STATISTICAL ANALYSIS PLAN

INCB 18424-271 / NCT02953678

A Single-Cohort, Phase 2 Study of Ruxolitinib in Combination With Corticosteroids for the Treatment of Steroid-Refractory Acute Graft-Versus-Host Disease

IND Number:	**77456**
Sponsor:	**Incyte Corporation** **1801 Augustine Cut-Off** **Wilmington, DE 19803**
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SAP Author:	[redacted]**, Biostatistics**
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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
AE	adverse event
BID	twice daily
BMI	body mass index
BMT CTN	Bone Marrow Transplant Clinical Trials Network
BSA	body surface area
CI	confidence interval
CR	complete response
CRF	case report form
CTCAE	Common Terminology Criteria for Adverse Events (v4.03)
DOR	duration of response
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	case report form
EOT	end of treatment
FDA	Food and Drug Administration
FFS	failure-free survival
GVHD	graft-versus-host disease
IVRS	interactive voice response system
JAK	Janus kinase
MAGIC	Mount Sinai Acute GHVD International Consortium
MedDRA	Medical Dictionary for Regulatory Activities
MF	myelofibrosis
MN-CIBMTR	Minnesota-Center for International Bone Marrow Transplant Research
NCI	National Cancer Institute
NRM	nonrelapse mortality
ORR	overall response rate
OS	overall survival
PK	pharmacokinetic
PR	partial response
SAE	serious adverse event
SAP	Statistical Analysis Plan
TEAE	treatment-emergent adverse event
VGPR	very good partial response
WHO	World Health Organization

1. INTRODUCTION

Ruxolitinib is a novel, potent, and selective inhibitor of the Janus kinases (JAKs) with selectivity for JAK1 and JAK2 (Quintás-Cardama et al 2010). Ruxolitinib potently inhibits JAK1 and JAK2 (IC_{50} < 5 nM), yet it does not significantly inhibit a broad panel of 28 kinases (< 30% inhibition) when tested at 200 nM (approximately 100 × the average IC_{50} value for JAK1 and JAK2 enzyme inhibition.

Section 1 of the Protocol provides a detailed description of the investigational products, target patient population, and the potential risks and benefits from the combination treatments. The purpose of this document is to provide a detailed Statistical Analysis Plan (SAP).

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 18424-271 Protocol Amendment 2 dated 04 OCT 2016 and case report form (CRF) approved 15 NOV 2016. Unless superseded by an amendment, this SAP will be effective for all subsequent Protocol amendments and electronic case report form (eCRF) versions.

2.2. Study Objectives

2.2.1. Primary Objectives

Assess the efficacy of ruxolitinib in combination with corticosteroids in subjects with Grades II to IV steroid-refractory acute graft-versus-host disease (GVHD).

2.2.2. Secondary Objectives

Secondary objectives include the following:

- Assess additional response and longer-term efficacy outcomes in the study population.
- Assess the incidence and severity of adverse events (AEs) and serious adverse events (SAEs).
- Evaluate the pharmacokinetics (PK) of ruxolitinib when administered in combination with corticosteroids.

[redacted]

[redacted]

2.3. Study Endpoints

2.3.1. Primary Endpoint

Overall response rate (ORR) at Day 28, defined as the proportion of subjects demonstrating a complete response (CR), very good partial response (VGPR), or partial response (PR).

2.3.2. Secondary Endpoints

Key secondary endpoint and other secondary endpoints are included in the following:

- Key secondary endpoint: Six-month duration of response (DOR), defined as the time from first response until GVHD progression or death. DOR will be assessed when all subjects complete the Day 180 visit.
- ORR, defined as the proportion of subjects demonstrating a CR, VGPR, or PR at Days 14, 56, and 100.
- Three-month DOR, defined as the time from first response until GVHD progression or death, when all subjects complete the Day 84 visit.
- Nonrelapse mortality (NRM), defined as the proportions of subjects who died due to causes other than malignancy relapse at Months 6, 9, 12, and 24.
- Relapse rate, defined as the proportion of subjects whose underlying malignancy relapses.
- Relapse-related mortality rate, defined as the proportion of subjects whose malignancy relapses and has a fatal outcome.
- Failure-free survival (FFS), defined as the proportion of subjects who are still alive, have not relapsed, have not required additional therapy for acute GVHD, and have not demonstrated signs or symptoms of chronic GVHD, at Month 6.
- Overall survival (OS), defined as the time from study enrollment (first day of ruxolitinib treatment) to death due to any cause.
- Summary of clinical safety data (eg, AEs, infections) will be tabulated and listed.
- Maximum observed plasma drug concentration (C_{max}), minimum observed plasma drug concentration (C_{min}), time of maximum observed plasma drug concentration (t_{max}), area under the plasma drug concentration versus time curve (AUC), and apparent clearance of study drug from plasma (CL/F).

[redacted]

3. STUDY DESIGN

This is an open-label, single-cohort, multicenter Phase 2 study of ruxolitinib in combination with corticosteroids for the treatment of steroid-refractory Grades II to IV acute GVHD. Eligible subjects will begin treatment at 5 mg twice daily (BID) ruxolitinib; if hematologic parameters are stable and no treatment-related toxicity is observed after the first 3 days of treatment, the dose may be increased to 10 mg BID. Ruxolitinib may be tapered after Day 180 provided the subject has achieved CR or VGPR and corticosteroids have been discontinued for at least 8 weeks. Corticosteroids will be administered at a starting dose of 2.0 mg/kg per day (unless otherwise indicated) on Day 1 and will be tapered as appropriate. Subjects will receive study treatment until treatment failure (progression of GVHD, no response, or requiring additional systemic therapy), unacceptable toxicity, or death. Continued use of anti-infective medications, GVHD prophylaxis medications (including calcineurin inhibitors), transfusion support, and topical steroid therapy is permitted.

Severity of GVHD will be assessed from screening through end of treatment (EOT) using the Mount Sinai Acute GHVD International Consortium (MAGIC) guidelines. Adverse events and SAEs will be assessed from the time of consent through 30 to 35 days after the EOT as per National Cancer Institute CTCAE v4.03. Subjects will be assessed for efficacy (including overall response, NRM, FFS, DOR, relapse rate, relapse-related mortality rates, and OS), safety (including AEs, SAEs, and clinical/laboratory assessments), [redacted]

3.1. Control of Type I Error

No formal statistical tests will be performed. All confidence intervals (CIs) will be 95%.

3.2. Sample Size Considerations

Approximately 70 subjects are planned for the final analysis of the primary endpoint of ORR. A second-line treatment demonstrating a true ORR of 60% would be considered clinically meaningful. With the assumed true rate of 60%, a sample size of 70 subjects would provide > 90% probability to have a 95% CI with lower limit of ≥ 40%.

An interim analysis will be conducted once 35 subjects complete the Day 28 visit. In this interim analysis, only futility will be assessed, and the trial will be terminated if the lower boundary is crossed.

A group sequential design method for 1 sample binary outcome data will be used to calculate the lower boundary of futility. The spending function of HSD(-4) will be used. For H0: p = 0.4, Ha: p = 0.6, and a 1-sided binomial test with alpha of 0.025, if ≤ 15 subjects respond at the time of the interim analysis, the study will be terminated. This will provide 70.03% probability for the response rate of 40% at the interim analysis.

If ≥ 37 subjects respond at the time of final analysis, the study outcome will be considered positive. These assumptions will provide 89.88% power for the response rate of 60% in the final analysis with Type I error of 0.0189.

3.3. Schedule of Assessments

See Appendix C for assessment schedules for this study.

4. DATA HANDLING DEFINITIONS AND CONVENTIONS

4.1. Scheduled Study Evaluations and Study Periods

4.1.1. Day 1

Day 1 is the date of first dose of ruxolitinib. For patients who started corticosteroids before ruxolitinib, all study visits will be counted based on Day 1 of study.

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 follows:

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 follows:

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 on or before the day of the first administration of study drug. When scheduled assessments and unscheduled assessments occur on the same day and time of the assessment or 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 study drug.

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. Body Surface Area

Body surface area (BSA) will be calculated based on the Mosteller (1987) formula as follows:

BSA (m^2) = {[weight (kg) × height (cm)] / 3600}^{½}

Sites will also record the BSA calculated per institutional standards.

4.2.4. 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 is started accordingly:

- Before the date of first administration of study drug 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 study drug 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 study drug. In the listing, it will be indicated whether a medication is prior only, concomitant only, or both prior and concomitant.

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

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

- For the starting date, impute as follows:
  - If the day is missing, then impute as the first day of the month.
  - If the month is missing, then impute as the first day of the year.
  - If the year is missing, then the medication will be considered both prior and concomitant.
- For the ending date, impute as follows:
  - If the day is missing, then impute as the last day of the month.
  - If the month is missing, then impute as the last day of the year.
  - If the year is missing, then the medication will be considered as ongoing until the end of the study.

5. STATISTICAL METHODOLOGY

5.1. General Methodology

Unless otherwise noted, SAS® software (SAS Institute Inc., Cary, NC; v9 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 single-cohort study. Eligible subjects will begin treatment at ruxolitinib 5 mg BID; if hematologic parameters are stable and no treatment-related toxicity is observed after the first 3 days of treatment, the dose may be increased to 10 mg BID. Corticosteroids will be administered at a starting dose of 2.0 mg/kg per day (unless otherwise indicated) on Day 1 and will be tapered as appropriate.

5.3. Analysis Populations

5.3.1. Efficacy Evaluable Population

The efficacy evaluable population includes all subjects enrolled in the study. Demographics, baseline characteristics, subject disposition, and all efficacy analyses will be conducted using the efficacy evaluable population.

5.3.2. Safety Evaluable Population

The safety evaluable population includes all subjects enrolled in the study who received at least 1 dose of study drug. Treatment groups for this population will be determined according to the actual treatment that the subject received on Day 1. All safety analyses will be conducted using the safety evaluable population.

5.3.3. Pharmacokinetic Evaluable Population

The pharmacokinetic evaluable population includes subjects who receive at least 1 dose of study drug and provide at least 1 plasma sample (1 PK measurement) after study drug administration. 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.

6. BASELINE, EXPOSURE, AND DISPOSITION VARIABLES AND ANALYSES

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

Demographic and baseline characteristics, disease history, and prior therapy will be summarized for the efficacy evaluable population and listed.

6.1.1. Demographics and Baseline Characteristics

Demographic and baseline characteristics include the following: age, sex, race, ethnicity, weight, height, BMI, BSA, and ECOG performance status.

6.1.2. Disease History

Cancer type, time since initial diagnosis, stage at diagnosis, current stage, disease histology, primary site of disease, mutation status, and site of metastatic disease at baseline will be summarized.

Time since diagnosis will be calculated as follows:

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

6.1.3. Prior Therapy

Number of subjects who received prior systemic therapy will be summarized for the efficacy evaluable population. Regimen name, component drugs, start and stop dates, 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 efficacy evaluable population. Radiotherapy type, body site, start and stop dates, 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 efficacy evaluable population. Date and description of the surgery/procedure will be listed.

6.1.4. Medical History

For subjects in the efficacy evaluable population, medical history will be summarized by system-organ class and preferred term and will be listed.

6.2. Disposition of Subjects

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

6.3. Protocol Deviations

Protocol deviations and violations collected on eCRF will be presented in the subject data listings.

6.4. Exposure

For subjects in the safety evaluable population, exposure to study drug (INCB018424) will be summarized descriptively as follows:

- **Duration of treatment with study drug:**

  Duration of treatment (days) = Date of last dose of study drug – Date of first dose of study drug + 1

- **Average daily dose of study drug:**

  Average daily dose of study drug (mg/day) = [total actual study drug dose taken (mg)] / [duration of treatment with study drug]

Summary for the planned exposure of corticosteroids will be provided.

6.5. Study Drug Compliance

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

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

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

Compliance of study drug will be summarized descriptively and listed.

6.6. Prior and Concomitant Medication

Prior medications and concomitant medications will be coded using the WHO Drug Dictionary. For subjects in the safety population, the number and percentage of subjects with prior and concomitant medications will be 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.

7. EFFICACY

Planned tables, figures, and listings are provided in Appendix A. All efficacy analyses will be performed using the efficacy evaluable population.

7.1. General Considerations

Missing observations will be handled for specific endpoints as detailed in the sections addressing each analysis.

7.2. Efficacy Hypotheses

No formal statistical tests will be performed.

7.3. Analyses of the Efficacy Parameters

7.3.1. Primary Efficacy Analysis

Overall response rate at Day 28 is defined as the proportion of subjects demonstrating a CR, VGPR, or PR as per standard criteria (see Appendix B).

The proportion of responders will be estimated with 95% CIs for the efficacy evaluable population. Confidence intervals will be calculated based on the exact method for binomial distributions. Summary statistics will be provided.

Subjects who have missing response data at Day 28 (includes withdrawal or death before Day 28) will be considered nonresponders. The primary analysis will be conducted when all subjects have completed Day 28 response assessments or discontinued.

7.3.2. Secondary and Efficacy Analysis

7.3.2.1. Duration of Response

Duration of response at Month 6 is the key secondary endpoint. For responders, the DOR is defined as the difference of the end of response and the start of response for subjects who have at least 1 response measurement. The start of a response will be the first visit where the subject achieves PR or better based on response criteria in Appendix B (MAGIC guidelines). The end of response will be the first visit after GVHD progression based on response criteria in Appendix B or death. Duration of response will be assessed using the Kaplan-Meier method for subjects who achieve a response. Median duration and 95% CI will be estimated. Subjects who are still responding at the time of database lock or discontinuation will be right-censored at the

time of last valid response assessment. Six-month DOR will be assessed when all subjects complete the Day 180 visit.

In addition, 3-month DOR will be assessed. Three-month DOR is defined as the time from first response until GVHD progression or death, when all subjects complete the Day 84 visit. Duration of response will be assessed using the Kaplan-Meier method for subjects who achieve a response.

7.3.2.2. Overall Response Rate

Overall response rate at Days 14, 56, and 100 is defined as the proportion of subjects demonstrating a CR, VGPR, or PR based on the MAGIC guidelines.

Subjects who have missing response data at Days 14, 56, and 100 (includes withdraw or death before these days) will be considered as nonresponders. The ORR on Days 14, 56, and 100 will be estimated with a 95% CI. The proportion of responders will be estimated with 95% CIs. Confidence intervals will be calculated based on the exact method for binomial distributions. Summary statistics will be provided.

7.3.2.3. Nonrelapse Mortality

Nonrelapse mortality is defined as the proportion of subjects who died due to causes other than malignancy relapse at Months 6, 9, 12, and 24.

Cumulative incidence functions of NRM will be estimated using Gray's method, and subjects with relapse-related mortality will be treated as competing risk and no observed mortality as censored at their last date known to be alive. Cumulative incidence rates of NRM at Months 6, 9, 12, and 24 will be estimated with 95% CI. Confidence intervals will be calculated based on the exact method for binomial distributions. Summary statistics will be provided.

7.3.2.4. Relapse Rate

Relapse rate is defined as the proportion of subjects whose underlying malignancy relapses. Primary disease relapse rate at Month 6 will be estimated with 95% CI. Confidence intervals will be calculated based on the exact method for binomial distributions. Cumulative incidence rate and summary statistics will be provided.

7.3.2.5. Relapse-Related Mortality Rate

Relapse-related mortality rate is defined as the proportion of subjects whose malignancy relapses and has a fatal outcome at Month 6. Relapse mortality rate will be provided with 95% CI. Confidence interval will be calculated based on the exact method for binomial distributions. Cumulative incidence rate and summary statistics will be provided.

7.3.2.6. Failure-Free Survival

Failure-free survival, defined as the proportion of subjects who are still alive, have not relapsed, have not required additional therapy for acute GVHD, and have not demonstrated signs or symptoms of chronic GVHD, at Month 6. The Kaplan-Meier method will be used to estimate the FFS time distribution and the median survival. Subjects with no observed death or loss to follow-up or have not relapsed, have not required additional therapy for acute GVHD, and have

not demonstrated signs or symptoms of chronic GVHD, at Month 6 will be treated as censored at Month 6. Survival rate at Month 6 will be estimated with 95% CI. The 95% CI will be calculated using the Brookmeyer and Crowley's method (Brookmeyer and Crowley 1982). Summary statistics will be provided.

7.3.2.7. Overall Survival

Overall survival is defined as the time from study enrollment (first date of ruxolitinib treatment) to death due to any cause. The Kaplan-Meier method will be used to estimate the survival time distribution and the median survival. Subjects with no observed death or loss to follow-up will be treated as censored at their last date known to be alive. Survival rate at Month 6 will be estimated with 95% CI. The 95% CI will be calculated using the Brookmeyer and Crowley's method (Brookmeyer and Crowley 1982). Summary statistics will be provided.

7.4. Pharmacokinetic Analyses

Noncompartmental analysis of the observed PK concentration data will be performed, and PK parameters, such as C_{max}, t_{max}, AUC, and $t_{½}$, will be generated and summarized wherever possible. Planned tables, listings, and figures are listed in Appendix B.

The population PK of ruxolitinib in subjects with myelofibrosis (MF) has been established in the previous MF New Drug Application. First, the PK data from this study will be applied to validate the final PK model established in the MF population. If significant biases are observed in this validation process, then a new population PK model may be generated based on the data from this study, and the model development process will follow the methods below. The data from this study may be combined with data from other clinical studies to improve parameter estimation.

The model development process consists of base pharmacokinetic model development and covariate analysis. In the base model development, compartment models with first-order absorption and linear elimination will be tested for their ability to characterize the PK of ruxolitinib in combination with corticosteroids for the treatment of steroid-refractory acute GVHD. Interindividual variability will be modeled using an exponential error model and explored for each PK parameter. Proportional, additive, and mixed error (additive plus proportional) models will be individually evaluated for their ability to describe the magnitude of residual variability. The first-order conditional estimation method with the interaction option will be used.

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

The population PK data preparation will be performed using SAS v9.1 or later (SAS Institute Inc, Cary, NC). [redacted] The PK analyses will use NONMEM v7.1.0 or later (ICON Development Solutions, Dublin, Ireland).

[redacted]

8. SAFETY AND TOLERABILITY

8.1. General Considerations

The analyses for this section will be provided for the safety evaluable population. Summary tables may be replaced with listings when appropriate. For instance, an AE frequency table may be replaced with a listing if it only contains a few unique preferred terms reported on relatively few subjects.

8.2. Adverse Events

8.2.1. Adverse Event Definitions

A treatment-emergent adverse event (TEAE) is any AE either reported for the first time or the worsening of a pre-existing event after the first dose of study drug until 30 days after the last dose of study drug. Analysis of AEs (as discussed below) will be limited to TEAEs, but data listings will include all AEs regardless of their timing to study drug administration.

Adverse events will be tabulated by MedDRA preferred term and system organ class. Severity of AEs will be described and graded using the National Cancer Institute (NCI) CTCAE v4.03 (NCI 2010). The CTCAE reporting guidelines and grading details are available on the Cancer Therapy Evaluation Program website.

A grading (severity) scale is provided for each AE term. If the toxicity is not included in the CTCAE v4.03 criteria, then it will be rated on a scale of 1 to 4 as follows: 1 = mild, 2 = moderate, 3 = severe, and 4 = life-threatening. All toxicities will be graded based on the worst level reached, not the level they may have reached if they had not been treated. When the intensity of an AE changes over time for a reporting period (eg, between visits), then 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 study drug will be considered to be treatment-related AEs. If the investigator does not specify the relationship of the AE to study drug, then the AE will be considered to be treatment-related. The incidence of AEs and treatment-related AEs will be tabulated. Serious AEs will also be tabulated.

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

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

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

8.2.2. 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 TEAEs related to ruxolitinib
- Number (%) of subjects reporting any TEAEs related to corticosteroids
- Number (%) of subjects who temporarily interrupted ruxolitinib because of a TEAE
- Number (%) of subjects with ruxolitinib dose reductions because of TEAEs
- Number (%) of subjects who permanently discontinued ruxolitinib because of a TEAE
- Number (%) of subjects who permanently discontinued ruxolitinib or corticosteroids because of a TEAE
- Number (%) of subjects who withdrew from the study because of a TEAE
- Number (%) of subjects who had a fatal TEAE
- Number (%) of subjects who had a TEAE of special interest

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

- Number (%) of subjects reporting TEAEs by system organ class and preferred term
- Number (%) of subjects reporting TEAEs by preferred term in decreasing order of frequency
- Number (%) of subjects reporting TEAEs by system organ class, preferred term, and highest CTCAE grade
- Number (%) of subjects reporting any Grade 3 or 4 TEAEs by system organ class and preferred term
- Number (%) of subjects reporting treatment-related AEs by system organ class and preferred term
- Number (%) of subjects reporting treatment-related AEs by preferred term in decreasing order of frequency
- Number (%) of subjects reporting treatment-related AEs by system organ class, preferred term, and highest CTCAE grade
- Number (%) of subjects reporting fatal TEAEs by system organ class and preferred term
- Number (%) of subjects reporting treatment-emergent SAEs by system organ class and preferred term

- Number (%) of subjects reporting treatment-related SAEs by system organ class and preferred term
- Number (%) of subjects reporting TEAEs leading to dose reduction of ruxolitinib by system organ class and preferred term
- Number (%) of subjects reporting TEAEs leading to discontinuation of ruxolitinib by system organ class and preferred term
- Number (%) of subjects reporting treatment-emergent non-SAE by system organ class and preferred term

8.3. Clinical Laboratory Tests

8.3.1. Laboratory Value Definitions

Laboratory values and change from baseline values will be summarized descriptively by visit. The baseline value will be determined using the last nonmissing values collected before the first dose.

Laboratory test values outside the normal range will be assessed for severity based on CTCAE v4.03 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 central 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, associated central laboratory normal ranges will be applied. In the event that central laboratory normal ranges are not available, a set of standard normal ranges based on documented reference ranges will be applied to facilitate reporting the test results.

For numeric laboratory values, baseline value, postbaseline value, change from baseline, and percent change from baseline will be summarized by visit. In addition, mean change from baseline will be plotted over time for selected laboratory parameters.

Shift summaries will be presented showing the number and percentage of subjects with laboratory values of low, normal, and high at baseline along with change to the worst postbaseline visits. The denominator for the percentage calculation will use the number of subjects in the baseline category (ie, low, high, normal, 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. Separate tables will be provided for selected laboratory tests that have grading criteria in both high and low directions. 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

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 1. The abnormal values for subjects exhibiting clinically notable vital sign abnormalities will be listed. Alert vital signs are defined as an absolute value outside the defined range and percentage change from baseline greater than 25%. The abnormal values for subjects exhibiting alert vital sign abnormalities will also be listed.

Table 1: 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

Normal or abnormal 12-lead electrocardiograms (ECGs) will be collected and listed for each scheduled visit.

8.6. Analyses for the Data Monitoring Committee

No Data Monitoring Committee is planned.

9. INTERIM ANALYSES

An interim analysis will be conducted when 35 subjects complete the Day 28 visit. In this interim analysis, only futility will be assessed, and the study will be terminated if the lower boundary is crossed.

A group sequential design method for 1 sample binary outcome data will be used to calculate the lower boundary of futility. The spending function of HSD(-4) will be used. For H0: $p = 0.4$, Ha: $p = 0.6$, and a 1-sided binomial test with alpha of 0.025, if ≤ 15 subjects respond at the time of the interim analysis, the study will be terminated. This will provide 70.03% probability for the response rate of 40% at the interim analysis.

If ≥ 37 subjects respond at the time of final analysis, the study outcome will be considered positive. These assumptions will provide 89.88% power for the response rate of 60% in the final analysis with Type I error of 0.0189.

10. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 2.

Table 2: Statistical Analysis Plan Versions

SAP Version	Date
Original	15 JUN 2016
Amendment 1	13 SEP 2016
Amendment 2	09 OCT 2016
Amendment 3	24 JUL 2017

10.1. Changes to Protocol-Defined Analyses

1. Key secondary endpoint: 6-month DOR.
2. Updated interim analysis for futility.
3. Removed ECG analysis.

10.2. Changes to the Statistical Analysis Plan

SAP Amendment 1:

1. Sections 2.3.2 and 7.3.2.1: Key secondary endpoint was changed to 6-month DOR, and 3-month DOR was added as a secondary endpoint; duration of response analysis description was updated accordingly.
2. Sections 3.2 and 9: Modified language to reflect planned interim analysis for futility.
3. Section 3: Updated text regarding guidance on tapering of ruxolitinib to align with revisions made in Protocol Amendment 2.

SAP Amendment 2:

1. Section 7.3.1: Revised to indicate that if subjects have response assessments before Day 28 and discontinue the study, then the response assessments before Day 28 will be used for the overall responses rate at Day 28.
2. Section 7.3.2.2: Revised to indicate that if subjects have response assessments before scheduled visits and discontinue the study, the response assessments before the scheduled visits will be used for the overall responses rate at the next closest scheduled visits.

SAP Amendment 3:

1. Section 4.1.1: Revised definition of Day 1 to be based on first day of treatment of ruxolitinib.
2. Section 2.3.2 and 7.3.2.7: Clarified that study enrollment refers to the first date of ruxolitinib treatment (Day 1) for the overall survival definition.

3. Section 7.3.1: Revised to indicate that if subjects have response assessments before Day 28 and discontinue the study, then the subject will be considered as non-responder for the overall responses rate at Day 28.
4. Section 7.3.2.2: Revised to indicate that if subjects have response assessments before scheduled visits and discontinue the study, the subject will be considered as non-responder at that scheduled visit.
5. Section 7.3.3: Revised to include more detail on the summary statistics to be provided for other efficacy analyses. Modified to indicate that summary statistics will not be provided for chronic GVHD.
6. Section 8.2.2: Updated planed AE related outputs
7. Section 8.5: Revised to indicate that there will not be any ECG analysis; instead normal/abnormal status will be listed per CRF collection.
8. Appendix A: Updated the planned tables, listings, and figures as a result of the other changes to this SAP. Numbering was modified as necessary as a result of the modifications.

11. REFERENCES

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Martin PJ, Bachier CR, Klingemann HG, et al. Endpoints for clinical trials testing treatment of acute graft-versus-host disease: a joint statement. Biol Blood Marrow Transplant 2009;15:777 784.

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APPENDIX A. PLANNED TABLES, FIGURES, AND LISTINGS

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

Tables

Table No.	Title	Population	In-Text
1.1.1	Analysis Population	Enrolled	X
1.1.2	Summary of Subject Disposition	Enrolled	X
1.2.1	Summary of Demographic and Baseline Characteristics	Efficacy	X
1.2.2	Summary of Baseline Disease Characteristics	Efficacy	X
1.3.1	Summary of Medical History	Efficacy	
1.3.2	Summary of Cancer History	Efficacy	
1.3.3	Summary of Allogeneic Hematopoietic Stem Cell Transplant History	Efficacy	
1.4.1	Summary of Prior Medications	Efficacy	
1.4.2	Summary of Concomitant Medications	Efficacy	
1.4.3	Summary of Prior Anti-Cancer Therapy	Efficacy	X
1.4.4	Summary of Prior Anti-GVHD Therapy	Efficacy	
1.4.5	Summary of Prior Radiotherapy	Efficacy	
2.1.1	Summary of Overall Response Rate at Day 28	Efficacy	X
2.1.2	Summary of Overall Response Rate at Days 14, 56, and 100	Efficacy	X
2.1.3	Summary of Overall Response Rate at Interim Analysis	Efficacy	X
2.2.1	Summary of Duration of Response	Efficacy	X
2.2.2	Summary of Nonrelapse Mortality Rate	Efficacy	X
2.2.3	Summary of Relapse Rate and Relapse Mortality Rate	Efficacy	X
2.2.4	Kaplan-Meier Analysis of Failure-Free Survival	Efficacy	X
2.2.5	Kaplan-Meier Analysis of Overall Survival	Efficacy	X
[redacted]			
2.3.5	Summary of Stages of GVHD by Organ	Efficacy	
[redacted]			
2.3.8	Summary of Body Weight	Efficacy	
2.3.9	Summary of ECOG Status	Efficacy	
2.3.10	Summary of Correlative Study Parameters	Efficacy	
3.1.1	Summary of Ruxolitinib Exposure and Compliance	Safety	X
3.1.2	Summary of Corticosteroid Exposure	Safety	X
3.2.1	Overall Summary of Treatment-Emergent Adverse Events	Safety	X
3.2.2	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	
3.2.3	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X
3.2.4	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Highest Grade	Safety	

Table No.	Title	Population	In-Text
3.2.5	Summary of Ruxolitinib Treatment-Related, Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	
3.2.6	Summary of Ruxolitinib Treatment-Related, Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X
3.2.7	Summary of Ruxolitinib Treatment-Related, Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Highest Grade	Safety	
3.2.8	Summary of Treatment-Emergent Fatal Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.9	Summary of Treatment-Emergent Serious Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.10	Summary of Ruxolitinib Treatment-Related, Treatment-Emergent Serious Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	
3.2.11	Summary of Treatment-Emergent Adverse Events Leading to Ruxolitinib Dose Interruption By MedDRA System Organ Class and Preferred Term	Safety	
3.2.12	Summary of Treatment-Emergent Adverse Events Leading to Ruxolitinib Dose Reduction By MedDRA System Organ Class and Preferred Term	Safety	
3.2.13	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Ruxolitinib by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.14	Summary of Corticosteroids Treatment-Related, Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	
3.2.15	Summary of Corticosteroids Treatment-Related, Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X
3.2.16	Summary of Corticosteroids Treatment-Related, Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Highest Grade	Safety	
3.2.17	Summary of Corticosteroids Treatment-Related, Treatment-Emergent Serious Adverse Events By MedDRA System Organ Class and Preferred Term	Safety	X
3.2.18	Summary of Treatment-Emergent Adverse Events Leading to Corticosteroids Dose Interruption by MedDRA System Organ Class and Preferred Term	Safety	
3.2.19	Summary of Treatment-Emergent Adverse Events Leading to Corticosteroids Dose Reduction by MedDRA System Organ Class and Preferred Term	Safety	
3.2.20	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Corticosteroids by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.21	Summary of Treatment-Emergent Adverse Events Leading to Withdrawal From the Study By MedDRA System Organ Class and Preferred Term	Safety	
3.2.22	Summary of Treatment-Emergent Grade 3 or Higher Adverse Events By MedDRA System Organ Class and Preferred Term	Safety	
3.2.23	Summary of Treatment-Emergent Adverse Events of Special Interest	Safety	X
3.3.1	Summary of Laboratory Values – Hematology	Safety	
3.3.2	Shift Summary of Hematology Values – to the Worst Abnormal Value	Safety	

Table No.	Title	Population	In-Text
3.3.3	Shift Summary of Hematology Values in CTC Grade – to the Worst Abnormal Value	Safety	
3.3.4	Summary of Laboratory Values – Chemistry	Safety	
3.3.5	Shift Summary of Chemistry Values – to the Worst Abnormal Value	Safety	
3.3.6	Shift Summary of Chemistry Values in CTC Grade – to the Worst Abnormal Value	Safety	
3.4.1	Summary of Systolic Blood Pressure	Safety	
3.4.2	Summary of Diastolic Blood Pressure	Safety	
3.4.3	Summary of Pulse	Safety	
3.4.4	Summary of Body Temperature	Safety	
3.4.5	Summary of Respiratory Rate	Safety	

Figures

Figure No.	Title
4.2.1	Kaplan-Meier Estimate of Duration of Response
4.2.2	Kaplan-Meier Estimate of Overall Survival
4.2.3	Kaplan-Meier Estimate of Failure-Free Survival
4.2.4	Body Weight Over Time

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
2.4.1	Demographic and Baseline Characteristics
2.4.2	Medical History
2.4.3	GVHD and Cancer History
2.4.4	Prior and Concomitant Drug Treatments
2.4.5	Allogeneic Hematopoietic Stem Cell Transplant History
2.4.6	Prior Anti-GVHD Medication
2.4.7	Prior Radiotherapy
2.4.8	Prior Anti-Cancer Therapy
2.4.9	Immunosuppressive Medication
2.5.1	Ruxolitinib Exposure and Compliance
2.5.2	Corticosteroid Exposure
2.6.1	GVHD Symptoms and Response Assessment
2.6.2	Overall Survival Events and Assessment
2.6.3	Failure-Free Survival Events and Assessment
2.6.4	ECOG Performance Status
2.6.5	Duration of Response
2.6.6	Acute GVHD Staging and Grading
2.7.1	Adverse Events
2.7.2	Serious Adverse Events
2.7.3	Grade 3 or 4 Adverse Events
2.7.4	Adverse Events Leading to Interruption, Dose Reduction or Discontinuation of Ruxolitinib
2.7.5	Adverse Events Leading to Interruption, Dose Reduction or Discontinuation of Corticosteroids
2.7.6	Fatal Adverse Events
2.8.1	Clinical Laboratory Values – Hematology
2.8.2	Clinical Laboratory Values – Chemistry

Listing No.	Title
2.8.3	Abnormal Clinical Laboratory Values – Hematology
2.8.4	Abnormal Clinical Laboratory Values – Chemistry
2.8.5	PK Blood Sampling Times
2.9.1	Vital Signs
2.9.2	Abnormal Vital Signs
2.10.1	12-Lead ECG

APPENDIX B. MAGIC GUIDELINES FOR STAGING AND GRADING ACUTE GVHD

Acute GVHD Staging and Grading, MAGIC Guidelines

Stage	Skin (Active Erythema Only)	Liver (bilirubin)	Upper GI	Lower GI (stool output/day)
0	No active (erythematous) GVHD rash	< 2 mg/dL	No or intermittent nausea, vomiting, or anorexia	Adult: < 500 mL/day or < 3 episodes/day. Child: < 10 mL/kg per day or < 4 episodes/day.
1	Maculopapular rash < 25% BSA	2-3 mg/dL	Persistent nausea, vomiting, or anorexia	Adult: 500-999 mL/day or 3-4 episodes/day. Child: 10-19.9 mL/kg per day or 4-6 episodes/day.
2	Maculopapular rash 25%-50% BSA	3.1-6 mg/dL	–	Adult: 1000-1500 mL/day or 5-7 episodes/day. Child: 20-30 mL/kg per day or 7-10 episodes/day.
3	Maculopapular rash > 50% BSA	6.1-15 mg/dL	–	Adult: > 1500 mL/day or > 7 episodes/day. Child: > 30 mL/kg per day or > 10 episodes/day.
4	Generalized erythroderma (> 50%) with bullae	> 15 mg/dL	–	Severe abdominal pain with or without ileus or grossly bloody stool (regardless of stool volume).

Overall clinical grade (based on most severe target organ involvement):
Grade 0: No stage 1-4 of any organ.
Grade I: Stage 1-2 skin without liver, upper GI, or lower GI involvement.
Grade II: Stage 3 rash and/or stage 1 liver and/or stage 1 upper GI and/or stage 1 lower GI.
Grade III: Stage 2-3 liver and/or stage 2-3 lower GI, with stage 0-3 skin and/or stage 0-1 upper GI.
Grade IV: Stage 4 skin, liver, or lower GI involvement, with stage 0-1 upper GI.

Response Definitions:

GVHD response assessments will be made with respect to changes in the organ stage relative to Study Day 1.

- Complete response (CR) is defined as a score of 0 for the GVHD grading in all evaluable organs. For a response to be scored as CR at Day 28 or later, the participant must still be in CR on that day and have had no intervening additional therapy for an earlier progression, mixed response (MR), or no response (NR).
- Very good partial response (VGPR) is defined as follows:
  - Skin: No rash, or residual erythematous rash involving < 25% of the body surface, without bullae (residual faint erythema and hyperpigmentation do not count).
  - Liver: Total serum bilirubin concentration < 2 mg/dL or < 25% of baseline at enrollment.
  - Gut:
    - Tolerating food or enteral feeding.
    - Predominantly formed stools.
    - No overt gastrointestinal bleeding or abdominal cramping.
    - No more than occasional nausea or vomiting.
- Partial response (PR) is defined as improvement in 1 stage in 1 or more organs involved with GVHD symptoms without progression in others. For a response to be scored as PR at Day 28 or later, the participant must still be in PR on that day and have had no intervening additional therapy for an earlier progression, MR, or NR.
- Mixed response is defined as improvement in 1 or more organs with deterioration in another organ manifesting symptoms of GVHD or development of symptoms of GVHD in a new organ.
- Progression of disease is defined as deterioration in at least 1 organ without any improvement in others.
- No response is defined as absence of any improvement or progression as defined. Subjects receiving secondary therapy (including need to re-escalate steroid dose to greater than the Day 1 dose), will be classified as nonresponders.

Source: CIBMTR 2009, Martin et al 2009, Harris et al 2016.

APPENDIX C. SCHEDULE OF ASSESSMENTS

Schedule of Assessments

Item	Protocol Section	Screening Phase	Treatment Phase[a]													EOT	Follow-Up Phase	
		D -28 to -1	D1	D3	D7	D14	D21	D28	D35	D42	D49	D56[b]	D100	D180	D365[c]		Safety[d]	Survival
Informed consent	7.1	X																
Inclusion/exclusion criteria	3	X																
Contact IVRS	7.2	X	X					X				X	X		X	X		X
Demography/disease history	7.3	X																
Prior/concomitant medications	7.4	X	X													X	X	
Supportive care medications	5.2.2.4	X	X													X	X	
AE assessment	7.5.1	X	X													X	X	
Physical examination	7.5.2	X	X		X	X	X	X	X	X	X	X	X		X	X	X	
Vital signs	7.5.3	X	X		X	X	X	X	X	X	X	X	X		X	X	X	
ECOG performance status	7.5.4	X	X		X	X	X	X	X	X	X	X	X		X	X	X	
12-lead ECG	7.5.5	X	As indicated													X		
Acute GVHD grading and response assessment	7.6.1	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	
[redacted]																		
Chimerism assessment	7.6.3	X	As indicated															
PTLD assessment	7.6.4		As indicated															

Schedule of Assessments (Continued)

Item	Protocol Section	Screening Phase	Treatment Phase[a]												EOT	Follow-Up Phase	
		D -28 to -1	D1	D3	D7	D14	D21	D28	D35	D42	D49	D56[b]	D100	D180	D365[c]		Safety[d]	Survival
Dispense study drug	5.1		X					X				X			X			
Study drug compliance	5.3		X					X				X			X	X		
Steroid dose monitoring	5.3		X													X		
Survival follow-up	6.4																	X[e]

ECG = electrocardiogram; PTLD = post-transplant lymphoproliferative disorder.
[a] A ± 2-day window is permitted to facilitate scheduling during the treatment phase.
[b] After Day 56, visits will occur every 28 days and will include all Day 56 assessments.
[c] The Day 365 visit will also serve as the regularly scheduled visit occurring every 28 days after Day 56 (ie, Day 364).
[d] Thirty to 35 days after EOT. For subjects withdrawing due to reasons other than GVHD progression, GVHD status should be assessed every 28 days.
[e] Every 8 weeks ± 7 days.

Laboratory Assessments

Item	Protocol Section	Screening Phase	Treatment Phase[a]													EOT	Safety Follow-Up
		D -28 to -1	D1[b]	D3	D7	D14	D21	D28	D35	D42	D49	D56[c]	D100	D180	D365[d]		
Chemistry panel	7.5.6.1	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X
Hematology	7.5.6.2	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X
Hepatitis screening	7.5.6.4	X															
Serum pregnancy test (childbearing females only)	7.5.6.3	X														X	
Urine pregnancy test[e] (childbearing females only)	7.5.6.3		X														
PK assessment[f]	7.7		X		X	X											
Correlative study blood collection	7.8	X	X		X	X		X				X[g]	X	X	X	X	

[a] A ± 2-day window is permitted to facilitate scheduling during the treatment phase.
[b] Day 1 laboratory assessments do not need to be repeated if screening assessments were performed in preceding 7 days.
[c] After Day 56, visits will occur every 28 days and will include all Day 56 assessments.
[d] The Day 365 visit will also serve as the regularly scheduled visit occurring every 28 days after Day 56 (ie, Day 364).
[e] Urine pregnancy tests are only required if medically indicated and should be confirmed with a serum pregnancy test.
[f] Samples to be collected at predose and at 1 hour ± 15 minutes, at 2 hours ± 30 minutes, and between 4 and 8 hours postdose.
[g] Day 56 only.

APPENDIX D. PLANNED TABLES AND FIGURES FOR PK ANALYSES

Tables

Table No.	Title
Table 1	Randomization of the Study
Table 2	Accuracy and Precision of the Plasma Assay Quality Control Samples
Table 3	Plasma Sample Collections Times With Deviations
Table 4	Summary of INCB018424 Pharmacokinetic Parameters From Observed Concentration Data
Table 5	Estimation of INCB018424 Population Pharmacokinetic Model Parameters
Table 6	Summary of INCB018424 Pharmacokinetic Parameters From Predicted Concentration Data
Table 7	Observed INCB018424 Plasma Concentrations for Individual Subjects
Table 8	INCB018424 Pharmacokinetic Parameters for Individual Subjects From Observed Concentration Data
Table 9	Predicted INCB018424 Plasma Concentrations for Individual Subjects From Final PK Model
Table 10	INCB018424 Pharmacokinetic Parameters for Individual Subjects From Predicted Concentration Data

Figures

Figure No.	Title
Figure 1	INCB 018424 Plasma Concentrations (Mean ± SE) Profile from Observed Concentration Data
Figure 2	Basic Goodness of fit diagnostic plots for population PK model
Figure 3	Additional Goodness of fit diagnostic plots for population PK model (optional)
Figure 4	Visual Predictive Check Plot
Figure 5	Individual Plot for Final PK