Official Title:	**A Phase 1/2, Open-Label, Dose Escalation, Safety and Tolerability Study of INCB050465 and Iitacitinib in Subjects With Previously Treated B-Cell Malignancies (CITADEL-101)**
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STATISTICAL ANALYSIS PLAN

INCB050465

INCB 50465-101

A Phase 1, Open-Label, Dose-Escalation, Safety and Tolerability Study of INCB050465 Monotherapy and in Combination With INCB039110 in Subjects With Previously Treated B-Cell Malignancies

IND Number: 121,474
124,540 (combination with INCB039110)

Date of Plan: 26 JUN 2015

Based on: Protocol Amendment 3 dated 06 MAR 2015
CRF dated 03 FEB 2015

SPONSOR:

Incyte Corporation
1801 Augustine Cut-Off
Wilmington, DE 19803

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

STATISTICAL ANALYSIS PLAN APPROVAL

SAP:	INCB 50465-101 SAP
SAP Version:	Final
Submitter:	[redacted], Biostatistics
Date Submitted:	26 JUN 2015
Protocol Version:	Amendment 3 dated 06 MAR 2015
CRF Date:	03 FEB 2015

NOTE:

1. An amendment made before the release of unblinded data (eg, treatment assignment received by each subject) for a blinded study or database release for an open-label study must be included in an updated SAP.

2. An amendment made to the statistical analyses defined in the SAP that occurs after unblinding or database release must be documented in the final Clinical Study Report.

3. The approvers must ensure that all relevant functions are in agreement with the final SAP.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF ABBREVIATIONS

Abbreviation	Term
AE	adverse event
AUC	area under the concentration-time curve
BMI	body mass index
bpm	beats per minute
CI	confidence interval
CLL	chronic lymphocytic leukemia
CR	complete response
CRF	case report form
CTCAE	Common Terminology Criteria for Adverse Events
DLT	dose-limiting toxicity
[redacted]	[redacted]
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
FDA	Food and Drug Administration
ITT	intent-to-treat
MedDRA	Medical Dictionary for Regulatory Activities
MR	minor response
MTD	maximum tolerated dose
NE	not evaluable
ORR	overall response rate
PD	progressive disease
[redacted]	[redacted]
[redacted]	[redacted]
PK	pharmacokinetics
PP	per protocol
PR	partial response
PT	preferred term
QD	once daily
QTcF	Fridericia correction
RP2D	recommended Phase 2 dose
SAE	serious adverse event
SAP	Statistical Analysis Plan
SD	stable disease
SOC	system organ class

Abbreviation	Term
TEAE	treatment-emergent adverse event
VGPR	very good partial response
WHO	World Health Organization
WM	Waldenström macroglobulinemia

1. INTRODUCTION

This is a Phase 1, open-label, dose-escalation, safety and tolerability study of INCB050465 as monotherapy and in combination with INCB039110 in subjects with previously treated B-cell malignancies. The purpose of this Statistical Analysis Plan (SAP) is to define the methodology for analyzing and summarizing the data collected during the conduct of Study INCB 50465-101.

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 50465-101 Protocol Amendment 3 dated 06 MAR 2015 and case report form (CRF) approved 03 FEB 2015. Unless superseded by an amendment, this SAP will be effective for all subsequent Protocol amendments and CRF versions.

2.2. Study Objectives

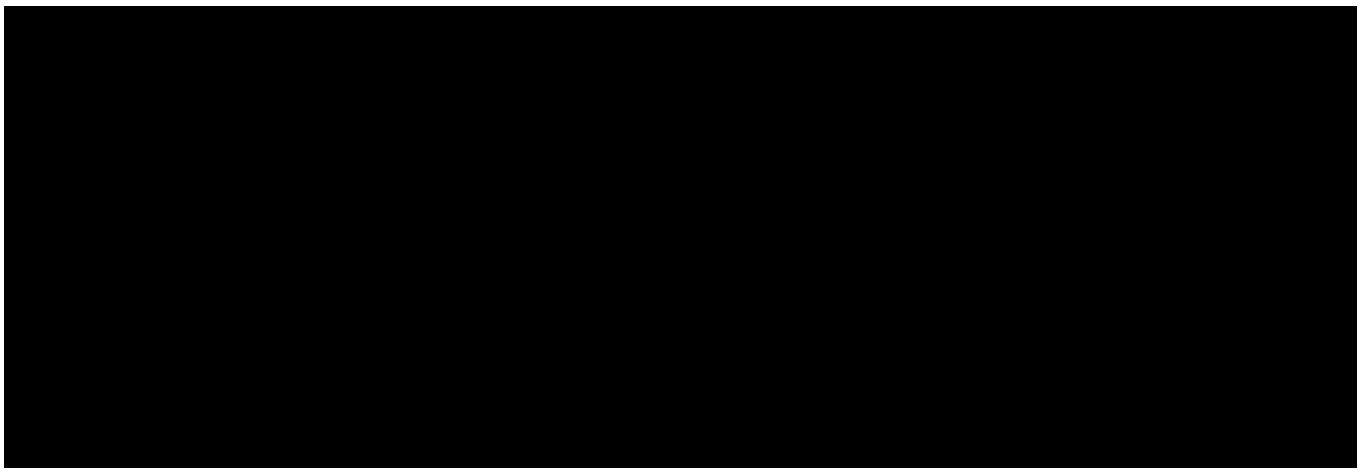
2.2.1. Primary Objective

- To assess the safety and tolerability of INCB050465 as monotherapy and in combination with INCB039110 and select doses for further evaluation.

2.2.2. Secondary Objectives

- To assess preliminary efficacy by assessing the overall response rate (ORR) of INCB050465 as monotherapy and in combination with INCB039110.

- To assess the pharmacokinetics (PK) of INCB050465 as monotherapy and in combination with INCB039110 and assess the effect of food on the PK of INCB050465.



2.3. Study Endpoints

2.3.1. Primary Endpoint

- Safety and tolerability of INCB050465 as a monotherapy and in combination with INCB039110 as assessed by summary of adverse events (AEs), clinical laboratory assessments, physical examination results, and 12-lead electrocardiograms (ECGs).

2.3.2. Secondary Endpoints

- Efficacy as measured by ORR, defined as the proportion of subjects achieving a minor response (MR, only among subjects with Waldenström macroglobulinemia [WM]), partial response (PR), very good partial response (VGPR, only among subjects with WM), and a complete response (CR) to INCB050465 as monotherapy and in combination with INCB039110 based on:
  - International Workshop on Chronic Lymphocytic Leukemia criteria for chronic lymphocytic leukemia (CLL; Hallek et al 2008, Cheson et al 2012).
  - VIth International Workshop on Waldenström Macroglobulinemia response assessment for subjects with WM (Owen et al 2013).
  - Revised response criteria for lymphoma for Hodgkin's lymphoma and non-Hodgkin's lymphoma (Cheson et al 2014).
- C_{max}, T_{max}, C_{min}, $AUC_{0\text{-}t}$, and $AUC_{0\text{-}\tau}$ at Cycle 1 Day 15 of INCB039110 in combination with INCB050465.
- C_{max}, T_{max}, C_{min}, $AUC_{0\text{-}t}$, and $AUC_{0\text{-}\tau}$ of INCB050465 as monotherapy and in combination with INCB039110.

[redacted]

3. STUDY DESIGN

The study consists of 3 parts. Monotherapy dose escalation (Part 1) will determine the maximum tolerated dose (MTD) of INCB050465 or, alternatively, a tolerated dose that produces substantial pharmacologic target inhibition; this dose may be chosen for further evaluation and potential use in a Phase 2 clinical study as the recommended Phase 2 dose (RP2D). Dose escalation will be conducted with a 3 + 3 design, with the exception that the first cohort (dose level of 5 mg once daily [QD]) will be a single subject cohort.

Part 2 will evaluate the combination of INCB050465 and INCB039110 to determine the MTD of the combination or, alternatively, a tolerated dose that produces substantial pharmacologic inhibition of the targets and will be considered the recommended dose of the combination. Dose escalation will be conducted with a 3 + 3 design with a starting dose of INCB050465 approximately 25% (rounded down to the nearest tablet size combination) below the RP2D determined in Part 1 followed by 1 escalation of INCB050465 to the RP2D determined in Part 1, each in combination with INCB039110 at 300 mg QD. Other dose levels of INCB050465 and INCB039110 will be explored depending on observed toxicities.

Expansion (Part 3), which consists of 4 cohorts, will evaluate the chosen dose(s) of INCB050465 as monotherapy and in combination with INCB039110. In Expansion Cohort A, approximately 15 subjects with relapsed/refractory B-cell lymphoid malignancies will be treated with the selected dose of INCB050465 as a single agent. In Expansion Cohort B, approximately 15 subjects with relapsed/refractory Hodgkin's lymphoma will be treated with the selected dose of INCB050465 as a single agent. In Expansion Cohort C, approximately 15 subjects with relapsed/refractory diffuse large B-cell lymphoma will be treated with the recommended doses of the combination. In Expansion Cohort D, approximately 15 subjects with relapsed/refractory B-cell lymphoid malignancies will be treated with the recommended doses of the combination

Section 4 of the study Protocol provides more details on the study design.

3.1. Randomization

This study is an open-label, dose-escalation, and expansion study. There is no randomization in the study.

3.2. Control of Type I Error

All statistical analyses are exploratory in nature. Unless otherwise specified, all confidence intervals (CIs) provided will be at the 95% confidence level.

3.3. Sample Size Considerations

The total sample size estimate of up to approximately 90 subjects in this study is based on the enrollment of 1 single-subject cohort, followed by up to 4 dose levels of 3 to 6 subjects per dose level in subsequent cohorts in Part 1 monotherapy dose escalation, up to 4 dose levels of 3 to

6 subjects per dose level in Part 2 combination dose escalation, and the 4 expansion cohorts which will each enroll 15 subjects. The exact number of subjects treated will depend on the number of subjects required per dose level and the number of dose levels studied.

During the 3 + 3 dose escalation in Part 1 and Part 2, the probabilities of dose escalation from that dose level for various dose-limiting toxicity (DLT) rates are given in Table 1.

Table 1: Probability of Dose Escalation for Specific Dose-Limiting Toxicity Rates During 3 + 3 Dose Escalation

True DLT Rate	Probability of Dose Escalation
10%	90.6%
20%	70.9%
30%	49.4%
40%	30.9%
50%	17.2%
60%	8.2%

In the expansion cohorts, the evaluation of 15 subjects each will provide a ≥ 90% chance of identifying a toxicity with a true event rate of 15%.

3.4. Schedule of Assessments

The schedules for study visit assessments and laboratory sampling for the safety and efficacy variables defined for this study are provided in Section 6 of the Protocol.

4. DATA HANDLING DEFINITIONS AND CONVENTIONS

4.1. Scheduled Study Evaluations and Study Periods

4.1.1. Study Day 1

Day 1 is the date that the first dose of study treatment (INCB050465 for monotherapy; INCB050465 or INCB039110 for combination therapy) is administered to the subject.

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 prior to Day 1, then the study day at the visit/reporting date will be calculated as

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

4.1.3. Baseline Value

Baseline is the last nonmissing measurement obtained prior to the first administration of any study treatment. When scheduled assessments and unscheduled assessments occur on the same day and time of the assessment or first dose is not available, the following convention will be used 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. Analysis Windows

For parameters that will be summarized by visit, the nominal visit as recorded on the electronic CRF will be used. There will be no additional analysis windowing performed based on the assessment date.

4.1.5. Missing 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 cancer 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 last day of the month or the date that the subject discontinued treatment.
- Otherwise, the date that the subject discontinued treatment will be used as the date of the last dose.

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. Selection of Data in the Event of Multiple Records in a Window

Depending on the statistical analysis method, single values may be required for each analysis window. For example, change from baseline by visit usually requires a single value per visit. Unless otherwise noted throughout the rest of the SAP, when a single value is needed, the following rules will be used:

- If > 1 assessment occurs during the same nominal visit, then the record closest to the nominal day for that visit will be selected.
- If there are 2 assessments that are equidistant from the nominal day, then the data of the assessment after the scheduled study day will be used.
- The last measurement will be used if multiple measurements are taken on the same day.

4.1.7. Cycle Length and Duration

INCB050465 and INCB039110 will be self-administered continuously. One cycle will be approximately 21 days of treatment and subjects will receive treatment in continuous cycles.

Cycle 1 Day 1 is defined as the day of the first dose of the study drug. The date of the Day 1 visit of each cycle recorded on the CRF will be used as the actual Day 1 date of the cycle.

4.2. Variable Definitions

4.2.1. Age

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

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

4.2.2. Body Mass Index

Body mass index (BMI) will be calculated as follows:

BMI (kg/m^2) = (weight [kg]) / (height [m])^2

4.2.3. Prior and Concomitant Medication

Prior medication is defined as any nonstudy medication started before the first dose of study drug. Concomitant medication is defined as any nonstudy medication that was started as follows:

- Before the first dose of study drug and continuing after the first dose of study drug or
- On or after the first dose of study drug up to within 30 days after last dose of study drug.

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

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

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.

5.2. Treatment Groups

This is a Phase 1, open-label, dose-escalation study; therefore, there are no randomized treatment groups.

The efficacy endpoints, including ORR, [redacted] and change in target lesion size, will be summarized by disease subtype. Change in peripheral blood leukemic cells will only be analyzed for subjects with CLL. All other data, including baseline and safety, will be summarized by dose groups. In the event that several dose regimens tested are deemed substantially below the MTD, these doses may be combined for summary purposes.

5.3. Analysis Populations

5.3.1. Intent-to-Treat/Safety Population

The intent-to-treat (ITT) or safety population includes all subjects enrolled in the study who received at least 1 dose of any study treatment.

Demographics, baseline characteristics, subject disposition, study drug administration, and all safety and efficacy analyses will be conducted using the ITT/safety population.

5.3.2. Per-Protocol Population

Subjects in the ITT population who are considered to be compliant with the Protocol compose the per-protocol (PP) population.

The following procedures will be performed to identify those subjects who are to be excluded from the PP population prior to the database freeze:

- Clinical review of Protocol deviations/violations.
- Clinical review of concomitant medications as defined in Sections 5.9 and 5.10 of the Protocol.
- Clinical review of the drug accountability listing.

The determination of subjects being considered for exclusion from the PP population by the clinical team will be prepared and signed prior to database freeze.

The PP population may be used for sensitivity analysis of the efficacy endpoints.

5.3.3. Pharmacokinetic [redacted] valuable Population

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

[redacted]

6. BASELINE, EXPOSURE, AND DISPOSITION VARIABLES AND ANALYSES

See Appendix A for a list of data displays.

6.1. Baseline

6.1.1. Demographics and Baseline Disease Characteristics

The following demographic characteristics will be summarized and listed: age, sex, race, ethnicity, weight, height, and BMI.

Size of spleen and liver by manual palpation, and ECOG performance status at baseline will be summarized.

6.1.2. Disease History

Disease history, including disease subtype and markers, time since diagnosis, results from cytogenetic testing with identification of high-risk CLL subjects, Ann Arbor staging, International Prognostic Index, and presence of B-symptoms at baseline, will be summarized and listed. For subjects with CLL or small lymphocytic lymphoma, Rai staging and markers will be summarized and listed.

Time since diagnosis will be calculated as follows:

Time since diagnosis (years) = (Day 1 date – date of diagnosis + 1) / 365.25

6.1.3. Prior Therapy

Number of prior systemic therapy regimens will be summarized. Regimen name, component drugs, start and stop date, best response, reason for discontinuation, and date of relapse/progression will be listed.

Number of subjects who received prior radiation will be summarized. Radiotherapy type, body site, start and stop date, and total dose will be listed.

Number of subjects who had stem cell transplant will be summarized. Transplant date, type, source cell, setting (primary or relapse), best response, and drugs used with the transplant will be listed.

Number of subjects who had prior surgery or surgical procedure for lymphoma will be summarized. Surgery date and description of the surgery or surgical procedure will be listed.

6.1.4. Medical History

Medical history will be coded to system organ class (SOC) and preferred term (PT) using MedDRA coding dictionary. Medical history will be summarized by SOC and PT and listed.

6.2. Disposition of Subjects

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

6.3. Protocol Deviations

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

6.4. Exposure

For subjects in the safety population, duration of treatment, average daily dose (mg), and dose modifications will be summarized descriptively. The summaries will be provided separately for

INCB050465 and INCB039110 when applicable. Administrations of the study drug will be listed.

- **Duration of treatment:** The number of study days from Day 1 to the last day of INCB050465 or INCB039110 taken by the subject.
- **Average daily dose (mg/day):** Total dose taken by the subject divided by duration of treatment in days.
- **Dose modifications:** Number of subjects who had dose reduction, interruption, and escalation will be summarized.

6.5. Study Drug Compliance

For subjects in the safety population, overall compliance (%) of INCB050465 and INCB039110, when applicable, will be calculated separately as follows:

Compliance (%) = 100 × (total dose actually taken [mg]) / (total intended dose [mg])

Total intended dose is defined as the sum of the doses prescribed by the investigator accounting for dose modifications.

Study drug compliance will be summarized descriptively and listed.

6.6. Prior and Concomitant Medication

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

7. EFFICACY

See Appendix A for a list of data displays.

7.1. Efficacy Hypotheses

Not applicable.

7.2. Analysis of the Efficacy Parameters

7.2.1. Response Assessment

An objective assessment of disease status is required at baseline (screening) using a method that is appropriate for the disease subtype, per established and modified guidelines (Hallek et al 2008,

Cheson et al 2014, Cheson et al 2012, Owen et al 2013). Disease status will be assessed by the site every 9 weeks following Cycle 1 Day 1. For subjects in Part 3 Expansion Cohorts, the sponsor may also have disease status assessed by a central imaging vendor.

Response status will be recorded at each postbaseline disease assessment visit as CR, VGPR (only for subjects with WM), PR, MR (only for subjects with WM), stable disease (SD), progressive disease (PD), or not evaluable (NE).

7.2.2. Best Overall Response and Overall Response Rate

Best overall response is the best response recorded during the study treatment prior to and including the first PD, in the order of CR, VGPR, PR, MR, SD, PD, and NE. In the case of SD, assessment must meet the SD criteria at least once on or after Day 42. Subjects who fail to meet this criterion will have best response of PD if the next available assessment after the initial assessment indicates PD or will have best response of NE if there are no additional assessments available.

A subject is considered a responder if they have a best overall response of CR or PR (CR, VGPR, PR, or MR for subjects with WM postbaseline.

The ORR is the proportion of responders. Subjects who do not have sufficient baseline or on-study response assessment information to be adequately assessed for response status will be included in the denominators in the calculation of ORR.

Best overall response will be summarized descriptively. The ORR will be estimated with 95% CIs. Confidence intervals will be calculated based on the exact method for binomial distributions.

[redacted]

7.2.5. Best Change in Target Lesion Size

For subjects with measurable lesions at baseline, target lesion sizes will be measured by sum of product of diameters. The best percentage change from baseline, defined as the largest decrease in target lesion sizes during the study, will be summarized, and a waterfall plot of the best percentage change will be generated. Note that for subjects who only have increases in target lesion sizes from baseline, the smallest increase will be considered as the best change from baseline.

Target lesions considered "too small to measure" will be assigned a default value of 5 mm × 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 that a target lesion is unaccounted for in a particular postbaseline timepoint (ie, the assessment is missing or NE), then the overall sum of target lesions will not be evaluable for that postbaseline timepoint.

7.2.6. Change in Peripheral Blood Leukemic Cells

For subjects with CLL, changes in peripheral blood leukemic cells, including neutrophils, platelets, hemoglobin, and lymphocytes, from baseline to each post-treatment assessment will be summarized descriptively.

7.3. Pharmacokinetic Analyses

7.3.1. Blood Sample Collection

Pharmacokinetic samples will be obtained at predose, 0.5, 1, 2, 4, 6, 8, and 12 (if possible) hours postdose on Cycle 1 Day 1, Cycle 1 Day 15, and Cycle 2 Day 1 (only required for subjects enrolled in the food-effect expansion cohort) and at predose on Cycle 1 Day 8. On Cycle 1 Day 1, study subjects should have fasted overnight; the clinic visit should be scheduled in the morning. A predose PK sample will be taken, followed by administration of the INCB050465 only. For subjects receiving the combination, administration of INCB039110 should be started on Day 1 after INCB050465 PK sampling is complete in Part 2 and Part 3 Cohorts C and D. On Cycle 1 Day 8 and Day 15, subjects will refrain from taking study drug in the morning before arriving at the research unit. A trough (predose) PK sample will be taken, followed by administration of the study drug. On Cycle 2 Day 1, study subjects in the expansion cohort Cohort A only will be required to undergo PK testing after fed administration on Cycle 2 Day 1 only.

7.3.2. Urine Sample Collection

Urine will be collected from each subject on Cycle 1 Day 15 after morning dose and a predose void. A complete urine output collection will be collected from hour 0 (after morning dose) through 8 hours after the first dose of study drug or through 12 hours after the morning dose if a 12-hour postdose PK sample is being performed.

7.3.3. Bioanalytical Methodology and Analysis

The plasma and urine samples will be analyzed for INCB050465 and INCB039110 by a validated assay and will be collected from all subjects enrolled in this study. [redacted]

7.3.4. Pharmacokinetic Analysis

The PK calculations will be performed, if appropriate, using commercial software such as WinNonlin® (Pharsight Corporation, Mountain View, CA). Nominal times will be used in all cases, except when the difference between the actual time and nominal time is greater than 5 minutes for samples collected up to 4 hours after administration and greater than 15 minutes for samples collected more than 4 hours after administration; in these cases, actual time will be used for PK analysis. Additional details of analyses will be described in the SAP.

[redacted]

8. SAFETY AND TOLERABILITY

See Appendix A for a list of data displays.

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 AEs occurring within 30 days of the last administration of study drug.

8.2. Adverse Events

8.2.1. Adverse Event Definitions

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

Adverse events will be coded to SOC and PT using MedDRA coding dictionary. Adverse events will be tabulated by MedDRA SOC and PT. Severity of AEs will be described and graded using the National Cancer Institute CTCAE v4.03. The CTCAE reporting guidelines and grading details are available on the Cancer Therapy Evaluation Program website (http://ctep.cancer.gov/).

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 1 to 4 scale as follows: (1) mild, (2) moderate, (3) severe, (4) life-threatening. All toxicities will be graded based on the worst level reached, not the level that they may have reached if they had not been treated. When the intensity of an AE changes over time for a reporting period (eg, between visits), each change in intensity will be reported as an AE until the event resolves.

The subset of AEs considered by the investigator to be related to INCB050465 or INCB039110 (when applicable) will be considered to be treatment-related AEs. If the investigator does not specify the relationship of the AE to study drug, the AE will be considered to be treatment related. The incidence of AEs and treatment-related AEs will be tabulated. In addition, serious adverse events (SAEs) will be tabulated.

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

- An unresolved missing causality will be considered treatment related. For subjects receiving monotherapy, the event will be considered treatment related to INCB050465 only, and for subjects receiving combination therapy, the event will be considered treatment related to both investigational agents.

- 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. Therefore, a missing onset date will be considered treatment emergent, with the following examples illustrating exceptions:

- If the stop/resolution date is before the first dose date on Day 1, then the AE will not be considered treatment emergent.

- If both the month and day are missing, and the last day of the year is before the first dose date on Day 1, then the AE will not be considered treatment emergent.

- If only the day is missing, and the last day of the month is before the first dose date on Day 1, then the AE will not be considered treatment emergent.

- If only the day is missing, and the first day of the month is after the first dose date on Day 1, then the AE will be considered treatment emergent.

8.2.2. Dose-Limiting Toxicities

The DLTs during the first cycle of study drug will be listed for subjects in Part 1 and Part 2.

8.2.3. Adverse Event Summaries

An overall summary of AEs will include the following:

- Number (%) of subjects reporting any TEAEs

- Number (%) of subjects reporting any SAEs

- Number (%) of subjects reporting any Grade 3 or 4 TEAEs

- Number (%) of subjects reporting any INCB050465-related TEAEs

- Number (%) of subjects reporting any INCB039110-related TEAEs
- Number (%) of subjects who had a fatal TEAE
- Number (%) of subjects who withdrew from study due to a TEAE
- Number (%) of subjects who temporarily interrupted INCB050465 due to a TEAE
- Number (%) of subjects with INCB050465 dose reductions due to a TEAE
- Number (%) of subjects who permanently discontinued INCB050465 due to a TEAE
- Number (%) of subjects who temporarily interrupted INCB039110 due to a TEAE
- Number (%) of subjects with INCB039110 dose reductions due to a TEAE
- Number (%) of subjects who permanently discontinued INCB039110 due to a TEAE

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

- Number (%) of subjects reporting TEAEs by SOC and PT
- Number (%) of subjects reporting TEAEs by PT in decreasing order of frequency
- Number (%) of subjects reporting TEAEs by SOC, PT, and maximum severity
- Number (%) of subjects reporting Grade 3 or 4 TEAEs by SOC and PT
- Number (%) of subjects reporting INCB050465 treatment-related AEs by SOC and PT
- Number (%) of subjects reporting INCB050465 treatment-related AEs by PT in decreasing order of frequency
- Number (%) of subjects reporting INCB050465 treatment-related AEs by SOC, PT, and maximum severity
- Number (%) of subjects reporting INCB039110 treatment-related AEs by SOC and PT
- Number (%) of subjects reporting INCB039110 treatment-related AEs by PT in decreasing order of frequency
- Number (%) of subjects reporting INCB039110 treatment-related AEs by SOC, PT, and maximum severity
- Number (%) of subjects reporting TEAEs leading to death by SOC and PT

- Number (%) of subjects reporting treatment-emergent SAEs by SOC and PT
- Number (%) of subjects reporting INCB050465 treatment-related SAEs by SOC and PT
- Number (%) of subjects reporting INCB039110 treatment-related SAEs by SOC and PT
- Number (%) of subjects reporting TEAEs leading to INCB050465 dose interruption by SOC and PT
- Number (%) of subjects reporting TEAEs leading to INCB050465 dose reduction by SOC and PT
- Number (%) of subjects reporting TEAEs leading to discontinuation of INCB050465 by SOC and PT
- Number (%) of subjects reporting TEAEs leading to INCB039110 dose interruption by SOC and PT
- Number (%) of subjects reporting TEAEs leading to INCB039110 dose reduction by SOC and PT
- Number (%) of subjects reporting TEAEs leading to discontinuation of INCB039110 by SOC and PT
- Number (%) of subjects reporting TEAEs leading to withdrawal from the study by SOC and PT

8.3. Clinical Laboratory Tests

8.3.1. Laboratory Value Definitions

All test results and associated normal ranges will be summarized in SI units.

For numeric laboratory results, the change and percentage change from baseline will be calculated using the last nonmissing value before the first dose of study drug as the baseline value.

When applicable, laboratory test values will be assessed for severity based on CTCAE v4.03. For specific laboratory parameters requiring clinical intervention to grade, the classification according to the quantitative component will be provided.

8.3.2. Laboratory Value Summaries

For numeric laboratory values, baseline value, postbaseline value, change from baseline, and percentage change from baseline will be summarized by visit. In addition, mean laboratory

values will be plotted over time for hemoglobin, platelet counts, white blood cell, neutrophils, and lymphocytes.

Shift summaries will be presented showing number and percentage of subjects with the laboratory values being low, normal, and high at baseline and at each of the scheduled postbaseline visits. The denominator for the percentage calculation will use the number of subjects in the baseline category (ie, low, high, normal, and missing).

For the laboratory parameters that have CTCAE grading, shift tables will also be presented showing change in CTCAE severity grade from baseline to worst grade postbaseline. All postbaseline values will be included when summarizing worst postbaseline grade. The denominator for the percentage calculation will be the number of subjects in the baseline category.

Categorical laboratory data will be tabulated by visit at baseline and postbaseline visits where appropriate.

8.4. Vital Signs

Vital signs, including systolic blood pressure, diastolic blood pressure, pulse, and body temperature, will be taken in the seated position for each subject during the study in accordance with the schedule of assessments. Change and percentage change from baseline will be calculated using the last nonmissing value before first dose of study drug as the baseline value.

Criteria for clinically notable vital sign abnormalities are defined in Table 3. The abnormal values for subjects exhibiting clinically notable vital sign abnormalities will be listed.

Table 3: Criteria for Clinically Notable Vital Sign Abnormalities

Parameter	High Threshold	Low Threshold
Systolic blood pressure	> 155 mm Hg	< 85 mm Hg
Diastolic blood pressure	> 100 mm Hg	< 40 mm Hg
Pulse	> 100 bpm	< 45 bpm
Temperature	> 38ºC	< 35.5ºC

bpm = beats per minute.

Alert vital signs are defined as an absolute value outside the defined range and absolute percentage change > 25%. The abnormal values for subjects exhibiting alert vital sign abnormalities will be listed.

8.5. Electrocardiograms

Twelve-lead ECGs including PR, QRS, QT, QTcF, and RR intervals will be obtained for each subject during the study in accordance with the schedule of assessments. Descriptive statistics and mean change from baseline will be determined for each ECG parameter at each assessment time. Change and percentage change from baseline will be calculated using the average of all nonmissing values prior to the first dose of study drug as the baseline value.

Criteria for clinically notable ECG abnormalities are defined in Table 4. The abnormal values for subjects exhibiting clinically notable ECG abnormalities will be listed.

Table 4: Criteria for Clinically Notable Electrocardiogram Abnormalities

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

QTcF = Fridericia correction.

Alert ECG values are defined as an absolute value outside the defined range and absolute percentage change > 25% (30% for QRS) interval. The abnormal values for subjects exhibiting alert ECG abnormalities will be listed.

Outliers of QT and QTc values, defined as absolute values > 450 ms or change from baseline > 30 ms, will also be listed.

9. INTERIM ANALYSES

There is no planned, formal interim analysis for this study. Periodic review of accrued clinical data will be conducted by Incyte. 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(s) additional subjects should be treated in the study.

10. CHANGES AND MODIFICATIONS TO THE STATISTICAL ANALYSIS PLAN

All versions of the SAP are listed in Table 5.

Table 5: SAP Versions

SAP Version	Date
Original	26 JUN 2015

10.1. Changes to Protocol-Defined Analyses

Not applicable.

10.2. Changes to the Statistical Analysis Plan

Not applicable.

11. REFERENCES

Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. J Clin Oncol 2014;32:3059-3068.

Cheson BD, Byrd JC, Rai KR, et al. Novel targeted agents and the need to refine clinical end points in chronic lymphocytic leukemia. J Clin Oncol 2012;30:2820-2822.

US Food and Drug Administration (FDA). Guidance for industry: clinical trial endpoints for the approval of cancer drugs and biologics. 2007. www.fda.gov/downloads/drugsGuidanceComplianceRegulatoyInformation/Guidance/UCM071590.pdf. Accessed June 22, 2015.

Hallek M, Cheson BD, Catovsky D, et al. Guidelines for the diagnosis and treatment of chronic lymphocytic leukemia: a report from the International Workshop on Chronic Lymphocytic Leukemia updating the National Cancer Institute-Working Group 1996 guidelines. Blood 2008;111:5446-5456.

Owen RG, Kyle RA, Stone MJ, et al. Response assessment in Waldenström macroglobulinaemia: update from the VIth International Workshop. Br J Haematol 2013;160:171-176.

APPENDIX A. PLANNED TABLES, FIGURES, AND LISTINGS

This appendix provides a list of the planned tables, figures, and listings for the CSR. Shells are provided for nonstandard tables. The list of tables, figures, listings 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				
1.1.1	Analysis Populations	ITT	X	X
1.1.2	Summary of Subject Disposition	ITT	X	X
1.2.1	Summary of Demographics	ITT		X
1.2.2	Summary of Baseline Disease Characteristics	ITT		X
1.3.1	Summary of Disease History	ITT		X
1.3.2	Summary of Prior Cancer Therapy	ITT		X
1.3.3	Summary of Medical History	ITT	X	
1.4.1	Summary of Prior Medications	ITT	X	
1.4.2	Summary of Concomitant Medications	ITT	X	
Efficacy				
2.2.1	Summary of Best Overall Response and Overall Response Rate	ITT		
[redacted]				
2.3.3	Summary of Best Change in Target Lesion Size	ITT		X
2.3.4	Summary of Peripheral Leukemic Blood Cells	ITT		X
Safety				
3.1.1	Summary of Study Drug Exposure and Compliance	Safety		X
3.2.1	Overall Summary of Treatment-Emergent Adverse Events	Safety	X	X
3.2.2	Summary of Treatment-Emergent Adverse Events By MedDRA System Organ Class and Preferred Term	Safety	X	
3.2.3	Summary of Treatment-Emergent Adverse Events By MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X	X
3.2.4	Summary of Treatment-Emergent Adverse Events By MedDRA System Organ Class, Preferred Term, and Maximum Severity	Safety	X	
3.2.5	Summary of Grade 3 or 4 Treatment-Emergent Adverse Events By MedDRA System Organ Class and Preferred Term	Safety	X	X
3.2.6	Summary of INCB050465 Treatment-Related Adverse Events By MedDRA System Organ Class and Preferred Term	Safety	X	
3.2.7	Summary of INCB050465 Treatment-Related Adverse Events By MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X	
3.2.8	Summary of INCB050465 Treatment-Related Adverse Events By MedDRA System Organ Class, Preferred Term, and Maximum Severity	Safety	X	
3.2.9	Summary of INCB039110 Treatment-Related Adverse Events By MedDRA System Organ Class and Preferred Term	Safety	X	

Table No.	Title	Population	Standard	In Text
3.2.10	Summary of INCB039110 Treatment-Related Adverse Events By MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X	
3.2.11	Summary of INCB039110 Treatment-Related Adverse Events By MedDRA System Organ Class, Preferred Term, and Maximum Severity	Safety	X	
3.2.12	Summary of Treatment-Emergent Adverse Events Leading to Death By MedDRA System Organ Class and Preferred Term	Safety	X	X
3.2.13	Summary of Treatment-Emergent Serious Adverse Events By MedDRA System Organ Class and Preferred Term	Safety	X	X
3.2.14	Summary of Serious INCB050465 Treatment-Related Adverse Events By MedDRA System Organ Class and Preferred Term	Safety	X	
3.2.15	Summary of Serious INCB039110 Treatment-Related Adverse Events By MedDRA System Organ Class and Preferred Term	Safety	X	
3.2.16	Summary of Treatment-Emergent Adverse Events Leading to INCB050465 Dose Interruption By MedDRA System Organ Class and Preferred Term	Safety	X	
3.2.17	Summary of Treatment-Emergent Adverse Events Leading to INCB050465 Dose Reduction By MedDRA System Organ Class and Preferred Term	Safety	X	
3.2.18	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of INCB050465 By MedDRA System Organ Class and Preferred Term	Safety	X	X
3.2.19	Summary of Treatment-Emergent Adverse Events Leading to INCB039110 Dose Interruption By MedDRA System Organ Class and Preferred Term	Safety	X	
3.2.20	Summary of Treatment-Emergent Adverse Events Leading to INCB039110 Dose Reduction By MedDRA System Organ Class and Preferred Term	Safety	X	
3.2.21	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of INCB039110 By MedDRA System Organ Class and Preferred Term	Safety	X	X
3.2.22	Summary of Treatment-Emergent Adverse Events Leading to Withdrawal From the Study By MedDRA System Organ Class and Preferred Term	Safety	X	X
3.3.1	Summary of Laboratory Values - Hematology	Safety	X	
3.3.2	Shift Summary of Hematology Values	Safety	X	
3.3.3	Shift Summary of Laboratory Values in CTC Grade - To the Worst Abnormal Value – Hematology	Safety	X	X
3.3.4	Summary of Laboratory Values - Chemistry	Safety	X	
3.3.5	Shift Summary of Chemistry Values	Safety	X	
3.3.6	Shift Summary of Laboratory Values in CTC Grade - To the Worst Abnormal Value – Chemistry	Safety	X	
3.3.7	Summary of Laboratory Values - Urinalysis	Safety	X	
3.3.8	Shift Summary of Urinalysis Values	Safety	X	
3.3.9	Summary of Laboratory Values - Coagulation	Safety	X	
3.3.10	Shift Summary of Coagulation Values	Safety	X	
3.4.1	Summary of Systolic Blood Pressure	Safety	X	
3.4.2	Summary of Diastolic Blood Pressure	Safety	X	
3.4.3	Summary of Pulse	Safety	X	
3.4.4	Summary of Body Temperature	Safety	X	
3.4.5	Summary of Weight	Safety	X	

Table No.	Title	Population	Standard	In Text
3.5.1	Summary of 12-Lead ECG: PR Interval Values	Safety	X	
3.5.2	Summary of 12-Lead ECG: QRS Interval Values	Safety	X	
3.5.3	Summary of 12-Lead ECG: QT Interval Values	Safety	X	
3.5.4	Summary of 12-Lead ECG: QTcB Interval Values	Safety	X	
3.5.5	Summary of 12-Lead ECG: QTcF Interval Values	Safety	X	
3.5.6	Summary of 12-Lead ECG: RR Interval Values	Safety	X	
3.5.7	Outliers of QT, QTcB, and QTcF Interval Values	Safety	X	

Figures

Figure No.	Title
[redacted]	
4.3.3	Waterfall Plot of Best Percent Change of Target Lesion Size from Baseline
4.6	Line Graph of Mean Values over Time for Selected Laboratory Values

Listings

Listing No.	Title
2.1.1	Subject Enrollment and Disposition Status
2.1.2	Subject Inclusion and Exclusion Criteria
2.2	Protocol Deviations/Violations
2.3	Analysis Population
2.4.1	Demographic and Baseline Characteristics
2.4.2	Disease History
2.4.3	Prior Radiation Treatments
2.4.4	Prior Systemic Therapy
2.4.5	Prior Stem Cell Transplant
2.4.6	Prior Surgery/Procedure
2.4.7	Medical History
2.4.8	Prior and Concomitant Medication
2.6.1	Best Overall Response, [redacted]
2.6.2	Overall Response assessment by Visit
2.6.3	Response Assessment: Target Lesions
2.6.4	Response Assessment: Non-target Lesions
2.7.1	Study Drug Administration and Compliance
2.7.2	Adverse Events
2.7.3	Dose-limiting Toxicities in Cycle 1
2.7.4	Serious Adverse Events
2.7.5	Grade 3 or 4 Adverse Events
2.7.6	Fatal Adverse Events
2.7.7	Treatment Related Adverse Events
2.7.8	Adverse Events Leading to Withdrawal From Study
2.7.9	Adverse Events Leading to Interruption, Reduction or Discontinuation of INCB050465 or INCB039110
2.8.1	Clinical Laboratory Values by Test and Visit
2.8.2	Abnormal Clinical Laboratory Values

Listing No.	Title
2.8.3	Clinical Laboratory Values by Visit and Test
2.9.1	Vital Signs
2.9.2	Abnormal Vital Sign Values
2.9.3	Alert Vital Sign Values
2.10.1	12-Lead ECG Values
2.10.2	Abnormal 12-Lead ECG Values
2.10.3	Alert 12-Lead ECG Values
2.10.4	Outliers of QT, QTcB, and QTcF Interval Values from 12-Lead ECG
2.11	ECOG status

Table 1.2.1

Summary of Demographics
(Population: ITT)

Variable	Dose Group: Dose 1 (N=xxx)	Dose 2 (N=xxx)	Dose 3 (N=xxx)	Total (N=xxx)
Age (yrs)				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x
Age Group				
<=65 years	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
>65 years	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Sex				
Male	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Female	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Race				
White	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Black or African American	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Asian	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Native Hawaiian or Other Pacific Islander	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
American Indian or Alaska Native	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Other	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Ethnicity				
Hispanic or Latino	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Not Hispanic or Latino	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Height (cm)				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx

Max	xx.x	xx.x	xx.x	xx.x
Weight (kg)				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x
Body Mass Index (kg/m^2)				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x

PROGRAM\OUTPUT: xxxxx.SAS\xxxxx.LST DATE(TIME): DDMMMYY(HH:MM)
Reference: Listing 16.x.x.x.x

Table 1.2.2

Summary of Baseline Disease Characteristics
(Population: ITT)

Variable	Dose Group: Dose 1 (N=xxx)	Dose 2 (N=xxx)	Dose 3 (N=xxx)	Total (N=xxx)
ECOG Status				
0	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
1	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
2	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
3	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
4	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
5	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Spleen Palpable?				
Yes	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
No	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Spleen Size (cm) [a]				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x
Liver Palpable?				
Yes	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
No	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Liver Size (cm) [b]				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x

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[a] from the left costal margin to the point of greatest splenic protrusion
[b] from the right costal margin to the point of greatest liver protrusion

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

Table 1.3.1

Summary of Disease History
(Population: ITT)

Variable	Dose Group: Dose 1 (N=xxx)	Dose 2 (N=xxx)	Dose 3 (N=xxx)	Total (N=xxx)
Time since Initial Diagnosis (Years)				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x
Disease Subtype				
CLL/SLL	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
B-cell prolymphocytic leukemia	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
…				
Follicular Lymphoma Grade				
Grade I	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Grade II	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Grade III	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Diffuse Large B-Cell Lymphoma				
Germinal center type (GC)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Activated B-Cell type (ABC)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Unknown	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Not Done	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
B-cell CLL/SLL Rai Staging				
Stage I	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage II	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage III	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stage IV	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
B-cell CLL/SLL ZAP70 Marker				
Positive	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Negative	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)

Not Done	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
B-cell CLL/SLL IgVH Marker				
Mutated	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Unmutated	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Not Done	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
B-cell CLL/SLL CD38 Marker				
Positive	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Negative	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Not Done	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Cytogenetics				
No chromosome abnormality/translocation found	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Chromosome abnormality/translocation found	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Not Done	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Ann Arbor Staging				
I	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
II	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
III	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
IV	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
International Prognostic Index				
Low risk	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Low-Intermediate risk	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
High-Intermediate risk	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
High risk	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Not appropriate for histologic subtype	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Are B-symptoms present?				
No	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Yes	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Fever	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Night Sweat	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Weight Loss	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)

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

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

Table 1.3.2

Summary of Prior Cancer Therapy
(Population: ITT)

Variable	Dose Group: Dose 1 (N=xxx)	Dose 2 (N=xxx)	Dose 3 (N=xxx)	Total (N=xxx)
Subjects with Prior Systemic Therapy	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Number of Prior Systemic Therapy Regimens				
1	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
2	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
3	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
4	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
>=5	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Subjects with Prior Radiation	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Subjects with Prior hematopoietic Stem Cell Transplant	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Subjects with Prior Surgery or Surgical Procedure for Lymphoma	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)

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

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

Table 2.2.1

Summary of Best Overall Response and Overall Response Rate
(Population: ITT)

Variable	Dose Group: Dose 1 (N=xxx)	Dose 2 (N=xxx)	Dose 3 (N=xxx)	Total (N=xxx)
Best Overall Response				
Complete Response	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Partial Response	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stable Disease	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Progressive Disease	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Not Evaluable	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Not Assessed	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Overall Response[a]	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
95% CI for Overall Response Rate[b]	xx.x - xx.x	xx.x - xx.x	xx.x - xx.x	xx.x - xx.x

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

[a] Subjects who have a best overall response of complete response or partial response.
[b] Confidence intervals are calculated based on the exact method for binomial distributions.

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

For disease subtype: Waldenström's macroglobulinemia

Table 2.2.1

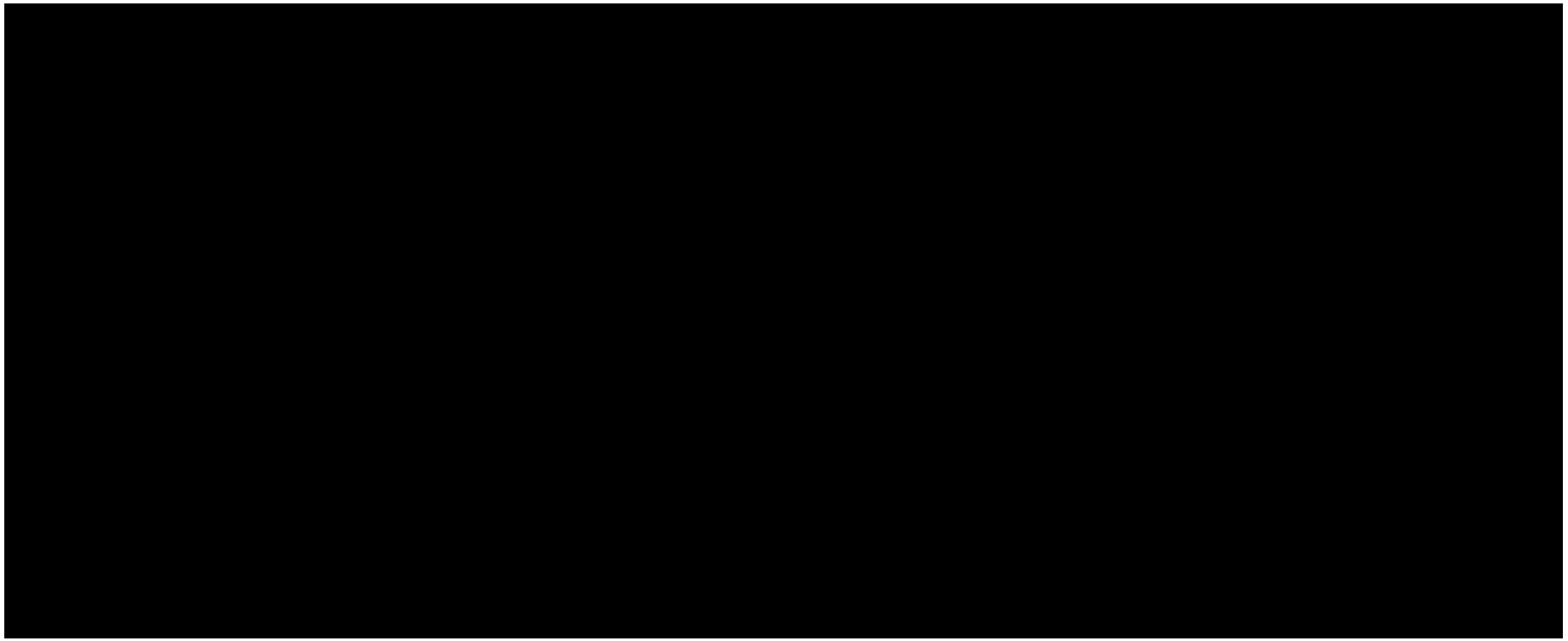
Summary of Best Overall Response and Overall Response Rate
(Population: ITT)

	Dose Group			
Variable	Dose 1 (N=xxx)	Dose 2 (N=xxx)	Dose 3 (N=xxx)	Total (N=xxx)
Best Overall Response				
Complete Response	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Very Good Partial Response	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Partial Response	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Minor Response	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Stable Disease	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Progressive Disease	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Not Evaluable	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Not Assessed	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Overall Response[a]	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
95% CI for Overall Response Rate[b]	xx.x – xx.x	xx.x – xx.x	xx.x – xx.x	xx.x – xx.x

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

[a] Subjects who have a best overall response of complete response, very good partial response, partial response, or minor response.
[b] Confidence intervals are calculated based on the exact method for binomial distributions.

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



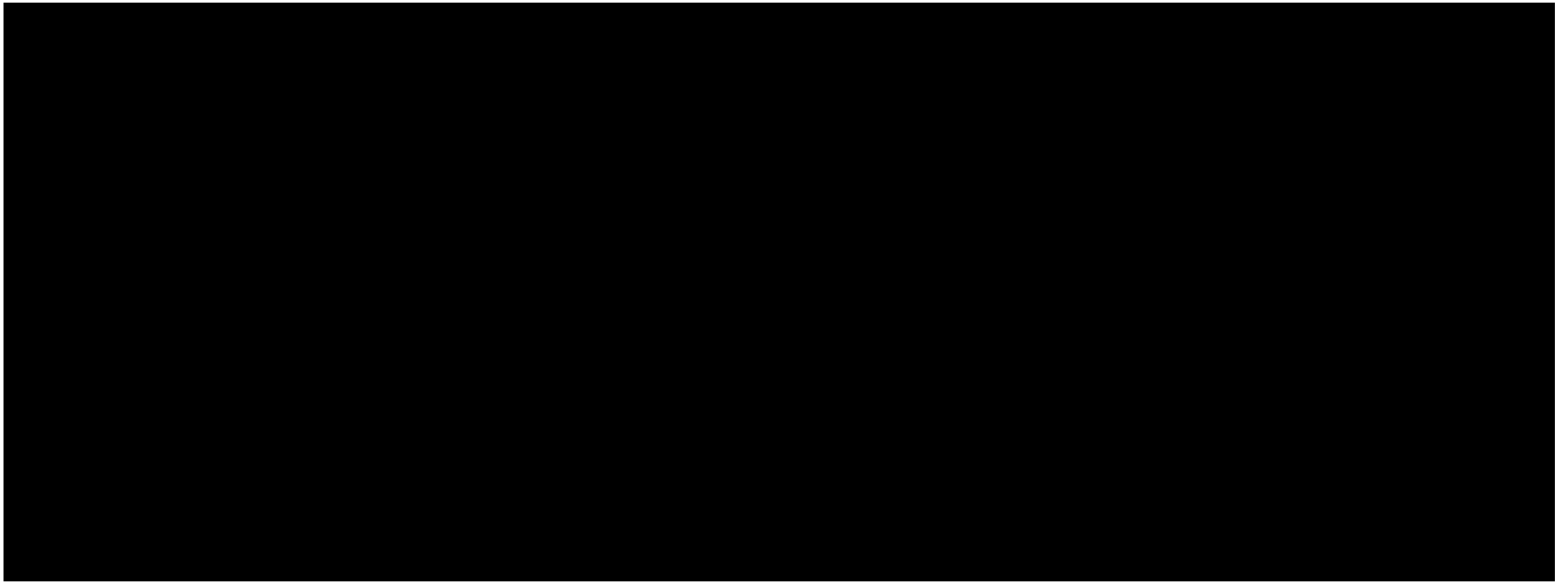


Table 2.3.3
Summary of Best Change in Target Lesion Size
(Population: ITT)

Variable	Dose Group: Dose 1 (N=xxx)	Dose 2 (N=xxx)	Dose 3 (N=xxx)	Total (N=xxx)
Sum of Product of Diameters [SPD], cm^2				
Baseline				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x
Best Change				
Measured				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x
Change				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x
Percent Change				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x

PROGRAM\OUTPUT: xxxxx.SAS\xxxxx.LST DATE(TIME): DDMMMYY(HH:MM)
Reference: Listing 16.x.x.x.x

Table 2.3.4

Summary of Peripheral Leukemic Blood Cells
(Population: ITT)

Variable	Dose Group: Dose 1 (N=xxx)	Dose 2 (N=xxx)	Dose 3 (N=xxx)	Total (N=xxx)
Neutrophils				
Baseline				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x
Cycle 1 Day 8				
Measured				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x
Change				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x
Percent Change				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x

Repeat for other visits

...

Repeat for platelets, hemoglobin and lymphocytes

PROGRAM\OUTPUT: xxxxx.SAS\xxxxx.LST DATE(TIME): DDMMMYY(HH:MM)
Reference: Listing 16.x.x.x.x

Table 3.1.1

Summary of Study Drug Exposure and Compliance
(Population: Safety)

Variable	Dose Group: Dose 1 (N=xxx)	Dose 2 (N=xxx)	Dose 3 (N=xxx)	Total (N=xxx)
Duration of INCB050465 Treatment (days) [a]				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x
Average Daily Dose of INCB050465 (mg/day) [b]				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x
Subjects Who Had INCB050465 Dose Interruption	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Subjects Who Had INCB050465 Dose Reduction	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
From xxxx to xxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
From xxxx to xxx	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Etc…	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Compliance With INCB050465 [c] (%)				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x

<the following is for combination therapy only>

Duration of INCB039110 Treatment (days) [a]				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x
Average Daily Dose of INCB039110 (mg/day) [b]				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x
Subjects Who Had INCB039110 Dose Interruption	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Subjects Who Had INCB039110 Dose Reduction	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
From 400 mg QD to 300 mg QD	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
From 300 mg QD to 200 mg QD	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Etc…	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)	xxx (xxx.x)
Compliance with INCB039110[c] (%)				
N	xxx	xxx	xxx	xxx
Mean	xx.xx	xx.xx	xx.xx	xx.xx
STD	xx.xxx	xx.xxx	xx.xxx	xx.xxx
Min	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx
Max	xx.x	xx.x	xx.x	xx.x

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

[a] Duration of treatment (days) = Date of last dose – Date of first dose + 1.
[b] Average daily dose (mg/day) = [total actual dose taken (mg)] / [duration of treatment (days)].
[c] Compliance (%) = 100 × (total dose actually taken [mg]) / (total intended dose [mg]).

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