ Class and Preferred Term	Phase 2 Safety	X	
3.2.21.1	Summary of Treatment-Emergent Adverse Events Leading to Withdrawal From the Study By MedDRA System Organ Class and Preferred Term	Phase 1 Safety	X	X
3.2.21.2	Summary of Treatment-Emergent Adverse Events Leading to Withdrawal From the Study By MedDRA System Organ Class and Preferred Term	Phase 2 Safety	X	X
3.2.22.1	Summary of Treatment-Emergent Adverse Events Leading to Dose Reduction By MedDRA System Organ Class and Preferred Term	Phase 1 Safety	X	
3.2.22.2	Summary of Treatment-Emergent Adverse Events Leading to Dose Reduction By MedDRA System Organ Class and Preferred Term	Phase 2 Safety	X	
3.2.23.1	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Drug Medication By MedDRA System Organ Class and Preferred Term	Phase 1 Safety	X	X
3.2.23.2	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Drug Medication By MedDRA System Organ Class and Preferred Term	Phase 2 Safety	X	X
3.2.25.1	Summary of Treatment-Emergent Immune-Related Adverse Events By MedDRA System Organ Class and Preferred Term (Investigator Determined)	Phase 1 Safety	X	X
3.2.25.2	Summary of Treatment-Emergent Immune-Related Adverse Events By MedDRA System Organ Class and Preferred Term (Investigator Determined)	Phase 2 Safety	X	X
3.2.26.1	Summary of Grade 3 or Higher Treatment-Emergent Immune-Related Adverse Events By MedDRA System Organ Class and Preferred Term (Investigator Determined)	Phase 1 Safety	X	X
3.2.26.2	Summary of Grade 3 or Higher Treatment-Emergent Immune-Related Adverse Events By MedDRA System Organ Class and Preferred Term (Investigator Determined)	Phase 2 Safety	X	X
3.2.27.1	Summary of Treatment-Emergent Immune-Related Adverse Events By MedDRA System Organ Class and Preferred Term (With Grade Specific)	Phase 1 Safety	X	X
3.2.27.2	Summary of Treatment-Emergent Immune-Related Adverse Events By MedDRA System Organ Class and Preferred Term (With Grade Specific)	Phase 2 Safety	X	X
3.2.28.1	Summary of Treatment-Emergent Immune-Related Adverse Events By MedDRA System Organ Class and Preferred Term (Regardless of Grade)	Phase 1 Safety	X	X

Table No.	Title	Population	Standard	In-Text
3.2.28.2	Summary of Treatment-Emergent Immune-Related Adverse Events By MedDRA System Organ Class and Preferred Term (Regardless of Grade)	Phase 2 Safety	X	X
3.2.29.1	Summary of Grade 3 or Higher Treatment-Emergent Immune-Related Adverse Events By MedDRA System Organ Class and Preferred Term	Phase 1 Safety	X	X
3.2.29.2	Summary of Grade 3 or Higher Treatment-Emergent Immune-Related Adverse Events By MedDRA System Organ Class and Preferred Term	Phase 2 Safety	X	X
3.2.30.1	Summary of Adverse Events of Special Interest By MedDRA System Organ Class and Preferred Term	Phase 1 Safety	X	X
3.2.30.2	Summary of Adverse Events of Special Interest By MedDRA System Organ Class and Preferred Term	Phase 2 Safety	X	X
Lab				
3.3.1	Summary of Laboratory Values - Hematology	Phase 1 Safety	X	
3.3.2	Summary of Laboratory Values - Hematology	Phase 2 Safety	X	
3.3.3	Summary of Laboratory Values - Chemistry	Phase 1 Safety	X	
3.3.4	Summary of Laboratory Values - Chemistry	Phase 2 Safety	X	
3.3.5.1	Shift Summary of Laboratory Values in CTC Grade - To the Worst Abnormal Value (Tests with One Directional CTC Grade)	Phase 1 Safety	X	X
3.3.5.2	Shift Summary of Laboratory Values in CTC Grade - To the Worst Abnormal Value (Tests with One Directional CTC Grade)	Phase 2 Safety	X	X
3.3.6.1	Shift Summary of Laboratory Values in CTC Grade - To the Worst Abnormal Value (Tests with Two Directional CTC Grade)	Phase 1 Safety	X	
3.3.6.2	Shift Summary of Laboratory Values in CTC Grade - To the Worst Abnormal Value (Tests with Two Directional CTC Grade)	Phase 2 Safety	X	
3.4.1.1	Summary of Systolic Blood Pressure	Phase 1 Safety	X	
3.4.1.2	Summary of Systolic Blood Pressure	Phase 2 Safety	X	
3.4.2.1	Summary of Diastolic Blood Pressure	Phase 1 Safety	X	
3.4.2.2	Summary of Diastolic Blood Pressure	Phase 2 Safety	X	
3.4.3.1	Summary of Heart Rate	Phase 1 Safety	X	
3.4.3.2	Summary of Heart Rate	Phase 2 Safety	X	
3.4.4.1	Summary of Body Temperature	Phase 1 Safety	X	
3.4.4.2	Summary of Body Temperature	Phase 2 Safety	X	
3.4.5.1	Summary of Respiration Rate	Phase 1 Safety	X	
3.4.5.2	Summary of Respiration Rate	Phase 2 Safety	X	
3.4.6.1	Summary of Subjects with Clinically Notable Vital Signs	Phase 1 Safety	X	
3.4.6.2	Summary of Subjects with Clinically Notable Vital Signs	Phase 2 Safety	X	
3.5.1.1	Summary of 12-Lead ECG: PR Interval Values	Phase 1 Safety	X	
3.5.1.2	Summary of 12-Lead ECG: PR Interval Values	Phase 2 Safety	X	
3.5.2.1	Summary of 12-Lead ECG: QRS Interval Values	Phase 1 Safety	X	
3.5.2.2	Summary of 12-Lead ECG: QRS Interval Values	Phase 2 Safety	X	

Table No.	Title	Population	Standard	In-Text
3.5.3.1	Summary of 12-Lead ECG: QT Interval Values	Phase 1 Safety	X	
3.5.3.2	Summary of 12-Lead ECG: QT Interval Values	Phase 2 Safety	X	
3.5.4.1	Summary of 12-Lead ECG: QTcB Interval Values	Phase 1 Safety	X	
3.5.4.2	Summary of 12-Lead ECG: QTcB Interval Values	Phase 2 Safety	X	
3.5.5.1	Summary of 12-Lead ECG: QTcF Interval Values	Phase 1 Safety	X	
3.5.5.2	Summary of 12-Lead ECG: QTcF Interval Values	Phase 2 Safety	X	
3.5.6.1	Summary of 12-Lead ECG: RR Interval Values	Phase 1 Safety	X	
3.5.6.2	Summary of 12-Lead ECG: RR Interval Values	Phase 2 Safety	X	
3.5.7.1	Summary of Treatment Emergent, Clinically Significant ECG Abnormality from Baseline	Phase 1 Safety		X
3.5.7.2	Summary of Clinically Notable ECG Abnormalities	Phase 2 Safety		X

Figures

Figure No.	Title
4.1	Kaplan-Meier Plot of Progression-free Survival by Treatment Group
4.2	Waterfall plot of largest percent reduction in sum of target lesion lengths
4.3	Percent change from baseline over time in sum of target lesion lengths
4.4	Line Graph of Selected Laboratory Values by Study Day
4.5	Box-and-Whisker Plot of Selected Laboratory Values by Study Visit

Listings

Listing No.	Title
16.2.1.1	Subject Enrollment and Disposition Status
16.2.1.2	Subject Inclusion and Exclusion Criteria
16.2.1.3	Medical History
16.2.1.4	Oncology Disease History
16.2.1.5	Systemic Cancer Medication History
16.2.1.6	Prior Surgery
16.2.1.7	Prior Radiotherapy
16.2.2	Protocol Deviations/Violations
16.2.3.1	Demographic and Baseline Characteristics
16.2.3.2	Baseline Disease Characteristics
16.2.3.3	Prior and Concomitant Drug Treatments
16.2.4.1	Study Drug Compliance
16.2.5.1	PFS Events and Assessments
16.2.6.1	Investigator Reported Assessment by RECIST Criteria
16.2.6.2	Target Lesions
16.2.6.3	Non-target Lesions
16.2.6.4	New Lesions
16.2.6.5	Percent Reduction in Sum of Target Lesion Lengths
16.2.6.6	Time to Disease Progression
16.2.6.7	ECOG Status

Listing No.	Title
16.2.7.1	Study Drug Administration
16.2.7.2	Adverse Events
16.2.7.3	Dose-limiting Toxicities
16.2.7.4	Serious Adverse Events
16.2.7.5	Adverse Events Leading to Study Drug Discontinuation
16.2.7.6	Deaths
16.2.8.1	Clinical Laboratory Values (Hematology)
16.2.8.2	Clinical Laboratory Values (Chemistry)
16.2.8.3	Clinical Laboratory Values (Coagulation)
16.2.8.4	Clinical Laboratory Values (Endocrine and CRP)
16.2.8.5	Abnormal Clinical Laboratory Values (Hematology)
16.2.8.6	Abnormal Clinical Laboratory Values (Chemistry)
16.2.8.7	Abnormal Clinical Laboratory Values (Coagulation)
16.2.8.8	Abnormal Clinical Laboratory Values (Endocrine and CRP)
16.2.9.6	Urinalysis Values
16.2.10.1	Vital Signs
16.2.10.2	Abnormal Vital Sign Values
16.2.11.1	12-Lead ECG Values
16.2.11.2	Abnormal 12-Lead ECG Values
16.2.12.2	Body Weight
16.2.13	Symptoms of Serotonin Syndrome
16.2.14	CA19-9

PROTOCOL: INCB XXXXX-XXX (Page 1 of YYYY)
DRUG/INDICATION: xxxxxxxxxxx/xxxxxxxxxxxxx VERSION: Final

Table 1.3.1.1

Summary of Baseline Disease Characteristics
(Population: Phase 1 Intent-to-Treat Subjects)

	Treatment Group			
Variable	Dose 1 (N=xxx)	Dose 2 (N=xxx)	Dose 3 (N=xxx)	Total (N=xxx)

This table follows the same shell as that
for 14.1.3.1.2

PROGRAM\OUTPUT: T_MHIST.SAS\T_MHIST1.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.x.x.x.x

PROTOCOL: INCB XXXXX-XXX (Page 1 of YYYY)
DRUG/INDICATION: xxxxxxxxxxx/xxxxxxxxxxxxx VERSION: Final

Table 1.3.1.2

Summary of Baseline Disease Characteristics
(Population: Phase 2 Intent-to-Treat Subjects)

Variable	Total	Treatment Group: Cancer Type 1 (N=xxx)	Treatment Group: Cancer Type 2 (N=xxx)	Treatment Group: Cancer Type 3 (N=xxx)
Prior Systemic Therapy				
Yes		xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
No		xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage at Initial Diagnosis				
Stage 0		xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage 1A		xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage 2B		xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage 2A		xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage 2B		xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage 2C		xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage 3A		xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage 3B		xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage 3C		xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage 4		xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)

PROGRAM\OUTPUT: T_MHIST.SAS\T_MHIST1.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.x.x.x.x

PROTOCOL: INCB XXXXX-XXX (Page 2 of YYYY)
DRUG/INDICATION: xxxxxxxxxxx/xxxxxxxxxxxxx VERSION: Final

Table 1.3.1.2

Summary of Baseline Disease Characteristics
(Population: Phase 2 Intent-to-Treat Subjects)

	Treatment Group		
Variable	Cancer Type 1 (N=xxx)	Cancer Type 2 (N=xxx)	Cancer Type 3 (N=xxx)
Current Staging			
Stage 0	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage 1A	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage 2B	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage 2A	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage 2B	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage 2C	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage 3A	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage 3B	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage 3C	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage 4	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Distant Metastasis			
Yes	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
No	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Sites of Metastatic Disease			
xxxxxxxxxxxxxxxxxxxxxxxxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
xxxxxxxxxxxxxxxxxxxxxxxxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
xxxxxxxxxxxxxxxxxxxxxxxxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)

PROGRAM\OUTPUT: T_MHIST.SAS\T_MHIST1.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.x.x.x.x

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Table 1.3.2.1

Summary of General Medical History
(Population: Phase 1 Intent-to-Treat Subjects)

	Treatment Group			
Variable	Dose 1 (N=xxx)	Dose 2 (N=xxx)	Dose 3 (N=xxx)	Total (N=xxx)

This table follows the same shell as
that for 1.3.2.2

PROGRAM\OUTPUT: T_MHIST.SAS\T_MHIST1.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.x.x.x.x

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Table 1.3.2.2

Summary of General Medical History
(Population: Phase 2 Intent-to-Treat Subjects)

MedDRA Organ Class/ MedDRA Preferred Term	Treatment Group: Cancer Type 1 (N=xxx)	Cancer Type 2 (N=xxx)	Cancer Type 3 (N=xxx)
Number (%) of Subjects with any General Medical History	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
xxxxxxxxxxxxxxxxxxxxxxxxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
xxxxxxxxxxxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
xxxxxxxxxxxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
xxxxxxxxxxxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
xxxxxxxxxxxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
xxxxxxxxxxxxxxxxxxxxxxxxxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
xxxxxxxxxxxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
xxxxxxxxxxxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
xxxxxxxxxxxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
xxxxxxxxxxxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
xxxxxxxxxxxxxxxxxxxxxxxxxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
xxxxxxxxxxxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
xxxxxxxxxxxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
xxxxxxxxxxxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
xxxxxxxxxxxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)

PROGRAM\OUTPUT: T_MHIST.SAS\T_MHIST1.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.x.x.x.x

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Table 1.4.1.1

Summary of Prior Medications
(Population: Phase 1 Intent-to-Treat Subjects)

	Treatment Group			
Variable	Dose 1 (N=xxx)	Dose 2 (N=xxx)	Dose 3 (N=xxx)	Total (N=xxx)

This table follows the same shell as
that for 1.4.1.2

PROGRAM\OUTPUT: T_MHIST.SAS\T_MHIST1.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.x.x.x.x

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Table 1.4.1.2

Summary of Prior Medications
(Population: Phase 2 Intent-to-Treat Subjects)

MedDRA Organ Class/ MedDRA Preferred Term	Treatment Group		
	Cancer Type 1 (N=xxx)	Cancer Type 2 (N=xxx)	Cancer Type 3 (N=xxx)
Subjects With Any Prior Medication	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
WHO Drug Class 1	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
WHO Preferred Term 1	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
WHO Preferred Term 2	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
WHO Preferred Term 3	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
WHO Preferred Term 4	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
WHO Drug Class 2	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
WHO Preferred Term 1	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
WHO Preferred Term 2	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
WHO Preferred Term 3	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
WHO Preferred Term 4	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
WHO Drug Class 3	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
WHO Preferred Term 1	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
WHO Preferred Term 2	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
WHO Preferred Term 3	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
WHO Preferred Term 4	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)

PROGRAM\OUTPUT: T XXXXXX\XXXXXX.SAS\XXXXXX.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.x.x.x.x

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Table 1.4.2.1

Summary of Concomitant Medications
(Population: Phase 1 Intent-to-Treat Subjects)

	Treatment Group			
Variable	Dose 1 (N=xxx)	Dose 2 (N=xxx)	Dose 3 (N=xxx)	Total (N=xxx)

This table follows the same shell as
that for 1.4.2.2

PROGRAM\OUTPUT: T_MHIST.SAS\T_MHIST1.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.x.x.x.x

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Table 1.4.2.2

Summary of Concomitant Medications
(Population: Phase 2 Intent-to-Treat Subjects)

MedDRA Organ Class/ MedDRA Preferred Term	Treatment Group: Cancer Type 1 (N=xxx)	Cancer Type 2 (N=xxx)	Cancer Type 3 (N=xxx)

This table follows the same shell as that for 1.4.1.2

PROGRAM\OUTPUT: T XXXXXX\XXXXXX.SAS\XXXXXX.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.x.x.x.x

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DRUG/INDICATION: xxxxxxxxxxx/xxxxxxxxxxxxx VERSION: Final

Table 1.4.3.1

Summary of Prior Medications for Cancer
(Population: Phase 1 Intent-to-Treat Subjects)

	Treatment Group			
Variable	Dose 1 (N=xxx)	Dose 2 (N=xxx)	Dose 3 (N=xxx)	Total (N=xxx)

This table follows the same shell as
that for 1.4.3.2

PROGRAM\OUTPUT: T_MHIST.SAS\T_MHIST1.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.x.x.x.x

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Table 1.4.3.2

Summary of Prior Medications for Cancer
(Population: Phase 2 Intent-to-Treat Subjects)

MedDRA Organ Class/ MedDRA Preferred Term	Treatment Group: Cancer Type 1 (N=xxx)	Cancer Type 2 (N=xxx)	Cancer Type 3 (N=xxx)

This table follows the same shell as that for 1.4.1.2

PROGRAM\OUTPUT: T XXXXXX\XXXXXX.SAS\XXXXXX.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.x.x.x.x

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Table 2.1.1

Kaplan-Meier Analysis of Progression-Free Survival by RECIST Criteria
(Population: Phase 1 Intent-to-Treat Subjects)

	Treatment Group		
Variable	Cohort 1 (N=xxx)	Cohort 2 (N=xxx)	Cohort 3 (N=xxx)
Number (%) of Subjects with Disease Progression or Death [1]			
Observed	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Deaths	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Disease Progression	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Censored	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Median Time to Event (95% CI) [3]	##.# (##.#,##.#)	##.# (##.#,##.#)	##.# (##.#,##.#)
Month 3 Survival Rate (95% CI)	##.# (##.#,##.#)	##.# (##.#,##.#)	##.# (##.#,##.#)
Month 6 Survival Rate (95% CI)	##.# (##.#,##.#)	##.# (##.#,##.#)	##.# (##.#,##.#)
Month 9 Survival Rate (95% CI)	##.# (##.#,##.#)	##.# (##.#,##.#)	##.# (##.#,##.#)
Month 12 Survival Rate (95% CI)	##.# (##.#,##.#)	##.# (##.#,##.#)	##.# (##.#,##.#)

PROGRAM\OUTPUT: T XXXXXX\XXXXXX.SAS\XXXXXX.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.x.x.x.x
[1] Progression free survival was the first occurrence of death or progressive disease by RECIST 1.1
[2] The median time and the 95% CI were estimated using Brookmeyer and Crowley.

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Table 2.1.2

Kaplan-Meier Analysis of Progression-Free Survival by RECIST Criteria
(Population: Phase 2 Intent-to-Treat Subjects)

Variable	Treatment Group: Cancer Type 1 (N=xxx)	Cancer Type 2 (N=xxx)	Cancer Type 3 (N=xxx)
Number (%) of Subjects with Disease Progression or Death [1]			
Observed	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Deaths	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Disease Progression	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Censored	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Median Time to Event (95% CI) [3]	##.# (##.#,##.#)	##.# (##.#,##.#)	##.# (##.#,##.#)
Month 3 Survival Rate (95% CI)	##.# (##.#,##.#)	##.# (##.#,##.#)	##.# (##.#,##.#)
Month 6 Survival Rate (95% CI)	##.# (##.#,##.#)	##.# (##.#,##.#)	##.# (##.#,##.#)
Month 9 Survival Rate (95% CI)	##.# (##.#,##.#)	##.# (##.#,##.#)	##.# (##.#,##.#)
Month 12 Survival Rate (95% CI)	##.# (##.#,##.#)	##.# (##.#,##.#)	##.# (##.#,##.#)

PROGRAM\OUTPUT: T XXXXXX\XXXXXX.SAS\XXXXXX.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.x.x.x.x
[1] Progression free survival was the first occurrence of death or progressive disease by RECIST 1.1
[2] The median time and the 95% CI were estimated using Brookmeyer and Crowley.

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Table 2.2.1.1

Summary of Best Response by RECIST Criteria
(Population: Phase 1 Intent-to-Treat Subjects)

	Treatment Group		
Variable	Dose 1 (N=xxx)	Dose 2 (N=xxx)	Dose 3 (N=xxx)
Overall Response	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Complete Response	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Partial Response	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stable Disease	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Progressive Disease	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Unable to Evaluate	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)

PROGRAM\OUTPUT: T_MHIST.SAS\T_MHIST1.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.x.x.x.x

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Table 2.2.1.2

Summary of Best Response by RECIST Criteria
(Population: Phase 2 Intent-to-Treat Subjects)

Variable	Treatment Group		
	Cancer Type 1 (N=xxx)	Cancer Type 2 (N=xxx)	Cancer Type 3 (N=xxx)
Overall Response	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Complete Response	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Partial Response	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stable Disease	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Progressive Disease	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Unable to Evaluate	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)

PROGRAM\OUTPUT: T XXXXXX\XXXXXX.SAS\XXXXXX.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.x.x.x.x

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Table 2.2.4.1

Summary of Duration of Response
(Population: Phase 1 Intent-to-Treat Subjects)

Variable	Treatment Group: Dose 1 (N=xxx)	Dose 2 (N=xxx)	Dose 3 (N=xxx)

This table follows the same shell as that for 2.2.5.2

PROGRAM\OUTPUT: T XXXXXX\XXXXXX.SAS\XXXXXX.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.x.x.x.x
[1] The median time and the 95% CI was estimated using Brookmeyer and Crowley.

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Table 2.2.4.2

Summary of Duration of Response
(Population: Phase 2 Intent-to-Treat Subjects)

Variable	Treatment Group: Cancer Type 1 (N=xxx)	Cancer Type 2 (N=xxx)	Cancer Type 3 (N=xxx)
RECIST Criteria			
Number of Responders (%)	### (xxx.x)	### (xxx.x)	### (xxx.x)
Median Duration of Response (Range) [1]	##.# (##.#,##.#)	##.# (##.#,##.#)	##.# (##.#,##.#)

PROGRAM\OUTPUT: T XXXXXX\XXXXXX.SAS\XXXXXX.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.x.x.x.x
[1] The median time and the 95% CI was estimated using Brookmeyer and Crowley.

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DRUG/INDICATION: xxxxxxxxxxx/xxxxxxxxxxxxx VERSION: Final

TABLE 3.1.1.1

Summary of Exposure and Duration of Exposure to INCB024360 and MEDI4736
(Population: Phase 1 Intent-to-Treat Subjects)

	Treatment Group		
	Dose 1 (N=xxx)	Dose 2 (N=xxx)	Dose 3 (N=xxx)

This table follows the same shell as that for 3.1.1.2

FOLDER\PROGRAM\OUTPUT: XXXXXX\XXXXXX.SAS\XXXXXX.LST DATE(TIME): MMDDYYYY(hh:mm)

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TABLE 3.1.1.2

Summary of Exposure and Duration of Exposure to INCB024360 and MEDI4736
(Population: Phase 2 Intent-to-Treat Subjects)

	Treatment Group		
	Cancer Type 1 (N=xxx)	Cancer Type 2 (N=xxx)	Cancer Type 3 (N=xxx)
Days of Exposure to INCB024360			
N	###	###	###
Mean (STD)	##.## (#.###)	##.## (#.###)	##.## (#.###)
Median	##.##	##.##	##.##
(Q1,Q3)	(##.##,##.##)	(##.##,##.##)	(##.##,##.##)
(MIN,MAX)	(##.##,##.##)	(##.##,##.##)	(##.##,##.##)
Average Daily Dose (mg) of INCB024360			
N	###	###	###
Mean (STD)	##.## (#.###)	##.## (#.###)	##.## (#.###)
Median	##.##	##.##	##.##
(Q1,Q3)	(##.##,##.##)	(##.##,##.##)	(##.##,##.##)
(MIN,MAX)	(##.##,##.##)	(##.##,##.##)	(##.##,##.##)
Dose Intensity (%) of INCB024360			
N	###	###	###
Mean (STD)	##.## (#.###)	##.## (#.###)	##.## (#.###)
Median	##.##	##.##	##.##
(Q1,Q3)	(##.##,##.##)	(##.##,##.##)	(##.##,##.##)
(MIN,MAX)	(##.##,##.##)	(##.##,##.##)	(##.##,##.##)

FOLDER\PROGRAM\OUTPUT: XXXXXX\XXXXXX.SAS\XXXXXX.LST DATE(TIME): MMDDYYYY(hh:mm)

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DRUG/INDICATION: xxxxxxxxxxx/xxxxxxxxxxxxx VERSION: Final

TABLE 3.1.1.2

Summary of Exposure and Duration of Exposure to INCB024360 and MEDI4736
(Population: Phase 2 Intent-to-Treat Subjects)

	Treatment Group		
	Cancer Type 1 (N=xxx)	Cancer Type 2 (N=xxx)	Cancer Type 3 (N=xxx)
Days of Exposure to MEDI4736			
N	###	###	###
Mean (STD)	##.## (#.###)	##.## (#.###)	##.## (#.###)
Median	##.##	##.##	##.##
(Q1,Q3)	(##.##,##.##)	(##.##,##.##)	(##.##,##.##)
(MIN,MAX)	(##.##,##.##)	(##.##,##.##)	(##.##,##.##)
Number of Doses of MEDI4736			
0	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
1	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
2	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
3	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
4	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)

FOLDER\PROGRAM\OUTPUT: XXXXXX\XXXXXX.SAS\XXXXXX.LST DATE(TIME): MMDDYYYY(hh:mm)

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Table 3.5.7.1

Summary of Treatment Emergent, Clinically Significant ECG Abnormality from Baseline
(Population: Phase 1 Safety Subjects)

MedDRA Organ Class/ MedDRA Preferred Term	Treatment Group		
	Cohort 1 (N=xxx)	Cohort 2 (N=xxx)	Cohort 3 (N=xxx)
Number (%) of Subjects With a Postbaseline ECG Evaluation	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Number (%) of Subjects With a Clinically Significant Post-Baseline ECG Abnormality	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)

PROGRAM\OUTPUT: T XXXXXX\XXXXXX.SAS\XXXXXX.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.x.x.x.x

Signature Manifest

Document Number: IC-STS-SAP-0048 **Revision:** 0

Title: INCB24360-203 Statistical Analysis Plan

All dates and times are in Eastern Standard Time.

INCB24360-203 SAP

Approval

Name/Signature	Title	Date	Meaning/Reason
[redacted]		26 Nov 2014, 03:08:47 PM	Approved
		26 Nov 2014, 03:20:58 PM	Approved
		04 Dec 2014, 02:11:35 PM	Approved
		09 Dec 2014, 10:58:15 AM	Approved