STATISTICAL ANALYSIS PLAN

Epacadostat, Nivolumab

INCB 24360-204 / NCT02327078

(CA209)

A Phase 1/2 Study of the Safety, Tolerability, and Efficacy of Epacadostat Administered in Combination With Nivolumab in Select Advanced Cancers

IND Number:	**122,945**
EudraCT Number:	**2016-002423-29**
Sponsor:	**Incyte Corporation** **1801 Augustine Cut-Off** **Wilmington, DE 19803** **(In collaboration with Bristol-Myers Squibb)**
Protocol Version:	**Protocol Amendment 8 dated 31 MAY 2018**
CRF Approval Date:	**14 SEP 2018**
SAP Version:	**Amendment 1**
SAP Author:	[redacted] **PhD** [redacted]
Date of Plan:	**05 MAR 2019**

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

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

Abbreviation	Term
[redacted]	[redacted]
AE	adverse event
ALT	alanine aminotransferase
AST	aspartate aminotransferase
[redacted]	[redacted]
[redacted]	[redacted]
BID	twice daily
CI	confidence interval
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
CR	complete response
CRC	colorectal cancer
CRF	case report form
CSF	cerebrospinal fluid
CTCAE	Common Terminology Criteria for Adverse Events
DLBCL	diffuse large B-cell lymphoma
DOR	duration of response
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
EGFR	epidermal growth factor receptor
EOT	end of treatment
FDA	Food and Drug Administration
FAS	full analysis set
HL	Hodgkin lymphoma
HPV	human papilloma virus
IDO	indoleamine 2,3–dioxygenase
I/O	immuno-oncology
IV	intravenously
MedDRA	Medical Dictionary for Regulatory Activities
MEL	melanoma
MTD	maximum tolerated dose

Abbreviation	Term
NCI	National Cancer Institute
NE	not evaluable
NHL	non-Hodgkin lymphoma
NSCLC	non–small cell lung cancer
ORR	overall response rate
OS	overall survival
PAD	pharmacologically active dose
PD	progressive disease
PD-L1	programmed death-ligand 1
PFS	progression-free survival
[redacted]	[redacted]
PR	partial response
Q2W	every 2 weeks
Q3W	every 3 weeks
Q4W	every 4 weeks
RANO	Response Assessment in Neuro-Oncology
RD	relapsed disease
RECIST	Response Evaluation Criteria in Solid Tumors
RP2D	recommended Phase 2 dose
TIL	tumor-infiltrating lymphocyte
TNM	tumor, node, metastasis (classification system)
SAE	serious adverse event
SAP	Statistical Analysis Plan
SCCHN	squamous cell carcinoma of the head and neck
SD	stable disease
[redacted]	[redacted]
[redacted]	[redacted]
TEAE	treatment-emergent adverse event
[redacted]	[redacted]
WHO	World Health Organization

1. INTRODUCTION

The INCB 24360-204 study is a Phase 1/2 dose-escalation and cohort expansion study of the safety, tolerability, and efficacy of epacadostat administered in combination with nivolumab or in combination of nivolumab and chemotherapy in subjects with selected advanced cancers. A detailed description of the investigational products, target patient population, rationale for doses to be examined, and potential risks and benefits of treatment with epacadostat and nivolumab or epacadostat in combination with nivolumab and chemotherapy 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 24360-204.

[redacted]

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 24360-204 Protocol Amendment 8 dated 31 MAY 2018 and case report form (CRF) dated 14 SEP 2018. 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

2.2.1.1. Phase 1

- **Part 1 Safety:** To assess the safety and tolerability of epacadostat twice daily (BID) orally in combination with nivolumab, and to identify dose-limiting toxicities and the recommended Phase 2 dose (RP2D) of the combination immunotherapy, in subjects with select advanced (metastatic and/or unresectable) cancers (solid tumors and B-cell non-Hodgkin lymphoma [NHL] or Hodgkin lymphoma [HL]).
- **Part 2 Safety:** To assess the safety and tolerability and to determine a maximum tolerated dose (MTD) and/or pharmacologically active dose (PAD) of epacadostat in combination with nivolumab and chemotherapy in subjects with advanced or metastatic squamous cell carcinoma of head and neck (SCCHN) and in subjects with advanced or metastatic non–small cell lung cancer (NSCLC).

2.2.1.2. Phase 2

- **Efficacy:**
  - To assess objective response rate (ORR) and progression-free survival (PFS) at 6 months in subjects with select solid tumors or subjects with diffuse large B-cell lymphoma (DLBCL).
  - To assess overall survival (OS) at 9 months for subjects with glioblastoma.

2.2.2. Secondary Objectives

2.2.2.1. Phase 1

- **Part 1 Efficacy:** To assess the preliminary antitumor activity of the combination of epacadostat and nivolumab in subjects with select advanced solid tumors, B-cell NHL or HL, or glioblastoma by assessing ORR.
- **Part 2 Efficacy:** To explore the preliminary efficacy of epacadostat administered in combination with nivolumab and chemotherapy in subjects with advanced or metastatic SCCHN and advanced or metastatic NSCLC by assessing ORR, duration of response (DOR), and PFS.

2.2.2.2. Phase 2

- **Efficacy:**
  - To assess the preliminary antitumor activity of the combination of epacadostat and nivolumab in subjects with select advanced solid tumors and DLBCL by assessing DOR and duration of disease control.
  - To evaluate OS in subjects with select solid tumors and DLBCL.
  - To evaluate ORR, PFS, DOR, and duration of disease control for subjects with glioblastoma.
- **Safety:**
  - To assess the safety and tolerability of epacadostat BID orally when given in combination with nivolumab 240 mg every 2 weeks.
  - To assess the safety and tolerability of epacadostat BID orally when given in combination with nivolumab 480 mg every 4 weeks.

2.3. Study Endpoints

2.3.1. Primary Endpoints

2.3.1.1. Phase 1

- **Safety:** In Part 1 and Part 2 of Phase 1 of the study, all subjects who receive at least 1 dose of epacadostat or nivolumab will be assessed for safety by monitoring the frequency and severity of adverse events (AEs), serious adverse events (SAEs), and deaths.

2.3.1.2. Phase 2

- **Efficacy:**
  - The ORR and PFS at 6 months will be assessed based on RECIST v1.1 criteria for subjects with select solid tumors or Cheson criteria (Cheson et al 2007) for subjects with DLBCL.
  - OS will be assessed at 9 months for subjects with glioblastoma as determined by death due to any cause.

2.3.2. Secondary Endpoints

2.3.2.1. Phase 1

- **Part 1 Efficacy:** The ORR will be assessed per RECIST v1.1 and modified RECIST for subjects with select advanced solid tumors, Cheson and modified Cheson criteria for B-cell NHL or HL, and Response Assessment in Neuro-Oncology (RANO) and modified RANO criteria for glioblastoma.
- **Part 2 Efficacy:** The ORR, DOR, and PFS will be assessed per RECIST v1.1 and modified RECIST for subjects with advanced or metastatic SCCHN and advanced or metastatic NSCLC treated with epacadostat in combination with nivolumab and chemotherapy.

2.3.2.2. Phase 2

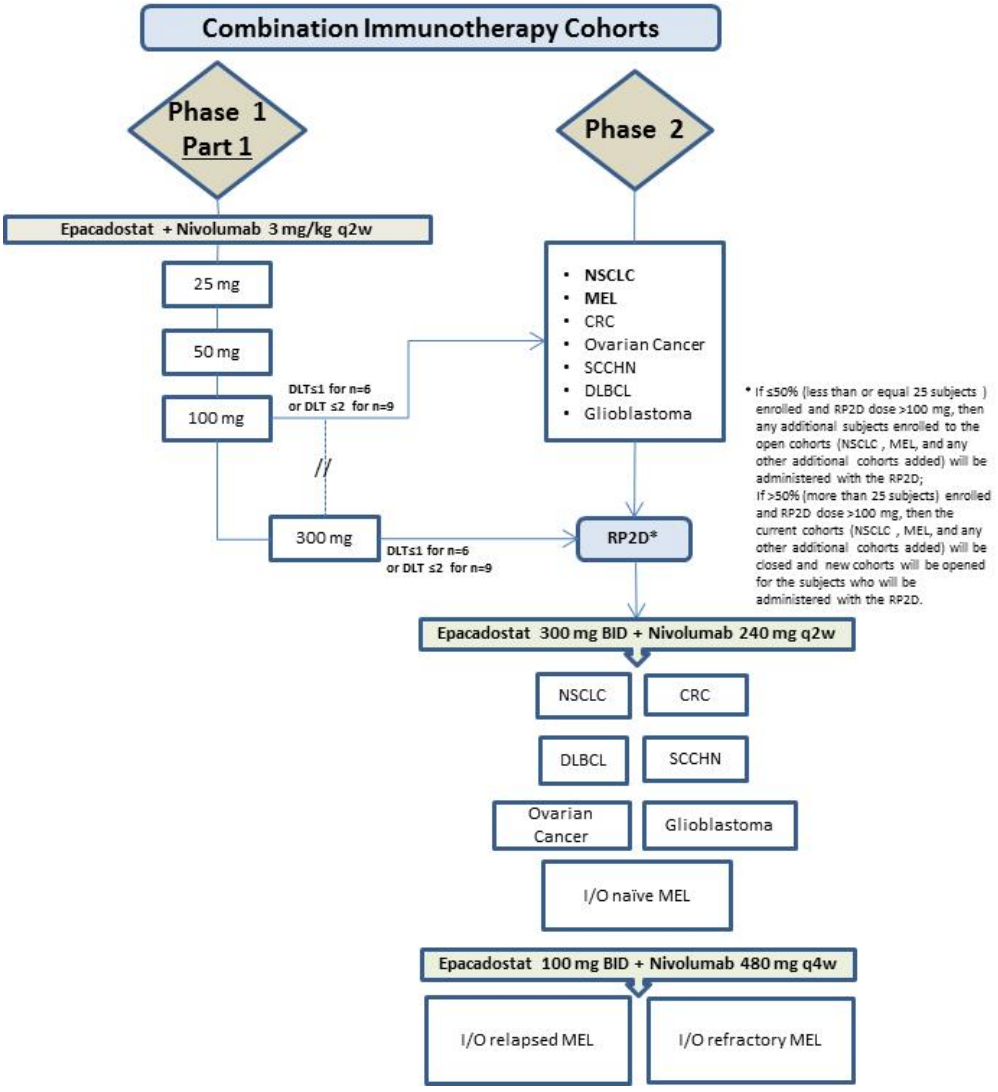
- **Efficacy:** The DOR and duration of disease control will be assessed based on RECIST v1.1 criteria and modified RECIST for select solid tumors, Cheson and modified Cheson criteria for DLBCL, or RANO and modified RANO criteria for subjects with glioblastoma. Overall survival will be evaluated for solid tumors and DLBCL cohorts. Objective response rate and PFS will be assessed for glioblastoma per modified RANO.
- **Safety:** All subjects who receive at least 1 dose of epacadostat or nivolumab will be assessed for safety by monitoring the frequency and severity of AEs, SAEs, and deaths.

3. STUDY DESIGN

This is a Phase 1/2, open-label study that will be conducted in 2 phases. Phase 1 of the study will consist of 2 parts (Part 1 and Part 2).

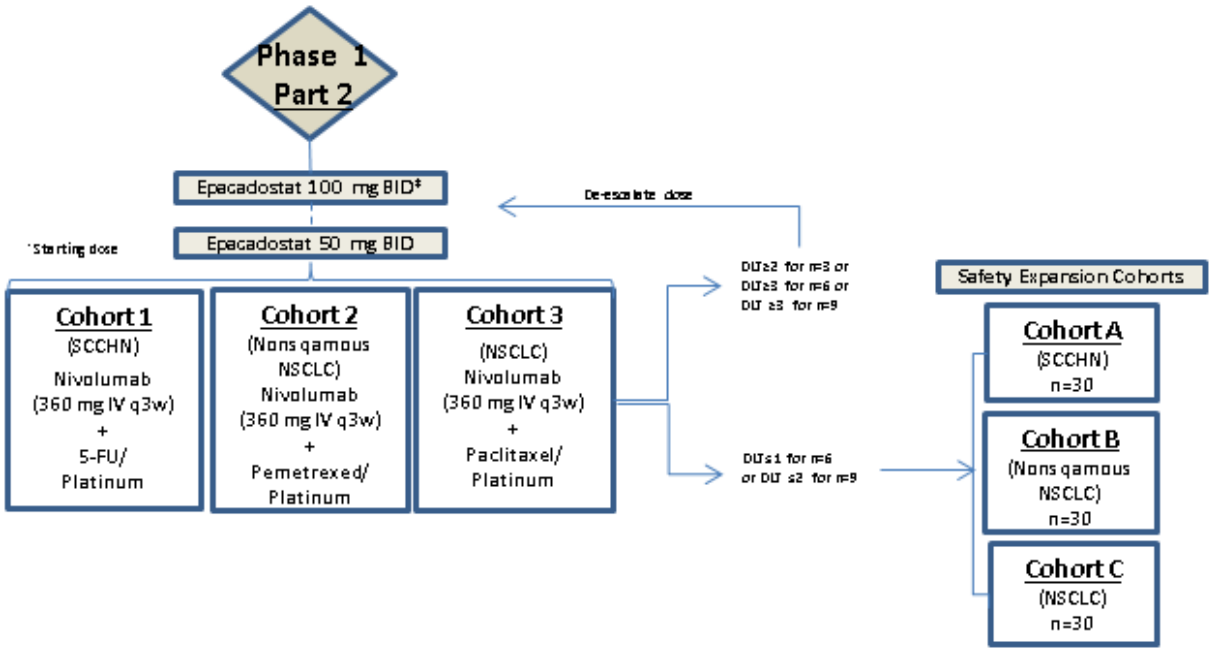
Part 1 of Phase 1 will consist of a dose-escalation design to determine the MTD or PAD of epacadostat administered with nivolumab (BMS-936558) 3 mg/kg in subjects with select advanced solid tumors and lymphomas including melanoma (MEL), NSCLC, colorectal cancer (CRC), SCCHN, ovarian cancer, and B cell NHL or HL including DLBCL (see Figure 1).

Figure 1: Study Design for Combination Immunotherapy Cohorts (Phase 1 Part 1 and Phase 2)



Part 2 of Phase 1 will evaluate the preliminary safety of epacadostat in combination with nivolumab and several chemotherapy regimens (defined as combination chemo-immunotherapy) in subjects with SCCHN and NSCLC by using a dose de-escalation design. The starting dose of epacadostat in Part 2 will be the RP2D of epacadostat selected for the use of combination immunotherapy in Part 1. Initial dose-finding cohorts in Part 2 will be expanded to safety expansion cohorts and will further evaluate tolerated dose(s) of epacadostat when given in combination with nivolumab and chemotherapy regimens (see Figure 2).

Figure 2: Study Design for Combination Chemo-Immunotherapy Cohorts (Part 2 of Phase 1 Only)



Phase 2 of the study will include 9 expansion cohorts in tumor types tested in Phase 1 Part 1 (expect DLBCL will be the only lymphoma permitted) with a) historically good activity under nivolumab monotherapy, and b) with historically low activity with nivolumab monotherapy. In Phase 2 of the study, nivolumab will be administered at 240 mg intravenously (IV) every 2 weeks or 480 mg IV every 4 weeks for specific tumor types as described in Figure 1.

3.1. Randomization

Not applicable.

3.2. Control of Type I Error

The level of significance for the each of the 2 primary endpoints in Phase 2 is 1-sided 2.5% for the NSCLC, MEL (including immuno-oncology (I/O)-naive, I/O-relapsed, and I/O-refractory cohorts), SCCHN, DLBCL, ovarian cancer, and CRC cohorts, which is based on Bonferroni correction for Type I error 5% due to dual primary endpoints. The level of significance is 1-sided 5% for the glioblastoma cohort.

3.3. Sample Size Considerations

3.3.1. Cohort Size in Part 1 and Part 2 of Phase 1

The primary objective of Phase 1 Part 1 is to determine the RP2D of epacadostat in combination with nivolumab, and the primary objective of Phase 1 Part 2 is to determine the safe dose of epacadostat in combination with nivolumab and chemotherapy. The total number of subjects will depend on the number of dose levels tested before the MTD or PAD is established. Up to approximately 63 subjects (9 subjects per dose level for 7 dose levels) will be enrolled in Part 1 of Phase 1 for the dose escalation of epacadostat when administered with nivolumab (the combination immunotherapy cohorts). Up to 81 subjects (9 subjects per dose level for up to 3 dose levels in 3 combination chemo-immunotherapy cohorts) will be enrolled in Part 2 of Phase 1 for the dose finding of epacadostat in combination with nivolumab and chemotherapy (the combination chemo-immunotherapy cohorts). Additionally, 30 subjects will be enrolled into each of the safety expansion of combination chemo-immunotherapy cohorts (epacadostat + nivolumab + chemotherapy): Cohort A, Cohort B, and Cohort C. Table 1 below tabulates the probability of observing a toxicity in a cohort of 30 subjects for various event rates. Overall sample size in Phase 1 (Part 1 and Part 2) will be up to approximately 234 subjects.

Table 1: Probability of Observing a Toxicity for Various Safety Event Rates

True Probability of Subjects Having an AE	Probability of Observing an AE
5%	78.5%
10%	95.8%
15%	99.2%
20%	99.9%

3.3.2. Sample Size in Phase 2

The sample size of 25 subjects are expected to be enrolled in each of the 4 low historic response expansion cohorts (CRC, SCCHN, ovarian cancer, and DLBCL) as well as the I/O-relapsed MEL and I/O-refractory MEL cohorts, and 50 subjects in each of the 2 higher historic ORR cohorts (NSCLC and I/O-naive MEL). The sample size for each independent cohort yields a power of 80% to detect the following: 1) A target ORR of 17% to 26% increase (Ha) from historical response rate (H0), or 2) a PFS rate at 24 weeks of 14% to 22% increase (Ha) from historical survival probability (H0). This assumes a 1-sided alpha of 2.5% (based on Bonferroni adjustment due to dual primary endpoints), 10% lost to follow-up, enrollment period of 6 to 10 months (depends on cohort), and 6 to 10 months of follow-up (depends on cohort) after last subject enrolled. See details in Table 2. Twenty-eight subjects are expected to be enrolled in the glioblastoma cohort. This sample size for the glioblastoma cohort yields a power of 80% to detect an OS rate at 9 months of 25% increase (Ha) from historical survival probability (H0). This assumes a 1-sided alpha of 5%, 10% lost to follow-up, enrollment period of 4 months, and 9 months of follow-up after last subject enrolled. Details are shown in Table 3.

Table 2: Sample Size Calculation for Each Cohort: Comparing to a Known Proportion

Tumor Type (Cohort)	ORR		PFS at 6 Months		Accrual Time	Minimum Follow-Up Time	Sample Size
	H0	Ha	H0	Ha			
NSCLC	24%	43%	45%	65%	6 months	6 months	50
I/O-naive MEL	32%	52%	50%	67%	6 months	10 months	50
I/O-relapsed MEL	5%	22%	5%	19%	10 months	6 months	25
I/O-refractory MEL	5%	22%	5%	19%	10 months	6 months	25
SCCHN	19%	44%	15%	37%	10 months	6 months	25
DLBCL	5%	22%	15%	37%	10 months	6 months	25
Ovarian cancer	20%	46%	15%	37%	10 months	6 months	25
CRC	5%	22%	15%	37%	10 months	6 months	25

Table 3: Sample Size Calculation for Glioblastoma Cohort: Comparing to a Known Proportion

Tumor Type (Cohort)	OS at 36 Weeks		Accrual Time	Minimum Follow-Up Time	Sample Size
	H0	Ha			
Glioblastoma	50%	75%	4 months	9 months	28

3.4. Schedule of Assessments

See Protocol Amendment 8 dated 31 MAY 2018 for a full description of all study procedures and assessment schedules for this study.

4. DATA HANDLING DEFINITIONS AND CONVENTIONS

4.1. Scheduled Study Evaluations and Study Periods

4.1.1. Day 1

Day 1 is the date of first dose of study treatment, including epacadostat or nivolumab or the chemotherapy drugs.

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. Baseline Value

Baseline is defined as the last nonmissing measurement obtained before the first dose of study treatment is administered, unless otherwise defined.

4.1.4. Handling of Missing and Incomplete Data

In general, values for missing data will not be imputed unless methods for handling missing data are specified in this section or relevant sections.

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

- If only the day is missing, then use the first day of the month.
- If both the month and day are missing, then use 01 JAN of the year.
- Time since cancer diagnosis will be missing if the diagnosis date is completely missing.

Missing or partial date of last dose will be handled as follows:

- If only the day is missing, then the imputed date of the last dose will be the earlier date of the last day of the month or the date that the subject discontinued treatment.
- Otherwise, the date that the subject discontinued treatment will be used as the date of the last dose.

When calculating PFS, DOR, and OS, partial date of death will be handled as follows in the calculation:

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

4.1.5. Cycle Length and Duration

Cycle 1 Day 1 is defined as the day of the first dose of study treatment. Subsequent cycles have Day 1 as the corresponding visit date associated with the corresponding cycle.

4.2. Variable Definitions

4.2.1. Prior and Concomitant Medication

Prior medication is defined as any nonstudy drug started before the administration of first dose of study treatment.

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

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

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

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

5. STATISTICAL METHODOLOGY

5.1. General Methodology

Unless otherwise noted, SAS® software (SAS Institute Inc, Cary, NC; v9.1 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.

5.2. Treatment Groups

Data from Phase 1 Part 1, Phase 1 Part 2, and Phase 2 will be summarized separately.

For Phase 1 Part 1, data will be summarized by initial assigned dose levels. Disease-specific outputs, such as cancer history and prior medication for cancer, will be provided by cancer type and initial assigned dose level. Efficacy data will only be listed. All data listings will be grouped by cancer type and initial assigned dose level.

For Phase 1 Part 2, only 6 subjects with SCCHN, 3 subjects with nonsquamous NSCLC, and 3 subjects with NSCLC have been treated with epacadostat 100 mg BID, nivolumab 360 mg Q3W plus fluorouracil/platinum, pemetrexed/platinum, or paclitaxel/platinum, respectively. Summary tables will be provided for subject disposition, demographics, and exposure to epacadostat. Listings will be provided for all data in Phase 1 Part 2, grouped by cancer type and chemo-immunotherapy combination. Selected AE summary tables may also be provided.

For Phase 2, all efficacy data, demographics, baseline characteristics, cancer history, and prior medications for cancer will be summarized by cancer type/cohort and initial assigned dose level. Disposition, other baseline and safety data will be pooled for all Phase 2 cohorts and summarized by initial assigned dose level. For the purpose of summary tables, data from subjects treated with epacadostat 100 mg BID/nivolumab 240 mg Q2W and epacadostat 100 mg BID/nivolumab 480 mg Q4W will be combined due to the equivalence and interchangeability of the 2 dosing frequencies of nivolumab. Listings will be grouped by cancer type/cohort and initial assigned dose level.

5.3. Analysis Populations

5.3.1. Full Analysis Set

The full analysis set (FAS) will include all subjects enrolled in the study who take at least 1 dose of study drug. The FAS will be used for the summary of demographics, baseline characteristics, and subject disposition and analyses of all efficacy data.

5.3.2. Safety Population

The safety population will include all subjects enrolled in the study who received at least 1 dose of study drug. All safety analyses will be conducted using the safety population.

[redacted]

6. BASELINE, EXPOSURE, AND DISPOSITION VARIABLES AND ANALYSES

Appendix A provides a list of planned tables, figures, and listings.

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

6.1.1. Demographics and Baseline Disease Characteristics

The following demographics will be summarized for the FAS: age and age group (< 65 years old vs ≥ 65 years old), sex, race, ethnicity, weight, height. Additionally, ECOG performance status will be summarized.

6.1.2. Disease History

The disease history will be summarized by cancer types:

- NSCLC
  - Time since diagnosis; stage at initial diagnosis; tumor, node, metastasis (TNM) classification; histopathology; prior treatment with tyrosine-kinase inhibitor; tumor-infiltrating lymphocytes (TILs) at initial diagnosis; current stage; current TILs; current sites of metastases; epidermal growth factor receptor (EGFR) mutation status; KRAS mutation status; anaplastic lymphoma kinase re-arrangement status; smoking history (never smoked vs former smoker vs current smoker vs unknown); PD-L1 status (positive vs negative vs unknown); and IDO1 status (positive vs negative vs unknown)
- MEL
  - Time since diagnosis, stage at initial diagnosis, TNM classification, and TILs at initial diagnosis, primary site of disease, current stage, current M classification, current TILs, current sites of disease, BRAF mutation status, baseline serum LDH level (elevated vs normal), PD-L1 status (positive vs negative vs unknown), and IDO1 status (positive vs negative vs unknown)

- SCCHN
  - Time since initial diagnosis, stage at initial diagnosis, site of primary tumor, differentiation of tumor, TNM classification, TILs at initial diagnosis, current stage, currently reported TILs, current sites of disease, human papilloma virus (HPV) status, derived HPV status (positive if site of primary tumor is oropharynx and HPV marker or p16 marker is positive), EGFR mutation status, p53 status, smoking history (never smoked vs former smoker vs current smoker vs unknown), PD-L1 status (positive vs negative vs unknown), and IDO1 status (positive vs negative vs unknown)
- Ovarian cancer
  - Time since initial diagnosis, International Federation of Gynecology and Obstetrics staging grade, histology, TILs at initial diagnosis, current stage, currently reported TILs, current sites of disease, BRCA testing
- CRC
  - Time since diagnosis, primary site of disease, histology, stage at initial diagnosis, TILs at initial diagnosis, current stage, current TILs, current sites of metastases, KRAS mutation status, BRAF mutation status, EGFR mutation status, microsatellite instability, p53 status
- DLBCL or other B-cell lymphomas
  - Time since diagnosis, disease subtype, cytogenetics, Ann Arbor staging, International Prognostic Index
- Glioblastoma
  - Time since initial diagnosis; basis of initial diagnosis; initial tumor WHO grade; any infratentorial, supratentorial, or cerebrospinal fluid (CSF) involvement at initial diagnosis; cerebral hemisphere (left or right) at initial diagnosis; TILs at initial diagnosis; current tumor WHO grade; any current infratentorial, supratentorial, or CSF involvement; current cerebral hemisphere (left or right); multifocal disease (yes or no); current sites of disease; MGMT status

6.1.3. Prior Therapy

The number of prior systemic cancer therapy regimens will be summarized. The component drugs of prior systemic therapy regimens will be coded using the WHO Drug Dictionary. Number and percentage of subjects receiving each drug will be summarized by WHO drug class and WHO drug preferred term. Regimen name, component drugs, start and stop date, purpose of the regimen, best response, reason for discontinuation, and date of relapse/progression will be listed. Additionally, number of prior systemic therapy in advanced or metastatic setting will be summarized for all cancer types as applicable.

The number of subjects who received prior radiation will be summarized. Radiotherapy type, body site, start and stop date, total dose, and best response will be listed. Radiotherapy technique/method will also be listed for subjects with glioblastoma.

The number of subjects who had prior surgery or surgical procedure(s) for the malignancies under study will be summarized. Date and description of the surgery/procedure will be listed. Extent of resection will also be listed for subjects with glioblastoma.

For subjects with lymphoma, the number of subjects who had hematopoietic stem cell transplant will be summarized. The date/type of transplant, source of cells, line of therapy setting, best response, regimen name, and drug used with the transplant will be listed.

6.2. Disposition of Subjects

The number and percentage of subjects who were treated, discontinued study treatment (with a primary reason for discontinuation), and who were withdrawn from the study (with a primary reason for withdrawal) will be summarized for the FAS population.

6.3. Protocol Deviations

Protocol deviations captured on the Protocol Deviation CRF will be summarized and listed.

6.4. Exposure

For subjects in the safety population, descriptive statistics will be provided for duration of treatment with epacadostat, average reported daily dose of epacadostat, and dose modifications of epacadostat and duration of treatment with nivolumab, number of doses of nivolumab, and dose modifications of nivolumab.

- **Duration of treatment with epacadostat (days):** The duration of treatment will be the number of study days between Day 1 and the last nonzero dosing record of epacadostat taken by the subject.
- **Average reported daily dose of epacadostat (mg/day):** Total reported epacadostat dose taken (mg) / duration of treatment with epacadostat (days).
- **Epacadostat dose modifications:** The number of subjects who had epacadostat dose reductions and/or interruptions will be summarized.
- **Duration of treatment with nivolumab (days):** The duration of treatment will be the number of study days between Day 1 and the last nonzero dosing record of nivolumab taken by the subject.
- **Number of doses of nivolumab:** The number of doses of nivolumab for a subject will be the number of administered infusions of nivolumab recorded on the nivolumab dosing CRF.
- **Nivolumab dose modifications:** The number of subjects who had nivolumab dose interruptions will be summarized.

6.5. Study Drug Compliance

For subjects in the safety population, overall compliance (%) for epacadostat will be calculated for all subjects as follows:

Overall Compliance (%) = 100 × [total dosage taken] / [intended dosage].

Intended dosage is defined as the sum of the doses (total dosage, not number of 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 FAS population, medical history will be summarized. 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 Medications

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

7. EFFICACY

Appendix A provides a list of planned tables, figures, and listings. Sample data displays are included in a separate document.

7.1. Efficacy Hypotheses

Not applicable.

7.2. Analysis of the Efficacy Parameters

7.2.1. Response Assessment

For subjects with solid tumors (NSCLC, MEL, CRC, ovarian cancer, and SCCHN), overall response will be evaluated as complete response (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 per RECIST v1.1.

For subjects with lymphomas, including DLBCL, overall response will be evaluated as CR, PR, SD, relapsed disease (RD)/PD, or NE at each postbaseline radiological assessment per Cheson criteria. (At the time of the SAP Amendment 1, no Waldenström's macroglobulinemia subjects have been enrolled in the study).

For subjects with glioblastoma, overall response will be evaluated as CR, PR, SD, PD, or NE at each postbaseline radiological assessment per RANO criteria. Complete response/PR must be confirmed by a consecutive assessment $\geq$ 4 weeks apart.

7.2.2. Best Overall Response and Objective Response Rate

In general, best overall response is determined at subject level using the best response achieved postbaseline, before and including the first PD, in the order of CR, PR, SD, PD (RD/PD for subjects with lymphoma), and NE. In the case of SD, assessments must meet the SD criteria at least once after starting treatment at a minimum interval of 49 days. Subjects that fail to meet these criteria will have best response of PD if the next available assessment after the initial assessment indicates PD or NE if there are no additional assessments available.

Overall ORR is defined as the proportion of subjects with best response of CR or PR (objective responders). Subjects who do not have sufficient baseline or on-study response assessment information to be adequately assessed for response status will be included in the denominators in the calculation of ORR.

Best overall response as determined will be summarized descriptively. The ORR and its 95% confidence intervals (CIs) will be calculated. Confidence intervals will be calculated based on the exact method (ie, Clopper-Pearson) for binomial distributions. For the Phase 2 I/O-naive MEL, NSCLC, and SCCHN cohorts, best overall response and ORR will be summarized similarly by PD-L1 status (positive vs negative vs unknown) and by IDO1 status (positive vs negative vs unknown).

7.2.3. Progression-Free Survival

Progression-free survival is defined as the number of days from the first dose administration to the earlier of death or disease PD (PD/RD for subjects with lymphoma). Time-to-event data will be analyzed by the Kaplan-Meier method. Censoring for PFS will follow the algorithm outlined in Table 4, which is based on FDA guidance (FDA 2007). The Kaplan-Meier estimate of median PFS and its 95% CIs will be provided, with the CIs calculated using the generalized Brookmeyer and Crowley's method (1982) with log-log transformation (Klein and Moeschberger 1997). Progression-free survival rates at Months 6, 12, and 18, when applicable, will also be provided with 95% CIs calculated using Greenwood's formula to estimate the standard error. For the Phase 2 I/O-naive MEL, NSCLC, and SCCHN cohorts, PFS data will be summarized similarly by PD-L1 status (positive vs negative vs unknown) and by IDO1 status (positive vs negative vs unknown).

7.2.4. Duration 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 the first overall response of PD (PD/RD for subjects with lymphoma). Censoring of DOR will follow the same algorithm as the censoring of PFS (see Table 4). The Kaplan-Meier estimate of median DOR and its 95% CIs will be provided, with the CIs calculated using the generalized Brookmeyer and Crowley's method (1982) with log-log transformation (Klein and Moeschberger 1997). Event-free survival rates at Months 6, 12, and 18, when applicable, will also be provided with 95% CIs calculated using Greenwood's formula to estimate the standard error.

7.2.5. Duration of Disease Control

Duration of disease control is defined as the time from the first dose of study treatment to the first date of tumor assessment of PD (PD/RD for subjects with lymphoma) or death for subjects who had SD or better. Censoring of duration of disease control will follow the same algorithm as the censoring of PFS (see Table 4). . The Kaplan-Meier estimate of median duration of disease control and its 95% CIs will be provided, with the CIs calculated using the generalized Brookmeyer and Crowley's method (1982) with log-log transformation (Klein and Moeschberger 1997). Event-free survival rates at Months 6, 12, and 18, when applicable, will also be provided with 95% CIs calculated using Greenwood's formula to estimate the standard error.

7.2.6. Overall Survival

Overall survival is defined as the time from the date of the first dose of study treatment to death due to any cause. For subjects who are still alive at the time of the analysis, OS will be censored on the date the subjects are last known to be alive. The Kaplan-Meier estimate of median OS and its 95% CIs will be provided, with the CIs calculated using the generalized Brookmeyer and Crowley's method (1982) with log-log transformation (Klein and Moeschberger 1997). Survival rates at Months 6, 12, and 18, when applicable, will also be provided with 95% CIs calculated using Greenwood's formula to estimate the standard error.

Table 4: Evaluation and Censoring of Progression-Free Survival

Situation	Outcome	Date of Progression or Censoring
No baseline tumor assessments or no valid post baseline response assessment	Censored	Day 1
Progression documented between scheduled visits	Progressed	Date of first overall response of PD
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) on/before starting a new anticancer treatment
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 assessment	Censored	Date of last valid radiologic assessment (not NE and not missing) before the missed assessment

Source: FDA 2007.

7.2.7. Largest Percentage Reduction in Target Lesion Size

For subjects with solid tumors, the percentage change from baseline in the sum of the longest diameters of target lesions will be derived for each postbaseline period at which a valid target lesion assessment is provided. The best percentage change from baseline, defined as the largest decrease in the sum of diameters, will be derived for waterfall plots and potential exploratory analyses.

For subjects with lymphoma, including DLBCL, target lesion sizes will be measured by the sum of product of the longest diameter and the longest perpendicular diameter. The best percentage change from baseline, defined as the largest decrease in target lesion sizes during the study, will be summarized, and a waterfall plot will be generated.

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

[redacted]

9. SAFETY AND TOLERABILITY

Appendix A provides a list of planned tables, figures, and listings. Sample data displays are included in a separate document.

9.1. General Considerations

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.

9.2. Adverse Events

9.2.1. 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 the first dose of study treatment and up to 100 days after the last dose of study treatment. Analysis of AEs (as discussed below) will be limited to TEAEs, but data listings will include all AEs regardless of their timing to study treatment 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 NCI 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 epacadostat, nivolumab, or the chemotherapy regimens (as applicable) will be considered to be treatment-related AEs. If the investigator does not specify the relationship of the AE to study treatment, the AE will be considered to be treatment-related. The incidence of AEs and treatment-related AEs will be tabulated. Serious AEs will also be tabulated. The TEAEs leading to death by MedDRA system organ class and preferred term 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.

9.2.2. Adverse Event Summaries

An overall summary of AEs by treatment group will include the following:

- Number (%) of subjects reporting any TEAEs
- Number (%) of subjects reporting any epacadostat treatment-related TEAEs
- Number (%) of subjects reporting any Grade 3 or 4 epacadostat treatment-related TEAEs
- Number (%) of subjects reporting any nivolumab treatment-related TEAEs
- Number (%) of subjects reporting any Grade 3 or 4 nivolumab treatment-related TEAEs
- Number (%) of subjects reporting any treatment-related TEAEs (epacadostat or nivolumab)
- Number (%) of subjects reporting any Grade 3 or 4 treatment-related TEAEs (epacadostat or nivolumab)
- Number (%) of subjects reporting any serious TEAEs
- Number (%) of subjects reporting any Grade 3 or 4 TEAEs
- Number (%) of subjects who temporarily interrupted epacadostat or nivolumab because of TEAEs
- Number (%) of subjects who temporarily interrupted epacadostat or nivolumab because of TEAEs related to epacadostat or nivolumab
- Number (%) of subjects who permanently discontinued epacadostat or nivolumab because of TEAEs
- Number (%) of subjects who permanently discontinued epacadostat or nivolumab because of TEAEs related to epacadostat or nivolumab
- Number (%) of subjects who permanently discontinued epacadostat or nivolumab because of Grade 3 or 4 TEAEs related to epacadostat or nivolumab

- Number (%) of subjects with epacadostat or nivolumab dose reductions because of TEAEs
- Number (%) of subjects with epacadostat or nivolumab dose reductions because of TEAEs related to epacadostat or nivolumab
- Number (%) of subjects who had a TEAE leading to death

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

- Summary of TEAEs by system organ class and preferred term
- Summary of TEAEs by preferred term in decreasing order of frequency
- Summary of TEAEs by system organ class, preferred term, and maximum severity
- Summary of any Grade 3 or 4 TEAEs by system organ class and preferred term
- Summary of Grade 3 or 4 TEAEs by preferred term in decreasing order of frequency
- Summary of treatment-emergent serious TEAEs by system organ class and preferred term
- Summary of treatment-emergent serious TEAEs by preferred term in decreasing order of frequency
- Summary of epacadostat or nivolumab treatment-related AEs by system organ class and preferred term
- Summary of epacadostat or nivolumab treatment-related AEs by preferred term in decreasing order of frequency
- Summary of Grade 3 or 4 epacadostat or nivolumab treatment-related AEs by system organ class and preferred term
- Summary of Grade 3 or 4 epacadostat or nivolumab treatment-related AEs by preferred term in decreasing order of frequency
- Summary of TEAEs leading to death by system organ class and preferred term
- Summary of TEAEs leading to dose reduction of epacadostat or nivolumab by system organ class and preferred term
- Summary of TEAEs leading to dose interruption of epacadostat or nivolumab by system organ class and preferred term
- Summary of TEAEs leading to discontinuation of epacadostat or nivolumab by system organ class and preferred term
- Summary of nonserious TEAEs by system organ class and preferred term
- Summary of epacadostat or nivolumab treatment-related AEs leading to dose reduction of epacadostat or nivolumab by system organ class and preferred term
- Summary of epacadostat or nivolumab treatment-related AEs leading to dose interruption of epacadostat or nivolumab by system organ class and preferred term

- Summary of epacadostat or nivolumab treatment-related AEs leading to discontinuation of epacadostat or nivolumab by system organ class and preferred term
- Summary of Grade 3 or 4 epacadostat or nivolumab treatment-related AEs leading to discontinuation of epacadostat or nivolumab by system organ class and preferred term
- Summary of treatment emergent rash events – nivolumab program
- Summary of treatment-emergent immune-related AEs per sponsor-specified list by system organ class and preferred term – nivolumab program
- Summary of Grade 3 or 4 treatment-emergent immune-related AEs per sponsor-specified list by system organ class and preferred term – nivolumab program
- Summary of epacadostat or nivolumab treatment-related immune-related AEs per sponsor-specified list by system organ class and preferred term – nivolumab program
- Summary of Grade 3 or 4 epacadostat or nivolumab treatment-related immune-related AEs per sponsor-specified list by system organ class and preferred term – nivolumab program

The last 5 summaries will be based on the pre-specified list of AE preferred terms included as immune-related AEs in the nivolumab program.

9.3. Clinical Laboratory Tests

9.3.1. 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 to the first dose of study treatment. For baseline laboratory candidates with the same date and time, the laboratory value with the smallest laboratory sequence number will be defined as baseline.

Laboratory test values will be assessed for severity based on the numerical component of the CTCAE v4.03 grade.

9.3.2. Laboratory Value Summaries

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

When there are multiple nonmissing laboratory values for a subject's particular test within a visit window, the laboratory value with the smallest laboratory sequence number will be used for by-visit tabulations and summaries.

Numeric laboratory values and change from baseline will be summarized descriptively by visit, and non-numeric test values will be tabulated by visit when necessary. In addition, line graphs will be provided for alanine aminotransferase (ALT) and aspartate aminotransferase (AST).

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.

Shift tables will be presented showing change in CTCAE grade from baseline to worst grade postbaseline. Separate summaries for high and low laboratory values will be provided when the laboratory parameter has both high and low grading criteria. The denominator for the percentage calculation will be the number of subjects in the baseline category.

9.4. Vital Signs

Change and percentage change from baseline for vital signs will be calculated using the last nonmissing value before first dose of study treatment as the baseline value. Vital sign values and change from baseline will be summarized by visit and listed.

Thresholds of clinically notable vital sign abnormalities are defined in Table 5. The abnormal values for subjects exhibiting clinically notable vital sign abnormalities will be flagged in the listing.

Table 5: 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
Pulse	> 100 bpm	< 45 bpm
Temperature	> 38ºC	< 35.5ºC
Respiratory rate	> 24 breaths/min	< 8 breaths/min

9.5. Electrocardiograms

Number and percentage of subjects with clinically significant ECG abnormality as reported on the CRF will be summarized. All ECG results will be listed and values outside the threshold values according to Table 6 will be flagged in the listing.

Table 6: Criteria for Clinically Notable Electrocardiogram Abnormalities

Parameter	High Threshold	Low Threshold
QTcF, QTcB	> 470 ms	< 295 ms
PR	> 220 ms	< 75 ms
QRS	> 120 ms	< 50 ms
QT	> 500 ms	< 300 ms
RR	> 1500 ms	< 600 ms

QTcB = Bazett's correction; QTcF = Fridericia correction.

10. INTERIM ANALYSES

No formal interim analysis for futility or efficacy is planned for this study. An interim safety analysis is planned for Phase 2 after 20 subjects have been enrolled and treated for 8 weeks and then every 3 months thereafter. Refer to Protocol Section 9.6 for more details on the safety interim analysis.

11. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 7.

Table 7: Statistical Analysis Plan Versions

SAP Version	Date
Original	14 OCT 2015
Amendment 1	05 MAR 2019

11.1. Changes to Protocol Defined Analyses

The per protocol population and analysis based on per protocol population will not be conducted.

Analyses of efficacy endpoints per modified response criteria will not be conducted due to the limited number of subjects that had pseudo progression per modified response criteria.

11.2. Changes to the Statistical Analysis Plan

11.2.1. Amendment 1

The overall rationale for SAP Amendment 1 is to reflect changes in the study design and the analyses to align with Protocol Amendment 8. The SAP was modified throughout as necessary.

Other minor updates include:

- Section 4.1.4, Handling of Missing and Incomplete Data was added.
- Section 7.1.8, Eastern Cooperative Oncology Group Performance Status was removed, as ECOG is not an endpoint of the study.
- [redacted]
- Section 10, Interim Analyses was updated.
- Section 11.1, Changes to Protocol-Defined Analyses was updated.
- Appendix A, Laboratory Tests: Required Analytes and Appendix B, Laboratory Grading were removed.
- Appendix C, Planned Tables, Figures, and Listings was updated to Appendix A and modified to remove sample table shells, as they will now be provided in a separate document.

12. REFERENCES

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

Cheson BD, Pfistner B, Juweid ME, et al. Revised response criteria for malignant lymphoma. J Clin Oncol 2007;25:579-586.

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 April 27, 2012.

Klein JP, Moeschberger ML. Survival analysis: techniques for censored and truncated data. New York, NY: Springer; 1997.

APPENDIX A. PLANNED TABLES, FIGURES, AND LISTINGS

This appendix provides a list of the planned tables, figures, and listings for the clinical study report.

Tables

Table No.	Title	Population	Phase 1 Part 1	Phase 1 Part 2	Phase 2
1.1.1	Analysis Populations	FAS	X		X
1.1.2	Summary of Subject Disposition	FAS	X	X	X
1.1.3	Summary of Number of Subjects Enrolled by Country and Site	FAS	X		X
1.1.4	Summary of Protocol Deviations	FAS	X		X
1.2.1	Summary of Demographics and Baseline Characteristics	FAS	X	X	X; by cancer cohorts
1.3.1	Summary of Disease History	FAS	X; by cancer types		X; by cancer cohorts
1.4.1	Summary of Prior Medications	FAS	X		X
1.4.2	Summary of Concomitant Medications	FAS	X		X
1.4.3	Summary of Prior Therapy for Cancer	FAS	X; by cancer types		X; by cancer cohorts
1.4.4	Summary of Prior Systematic Cancer Therapy by WHO Drug Class and Preferred Term	FAS	X; by cancer types		X; by cancer cohorts
1.5.1	Summary of Medical History	FAS	X		X
2.1.1	Summary of Best Response and Objective Response Rate	FAS			X; by cancer cohorts
2.1.2	Summary of Best Response and Objective Response Rate by PD-L1 Status	FAS			X; by cancer cohort for I/O naive MEL, NSCLC and SCCHN
2.1.3	Summary of Best Response and Objective Response Rate by IDO1 Status	FAS			X; by cancer cohort for I/O naive MEL, NSCLC and SCCHN
2.2.1	Kaplan-Meier Analysis of Progression-Free Survival	FAS			X; by cancer cohorts
2.2.2	Kaplan-Meier Analysis of Progression-Free Survival by PD-L1 Status	FAS			X; by cancer cohort for I/O naive MEL, NSCLC and SCCHN

Table No.	Title	Population	Phase 1 Part 1	Phase 1 Part 2	Phase 2
2.2.3	Kaplan-Meier Analysis of Progression-Free Survival by IDO1 Status	FAS			X; by cancer cohort for I/O naive MEL, NSCLC and SCCHN
2.2.4	Summary of Duration of Response	FAS			X; by cancer cohorts
2.2.5	Summary of Duration of Disease Control	FAS			X; by cancer cohorts
2.2.6	Summary of Overall Survival	FAS			X; by cancer cohorts
2.3.1	Summary of Best Change in Target Lesion Size	FAS			X; by cancer cohorts
3.1	Summary of Exposure to Epacadostat and Nivolumab	Safety	X	X	X
3.2.1	Overall Summary of Treatment-Emergent Adverse Events	Safety	X		X
3.2.2	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X		X
3.2.3	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X		X
3.2.4	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Safety	X		X
3.2.6	Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X		X
3.2.7	Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X		X
3.2.8	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X		X
3.2.9	Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X		X
3.2.10	Summary of Epacadostat or Nivolumab Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X		X
3.2.11	Summary of Epacadostat or Nivolumab Treatment-Related Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X		X
3.2.14	Summary of Grade 3 or 4 Epacadostat or Nivolumab Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X		X

Table No.	Title	Population	Phase 1 Part 1	Phase 1 Part 2	Phase 2
3.2.25	Summary of Grade 3 or 4 Epacadostat or Nivolumab Treatment-Related Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X		X
3.2.16	Summary of TEAEs Leading to Death by MedDRA System Organ Class and Preferred Term	Safety	X		X
3.2.18	Summary of Treatment-Emergent Adverse Events Leading to Dose Reduction of Epacadostat or Nivolumab by MedDRA System Organ Class and Preferred Term	Safety	X		X
3.2.19	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption of Epacadostat or Nivolumab by MedDRA System Organ Class and Preferred Term	Safety	X		X
3.2.20	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Epacadostat or Nivolumab by MedDRA System Organ Class and Preferred Term	Safety	X		X
3.2.24	Summary of Nonserious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X		X
3.2.26	Summary of Epacadostat or Nivolumab Treatment-Related Adverse Events Leading to Dose Reduction of Epacadostat or Nivolumab by MedDRA System Organ Class and Preferred Term	Safety	X		X
3.2.27	Summary of Epacadostat or Nivolumab Treatment-Related Adverse Events Leading to Dose Interruption of Epacadostat or Nivolumab by MedDRA System Organ Class and Preferred Term	Safety	X		X
3.2.28	Summary of Epacadostat or Nivolumab Treatment-Related Adverse Events Leading to Discontinuation of Epacadostat or Nivolumab by MedDRA System Organ Class and Preferred Term	Safety	X		X
3.2.29	Summary of Grade 3 and 4 Epacadostat or Nivolumab Treatment-Related Adverse Events Leading to Discontinuation of Epacadostat or Nivolumab by MedDRA System Organ Class and Preferred Term	Safety	X		X
3.2.30	Summary of Treatment Emergent Rash Events – Nivolumab Program	Safety	X		X
3.2.31	Summary of Treatment-Emergent Immune-Related Adverse Events per Sponsor-Specified List by MedDRA System Organ Class and Preferred Term – Nivolumab Program	Safety	X		X

Table No.	Title	Population	Phase 1 Part 1	Phase 1 Part 2	Phase 2
3.2.32	Summary of Grade 3 or 4 Treatment-Emergent Immune-Related Adverse Events per Sponsor-Specified List by MedDRA System Organ Class and Preferred Term – Nivolumab Program	Safety	X		X
3.2.33	Summary of Epacadostat or Nivolumab Treatment-Related Immune-Related Adverse Events per Sponsor-Specified List by MedDRA System Organ Class and Preferred Term – Nivolumab Program	Safety	X		X
3.2.34	Summary of Grade 3 or 4 Epacadostat or Nivolumab Treatment-Related Immune-Related Adverse Events per Sponsor-Specified List by MedDRA System Organ Class and Preferred Term – Nivolumab Program	Safety	X		X
3.3.1.1	Summary of Laboratory Values – Hematology	Safety	X		X
3.3.1.2	Summary of Laboratory Values – Chemistry	Safety	X		X
3.3.3.1	Shift Summary of Laboratory Values in CTC Grade – Hematology	Safety	X		X
3.3.2.2	Shift Summary of Laboratory Values in CTC Grade – Chemistry	Safety	X		X
3.4.1	Summary of Systolic Blood Pressure	Safety	X		X
3.4.2	Summary of Diastolic Blood Pressure	Safety	X		X
3.4.3	Summary of Pulse	Safety	X		X
3.4.4	Summary of Respiratory Rate	Safety	X		X
3.4.5	Summary of Body Temperature	Safety	X		X
3.5.9	Summary of Clinically Significant ECGs	Safety	X		X

Figures

Figure No.	Title	Population	Phase 1 Part 1	Phase 1 Part 2	Phase 2
4.1.1	Kaplan-Meier Plot of Progression-Free Survival	FAS			X; by cancer cohorts
4.1.2	Kaplan-Meier Plot of Progression-Free Survival by PD-L1 Status	FAS			X; by cancer cohort for I/O naive MEL, NSCLC and SCCHN
4.1.3	Kaplan-Meier Plot of Progression-Free Survival by IDO1 Status	FAS			X; by cancer cohort for I/O naive MEL, NSCLC and SCCHN
4.1.4	Kaplan-Meier Plot of Overall Survival	FAS			X; by cancer cohorts
4.3	Best Percentage Change From Baseline in Target Lesion Size	FAS			X; by cancer cohorts
4.6.1	Line Graph of Mean Values Over Time for Selected Laboratory Values (ALT, AST)	Safety	X		X

Listings

Listing No.	Title	Population	Phase 1 Part 1	Phase 1 Part 2	Phase 2
2.1.1	Subject Enrollment and Disposition Status	FAS	X	X	X
2.2	Protocol Deviations	FAS	X	X	X
2.3.1	Analysis Populations	FAS	X	X	X
2.4.1	Demographic and Baseline Characteristics	FAS	X	X	X
2.4.2	Oncology Disease History	FAS	X	X	X
2.4.3	Systemic Cancer Medication History	FAS	X	X	X
2.4.4	Radiotherapy History	FAS	X	X	X
2.4.5	Prior Surgery and Surgical Procedures	FAS	X	X	X
2.4.6	Prior Stem Cell Transplant	FAS	X; lymphoma subjects only		X; DLBCL only
2.4.7	Medical History	FAS	X	X	X
2.4.8	Prior and Concomitant Medications	FAS	X	X	X
2.5.1	Epacadostat Administration	Safety	X	X	X
2.5.2	Nivolumab Administration	Safety	X	X	X
2.5.3	Administration of Chemotherapy Regimens	Safety		X	
2.6.1	Overall Response Assessment	FAS	X	X	X
2.6.2	Progression-Free Survival, Duration of Response, Duration of Disease Control and Overall Survival	FAS	X	X	X
2.7.1	Adverse Events	Safety	X	X	X
2.7.2	Grade 3 and 4 Adverse Events	Safety	X	X	X
2.7.3	Treatment-Related Adverse Events	Safety	X	X	X
2.7.4	Serious Treatment-Emergent Adverse Events	Safety	X	X	X
2.7.5	Adverse Events Leading to Study Drug Discontinuation, Interruption or Reduction	Safety	X	X	X
2.7.6	Treatment-Emergent Adverse Events Leading to Death	Safety	X	X	X
2.7.7	Immune-Related Adverse Events per Sponsor-Specified List – Nivolumab Program	Safety	X	X	X
2.7.8	Dose-Limiting Toxicities	Safety	X	X	
2.8.1	Clinical Laboratory Values – Hematology	Safety	X	X	X
2.8.2	Clinical Laboratory Values – Chemistry	Safety	X	X	X
2.8.3	Abnormal Clinical Laboratory Values	Safety	X	X	X
2.9.1	Vital Sign Values	Safety	X	X	X
2.10.1	12-Lead ECG Values	Safety	X	X	X

Signature Manifest

Document Number: IC-STS-SAP-0134 **Revision:** 0

Title: INCB 24360-204 SAP Amendment 1

All dates and times are in Eastern Standard Time.

APPROVAL: 24360-204 SAP Amendment 1

Approval and Release

Name/Signature	Title	Date	Meaning/Reason
[redacted]	[redacted]	05 Mar 2019, 10:36:52 AM	Approved
[redacted]	[redacted]	05 Mar 2019, 05:10:57 PM	Approved
[redacted]	[redacted]	08 Mar 2019, 09:44:48 AM	Approved