Official Title: **A Phase 1/2 Study Exploring the Safety, Tolerability, and Efficacy of INCAGN01949 in Combination With Immune Therapies in Subjects With Advanced or Metastatic Malignancies**

NCT Number: NCT03241173

Document Date: Statistical Analysis Plan Version 1: 06 February 2018

STATISTICAL ANALYSIS PLAN

INCAGN 1949-201

A Phase 1/2 Study Exploring the Safety, Tolerability, and Efficacy of INCAGN01949 in Combination With Immune Therapies in Subjects With Advanced or Metastatic Malignancies

IND Number:	**135,378**
Sponsor:	**Incyte Biosciences International Sàrl** **Route de la Corniche 1** **1066 Epalinges, Switzerland**
Protocol Version:	**Protocol Amendment 1 dated 14 JUN 2017**
CRF Approval Date:	**04 OCT 2017**
SAP Version:	**Original**
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[redacted]	[redacted]

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

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LIST OF ABBREVIATIONS

Abbreviation	Term
[redacted]	[redacted]
AE	adverse event
[redacted]	[redacted]
BOR	best overall response
CI	confidence interval
[redacted]	[redacted]
[redacted]	[redacted]
CR	complete response
CRF	case report form
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
DLT	dose-limiting toxicity
DMC	Data Monitoring Committee
DOR	duration of response
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
EOS	end of study
EOT	end of treatment
FAS	full analysis set
FDA	Food and Drug Administration
Ipi	ipilimumab
irAE	immune-related AE
JTc	corrected JT interval
KM	Kaplan-Meier
λ_z	terminal phase rate constant
MedDRA	Medical Dictionary for Regulatory Activities
mRECIST	modified Response Evaluation Criteria in Solid Tumors
MTD	maximum tolerated dose
NE	not evaluable
Nivo	nivolumab
ORR	objective response rate
OS	overall survival
PAD	pharmacologically active dose

Abbreviation	Term
PD	progressive disease
PD-1	programmed death-1
PD-L1	programmed death ligand-1
PFS	progression-free survival
[redacted]	[redacted]
PoS	probability of success
PR	partial response
PT	preferred term
Q2W	every 2 weeks
QRS	QRS is the combination of three of the graphical deflections on an ECG. It is usually the most central and most visually obvious part of the tracing. It corresponds to the depolarization of the right and left ventricles of the human heart.
QTcF	QT interval corrected using the Fridericia formula
RCC	renal cell carcinoma
RECIST	Response Evaluation Criteria in Solid Tumors
RP2D	recommended Phase 2 dose
RR	RR is the interval from the beginning of a QRS complex to the beginning of the next QRS complex
SAE	serious adverse event
SAP	Statistical Analysis Plan
SCCHN	squamous cell carcinoma of the head and neck
SD	stable disease
SOC	system organ class
TEAE	treatment-emergent adverse event
TFLs	tables, figures, and listings
[redacted]	[redacted]
WHO	World Health Organization

1. INTRODUCTION

This is an open-label, nonrandomized, Phase 1/2 study to determine the safety, tolerability, and efficacy of INCAGN01949 when given in combination with immune therapies. Phase 1 will consist of 2 parts. Dose escalation (Part 1) will consist of a 3 + 3 + 3 design to determine the MTD, or PAD, defined as a dose that provides a maximal biochemical effect [redacted] of INCAGN01949 when given in combination with immune therapies. The safety expansion (Part 2) will further explore tolerated doses of INCAGN01949 given as a run-in of 2 doses followed by concomitant immune therapies. Subjects with advanced or metastatic cervical cancer, endometrial cancer, gastric cancer (including stomach and gastroesophageal junction cancer), esophageal cancer, hepatocellular carcinoma, melanoma, Merkel cell carcinoma, mesothelioma, microsatellite instability-high colorectal cancer, non–small cell lung cancer, ovarian cancer, SCCHN, small cell lung cancer, RCC, triple-negative breast cancer, and urothelial carcinoma who have progressed after treatment with available therapies that are known to confer clinical benefit, who are intolerant to treatment, or who refuse standard of care will be enrolled in both parts of Phase 1. The Phase 2 expansion will further evaluate the safety, tolerability, and efficacy of the recommended dose(s) of INCAGN01949 selected in Phase 1 when given in combination with immune therapies. Subjects with advanced or metastatic urothelial carcinoma or RCC will be enrolled in Phase 2.

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in the Study INCAGN 1949-201 Protocol. The scope of this plan includes the interim and final analyses that are planned and will be executed by the Department of Biostatistics or designee.

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCAGN 1949-201 Protocol Amendment 1 dated 14 JUN 2017 and CRFs approved 04 OCT 2017. 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

Phase 1

- To evaluate the safety, tolerability, and DLTs of INCAGN01949 in combination with immune therapies and to define the recommended dose(s) of INCAGN01949 when given in combination with immune therapies.

Phase 2

- To evaluate the efficacy of INCAGN01949 when given in combination with immune therapies by assessing ORR per RECIST v1.1.

2.2.2. Secondary Objectives

Phase 1 and Phase 2

- To evaluate the efficacy of INCAGN01949 when given in combination with immune therapies by assessing ORR, DOR, DCR, duration of disease control, and PFS per RECIST v1.1 and mRECIST.
- To evaluate the efficacy of INCAGN01949 when given in combination with immune therapies with respect to 1-year and 2-year OS.
- To evaluate the safety and tolerability of INCAGN01949 when given in combination with immune therapies.

[redacted]

[redacted]

2.3. Study Endpoints

2.3.1. Primary Endpoints

- Safety and tolerability will be assessed by monitoring frequency, duration, and severity of AEs.
- ORR, defined as the percentage of subjects having CR or PR, will be determined by investigator assessment of radiographic disease assessments per RECIST v1.1.

2.3.2. Secondary Endpoints

- ORR, defined as the percentage of subjects having CR or PR, will be determined by investigator assessment of radiographic disease assessments per RECIST v1.1 and mRECIST.
- DOR, defined as the time from the earliest date of disease response (CR or PR) until earliest date of disease progression or death due to any cause, if occurring sooner than progression, will be determined by investigator assessment of radiographic disease assessments per RECIST v1.1 and mRECIST.
- Disease control rate, defined as the percentage of subjects having CR, PR, or SD, will be determined by investigator assessment of radiographic disease assessments per RECIST v1.1 and mRECIST.
- Duration of disease control (CR, PR, and SD) as measured from first report of SD or better until disease progression or death from any cause, if occurring sooner than progression, will be determined by investigator assessment of radiographic disease per RECIST v1.1 and mRECIST.
- PFS, defined as the time from the start of combination therapy until the earliest date of disease progression or death due to any cause, if occurring sooner than progression, as determined by investigator assessment of objective radiographic disease assessments per RECIST v1.1 and mRECIST.
- OS determined from the start of combination therapy until death due to any cause. Survival analyses will occur at 1-year, 2-years, and at the end of the study.
- Safety and tolerability will be assessed by monitoring frequency, duration, and severity of AEs.

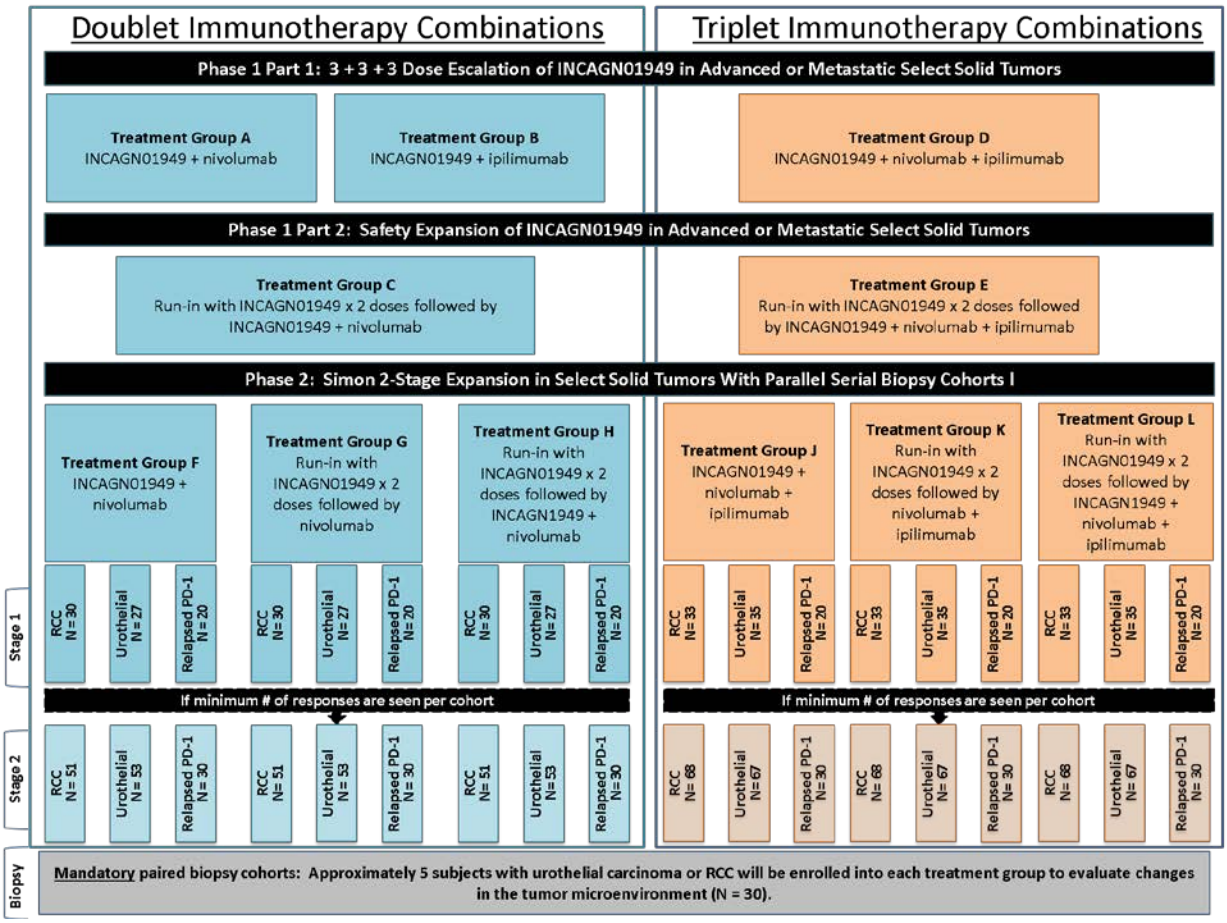
[redacted]

3. STUDY DESIGN

This is an open-label, nonrandomized, Phase 1/2 study to determine the safety, tolerability, and efficacy of INCAGN01949 when given in combination with immune therapies. The MTD or PAD of INCAGN01949 when given in combination with immune therapies will be determined in Phase 1 of the study. The Phase 2 expansion will further evaluate the safety, tolerability, and efficacy of the recommended dose(s) of INCAGN01949 selected in Phase 1.

See Figure 1 for overall study design.

Figure 1: Overall Study Design



3.1. Phase 1

3.1.1. Part 1 – Dose Escalation

The Part 1 will consist of a 3 + 3 + 3 dose escalation to determine the MTD or PAD, defined as a dose that provides a maximal biochemical effect, [redacted] of INCAGN01949 when given in combination with immune therapies. Phase 1 dose escalation will begin with 2 double treatment groups evaluating the MTD or PAD of INCAGN01949 plus nivolumab (Treatment A) and the MTD or PAD of INCAGN01949 plus ipilimumab (Treatment B), which will be explored in parallel. Dose escalation of the triplet immune therapy combinations (Treatment D) will proceed until the MTD or PAD of INCAGN01949 in combination with nivolumab and ipilimumab is determined; however, the dose of INCAGN01949 in the triplet combination will not exceed the lowest MTD of INCAGN01949 established in the applicable doublet combinations.

In Part 1 of the study, the MTD is defined as 1 dose level below that at which ≥ one-third of subjects in a particular cohort have DLTs. The PAD is defined as a dose that provides a maximal biochemical effect, [redacted] of INCAGN01949 when given in combination with immune therapies.

A DLT will be defined as the occurrence of any toxicity, with the exception of events clearly associated with the underlying disease, disease progression, a concomitant medication, or comorbidity; the list of toxicities that will be designated as dose limiting toxicities are provided in Table 8 of the Protocol.

The first 3 evaluable subjects enrolled within an INCAGN01949 dose cohort will be observed for the specified DLT observation period before the next dose cohort begins enrollment. If 0 DLTs occur in a cohort of 3 evaluable subjects, a new cohort of 3 evaluable subjects will be treated at the next higher dose level. If 1 of 3 evaluable subjects experiences a DLT, that cohort will be expanded to 6 evaluable subjects. If 1 of 6 evaluable subjects experiences a DLT, a new cohort of 3 evaluable subjects will be treated at the next higher dose level. If 2 of 6 evaluable subjects experience a DLT, that cohort will be expanded to 9 evaluable subjects. If $\geq$ 2 of 3, 3 of 6, or 3 of 9 evaluable subjects experience DLTs within a cohort, then that dose level will be determined to have exceeded the MTD, and the previous dose level will be considered the MTD. If only 3 evaluable subjects were treated at the MTD or PAD, then a minimum of 3 additional evaluable subjects will be enrolled before this dose is administered in Phase 2 of the study.

Additional subjects will be enrolled in a dose cohort to achieve the minimum of 3 evaluable subjects. Depending on treatment group, a subject must receive at least 2 doses of the cohort-specified dose of INCAGN01949, 2 doses of nivolumab, and 1 dose of ipilimumab, or must have had a DLT during the DLT observation period, to be considered evaluable. Subjects who dropout for reasons other than a DLT (eg, events clearly associated with the underlying disease, disease progression, concomitant medication, or comorbidity), during the DLT observation period will result in the subject being nonevaluable and the subject being replaced. Dose modifications should not be made during the DLT observation period without discussion with the medical monitor. The doses of INCAGN01949 to be evaluated in each treatment group are summarized in Table 1.

Table 1: INCAGN01949 Dose Levels and Cohorts

Cohort	Dose of INCAGN01949
-1	2 mg
1	7 mg
2	20 mg
3 (Starting Dose)	**70 mg**
4	200 mg
5	350 mg
6	700 mg

Note: A higher starting dose of INCAGN01949 was chosen based on safety data from the monotherapy study (INCAGN 1949-101).

3.1.2. Part 2 – Safety Expansion

Once an INCAGN01949 dose cohort in Treatment Group A is deemed tolerable, up to 6 subjects will be enrolled in Treatment Group C at the same dose of INCAGN01949. For example, if INCAGN01949 70 mg is tolerated in Treatment Group A, then 70 mg will be explored in up to

6 subjects in Treatment Group C. Likewise, once an INCAGN01949 dose in Treatment Group D is deemed tolerable, up to 6 subjects will be enrolled in Treatment Group E at the same dose of INCAGN01949. For example, if INCAGN01949 350 mg is tolerated in Treatment Group D, then 350 mg will be explored in up to 6 subjects in Treatment Group E. Doses of INCAGN01949 in Treatment Group C will be escalated in parallel to those explored in Treatment Group A but will not exceed the MTD of INCAGN01949 established in Treatment Group A. The same rules will apply with Treatment Groups D and E. Alternate dose administration schedules may also be explored depending on [redacted] safety results. The sponsor may elect to prioritize (or deprioritize) enrollment to specific dose cohorts based on emerging safety or efficacy data in collaboration with investigational sites.

If the cumulative incidence of Grade 3 or higher INCAGN01949-related AEs occurs in > 40% of subjects in a particular treatment group, then further enrollment will be interrupted until the sponsor, investigators, and regulatory authorities (if applicable) determine the appropriate course of action (eg, lower the dose of INCAGN01949, change dose frequency, etc).

3.2. Phase 2 – Dose Expansion

Phase 2 of the study will further evaluate the safety, tolerability, efficacy, [redacted] and pharmacologic activity of the immune therapy combinations in subjects with advanced or metastatic RCC or urothelial carcinoma. RCC- and urothelial carcinoma–specific cohorts will enroll subjects who are naive to immune therapies. Subjects who have relapsed following prior treatment with an anti–PD-1/L1 therapy will be enrolled into a relapsed cohort that will contain both RCC and urothelial carcinoma subjects. Additional tumor-specific cohorts may be added, by Protocol amendment, based on emerging data.

[redacted]

A Simon 2-stage design will be used with a stopping rule to allow for early termination of a particular tumor cohort within a given treatment group at the end of Stage 1 if there are insufficient responses observed. The design parameters for the individual Simon 2-stage designs are determined by historical response rates and will result in different sample sizes and different futility rules, depending on the historical response rate for the tumor type and treatment combination. The planned Simon 2-stage designs are summarized in Table 2. The same Simon 2-stage design parameters will be used for alternative dosing sequences in the same tumor type and treatment combination.

Table 2: Planned Simon 2-Stage Designs for Phase 2

Indication	Treatment Groups	r_1	n_1	r	n_2	n	p_0	p_1
RCC	F, G, H (INCAGN01949 + Nivo)	8	30	26	51	81	25%	40%
Urothelial	F, G, H (INCAGN01949 + Nivo)	6	27	21	53	80	20%	35%
Relapsed to anti–PD-1/L1	F, G, H (INCAGN01949 + Nivo)	2	20	8	30	50	10%	25%
RCC	J, K, L (INCAGN01949 + Nivo + Ipi)	14	33	48	68	101	40.4%	55%
Urothelial	J, K, L (INCAGN01949 + Nivo + Ipi)	10	35	33	67	102	26%	40%
Relapsed to anti–PD-1/L1	J, K, L (INCAGN01949 + Nivo + Ipi)	2	20	8	30	50	10%	25%

- r_1: if r_1 or fewer responses are observed during Stage 1, the study cohort is stopped early for futility.
- n_1: number of subjects initially enrolled in Stage 1.
- n_2: number of subjects enrolled in Stage 2.
- r: if r or fewer responses are observed by the end of Stage 2, then no further investigation of the drug combination is warranted in the selected tumor type and dosing schedule.
- n: total number of subjects.
- p_0: insufficient response rate.
- p_1: target response rate.

In Phase 2 of the study, toxicities will continue to be monitored. If the cumulative incidence of Grade 3 through Grade 5 INCAGN01949-related AEs occurs in > 40% of subjects in a particular treatment group after 6 subjects have been enrolled, then further enrollment in that treatment group will be interrupted until the sponsor, investigators, and regulatory authorities (if applicable) determine the appropriate course of action (eg, lower the dose of INCAGN01949, change dose frequency, etc). If a treatment group is discontinued due to toxicity, it may be re-initiated at a previously tested lower dose level and/or alternate dosing schedule. All AEs, regardless of the time of occurrence on study, may be considered for DLT determination purposes.

3.3. Control of Type I Error

For the primary efficacy endpoints, the 1-sided Type I error will be controlled at 0.05 for each individual cohort expansion. Note that this level of significance does not account for the multiple expansion cohorts. For other endpoints, CIs will be reported at a 95% confidence level.

During the Phase 1 portion of the study, telephone conferences will be scheduled by the sponsor with study investigators in order to review cohort-specific data and overall safety data, to agree on dose escalation, adjudicate individual high-grade AEs as potentially dose-limiting, and guide other major study decisions. An internal DMC will be assembled to monitor safety data and study conduct on a regular and ongoing basis. See Section 9 for details regarding the interim analyses conducted in this study.

3.4. Sample Size Considerations

3.4.1. Sample Size for Phase 1 Part 1

The primary objective in Phase 1 of the study is to determine the MTD or PAD of INCAGN01949 when given in combination with immune therapies. The total number of subjects will depend on the number of dose levels tested in each treatment group before the MTD or PAD is established. Approximately up to 108 subjects will be evaluated in Phase 1 Part 1 (9 subjects per dose level for 4 dose levels in 3 treatment groups). Dose escalation will follow the 3 + 3 + 3 design algorithm. Based on this algorithm, a minimum of 3 evaluable subjects will be enrolled in each cohort beginning with Cohort 3 (70 mg; starting dose) and a maximum of 9 evaluable subjects will be enrolled in each cohort. The probability of declaring a dose as safe for various DLT rates in the 3 + 3 + 3 is summarized in Table 3.

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

True DLT Rate	Probability of Dose Escalation
20%	78.4%
30%	56.1%
40%	35.0%
50%	18.9%
60%	8.8%

For example, if the true DLT rate is 50% at a given dose level, there is an 18.9% chance that the dose would be escalated. Furthermore, if the true DLT rate is 20%, there is a 78.4% chance that the dose would be escalated. If the MTD is not determined at the highest dose level tested during the study, then the MTD is at or above the highest dose level. The MTD is below the lowest dose level of INCAGN01949 if Cohort -1 is not well-tolerated. The PAD may be used in lieu of the MTD and/or prescribed doses may need to be altered in order to determine the MTD.

3.4.2. Sample Size for Phase 1 Part 2

Once an INCAGN01949 dose cohort in Treatment Group A is deemed tolerable, 6 subjects will be enrolled in Treatment Group C at the same dose of INCAGN01949. For example, if INCAGN01949 70 mg is tolerated in Treatment Group A, then 70 mg will be explored in 6 subjects in Treatment Group C. Likewise, once an INCAGN01949 dose cohort in Treatment Group D is deemed tolerable, 6 subjects will be enrolled in Treatment Group E at the same dose of INCAGN01949. For example, if 350 mg of INCAGN01949 is tolerated in Treatment Group D then 350 mg will be explored in 6 subjects in Treatment Group E.

3.4.3. Sample Size for Phase 2

Phase 2 will further evaluate the safety, tolerability, preliminary efficacy, [redacted] of the recommended dose of INCAGN01949 in combination with immune therapies as part of doublet and triplet drug expansion cohorts. In Phase 2, a Simon 2-stage design will be run for each tumor type within a given doublet or triplet drug expansion cohort.

The sample size for each tumor type within a given doublet or triplet expansion cohort will be guided by the Simon 2-stage design (Simon 1989). The planned Simon 2-stage designs are summarized in Table 2. Each Simon 2-stage design will have a stopping rule to allow early termination of a particular tumor type within the given treatment combination at the end of Stage 1 if there is insufficient response observed (calculated response rate < p_0%), while enrolling enough subjects to predict possible target responses (≥ p_1%) worthy of cohort expansion and potentially further evaluation in future studies. The individual Simon 2-stage designs run for each tumor type within each doublet or triplet expansion cohort will have design parameters that are determined by historical response rates. The same Simon 2-stage design parameters will be used for alternative dosing sequences in the same tumor type and treatment combination. For example, the urothelial cohorts in Treatment Groups F, G, and H will all use the same Simon 2-stage parameters.

In order to determine whether the target response rate (p_1%) is likely, an initial number of evaluable subjects (n_1 subjects) treated at the MTD or PAD and schedule of INCAGN01949 within the corresponding doublet or triplet expansion cohort will be enrolled in a cohort (Stage 1). If there are r_1 or fewer responses in the cohort, 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 tumor type in Stage 2. In the cohorts in which greater than r_1 responses are observed among the Stage 1 subjects, n_2 additional evaluable subjects will be treated in Stage 2 to estimate the response rate. At the end of Stage 2, if ≤ r subjects have responded among the n evaluable subjects, the doublet or triplet schedule will be declared nonpromising for that cohort. In other words, after the study is finished, if there is a sufficient number of responses in the 2 stages combined, the study doublet or triplet is considered promising; otherwise it is considered nonpromising. The detailed calculations for each tumor type–specific doublet and triplet cohort are based on a 1-sided Type I error of 0.05 and power of 85%. The individual p_0 and p_1 values for the tumor types within doublet or triplet expansion cohorts are listed in Table 2.

Formal quarterly safety reviews will be conducted to review efficacy and safety data with the obligation to hold a safety review meeting every 6 months.

[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 that the first dose of study drug (INCAGN0[redacted], nivolumab, or ipilimumab) is administered to the subjects.

4.1.2. Study Day

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

Day # = (Visit/Reporting Date – Day 1 date + 1).

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

Day # = (Visit/Reporting Date – Day 1 date).

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

4.1.3. Baseline Value

Baseline is the last nonmissing measurement obtained before the first administration of INCAGN0[redacted], nivolumab, or ipilimumab, unless otherwise defined.

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

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

4.1.4. Last Available Value

The last available value is the last nonmissing measurement obtained after starting INCAGN0[redacted], nivolumab, or ipilimumab and within 60 days after the last dose of INCAGN0[redacted], nivolumab or ipilimumab.

4.1.5. 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.

Partial disease diagnosis date will be handled as follows:

- If only the day is missing, then the imputed day will be the first of the month.
- If both the month and day are missing, then the imputed day and month will be 01 JAN.
- No imputation will be done if the 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 first 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.

For relevant efficacy endpoints, partial death date will be imputed as follows:

- If mmyyyy for the last contact date = mmyyyy for the death date, then the death date will be set to the day after the last contact date.
- If mmyyyy for the last contact 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.

4.1.6. Cycle Length and Duration

Cycle 1 Day 1 is the day that the first dose of INCAGN01949, nivolumab, or ipilimumab is administered.

- **INCAGN01949:** For all treatment groups, INCAGN01949 will be administered IV over a 30-minute period on Day 1 of each Q2W (ie, 14-day) cycle.
- **Nivolumab:** In the doublet Treatment Groups A, C, F, G, and H, nivolumab will be administered IV per instructions provided in the package insert at a dose of 240 mg Q2W (eg, 14 days). In the triplet Treatment Groups D, E, J, K, and L, nivolumab will be administered IV per instructions provided in the package insert at a dose of 3 mg/kg Q2W (eg, 14 days). In the concurrent dosing Treatment Groups A, D, F, and J, nivolumab dosing will begin on Cycle 1 Day 1. In the sequenced/run-in dosing Treatment Groups C, E, G, H, K, and L, nivolumab dosing will begin on Cycle 3 Day 1.
- **Ipilimumab:** In Treatment Groups B, D, E J, K, and L, ipilimumab will be administered IV per instructions provided in the package insert to subjects at a dose of 1 mg/kg Q6W (eg, 42 days). In the concurrent dosing Treatment Groups B, D, and J, ipilimumab dosing will begin on Cycle 1 Day 1. In the sequenced dosing Treatment Groups E, K, and L, ipilimumab dosing will begin on Cycle 3 Day 1.

Subjects will continue to receive INCAGN01949, nivolumab, and ipilimumab as defined in the Protocol as long as the subject is deriving benefit and has not met any of the Protocol-defined conditions for treatment withdrawal.

4.2. Variable Definitions

4.2.1. Variables to Be Derived Only If Not Provided on Case Report Form

The following variables will only be calculated if not reported on the CRF.

- 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 (ICF), using the following formula:

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

4.2.2. Prior and Concomitant Medication

Prior medication is defined as any nonstudy medication started before the first dose of INCAGN01949, nivolumab, or ipilimumab.

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

- Before the date of first administration of INCAGN01949, nivolumab, or ipilimumab and is ongoing throughout the study or ends on/after the date of first study drug administration.
- On/after the date of first administration of INCAGN01949, nivolumab, or ipilimumab and is ongoing or ends during the course of study drug.

A prior medication could also be classified as "both prior and concomitant medication" if the end date is on or after first dose of INCAGN01949, nivolumab, or ipilimumab. 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; Version 9 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.

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

5.2. Treatment Groups

This is a Phase 1/2, open-label, nonrandomized, multicenter, dose-escalation study. The starting dose of INCAGN01949 is 70 mg, and up to 4 doses will be tested. Data will be summarized overall and by treatment group. Treatment group is defined as the dose regimen and dose schedule initially assigned.

Dose escalation of the triplet immune therapy combinations will begin enrolling once all of the applicable doublet combinations have cleared 3 INCAGN01949 dose levels (see Table 1) or the MTD or PAD of INCAGN01949 has been determined (whichever occurs first). The starting dose of INCAGN01949 will be 2 dose levels below the last dose cohort deemed safe in the doublet combination. The triplet immune therapy combinations will be explored in parallel.

- Treatment Group A
  - INCAGN01949 + 240 mg Q2W nivolumab
- Treatment Group B
  - INCAGN01949 + 1 mg/kg Q6W ipilimumab
- Treatment Group C
  - Run-in with INCAGN01949 × 2 doses followed by INCAGN01949 + 240 mg Q2W nivolumab
- Treatment Group D
  - INCAGN01949 + 3 mg/kg Q2W nivolumab + 1 mg/kg Q6W ipilimumab
- Treatment Group E
  - Run-in with INCAGN01949 × 2 doses followed by INCAGN01949 + 3 mg/kg Q2W nivolumab + 1 mg/kg Q6W ipilimumab

5.3. Analysis Populations

5.3.1. Full Analysis Set

The FAS includes all subjects enrolled in the study who received at least 1 dose of INCAGN01949, nivolumab, or ipilimumab. The nivolumab FAS population includes all subjects in the FAS population who received at least 1 dose of nivolumab administered in mg or mg/kg. The ipilimumab FAS population includes all subjects in the FAS population who received at least 1 dose of ipilimumab.

Table summaries, unless otherwise indicated, will be provided by treatment group and tumor type–specific cohorts.

5.3.2. Response Evaluable Populations

The response evaluable population includes all subjects who received at least 1 dose of INCAGN01949, nivolumab, or ipilimumab, completed a baseline scan, and met at least 1 of the following criteria:

- The subject had ≥ 1 postbaseline scan.
- The subject was on the study for a minimum of 64 days of follow-up.
- The subject discontinued from treatment.

[redacted]

6. BASELINE, EXPOSURE, AND DISPOSITION VARIABLES AND ANALYSES

A list of data displays and sample data displays are provided in Appendix A and the sample data displays are provided in a separate document.

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

6.1.1. Demographic Characteristics

The following demographic characteristics will be summarized for the Phase 1 FAS population by treatment group and dose level and for the Phase 2 FAS population by tumor type: age, sex, race, ethnicity, and ECOG performance status.

6.1.2. Baseline Disease Characteristics and Disease History

For each type of tumor, primary tumor histology, time from initial diagnosis in months, stage at initial diagnosis, current stage of disease, current site of disease, and tumor markers will be summarized for all subjects in the Phase 1 Part 1 FAS population by treatment group and dose level and Phase 1 Part 2 FAS population by treatment group and tumor type.

6.1.3. Prior Therapy

Prior systemic cancer therapy regimens will be summarized by total number and by number of prior systemic cancer therapies taken for both advanced and metastatic disease for all subjects in the Phase 1 FAS population by dose level and treatment group and Phase 2 FAS population by tumor type and treatment group. 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.

Number of subjects who received prior radiation will be summarized for the Phase 2 FAS population. Radiotherapy type, body site, start and stop date, total dose, and best response will be listed.

Number of subjects who had prior surgery or surgical procedure for the malignancies under study will be summarized for the Phase 2 FAS population. Date and description of the surgery/procedure will be listed.

Number of subjects with prior immunotherapy and prior anti–PD-1/PD-L1 therapy will be summarized for the Phase 1 FAS population by dose level and treatment group and the Phase 2 FAS population by tumor type and treatment group. Prior immunotherapy type, start and stop date, total dose, and best response will be listed.

6.1.4. Medical History

For subjects in the Phase 1 FAS population by dose level and Phase 2 FAS population by tumor type, 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 as documented on the CRF.

6.2. Disposition of Subjects

The number and percentage of subjects who were enrolled, treated, completed the study, discontinued study treatment with a primary reason for discontinuation, and discontinued from the study with a primary reason for withdrawal will be summarized for the Phase 1 FAS population by dose level and treatment group and the Phase 2 population by tumor type and treatment group. The number of subjects enrolled by site will also be provided by treatment group.

6.3. Protocol Deviations and Violations

Protocol deviations and violations recorded on the CRF will be presented in a table and listing.

6.4. Exposure

6.4.1. Exposure for INCAGN01949

For subjects in the FAS population, exposure to INCAGN01949 will be summarized descriptively as the following:

- **Total number of infusions**: Total number of infusions per subject with a nonzero dose of INCAGN01949.
- **Dose administered per cycle**: The actual dose administered in mg per cycle.
- **Total dose administered in mg**: The total cumulative, actual dose administered (in mg) across cycles for each subject will be determined according to the following calculation:
  - For an infusion i, let C_i, V_i, and N be defined as above
  - Total dose administered (in mg) $= \sum_{i=1}^{N} C_i \times V_i$
- **Average dose in mg**: The average dose (in mg) will be the total dose administered (in mg) divided by the total number of infusions.

6.4.2. Exposure for Nivolumab

For subjects in the Phase 1 FAS population by dose level and treatment group and the Phase 2 FAS population by tumor type and treatment group, exposure to nivolumab will be summarized descriptively as the following:

- **Number of infusions**: Number of infusions of nivolumab for a subject will be the number of administered, nonzero infusions of nivolumab recorded on the Nivolumab Dosing CRF.

- **Average fixed dose**: The average fixed dose of nivolumab (mg) will be the sum of the doses of nivolumab recorded (mg) on the Nivolumab Dosing CRF divided by the number of infusions of nivolumab. Average dose of nivolumab (mg) will be summarized for subjects in the Phase 1 and Phase 2 nivolumab population.
- **Average weight-adjusted dose (mg/kg)**: The average weight-adjusted dose of nivolumab (mg/kg) will be the sum of the doses of nivolumab recorded (mg/kg) on the Nivolumab Dosing CRF divided by the number of infusions of nivolumab. Average-weight adjusted dose of nivolumab (mg/kg) will be summarized for subjects in the Phase 1 and Phase 2 nivolumab population.
- **Fixed dose administered per cycle (mg)**: The actual fixed dose administered in mg per cycle. Fixed dose administered per cycle of nivolumab (mg) will be summarized for subjects in the Phase 1 and Phase 2 nivolumab population.
- **Weight-adjusted dose administered per cycle (mg/kg)**: The actual weight-adjusted dose administered in mg/kg per cycle. Weight-adjusted dose administered per cycle of nivolumab (mg/kg) will be summarized for subjects in the Phase 1 and Phase 2 nivolumab population.

6.4.3. Exposure for Ipilimumab

For subjects in the Phase 1 FAS population by dose level and treatment group and the Phase 2 FAS population by tumor type and treatment group, exposure to ipilimumab will be summarized descriptively as the following:

- **Number of infusions**: Number of doses of ipilimumab for a subject will be the number of administered, nonzero infusions of ipilimumab recorded on the Ipilimumab Dosing CRF.
- **Dose administered per cycle (mg/kg)**: The actual dose of ipilimumab administered in mg/kg per cycle.
- **Average dose (mg/kg)**: The average dose of ipilimumab (mg/kg) will be the sum of the doses of ipilimumab recorded on the Ipilimumab Dosing CRF divided by the number of infusions of ipilimumab.

6.5. Prior and Concomitant Medication

Prior medications and concomitant medications will be coded using the WHO Drug Dictionary March 2017 version and summarized by WHO drug class and WHO drug term by dose level and treatment group in the Phase 1 FAS population and by tumor type and treatment group in the Phase 2 FAS population. Results will be summarized as number and percentage of subjects with prior and concomitant medications by PT and WHO drug class.

7. EFFICACY

Sample data displays are provided in a separate document.

7.1. General Considerations

The primary efficacy endpoint for this study is ORR per RECIST v1.1 assessed in the Phase 2 response evaluable population. Secondary efficacy endpoints of this study include ORR, DOR, duration of disease control, disease control rate, and PFS by investigator assessment based on RECIST v1.1 and mRECIST as well as OS assessed at 1 year, 2 years, and EOS.

7.2. Efficacy Hypotheses

Each Simon 2-stage design will test the null hypothesis that the true ORR is less than or equal to the clinically insignificant response rate p_0% against the alternative hypothesis that the true ORR is equal to the target rate of p_1%. For each Simon 2-stage design, the value for p_0 is determined by a historical response rate. The same values for $p_0$and $p_1$will be used for alternative dosing sequences in the same tumor type and treatment combination. For example, the gastric cohorts in Treatment Groups F, G, and H will all use the same value for p_0 and p_1.

7.3. Analysis of the Efficacy Parameter

7.3.1. Response Criteria

Overall disease status will be categorized using RECIST v1.1. Subjects will have their overall response evaluated as CR, PR, SD, PD, or NE at each postbaseline radiological assessment based on changes in target lesions, nontarget lesions, and appearance of new lesions.

7.3.2. Objective Response Rate and Best Overall Response

7.3.2.1. Confirmed ORR and Confirmed BOR by RECIST v1.1

Per RECIST v1.1, in nonrandomized trials where response is the primary endpoint, confirmation of PR and CR is required to ensure responses are not the result of measurement error. Therefore, a subject is defined as a confirmed objective responder if the subject has an overall response of CR or PR at any postbaseline visit that is confirmed at a subsequent timepoint at least 4 weeks later, before the first occurrence of PD. Confirmed objective responders will be assessed based on RECIST v1.1.

Confirmed ORR is defined as the proportion of subjects with confirmed overall responses. Confirmed ORR will be estimated with 95% CIs. Confidence intervals will be based on the method for Simon 2-stage CIs of response rates outlined in Koyama and Chen (2008).

Confirmed ORR will be summarized by treatment group and tumor type as primary endpoint for the Phase 2 response evaluable population.

In general, confirmed BOR is the best response recorded postbaseline before and including the first PD, in the order of CR, PR, SD, PD and NE, in which CR and PR must be confirmed at a subsequent timepoint at least 4 weeks after the CR or PR is observed. Responses of CR, PR, or

SD after the first assessment of PD will not be considered. In the case of SD, measurements must meet the SD criteria at least once after the date of first dose at a minimum interval of 49 days. Subjects that fail to meet this criterion will have confirmed BOR of PD if the next available assessment indicates PD or NE if there is no additional assessment available.

Under RECIST v1.1, if radiologic imaging shows CR or PR, a tumor assessment should be repeated at a minimum of 4 weeks to confirm the response in order to claim the CR or PR as the confirmed BOR. If there is no second CR or PR tumor assessment, the CR or PR will be unconfirmed. Table 4 lists the scenarios of responses that can occur after an unconfirmed CR or PR and provides a rule for determining the confirmed BOR in each scenario. A sensitivity analysis for the ORR, in which BOR is determined using unconfirmed PR and CR, is detailed in Section 7.3.2.2.

For determination of confirmed BOR, confirmatory scans with a response of NE will be subsequently followed by another scan at a minimum of 4 weeks. For example, in the case of PR at the first timepoint followed by NE at a subsequent timepoint, if a third scan shows a PR, then the confirmed BOR will be PR. There will be no third confirmatory scans performed for a loss of response. For example, if a response of PR at the first timepoint is followed by a response of SD or PD at a subsequent timepoint, the confirmed BOR will be determined using the rules in Table 4.

Table 4: Derivation of Confirmed Best Overall Response

Overall Response at First Timepoint	Overall Response at Subsequent Timepoint	Confirmed Best Overall Response
CR	CR	CR
CR	PR	SD, PD, or PR[a]
CR	SD	SD,[a] provided minimum criteria for SD duration are met; otherwise, PD
CR	PD	SD,[a] provided minimum criteria for SD duration are met; otherwise, PD
CR	NE	SD,[a] provided minimum criteria for SD duration are met; otherwise NE
PR	CR	PR
PR	PR	PR
PR	SD	SD
PR	PD	SD provided minimum criteria for SD duration are met; otherwise, PD
PR	NE	SD,[a] provided minimum criteria for SD duration are met; otherwise NE
NE	NE	NE

[a] If a CR is truly met at the first timepoint, then any disease seen at a subsequent timepoint, even disease meeting PR criteria relative to baseline, makes the disease PD at that point (since disease must have reappeared after CR). Confirmed BOR would depend on whether the minimum duration for SD was met. However, sometimes CR may be claimed when subsequent scans suggest small lesions were likely still present and in fact the subject had a PR, not a CR, at the first timepoint. Under these circumstances, the original CR should be changed to a PR, and the confirmed BOR is PR.

For subjects with measurable disease at baseline, the RECIST v1.1 assessment criteria presented in Table 5 can be used to determine the overall disease status at a given timepoint based on the target lesion, nontarget lesion, and new lesion assessment.

Table 5: RECIST Evaluation Criteria for Overall Response: Measurable Disease at Baseline

Target Lesions	Nontarget Lesions	New Lesions	Overall Response
CR	CR	No	CR
CR	Non-CR/non-PD	No	PR
CR	NE	No	PR
PR	Non-PD or NE	No	PR
SD	Non-PD or NE	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

7.3.2.1.1. Subgroup Analyses for Confirmed Best Overall Response Under RECIST v 1.1 in Phase 2

Subgroups will be formed based on the following subject characteristics and baseline variables for Phase 2 response evaluable subjects whose data are available:

- PD-L1 expression within tumor type: high, negative/low, unknown
- Number of prior therapies for advanced and metastatic disease within tumor type
- Subjects with > 1 postbaseline scan within tumor type
- Tumor-type disease characteristics for RCC and urothelial carcinoma

7.3.2.2. Unconfirmed ORR and Unconfirmed BOR by RECIST v1.1 – Sensitivity and Supportive Analyses for Confirmed ORR and Confirmed BOR by RECIST v1.1

A sensitivity analysis for the ORR assessed under RECIST v1.1 will be performed using unconfirmed CRs and PRs. The unconfirmed BOR is defined as the best response recorded postbaseline before and including the first PD, in the order of CR, PR, SD, PD, and NE. For this definition, responses of CR and PR do not need to be confirmed at a subsequent timepoint. In the case of SD, measurements must meet the SD criteria at least once after the date of first dose at a minimum interval of 49 (56-7) days. Subjects that fail to meet this criterion will have BOR of PD if the next available assessment indicates PD or NE if there is no additional assessment available.

Unconfirmed ORR will be summarized by treatment group and tumor type as a sensitivity analysis for the primary endpoint ORR for the Phase 2 response evaluable population and as a sensitivity analysis for the secondary endpoint ORR for the Phase 1 response evaluable population.

7.3.2.2.1. Subgroup Analyses for Unconfirmed Best Overall Response by RECIST v 1.1 in Phase 1

For the sensitivity analysis for unconfirmed BOR, subgroups will be formed based on subjects' prior treatment with an anti–PD-1/PD-L1 therapy within their tumor type (Yes/No) for Phase 1 response evaluable subjects and whose data are available.

7.3.2.3. Confirmed ORR and Confirmed BOR by mRECIST

Under mRECIST, if radiologic imaging shows CR or PR, a tumor assessment should be repeated at a minimum of 4 weeks to confirm the response in order to claim the CR or PR as the confirmed BOR. If there is no second CR or PR tumor assessment, the CR or PR will be unconfirmed. Table 4 lists the scenarios that can occur after an unconfirmed CR or PR and provides a rule for determining the confirmed BOR in each scenario. A sensitivity analysis will be performed for the ORR assessed under mRECIST, in which BOR is determined using unconfirmed PR and CR.

The mRECIST was adapted from RECIST v1.1 to include criteria that accounts for new lesions that can occur in immuno-oncology subjects before the occurrence of an SD, PR, or CR. Under mRECIST, if radiologic imaging shows PD, tumor assessment should be repeated at a minimum of 4 weeks but not more than 6 weeks later to confirm the progression. If there is no second PD tumor assessment in the 4- to 6-week follow-up time, the PD will be defined as unconfirmed. Table 6 lists the scenarios that can occur after an unconfirmed PD in at least 4 weeks and no more than 6 weeks and provides rules for determining whether or not the unconfirmed PD will be counted as an event in the corresponding scenario.

Table 6: Rules for Determining PD Event Status After an Unconfirmed PD Under mRECIST

Event Occurring After Unconfirmed PD in the Confirmation Window (4-6 weeks)	PD Event Status
Subject had EOS/EOT or started new anticancer therapy.	PD will be confirmed as a PD.
Subject had a confirmed PD.	PD will be confirmed as a PD.
Subject had an CR, PR, SD, or NE.	PD will not be considered as a PD and counted as corresponding CR, PR, SD, or NE for the second timepoint only.

Confirmed ORR by mRECIST will be summarized by treatment group and tumor type for the Phase 2 response evaluable population.

7.3.2.4. Unconfirmed ORR and Unconfirmed BOR by mRECIST – Sensitivity and Supportive Analyses for Confirmed ORR and Confirmed BOR by mRECIST

A sensitivity analysis for the ORR assessed under mRECIST will be performed using unconfirmed CRs and PRs. The unconfirmed BOR is defined as the best response recorded postbaseline before and including the first PD, in the order of CR, PR, SD, PD, and NE. For this definition, responses of CR and PR do not need to be confirmed at a subsequent timepoint. In the case of SD, measurements must meet the SD criteria at least once after the date of first dose at a minimum interval of 49 (56 – 7) days. Subjects that fail to meet this criterion will have confirmed BOR of PD if the next available assessment indicates PD or NE if there is no additional assessment available.

Unconfirmed ORR as assessed by mRECIST will be summarized by treatment group and dose level for the Phase 1 response evaluable population and by treatment group and tumor type for the Phase 2 response evaluable population.

7.3.3. Duration of Response

Duration of response will be assessed with RECIST v1.1 and mRECIST criteria.

Censoring of DOR will follow the same algorithm as the censoring of PFS (Table 7). Kaplan-Meier curves for DOR will be presented by cohort-specific tumor types. The KM estimate of median DOR will be presented with its 95% CI. The 95% CI will be calculated using Brookmeyer and Crowley's method (Brookmeyer and Crowley 1982). A swim plot for DOR will be generated under both RECIST v1.1 and mRECIST criteria.

Duration of response as assessed by RECIST v1.1 and mRECIST will be summarized by treatment group and dose level for the Phase 1 response evaluable population and by treatment group and tumor type for the Phase 2 response evaluable population.

7.3.3.1. Duration of Response by RECIST v1.1

Under RECIST v1.1, for unconfirmed objective responders, DOR is defined as the time from the first overall response contributing to an unconfirmed objective response (CR or PR) to the earlier of the subject's death from any cause or first assessment of PD.

7.3.3.2. Duration of Response by mRECIST

Under mRECIST, for unconfirmed objective responders, DOR is the time from the first unconfirmed overall response contributing to an unconfirmed objective response (CR or PR) to the earlier of the subject's death from any cause or first confirmed assessment of PD. Note that the criteria for the assessment of PD in DOR are the same with ORR, which are presented in Section 7.3.2.3.

7.3.4. Duration of Disease Control and Disease Control Rate

Duration of disease control (CR, PR, and SD) is defined as the time from the first report of SD or better until disease progression or death from any cause, if occurring sooner than progression, as determined by investigator assessment of radiographic disease per RECIST v1.1 and mRECIST. Note that the criteria for the assessment of PD in duration of disease control are the same with ORR, which are presented in Section 7.3.2.3.

The duration of disease control will be estimated with 95% CIs overall and by treatment group. Confidence intervals will be calculated based on the exact method for binomial distributions. Swim plots for duration of disease control will be generated separately for RECIST v1.1 and mRECIST criteria.

Disease control rate, defined as the proportion of subjects who have disease control (CR + PR + SD), as per RECIST v1.1 and mRECIST will be summarized. For the determination of DCR, response of CR and PR do not need to be confirmed at a subsequent timepoint. In the case of SD, measurements must meet the SD criteria at least after the date of first dose at a minimum of 49 days. Subjects who fail to meet this criterion will have confirmed BOR of PD if the next available assessment indicated PD or NE if there is no additional assessment available. Disease control rate will be estimated with 95% CIs.

Duration of disease control and DCR as assessed per RECIST v1.1 and mRECIST will be summarized by treatment group and dose level for the Phase 1 response evaluable population and by treatment group and tumor type for the Phase 2 response evaluable population.

7.3.5. Largest Percentage Reduction in Sum of Diameters of Target Lesions

For each subject in the FAS population with target lesions at baseline, target lesion sizes will be measured by sum of diameters. The best percentage change from baseline, defined as the largest decrease in target lesion size for each subject, will be summarized descriptively, and a waterfall plot of the best percentage change will be generated.

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 (ie, assessment missing or NE), then the overall sum of diameters for target lesions will not be evaluable for that postbaseline timepoint.

7.3.6. Percentage Change in Sum of Diameters of Target Lesions Over Time

For each subject in the FAS population with target lesions at baseline, target lesion sizes will be measured by sum of diameters. The percentage change in sum of diameter of target lesions over time will be listed and a spider plot will be generated.

7.3.7. Progression-Free Survival

Progression-free survival is defined as the length of time between the baseline visit (Day 1) and the earlier of death or PD as assessed by RECIST v1.1 and mRECIST. Date of death will be determined using the Death Report CRF, and analyses will be summarized for the FAS population.

Censoring for PFS will follow the algorithm outlined in Table 7 which is based on the FDA Guidance for Industry: Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics (FDA 2007).

Kaplan-Meier curves for PFS will be presented by cohort-specific tumor types. The KM estimate of median PFS will be presented with its 95% CI. The 95% CI will be calculated using the Brookmeyer and Crowley's method (1982).

Table 7: Evaluation and Censoring of Progression-Free Survival

Situation	Outcome	Date of Progression or Censoring
No baseline tumor assessments	Censored	Date of Day 1
No valid postbaseline response assessments	Censored	Date of Day 1
Progression documented between scheduled response assessments	Progressed	Date of first overall response of PD
No progression	Censored	Date of last valid radiologic assessment (not NE and not missing)
Study discontinuation for undocumented progression	Censored	Date of last valid radiologic assessment (not NE and not missing)
Study 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 progressive response assessment	Progressed	Date of death
Death between adequate response assessments	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 death

NE = not evaluable.

7.3.7.1. Progression-Free Survival by RECIST v1.1

Under RECIST v1.1, PFS is defined as the length of time between the baseline visit (Day 1) and the earlier of death or first assessment of PD as assessed by RECIST v1.1.

7.3.7.2. Progression-Free Survival by mRECIST

Under mRECIST, PFS is defined as the length of time between the baseline visit (Day 1) and the earlier of death or first confirmed assessment of PD (as described in Table 6).

7.3.8. Overall Survival

Overall survival is defined as the interval between Cycle 1 Day 1 and the date of death due to any cause. Date of death will be determined using the Death Report, the Survival Follow-Up, and the Subject Status CRFs. Subjects who are lost-to-follow-up or still alive at the time of analysis will be right-censored at the earlier of the date that the subject was last known alive and the clinical data cutoff date for the analysis. The last known alive date is defined as the later of the last study visit and the date the subject was last known alive from the Survival Follow-Up and Subject Status CRFs, and the analyses will be summarized for the FAS population.

Kaplan-Meier time to event curves will be presented by treatment groups. Median survival will be estimated using the Kaplan-Meier method. Kaplan-Meier estimates of 1-year and 2-year survival probabilities will be provided. Confidence intervals for median survival time will be calculated using the method of Brookmeyer and Crowley (1982).

[redacted]

8. SAFETY AND TOLERABILITY

Sample data displays are provided in a separate document.

8.1. 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 PTs reported on relatively few subjects.

Unless otherwise stated, table summaries will be limited to TEAEs.

8.2. Adverse Events

8.2.1. Adverse Event Definitions

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

Adverse events will be tabulated by MedDRA PT and SOC. Severity of AEs will be graded using the National Cancer Institute CTCAE. The CTCAE version 4.03 is used for this study. The CTCAE reporting guidelines and grading details are available on the Cancer Therapy Evaluation Program website.

The subset of AEs considered by the investigator to be related to INCAGN01949, nivolumab, or ipilimumab will be considered to be treatment-related AEs and will be summarized. 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. In addition, SAEs will also be tabulated.

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 5 as follows: 1 = mild, 2 = moderate, 3 = severe, 4 = life-threatening, and 5 = death related to AE. 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 collected as an AE until the event resolves. Only the worst grade will be reported in AE summaries. Also, the Grade 3 or higher AEs will be summarized.

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

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

For purposes of analysis, all AEs will be considered TEAEs unless the AE can unequivocally be defined as not treatment-emergent.

8.2.2. Dose-Limiting Toxicities

The number of subjects with DLTs and the type of DLT will be listed by dose level and treatment group. An AE for a subject will be identified as a DLT if the event is recorded as a Protocol-defined DLT on the AE CRF.

8.2.3. Adverse Events of Special Interest

8.2.3.1. Immune-Related Adverse Events

The number of subjects with irAEs and type of irAE will be listed by dose level and treatment group for the Phase 1 FAS population and by tumor type and treatment group in the Phase 2 FAS population. Adverse event terms will be reviewed periodically without respect to treatment group by the medical monitor and clinical scientist to determine which AE terms correspond to irAEs. This periodic review may also occur after database lock. The medical monitor and clinical scientist will also review investigator-reported irAEs to determine whether they qualify as irAEs. For example, a rash will be counted as an irAE even if the investigator did not report it as an irAE.

8.2.3.1.1. Adverse Events Identified as Incyte MedDRA Queries

Prospectively defined Incyte MedDRA Queries will be used to conduct analyses to evaluate the safety profile. Incyte MedDRA Queries are queries constructed by Incyte based on MedDRA PTs identified through review of standardized MedDRA queries for clinically relevant terms. Sets of included terms will be identified and archived before database lock for the individual studies. Incyte MedDRA Queries searches are to be conducted for the following TEAEs: hemorrhage events, dizziness, weight gain, thrombotic events, urinary tract infections, herpes zoster infections, tuberculosis, hepatitis B reactivation, and infections other than those stated previously. In addition, these other infections will be analyzed by subcategories of upper respiratory tract infections, lower respiratory tract infections, skin and soft tissue infections, alimentary tract infections, other viral infections, and miscellaneous infections with each tabulated by MedDRA PT.

8.2.3.2. Infusion-Related Reactions

Infusion-related reactions, defined as AEs that are identified as infusion related reaction by the investigator on the Infusion-Related Reaction CRF, will be summarized in a table and listing. The summaries will include the treatment group, dose level, cycle number, study day, date of

onset of AE, date of the associated infusion, and signs and symptoms of the infusion-related reaction.

8.2.4. Adverse Event Summaries

An overall summary of AEs by treatment group and by tumor type as applicable will include the following:

- Number (%) of subjects reporting any TEAEs
- Number (%) of subjects reporting any DLTs
- Number (%) of subjects reporting any SAEs
- Number (%) of subjects reporting any Grade 3 or higher TEAEs
- Number (%) of subjects reporting any TEAEs related to INCAGN01949
- Number (%) of subjects reporting any TEAEs related to nivolumab
- Number (%) of subjects reporting any TEAEs related to ipilimumab
- Number (%) of subjects who temporarily interrupted INCAGN01949 because of TEAEs
- Number (%) of subjects who temporarily interrupted nivolumab because of TEAEs
- Number (%) of subjects who temporarily interrupted ipilimumab because of TEAEs
- Number (%) of subjects who permanently discontinued INCAGN01949 because of TEAEs
- Number (%) of subjects with INCAGN01949 dose reductions because of TEAEs
- Number (%) of subjects who had a fatal TEAE
- Number (%) of subjects who withdrew from study because of an TEAE

The following summaries will be produced by MedDRA term:

- Summary of TEAEs by SOC and PT
- Summary of TEAEs by PT in decreasing order of frequency
- Summary of TEAEs by SOC, PT, and maximum severity
- Summary of Grade 3 or higher TEAEs by SOC and PT
- Summary of INCAGN0[redacted] treatment-related AEs by SOC and PT
- Summary of nivolumab treatment-related AEs by SOC and PT
- Summary of ipilimumab treatment-related AEs by SOC and PT
- Summary of Grade 3 or higher INCAGN01949 treatment-related AEs by PT in descending order of frequency
- Summary of Grade 3 or higher nivolumab treatment-related AEs by PT in descending order of frequency

- Summary of Grade 3 or higher ipilimumab treatment-related AEs by PT in descending order of frequency
- Summary of treatment-emergent SAEs by SOC and PT
- Summary of treatment-emergent SAEs by PT in descending order of frequency
- Summary of treatment-emergent non-SAE by SOC and PT.
- Summary of treatment-related SAEs by SOC and PT
- Summary of TEAEs leading to INCAGN01949 dose reduction by SOC and PT
- Summary of TEAEs leading to INCAGN01949 dose interruption by SOC and PT
- Summary of TEAEs leading to nivolumab dose interruption by SOC and PT
- Summary of TEAEs leading to ipilimumab dose interruption by SOC and PT
- Summary of TEAEs leading to discontinuation of INCAGN01949 by SOC and PT
- Summary of TEAEs leading to death by SOC and PT

8.3. Clinical Laboratory Tests

8.3.1. Laboratory Value Definitions

Laboratory values and change from baseline values will be summarized descriptively by visit. Baseline will be determined according to Section 4.1.3. If there are multiple values that meet the criteria for baseline, additional rules may be provided after consultation with the medical monitor to delineate which value will be defined as baseline.

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

8.3.2. Laboratory Value Summaries

All test results and associated normal ranges from local laboratories will be reported in SI units. 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, if query is unsuccessful at resolving the issue and analysis is mandatory, then the clinical scientist and medical monitor can provide a suitable normal range to be used in determining CTCAE grading and flags for above and below normal.

When there are multiple laboratory nonmissing values for a subject's particular test at a scheduled visit, the laboratory value with the smallest laboratory sequence number will be used in by-visit summaries (Table 8).

Table 8: Identification of Records for Postbaseline 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	

Numeric laboratory values will be summarized descriptively in SI units, and non-numeric test values will be tabulated when necessary. In addition, line graphs and box-and-whisker plots will be provided for hemoglobin, platelet counts, WBCs, and neutrophils.

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 FAS population. 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.

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

Values at each scheduled visit, change, and percentage change from baseline for vital signs, including systolic blood pressure, diastolic blood pressure, pulse, respiration rate, and body temperature, will be summarized descriptively.

Criteria for clinically notable vital sign abnormalities are defined in Table 9. 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 > 25% from baseline. The abnormal values for subjects exhibiting alert vital sign abnormalities will be listed.

Table 9: 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/min	< 8/min

8.5. Electrocardiograms

Twelve-lead ECGs including heart rate, PR, QRS, QT, QTcF, QTcB, JTC, and RR intervals will be obtained for each subject at the screening, EOT, and safety follow-up visits during the study. Values at each scheduled visit, change, and percentage change from baseline will be summarized for each ECG parameter. Baseline will be determined as the average of all nonmissing values before the first administration of INCAGN01949, nivolumab, or ipilimumab.

Criteria for clinically notable ECG abnormalities are defined in Table 10. Subjects exhibiting clinically notable ECG abnormalities will be listed with study visit and assigned treatment group. Abnormal values for subjects with alert ECG values, defined as both the absolute value and the percentage change from baseline being outside normal ranges, will be identified and listed.

Table 10: Criteria for Clinically Notable Electrocardiogram Abnormalities

Parameter	High Threshold	Low Threshold
QTcF	> 460 msec	< 295 msec
PR	> 220 msec	< 75 msec
QRS	> 120 msec	< 50 msec
QT	> 500 msec	< 300 msec
RR	> 1330 msec	< 600 msec

QTcF = Fridericia correction.

9. INTERIM ANALYSES

9.1. Overview of Interim Analyses

9.1.1. Interim Analyses for Safety

There will be no planned, formal interim analyses for the Phase 1 dose escalation portion of the study. The review of accrued clinical data will be conducted by Incyte and provided to study investigators via teleconferences at the end of Phase 1 of the study. Based on review of the most current safety data, the sponsor (in consultation with the study investigators and using the dose-escalation/de-escalation rules) will determine if and at what dose additional subjects should be treated in the study.

A DMC will be charged with evaluating interim safety results. The DMC will be composed of members who are internal to the sponsor but not members of the study team. The DMC members will include a medical monitor who will serve as the DMC chair and meeting facilitator, the head of biostatistics or a designee, the head of regulatory affairs or a designee, and the study medical monitor who will be a nonvoting member. The DMC will meet at least every 6 months starting after the first 10 subjects have been dosed to review the rate of DLTs and irAEs in each treatment group and the overall safety of the subjects treated with INCAGN01949, nivolumab, and ipilimumab. Additional operational details of the interim analyses, including TFLs provided to the DMC, will be provided in the DMC Charter. Additional safety analyses may be performed at the discretion of the DMC chair.

9.1.2. Interim Analyses for Futility

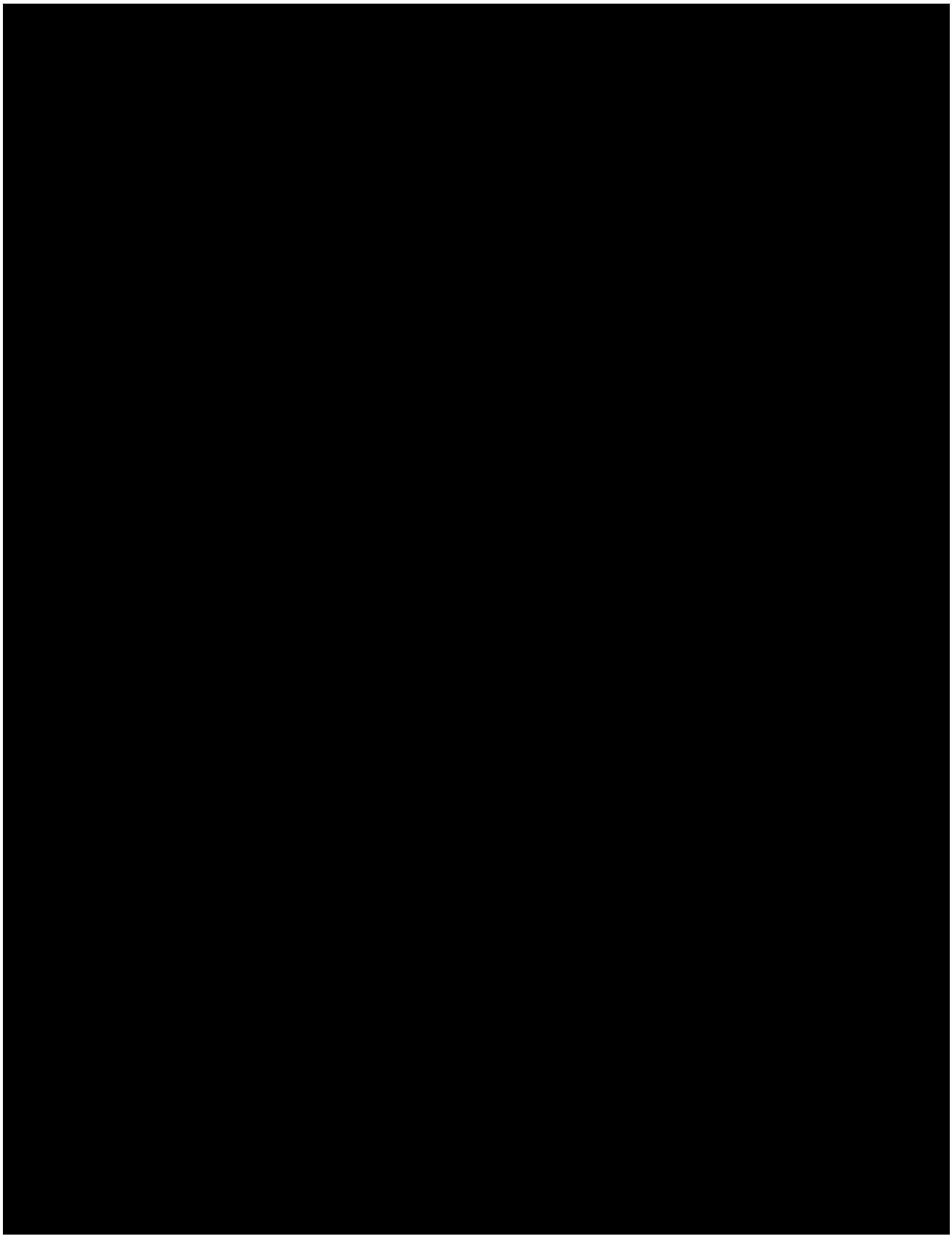
9.1.2.1. Simon 2-Stage Futility Rules

An interim analysis of efficacy will be conducted in Phase 2 by applying the Simon 2-stage design for each tumor within a given treatment group. During Stage 1, n_1 evaluable subjects treated at the recommended dose and schedule will be enrolled, and if r_1 or fewer responses are observed by the Week 16 assessment, then the cohort will be discontinued. To be counted as evaluable for the calculation in Stage 1, subjects must have discontinued from the study, reached the Week 16 assessment, or had at least 2 scans. As discussed in Section 3.2, the Simon 2-stage designs conducted for each tumor type within each treatment group have design parameters that are determined by historical response rates and will have different sample sizes and futility results depending on the historical response rate. The probability of early termination for Stage 1 in Treatment Groups F, G, and H is summarized in Table 11.

Table 11: Probability of Early Termination for Simon 2-Stage Design in Phase 2 in Treatment Groups F, G, and H

Cohort (Tumor Type)	p_0	p_1	Probability of Early Termination	
			Under H_0	Under H_A
RCC	25%	40%	0.6736	0.0940
Urothelial	20%	35%	0.7134	0.1148
Relapsed to anti–PD-1/L1	10%	25%	0.6769	0.0913

[redacted]



[redacted]

9.2. Data Cutoff for Interim Analysis

As discussed in Section 9.1.1, the DMC will meet every 6 months to review safety analyses. All efficacy and safety analyses will use a clinical data cutoff of 3 weeks before execution of the planned safety or interim analysis. This period will help ensure accuracy of the interim data by providing the sponsor time to perform data review, issue queries regarding data quality issues to sites, and to resolve such queries.

[redacted]

10. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 14.

Table 14: Statistical Analysis Plan Versions

SAP Version	Date
Original	06 FEB 2018

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 December 20, 2017.

Koyama T, Chen H. Proper inference from Simon's two-stage designs. Stat Med 2008;27:3145-3154.

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

[redacted]

APPENDIX A. PLANNED TABLES AND FIGURES

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

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

Tables

Table No.	Title	Population	Standard	In-Text
Baseline and Demographic Characteristics				
1.1	**Disposition**			
1.1.1.1	Analysis Populations	Phase 1 FAS Population	X	X
1.1.1.2	Analysis Populations	Phase 2 FAS Population	X	X
1.1.2.1	Summary of Subject Disposition	Phase 1 FAS Population	X	X
1.1.2.2	Summary of Subject Disposition	Phase 2 FAS Population	X	X
1.1.2.3	Summary of Subject Disposition	FAS Population	X	
1.1.3	Summary of Number of Subjects Enrolled by Country and Site	FAS Population	X	
1.2 Demography				
1.2.1	Summary of Demographics	Phase 1 FAS Population	X	X
1.2.2	Summary of Demographics – by Tumor Type	Phase 2 FAS Population	X	X
1.3 Baseline Characteristics				
1.3.1.1	Summary of Baseline Disease Characteristics and Disease History for Phase 1 Solid Tumor Types	Phase 1 FAS Population	X	
1.3.1.2.1	Summary of Baseline Disease Characteristics and Disease History for Phase 2 Solid Tumor Types	[redacted] Phase 2 FAS Population	X	
1.3.1.2.2	Summary of Baseline Disease Characteristics and Disease History	RCC Phase 2 FAS Population	X	

Table No.	Title	Population	Standard	In-Text
1.3.1.2.3	Summary of Baseline Disease Characteristics and Disease History	Urothelial Phase 2 FAS Population	X	
1.3.1.2.4	Summary of Baseline Disease Characteristics and Disease History	Relapsed PD-1 Phase 2 FAS Population	X	
1.4 Prior Medication and Concomitant Medication				
1.4.1.1	Summary of Prior Systemic Therapy	Phase 1 FAS Population		
1.4.1.2	Summary of Prior Systemic Therapy – by Tumor Type	Phase 2 FAS Population		
1.4.2.1	Summary of Prior Medications	Phase 1 FAS Population	X	
1.4.2.2	Summary of Prior Medications – by Tumor Type	Phase 2 FAS Population	X	
1.4.3	Summary of Prior Radiation – by Tumor Type	Phase 2 FAS Population		
1.4.4	Summary of Prior Surgery – by Tumor Type	Phase 2 FAS Population		
1.4.5.1	Summary of Concomitant Medications	Phase 1 FAS Population	X	
1.4.5.2	Summary of Concomitant Medications – by Tumor Type	Phase 2 FAS Population	X	
1.5 Others				
1.5.1	Summary of General Medical History	Phase 1 FAS Population	X	
1.5.2	Summary of General Medical History – by Tumor Type	Phase 2 FAS Population	X	
1.5.3	Summary of Protocol Deviations	FAS Population		X

Table No.	Title	Population	Standard	In-Text
2.1 Efficacy				
2.1.1.1	Summary of Confirmed Best Response, Duration of Response, and Duration of Disease Control Under RECIST v1.1 – by Treatment Group and Dose	Phase 1 Response Evaluable Population		X
2.1.1.2	Summary of Unconfirmed Best Response, Duration of Response, and Duration of Disease Control Under RECIST v1.1 – by Treatment Group and Dose	Phase 1 Response Evaluable Population		X
2.1.2.1	Summary of Confirmed Best Response, Duration of Response, and Duration of Disease Control Under RECIST v1.1 – by Treatment Group and Dose	Phase 2 Response Evaluable Population		X
2.1.2.2	Summary of Unconfirmed Best Response, Duration of Response, and Duration of Disease Control Under RECIST – by Treatment Group and Dose	Phase 2 Response Evaluable Population		X
2.1.3.1	Summary of Confirmed Best Response, Duration of Response, and Duration of Disease Control under mRECIST – by Treatment Group and Tumor Type	Phase 2 Response Evaluable Population		X
2.1.3.2	Summary of Unconfirmed Best Response, Duration of Response, and Duration of Disease Control Under mRECIST – by Treatment Group and Tumor Type	Phase 2 Response Evaluable Population		X
2.1.4.1	Summary of Progression-Free Survival Under RECIST v1.1	Phase 1 FAS Population		X
2.1.4.2	Summary of Progression-Free Survival Under RECIST v1.1 – by Tumor Type	Phase 2 FAS Population		X
2.1.5.1	Summary of Progression-Free Survival Under mRECIST	Phase 1 FAS Population		X
2.1.5.2	Summary of Progression-Free Survival under mRECIST – by Tumor Type	Phase 2 FAS Population		X
2.1.6.1	Summary of Overall Survival	Phase 1 FAS Population		X
2.1.6.2	Summary of Overall Survival – by Tumor Type	Phase 2 FAS Population		X

Table No.	Title	Population	Standard	In-Text
[redacted]				
Safety				
3.1 Dose Exposure				
3.1.1.1	Summary of INCAGN01949 Drug Exposure – by Treatment Group and Dose	Phase 1 FAS Population	X	X
3.1.1.2	Summary of INCAGN01949 Drug Exposure – by Treatment Group and Tumor Type	Phase 2 FAS Population	X	X
3.1.2.1	Summary of Nivolumab Drug Exposure – by Treatment Group and Dose	Phase 1 Nivolumab FAS Population	X	X
3.1.2.2	Summary of Nivolumab Drug Exposure – by Treatment Group and Tumor Type	Phase 2 Nivolumab FAS Population	X	X
3.1.3.1	Summary of Ipilimumab Drug Exposure – by Treatment Group and Dose	Phase 1 Ipilimumab FAS Population	X	X
3.1.3.2	Summary of Ipilimumab Drug Exposure – by Treatment Group and Tumor Type	Phase 2 Ipilimumab FAS Population	X	X
3.1.4.1	Summary of INCAGN01949 Drug Exposure by Visit – by Treatment Group and Dose	Phase 1 FAS Population		
3.1.4.2	Summary of INCAGN01949 Drug Exposure by Visit – by Treatment Group and Tumor Type	Phase 2 FAS Population		
3.1.5.1	Summary of Nivolumab Drug Exposure by Visit – by Treatment Group and Dose	Phase 1 Nivolumab FAS Population		
3.1.5.2	Summary of Nivolumab Drug Exposure by Visit – by Treatment Group and Tumor Type	Phase 2 Nivolumab FAS Population		

Table No.	Title	Population	Standard	In-Text
3.1.6.1	Summary of Ipilimumab Drug Exposure by Visit – by Treatment Group and Dose	Phase 1 Ipilimumab FAS Population		
3.1.6.2	Summary of Ipilimumab Drug Exposure by Visit – by Treatment Group and Tumor Type	Phase 2 Ipilimumab FAS Population		
3.2 Adverse Events				
3.2.1.1	Overall Summary of Treatment-Emergent Adverse Events – by Treatment Group and Dose	Phase 1 FAS Population	X	X
3.2.1.2	Overall Summary of Treatment-Emergent Adverse Events – by Treatment Group and Tumor Type	Phase 2 FAS Population	X	X
3.2.2.1	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – by Treatment Group and Dose	Phase 1 FAS Population	X	
3.2.3.1	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – by Treatment Group and Tumor Type	Phase 2 FAS Population	X	
3.2.4.1	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency – by Treatment Group and Dose	Phase 1 FAS Population	X	X
3.2.4.2	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency – by Treatment Group and Tumor Type	Phase 2 FAS Population	X	X
3.2.5.1	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity – by Treatment Group and Dose	Phase 1 FAS Population	X	
3.2.5.2	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity – by Treatment Group and Tumor Type	Phase 2 FAS Population	X	
3.2.6.1	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – by Treatment Group and Dose	Phase 1 FAS Population	X	X
3.2.6.2	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – by Treatment Group and Tumor Type	Phase 2 FAS Population	X	X
3.2.7.1	Summary of Any INCAGN01949 Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term – by Treatment Group and Dose	Phase 1 FAS Population	X	X
3.2.7.2	Summary of Any INCAGN01949 Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term – by Treatment Group and Tumor Type	Phase 2 FAS Population	X	X
3.2.8.1	Summary of Any Nivolumab Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term – by Treatment Group and Dose	Phase 1 Nivolumab FAS Population	X	X

Table No.	Title	Population	Standard	In-Text
3.2.8.2	Summary of Any Nivolumab Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term – by Treatment Group and Tumor Type	Phase 2 Nivolumab FAS Population	X	X
3.2.9.1	Summary of Any Ipilimumab Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term – by Treatment Group and Dose	Phase 1 Ipilimumab FAS Population	X	X
3.2.9.2	Summary of Any Ipilimumab Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term – by Treatment Group and Tumor Type	Phase 2 Ipilimumab FAS Population	X	X
3.2.10.1	Summary of Any Grade 3 or Higher INCAGN01949 Treatment-Related Adverse Events by MedDRA Preferred Term in Order of Decreasing Frequency – by Treatment Group and Dose	Phase 1 FAS Population	X	
3.2.10.2	Summary of Any Grade 3 or Higher INCAGN01949 Treatment-Related Adverse Events by MedDRA Preferred Term in Order of Decreasing Frequency – by Treatment Group and Tumor Type	Phase 2 FAS Population	X	
3.2.11.1	Summary of Any Grade 3 or Higher Nivolumab Treatment-Related Adverse Events by MedDRA Preferred Term in Order of Decreasing Frequency – by Treatment Group and Dose	Phase 1 Nivolumab FAS Population	X	
3.2.11.2	Summary of Any Grade 3 or Higher Nivolumab Treatment-Related Adverse Events by MedDRA Preferred Term in Order of Decreasing Frequency – by Treatment Group and Tumor Type	Phase 2 Nivolumab FAS Population	X	
3.2.12.1	Summary of Any Grade 3 or Higher Ipilimumab Treatment-Related Adverse Events by MedDRA Preferred Term in Order of Decreasing Frequency – by Treatment Group and Dose	Phase 1 Ipilimumab FAS Population	X	
3.2.12.2	Summary of Any Grade 3 or Higher Ipilimumab Treatment-Related Adverse Events by MedDRA Preferred Term in Order of Decreasing Frequency – by Treatment Group and Tumor Type	Phase 2 Ipilimumab FAS Population	X	
3.2.13.1	Summary of Any INCAGN01949 Treatment-Related Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term– by Treatment Group and Dose	Phase 1 FAS Population	X	
3.2.13.2	Summary of Any INCAGN01949 Treatment-Related Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term – by Treatment Group and Tumor Type	Phase 2 FAS Population	X	
3.2.14.1	Summary of Any Nivolumab Treatment-Related Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term – by Treatment Group and Dose	Phase 1 Nivolumab FAS Population	X	
3.2.14.2	Summary of Any Nivolumab Treatment-Related Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term – by Treatment Group and Tumor Type	Phase 2 Nivolumab FAS Population	X	

Table No.	Title	Population	Standard	In-Text
3.2.15.1	Summary of Any Ipilimumab Treatment-Related Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term– by Treatment Group and Dose	Phase 1 Ipilimumab FAS Population	X	
3.2.15.2	Summary of Any Ipilimumab Treatment-Related Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term – by Treatment Group and Tumor Type	Phase 2 Ipilimumab FAS Population	X	
3.2.16.1	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – by Treatment Group and Dose	Phase 1 FAS Population	X	
3.2.16.2	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – by Treatment Group and Tumor Type	Phase 2 FAS Population	X	
3.2.17.1	Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency – by Treatment Group and Dose	Phase 1 FAS Population		X
3.2.17.2	Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency – by Treatment Group and Tumor Type	Phase 2 FAS Population		X
3.2.18.1	Summary of Non-Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – by Treatment Group and Dose	Phase 1 FAS Population	X	
3.2.18.2	Summary of Non-Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – by Treatment Group and Tumor Type	Phase 2 FAS Population	X	
3.2.19.1	Summary of Treatment-Related Serious Adverse Events by MedDRA System Organ Class and Preferred Term – by Treatment Group and Dose	Phase 1 FAS Population	X	
3.2.19.2	Summary of Treatment-Related Serious Adverse Events by MedDRA System Organ Class and Preferred Term – by Treatment Group and Tumor Type	Phase 2 FAS Population	X	
3.2.20.1	Summary of Treatment-Emergent Adverse Events Leading to INCAGN01949 Dose Reduction by MedDRA System Organ Class and Preferred Term – by Treatment Group and Dose	Phase 1 FAS Population	X	
3.2.20.2	Summary of Treatment-Emergent Adverse Events Leading to INCAGN01949 Dose Reduction by MedDRA System Organ Class and Preferred Term – by Treatment Group and Tumor Type	Phase 2 FAS Population	X	
3.2.21.1	Summary of Treatment-Emergent Adverse Events Leading to INCAGN01949 Dose Interruption by MedDRA System Organ Class and Preferred Term – by Treatment Group and Dose	Phase 1 FAS Population		
3.2.21.2	Summary of Treatment-Emergent Adverse Events Leading to INCAGN01949 Dose Interruption by MedDRA System Organ Class and Preferred Term – by Treatment Group and Tumor Type	Phase 2 FAS Population		
3.2.22.1	Summary of Treatment-Emergent Adverse Events Leading to Nivolumab Dose Interruption by MedDRA System Organ Class and Preferred Term – by Treatment Group and Dose	Phase 1 FAS Population		

Table No.	Title	Population	Standard	In-Text
3.2.22.2	Summary of Treatment-Emergent Adverse Events Leading to Nivolumab Dose Interruption by MedDRA System Organ Class and Preferred Term – by Treatment Group and Tumor Type	Phase 2 FAS Population		
3.2.23.1	Summary of Treatment-Emergent Adverse Events Leading to Ipilimumab Dose Interruption by MedDRA System Organ Class and Preferred Term – by Treatment Group and Dose	Phase 1 FAS Population		
3.2.23.2	Summary of Treatment-Emergent Adverse Events Leading to Ipilimumab Dose Interruption by MedDRA System Organ Class and Preferred Term – by Treatment Group and Tumor Type	Phase 2 FAS Population		
3.2.24.1	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of INCAGN01949 by MedDRA System Organ Class and Preferred Term – by Treatment Group and Dose	Phase 1 FAS Population	X	
3.2.24.2	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of INCAGN01949 by MedDRA System Organ Class and Preferred Term – by Treatment Group and Tumor Type	Phase 2 FAS Population	X	
3.2.25.1	Summary of Treatment-Emergent Immune-Related Adverse Events (Investigator Identified) by MedDRA System Organ Class and Preferred Term – by Treatment Group and Dose	Phase 1 FAS Population		
3.2.25.2	Summary of Treatment-Emergent Immune-Related Adverse Events (Investigator Identified) by MedDRA System Organ Class and Preferred Term – by Treatment Group and Tumor Type	Phase 2 FAS Population		
3.2.26.1	Summary of Treatment-Emergent Immune-Related Adverse Events (Investigator Identified) by MedDRA System Organ Class, Preferred Term, and Maximum Severity – by Treatment Group and Dose	Phase 1 FAS Population		
3.2.26.2	Summary of Treatment-Emergent Immune-Related Adverse Events (Investigator Identified) by MedDRA System Organ Class, Preferred Term, and Maximum Severity – by Treatment Group and Tumor Type	Phase 2 FAS Population		
3.2.27.1	Summary of Grade 3 or Higher Treatment-Emergent Immune-Related Adverse Events (Investigator Identified) by MedDRA System Organ Class and Preferred Term – by Treatment Group and Dose	Phase 1 FAS Population		X
3.2.27.2	Summary of Grade 3 or Higher Treatment-Emergent Immune-Related Adverse Events (Investigator Identified) by MedDRA System Organ Class and Preferred Term – by Treatment Group and Tumor Type	Phase 2 FAS Population		X
3.2.28	Life Table Estimate of Time to First Grade 3 or Higher Treatment-Emergent Adverse Event – by Treatment Group and Tumor Type	Phase 2 FAS Population	X	
3.2.29.1	Summary of Adverse Events With a Fatal Outcome by System Organ Class and Preferred Term – by Treatment Group and Dose	Phase 1 FAS Population	X	
3.2.29.2	Summary of Adverse Events With a Fatal Outcome by System Organ Class and Preferred Term – by Treatment Group and Tumor Type	Phase 2 FAS Population	X	

Table No.	Title	Population	Standard	In-Text
3.2.30.1	Summary of Infusion Reactions – by Treatment Group and Dose	Phase 1 FAS Population		
3.2.30.2	Summary of Infusion Reactions – by Treatment Group and Tumor Type	Phase 2 FAS Population		
3.3 Laboratory				
3.3.1	Summary of Laboratory Values – Hematology	Phase 2 FAS Population	X	
3.3.2.1	Summary of Hematology Laboratory Values in CTC Grade – To the Worst Abnormal Value	Phase 1 FAS Population		
3.3.2.2	Summary of Hematology Laboratory Values in CTC Grade – To the Worst Abnormal Value	Phase 2 FAS Population		
3.3.3	Summary of Laboratory Values – Chemistry	Phase 2 FAS Population	X	
3.3.4.1	Summary of Chemistry Laboratory Values in CTC Grade – to the Worst Abnormal Value	Phase 1 FAS Population		
3.3.4.2	Summary of Chemistry Laboratory Values in CTC Grade – to the Worst Abnormal Value	Phase 2 FAS Population		
3.4 Vital Signs				
3.4.1.1	Summary of Systolic Blood Pressure (mmHg)	Phase 1 FAS Population	X	
3.4.1.2	Summary of Systolic Blood Pressure (mmHg) – by Tumor Type	Phase 2 FAS Population	X	
3.4.2.1	Summary of Diastolic Blood Pressure (mmHg)	Phase 1 FAS Population	X	
3.4.2.2	Summary of Diastolic Blood Pressure (mmHg) – by Tumor Type	Phase 2 FAS Population	X	
3.4.3.1	Summary of Heart Rate (bpm)	Phase 1 FAS Population	X	
3.4.3.2	Summary of Heart Rate (bpm) – by Tumor Type	Phase 2 FAS Population	X	
3.4.4.1	Summary of Respiration Rate (bpm)	Phase 1 FAS Population	X	
3.4.4.2	Summary of Respiration Rate (bpm) – by Tumor Type	Phase 2 FAS Population	X	

Table No.	Title	Population	Standard	In-Text
3.4.5.1	Summary of Body Temperature (°C)	Phase 1 FAS Population	X	
3.4.5.2	Summary of Body Temperature (°C) – by Tumor Type	Phase 2 FAS Population	X	
3.4.6.1	Summary of Weight (kg)	Phase 1 FAS Population	X	
3.4.6.2	Summary of Weight (kg) – by Tumor Type	Phase 2 FAS Population	X	
3.5 ECG				
3.5.1.1	Summary of PR Interval (msec) From Local Lab 12-Lead ECG	Phase 1 FAS Population	X	
3.5.1.2	Summary of PR Interval (msec) From Local Lab 12-Lead ECG – by Tumor Type	Phase 2 FAS Population	X	
3.5.2.1	Summary of RR Interval (msec) From Local Lab 12-Lead ECG	Phase 1 FAS Population	X	
3.5.2.2	Summary of RR Interval (msec) From Local Lab 12-Lead ECG – by Tumor Type	Phase 2 FAS Population	X	
3.5.3.1	Summary of QT Interval (msec) From Local l Lab 12-Lead ECG	Phase 1 FAS Population	X	
3.5.3.2	Summary of QT Interval (msec) From Local Lab 12-Lead ECG – by Tumor Type	Phase 2 FAS Population	X	
3.5.4.1	Summary of QRS Interval (msec) From Local Lab 12-Lead ECG	Phase 1 FAS Population	X	
3.5.4.2	Summary of QRS Interval (msec) From Local Lab 12-Lead ECG – by Tumor Type	Phase 2 FAS Population	X	
3.5.5.1	Summary of QTcB Interval (msec) From Local Lab 12-Lead ECG	Phase 1 FAS Population	X	
3.5.5.2	Summary of QTcB Interval (msec) From Local Lab 12-Lead ECG – by Tumor Type	Phase 2 FAS Population	X	
3.5.6.1	Summary of QTcF Interval (msec) From Local Lab 12-Lead ECG	Phase 1 FAS Population	X	
3.5.6.2	Summary of QTcF Interval (msec) From Local Lab 12-Lead ECG – by Tumor Type	Phase 2 FAS Population	X	

Table No.	Title	Population	Standard	In-Text
3.5.7.1	Summary of JTc Interval (msec) From Local Lab 12-Lead ECG	Phase 1 FAS Population		
3.5.7.2	Summary of JTc Interval (msec) From Local Lab 12-Lead ECG – by Tumor Type	Phase 2 FAS Population		
3.5.8.1	Summary of Heart Rate (beats/min) From Local Lab 12-Lead ECG	Phase 1 FAS Population	X	
3.5.8.2	Summary of Heart Rate (beats/min) From Local Lab 12-Lead ECG – by Tumor Type	Phase 2 FAS Population	X	
3.5.9.1	Summary of Alert Values of PR, QRS, QT, RR, and QTcF Interval Values From Local Lab 12-Lead ECG by Visit – by Treatment Group and Dose	Phase 1 FAS Population	X	X
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