Official Title:	GRAVITAS-309: A Phase 2/3 Study of Itacitinib and Corticosteroids as Initial Treatment for Chronic Graft-Versus-Host Disease
NCT Number:	NCT03584516
Document Date:	Statistical Analysis Plan Amendment Version 1: 03 March 2022

STATISTICAL ANALYSIS PLAN

GRAVITAS-309: A Phase 2/3 Study of Itacitinib and Corticosteroids as Initial Treatment for Chronic Graft-Versus-Host Disease

Sponsor:	**Incyte Corporation** **1801 Augustine Cut-Off** **Wilmington, DE 19803**
Protocol Version:	**Protocol Amendment 8 dated 30 SEP 2021**
CRF Approval Date:	**13 OCT 2021**
SAP Version:	**Amendment 1**
SAP Author:	[redacted]**, Biostatistics**
Date of Plan:	**03 MAR 2022**

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
aGVHD	acute graft-versus-host disease
AUC	area under the plasma or serum concentration-time curve
AUC_{0-t}	area under the plasma or serum concentration-time curve from time = 0 to the last measurable concentration at time = t
BID	twice daily
BMI	body mass index
BOR	best overall response
BSA	body surface area
cGVHD	chronic graft-versus-host disease
CI	confidence interval
Cl/F	apparent oral dose clearance
C_{max}	maximum observed plasma or serum concentration
C_{min}	minimum observed plasma or serum concentration
CMV	cytomegalovirus
CR	complete response
CRF	case report form
CTCAE	Common Terminology Criteria for Adverse Events
DLT	dose-limiting toxicity
DMC	Data Monitoring Committee
DoR	duration of response
EBV	Epstein-Barr virus
eCRF	electronic case report form
GVHD	graft-versus-host disease
ITT	intent-to-treat
MedDRA	Medical Dictionary for Regulatory Activities
MQ	MedDRA query
NCI	National Cancer Institute
NIH	National Institutes of Health
NRM	nonrelapse mortality
ORR	objective response rate
OS	overall survival
PK	pharmacokinetic
PR	partial response
PT	preferred term

Abbreviation	Term
QD	once daily
SAP	Statistical Analysis Plan
SOC	system organ class
TEAE	treatment-emergent adverse event
T_{max}	time to maximum concentration
WHO	World Health Organization

1. INTRODUCTION

This is a 2-part, Phase 2/3 study of itacitinib or placebo in combination with corticosteroids as initial treatment for cGVHD. Part 1 is a run-in that will employ a randomized, open-label, parallel-cohort design with the primary objective to assess the safety and tolerability of itacitinib in combination with corticosteroids in order to identify the appropriate dose of itacitinib in combination with corticosteroids as initial treatment for moderate or severe cGVHD. A total of 20 participants with moderate or severe cGVHD will be randomized 1:1 to itacitinib 200 mg QD plus corticosteroids or 300 mg QD plus corticosteroids.

Part 1 expansion is a Phase 2 with an initial safety run-in that will employ a randomized, open-label, parallel-cohort design with the primary objective to assess the safety and preliminary efficacy of itacitinib in combination with corticosteroids compared with corticosteroids monotherapy and identify the appropriate dosing/schedule of itacitinib in combination with corticosteroids as initial treatment for cGVHD for Part 2. A total of up to 140 participants (35 per treatment group) with moderate or severe cGVHD will be randomized 1:1 to 1 of 4 treatment groups: itacitinib 300 mg QD plus corticosteroids (Treatment Group A), itacitinib 400 mg QD plus corticosteroids (Treatment Group B), itacitinib 300 mg BID plus corticosteroids (Treatment Group C), or corticosteroids monotherapy (Treatment Group D). Randomization will be stratified by cGVHD risk status (moderate vs severe). Treatment Groups B and C will have an initial safety run-in of 10 participants to determine safety and tolerability of the dose before expansion. Participants enrolled in the safety run-in will be monitored continuously. Treatment Group C was discontinued as of Amendment 8, and participants in that treatment group who were ongoing were allowed to reduce to 400 mg QD plus corticosteroids.

The purpose of the original version of the SAP was to provide details of the statistical analyses that have been outlined in Part 1 of the Protocol.

The purpose of Amendment 1 is to provide details of the statistical analyses that have been outlined in Part 1 expansion of Protocol Amendment 8.

1.1. Preliminary Results From Part 1

Preliminary data from Part 1 were reviewed by an independent DMC, and the summary data are presented in the Protocol. The DMC recommended that 300 mg QD be chosen as the Part 2 dose of itacitinib as no differences emerged between the doses with respect to toxicity.

1.2. Rationale for Part 1 Expansion

Additional dosing regimens of itacitinib were selected for evaluation in combination with corticosteroids in an expansion to Part 1 of the study, and the underlying rationale is presented in the Protocol.

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This amendment of the SAP is based on INCB 39110-309 Protocol Amendment 8 dated 30 SEP 2021 and CRFs approved 13 OCT 2021.

2.2. Study Objectives and Endpoints

Study objectives and endpoints for Part 1 and Part 1 expansion are shown in Table 1.

Table 1: Objectives and Endpoints, Part 1 and Part 1 Expansion

Objectives	Endpoints
Primary	
To identify an appropriate dose of itacitinib in combination with corticosteroids as initial treatment for moderate or severe cGVHD.	Part 1: DLT data through Day 28 and additional data from clinical safety and laboratory assessments. Part 1 expansion: Incidence and severity of adverse events, across treatment cohorts.
Key Secondary (for Part 1 Expansion)	
To evaluate preliminary activity across treatment cohorts with respect to response rate at Month 3 and Month 6.	Response rate at Month 3 and Month 6, defined as the proportion of participants who demonstrate a CR or PR at each timepoint.
Secondary	
To evaluate the PK of itacitinib when administered in combination with corticosteroids in the study population.	C_{max}, C_{min}, T_{max}, AUC_{0-t}, and Cl/F.
To estimate efficacy outcomes for each treatment cohort.	Part 1: Response rate at Month 3, 6, and 12. Part 1 expansion: Response rate at Month 12. Response rate is defined as the proportion of participants who demonstrate either a CR or PR at each timepoint.
	Time to response, defined as the interval between randomization and first response.
	DoR, defined as the interval between first response and cGVHD progression, death, or initiation of new systemic cGVHD therapy.
	OS, defined as the interval between the date of randomization and the date of death due to any cause.
	NRM, defined as the proportion of participants who died due to causes other than a relapse of their primary hematologic disease.
	Proportion of participants with ≥ 50% reduction in daily corticosteroid dose at Day 180.

Table 1: Objectives and Endpoints, Part 1 and Part 1 Expansion (Continued)

Objectives	Endpoints
To estimate efficacy outcomes for each treatment cohort (continued).	Proportion of participants successfully tapered off all corticosteroids at Day 180.
	Relapse rate of malignant and nonmalignant hematologic diseases, defined as the proportion of participants whose underlying disease relapses.
	Time to primary hematologic disease relapse, defined as the interval between the date of randomization and the date of relapse.
[redacted]	

3. STUDY DESIGN

Part 1 is a run-in that will employ a randomized, open-label, parallel-cohort design to assess the safety and tolerability of itacitinib in combination with corticosteroids in order to identify the appropriate dose level for initial treatment of moderate or severe cGVHD. A total of 20 participants with moderate or severe cGVHD will be randomized 1:1 to itacitinib 200 mg QD plus corticosteroids or 300 mg QD plus corticosteroids. Itacitinib treatment will continue until treatment failure (cGVHD progression, death, or initiation of new systemic cGVHD therapy), unacceptable toxicity, or withdrawal of consent, for a maximum of 36 months. Participants may remain on study for a total of 37 months, including the treatment period, safety follow-up, and post-treatment GVHD follow-up, unless death or withdrawal of consent occurs earlier.

Chronic GVHD staging and grading will be assessed using NIH consensus guidelines (Jagasia et al 2015, Lee et al 2015); safety and tolerability will be assessed as per NCI CTCAE v4.03.

An analysis to determine the dose for further study will be performed once the 20th evaluable participant completes 28 days of study treatment. An external DMC will review data from this analysis and provide a recommendation on an appropriate dose for Part 2.

In Part 1, any participant who withdraws from treatment before the completion of the 28-day observation period for any reason other than a DLT (eg, not evaluable for DLT) may be replaced to ensure a minimum number of evaluable participants.

Part 1 expansion is a Phase 2 with an initial safety run-in that will employ a randomized, open-label, parallel-cohort design with the primary objective to assess the safety and preliminary efficacy of itacitinib in combination with corticosteroids compared with corticosteroids monotherapy and identify the appropriate dosing/schedule of itacitinib in combination with corticosteroids as initial treatment for cGVHD for Part 2. A total of up to 140 participants (35 per treatment group) with moderate or severe cGVHD will be randomized 1:1 to 1 of 4 treatment groups (see Table 2): itacitinib 300 mg QD plus corticosteroids (Treatment Group A), itacitinib 400 mg QD plus corticosteroids (Treatment Group B), itacitinib 300 mg BID plus corticosteroids (Treatment Group C), or corticosteroids monotherapy (Treatment Group D).

Table 2: Treatment Groups and Dose Levels and Schedules

Treatment Group	Dose Level and Schedule
A	Itacitinib 300 mg QD plus corticosteroids
B	Itacitinib 400 mg QD plus corticosteroids
C	Itacitinib 300 mg BID plus corticosteroids; may be decreased to 200 mg BID if a boundary is reached during safety run-in. This treatment group was discontinued due to concern of a potential increase in relapse rate. Participants in this treatment group who were ongoing were allowed to reduce to 400 mg QD plus corticosteroids.
D	Corticosteroids monotherapy

3.1. Randomization

3.1.1. Part 1

A total of 20 participants with moderate or severe cGVHD will be randomized 1:1 to itacitinib 200 mg QD plus corticosteroids or 300 mg QD plus corticosteroids.

3.1.2. Part 1 Expansion

A total of up to 140 participants (35 per treatment group) with moderate or severe cGVHD will be randomized 1:1 to 1 of 4 treatment groups: itacitinib 300 mg QD plus corticosteroids (Treatment Group A), itacitinib 400 mg QD plus corticosteroids (Treatment Group B), itacitinib 300 mg BID plus corticosteroids (Treatment Group C), or corticosteroids monotherapy (Treatment Group D).

Randomization will be stratified by cGVHD risk status (moderate vs severe). Treatment Groups B and C will have an initial safety run-in of 10 participants to determine safety and tolerability of the dose before expanding (see definition of DLT in Section 6.1.1.3 of the Protocol). Participants enrolled in the safety run-in will be monitored continuously using the Bayesian approach. Treatment Group C was discontinued as of Amendment 8, and participants in that treatment group who were ongoing were allowed to reduce to 400 mg QD plus corticosteroids.

3.2. Control of Type I Error

No formal statistical tests will be performed in Part 1 and Part 1 expansion. All CIs will be 95%.

3.3. Sample Size Considerations

3.3.1. Part 1

In Part 1, approximately 20 participants will be enrolled to achieve 10 randomly assigned participants in each of the 2 dose groups of itacitinib in order to identify an optimal dose for further study. This sample size was chosen based on typical Phase 1 studies employing a 3 + 3 design that enroll up to 9 participants in order to identify recommended Phase 2 doses. A sample size of 20 participants (10 per treatment group) allows for concurrent enrollment at 2 dose levels

that have been previously characterized in other disease settings and is expected to enable the clinical characterization of study treatment across 2 treatment cohorts. No formal statistical comparison will be performed between treatment groups.

3.3.2. Part 1 Expansion

Sample size in Part 1 expansion is based on clinical feasibility and consideration. No hypothesis test is planned for efficacy. Up to 35 participants will be enrolled into each treatment group. The toxicity of itacitinib will be monitored continuously for Treatment Groups B and C using a Bayesian approach. A total of up to 140 participants will be enrolled into Part 1 expansion of the study. Regarding the key secondary endpoint, Month 6 response rate, a table of Bayesian posterior probabilities and related descriptions are provided below. This posterior probability may be used to support decision-making on itacitinib dosing/schedule for Part 2, including decisions made by the DMC

Table 3 presents Bayesian posterior probability of demonstrating a clinically meaningful treatment difference [redacted] in Month 6 response rate between any itacitinib group and the corticosteroids-only group under various response rates at the end of the expansion.

Table 3: Bayesian Posterior Probability to Demonstrate That There Is a Clinically Meaningful Difference [redacted] Between Any Itacitinib Group and the Corticosteroids-Only Group

Responders in an Itacitinib Group (out of 35)	Responders in Corticosteroids-Only Group (out of 35)				
	18	19	20	21	22
25	64.3%	54.8%	45.0%	35.3%	26.4%
26	73.1%	64.4%	54.9%	44.8%	35.0%
27	80.9%	73.4%	64.7%	54.9%	44.7%
28	87.2%	81.3%	73.9%	65.0%	55.0%
29	92.1%	87.7%	81.9%	74.4%	65.3%
30	95.5%	92.6%	88.4%	82.6%	75.0%

Note: With a binomial likelihood, binomial (n, p) with s number of responders out of n participants, and a beta prior, Beta (a, b), the posterior is calculated as Beta(a+s, b+n-s).

Interpretation:

- [redacted]
- [redacted]

[redacted]

3.4. Schedule of Assessments

Refer to Protocol Amendment 8 dated 30 SEP 2021 for a full description of all study procedures and assessment schedules for this study.

4. DATA HANDLING DEFINITIONS AND CONVENTIONS

4.1. Scheduled Study Evaluations and Study Periods

4.1.1. Day 1

Day 1 is the date that the first dose of itacitinib is administered to the participants. For the corticosteroids-only group, Day 1 will be defined as the first nonmissing dose day.

4.1.2. Study Day

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

Day # = (visit/reporting date – Day 1 date + 1).

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

Day # = (visit/reporting date – Day 1 date).

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

4.1.3. Baseline Value

Baseline is the last nonmissing measurement obtained before the first administration of study treatment (eg, itacitinib with corticosteroids or corticosteroids only). When itacitinib and corticosteroids are started on different days, then the rules mentioned in Section 4.1.1 will be followed.

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

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

4.1.4. Last Available Value

The last available value is the last nonmissing measurement obtained after starting the study treatment.

4.1.5. Handling of Missing and Incomplete Data

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

4.2. Variable Definitions

4.2.1. Body Mass Index

Body mass index will be calculated as follows:

$$\text{BMI (kg/m}^2\text{)} = [\text{weight (kg)}] / [\text{height (m)}]^2$$

4.2.2. Body Surface Area

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

$$\text{BSA (m}^2\text{)} = \{[\text{weight (kg)} \times \text{height (cm)}] / 3600\}^{½}.$$

Sites will also record the BSA calculated per institutional standards.

4.2.3. Prior and Concomitant Medication

Prior medication is defined as any nonstudy medication started before the first dose of itacitinib or corticosteroids for participants on corticosteroids only in the Part 1 expansion.

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

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

A prior medication could also be classified as "both prior and concomitant medication" if the end date is on or after the first dose of itacitinib or corticosteroids only. Since corticosteroids are part of the study medication, they will not appear in the list of prior and concomitant medications unless prescribed for an indication other than GVHD. 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.

5. STATISTICAL METHODOLOGY

5.1. General Methodology

Unless otherwise noted, SAS® software (SAS Institute Inc, Cary, NC; v9.4 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 participants in each category.

5.2. Treatment Groups

5.2.1. Part 1

A total of 20 participants with moderate or severe cGVHD will be randomized 1:1 to itacitinib 200 mg QD plus corticosteroids or itacitinib 300 mg QD plus corticosteroids.

5.2.2. Part 1 Expansion

A total of up to 140 participants (35 per treatment group) with moderate or severe cGVHD will be randomized 1:1 to 1 of 4 treatment groups: itacitinib 300 mg QD plus corticosteroids (Treatment Group A), itacitinib 400 mg QD plus corticosteroids (Treatment Group B), itacitinib 300 mg BID plus corticosteroids (Treatment Group C), or corticosteroids monotherapy (Treatment Group D).

5.3. Analysis Populations

The populations that will be included in study-related analyses are described in Table 4.

Table 4: Populations for Analysis

Population	Description
ITT	All randomized participants
Safety	All enrolled/randomized participants who received at least 1 dose of study drug and/or reference therapy. Treatment groups for this population will be determined according to the actual treatment the participant received regardless of assigned study drug treatment.
Safety run-in	All participants enrolled in the safety run-in portion of the study who received at least 1 dose of study drug and/or reference therapy. Treatment groups for this population will be determined according to the treatment assignment on Day 1 regardless of the actual study drug the participant might take during their continued participation in the study.
PK evaluable	All participants who received at least 1 dose of study drug and/or reference therapy and provided at least 1 postdose plasma sample (1 PK measurement). The study pharmacokineticist will review data listings of study drug administration and sample records to identify participants to be excluded from analyses of PK data.

6. BASELINE, EXPOSURE, AND DISPOSITION VARIABLES AND ANALYSES

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

6.1. Baseline Demographics, Physical Characteristics, and Disease History

Demographic and baseline characteristics, disease history, and prior therapy will be summarized for the safety run-in and Part 1 expansion populations and listed.

6.1.1. Demographics and Baseline Characteristics

The following demographic and baseline characteristics will be summarized for the safety run-in population and Part 1 expansion: age, sex, race, ethnicity, weight (by sex), height, BMI, BSA, and Karnofsky performance status.

6.1.2. Disease History for Chronic Graft-Versus-Host Disease

Baseline cGVHD staging and grading, time since diagnosis of cGVHD, organs involved, aGVHD (yes/no) and grade, conditioning and prophylaxis therapy, donor type, and other details related to the disease under study and transplant will be summarized at baseline. Day 1 assessment will be used to determine baseline organ involvement.

Time since cGVHD diagnosis will be calculated as:

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

6.1.3. Medical History

For participants in the safety run-in population and participants in the Part 1 expansion, medical history will be summarized by assigned treatment group. This summation will include the number and percentage of participants for each body system/organ class as documented on the eCRF.

6.1.4. Primary Hematologic Disease and Transplant Characteristics

Summary will include disease-targeted medical and treatment history such as participant's primary hematologic disease, including diagnosis, prior therapy, disease stage at the time of transplantation, disease risk index, and details regarding allogeneic hematopoietic stem cell transplantation; prior and current GVHD prophylaxis; history of aGVHD; and current cGVHD staging information.

Cancer history and underlying hematologic disease will also be summarized.

6.2. Disposition of Participants

The number and percentage of participants who were randomized, treated, completed treatment, discontinued study treatment with a primary reason for discontinuation, and withdrew from the study with a primary reason for withdrawal will be summarized for the safety run-in population and the Part 1 expansion population.

6.3. Protocol Deviations

Protocol deviations recorded on the eCRF will be summarized and presented in the participant data listings.

6.4. Exposure

For participants in the safety run-in population and participants in the Part 1 expansion, exposure to itacitinib and corticosteroids will be summarized descriptively as follows.

- **Duration of treatment with itacitinib:**

  The exposure start date is when trt = itacitinib and exposure timepoint = first dose; when a participant does not have first dose record (but has other timepoints) as the exposure timepoint, exposure start date should be when trt = itacitinib and dose is not missing.

  Duration of treatment (days) = Date of last dose of itacitinib – Date of first dose of itacitinib + 1.

- **Average daily dose of itacitinib:**

  Average daily dose (mg/day) = Total actual itacitinib dose taken (mg) / Duration of treatment with itacitinib (days).

- **Dose modifications of itacitinib:**

  Numbers of participants who had itacitinib dose reduction and/or interruption will be summarized. Separate summaries will be generated for participants with dose change due to dose tapering (change of dose due to efficacy of treatment) and participants with dose change due to other reasons (potential safety concerns).

- **Duration of treatment with corticosteroids:**

  For corticosteroids, the first exposure start date is when the dose is not missing.

  Duration of treatment (days) = Date of last dose of corticosteroid – Date of first dose of corticosteroid + 1.

  If a participant is being treated with a corticosteroid prior to Day 1, study Day 1 will be used if no other data are available to conform to the definition provided in Section 4.1.1. If a participant is prescribed a corticosteroid for a flare during the course of the study, duration of treatment will be adjusted to account for the break in treatment between completing taper and starting of a short pulse for a flare.

- **Average daily dose of corticosteroids:**

  Average daily dose (mg/day) = Total actual corticosteroid dose taken (mg) / Duration of treatment with corticosteroids (days).

  Daily dose will account for how the doses are prescribed (eg, BID is converted to twice daily).

- **Reduction in daily dose of corticosteroids and successful tapering of corticosteroids**

  Numbers of participants who had dose reduction and/or interruption of corticosteroids will be summarized as follows:

  - Summary of number of participants with ≥ 50% reduction in daily corticosteroid dose at Day 180
  - Summary of participants successfully tapered off all corticosteroids at Day 180
  - Summary of number of participants with ≥ 50% reduction in daily corticosteroid dose by (4-week) time interval up to Month 6
  - Summary of participants successfully tapered off all corticosteroids by (4-week) time interval up to Month 6

Participants will be considered as having a competing risk at the time of cGVHD progression or start of a new systemic therapy for cGVHD, relapse of the underlying hematologic disease, or death.

Sensitivity analyses may be performed for participants who had their corticosteroid dose increased during the corticosteroid taper period for a non-GVHD medical condition.

6.5. Study Drug Compliance

For participants in the safety run-in population and participants in the Part 1 expansion, overall compliance (%) for the study treatment will be calculated for all participants as follows:

Compliance (%) = 100 × [total dose actually taken] / [total prescribed dose].

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

6.6. Prior and Concomitant Medication

For participants in the safety run-in population and participants in Part 1 expansion, prior medications and concomitant medications will be coded using the WHO Drug Dictionary and summarized by WHO drug class and WHO drug term. Results will be summarized as number and percentage of participants with prior and concomitant medications by PT and WHO drug class.

7. EFFICACY

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

7.1. General Considerations

In Part 1, all efficacy analyses will be performed using the safety run-in population. In Part 1 Expansion, all efficacy analyses will be performed using the safety population.

If there are not sufficient data for meaningful statistical inference, the planned analysis will not be performed, and only related summary statistics and/or listings will be provided.

In all efficacy analyses, initiation of new systemic anti-GVHD therapy includes 4 scenarios:

1. Initiation of new anti-GVHD therapy including a higher dose of corticosteroid than that used at Day 1.
2. The need for a second dose increase in corticosteroids.
3. A dose increase in corticosteroids that is not tapered back to the previous dose of corticosteroids within 6 weeks (± 2 days) of the increase.
4. Reintroduction of systemic corticosteroids that occurs after complete taper of corticosteroids due to response.

No formal statistical tests will be performed.

7.2. Primary Analysis

In Part 1, the primary objective is to identify an appropriate dose of itacitinib (200 mg QD or 300 mg QD) in combination with corticosteroids as initial treatment for moderate or severe cGVHD. The DLT data through Day 28 and additional data from clinical safety and laboratory assessments will be used as primary endpoints for this analysis.

In Part 1 Expansion, the primary objective is to identify an appropriate dose of itacitinib (300 mg QD, 400 mg QD, or 300 mg BID) in combination with corticosteroids as initial treatment for moderate or severe cGVHD. The selection of the dose is primarily based on the incidence and severity of AEs across treatment cohorts and will be supported by cGVHD response data (refer to Section 10.1.2 of the Protocol).

7.3. Analyses of the Secondary Efficacy Parameters

7.3.1. Response Rate

Response rate at 3, 6, and 12 months (Days 90, 180, and 365) is defined as the proportion of participants who achieved a response (CR or PR) at each of these timepoints based on an ITT population.

A participant will not be considered a responder for the analysis of ORR at 3, 6, and 12 months if any of the following events occurred at or prior to the response assessment at the predefined timepoint:

- cGVHD progression per NIH response criteria or initiation of a new systemic therapy for cGVHD

- Evidence of progression of the underlying hematologic disease
- Withdrawal from the study
- Death
- Response assessment missing (not performed) at the predefined timepoint

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.

Additional analyses may be performed based on evaluable subsets. An evaluable population will also be considered with participants who have completed 3, 6, or 12 months of follow-up as of the cutoff date or discontinued earlier because of new cGVHD progression. Presentations of ORR at Month 3 and Month 6 will include a footnote explaining what "evaluable" means (ie, participants who had at least 3 or 6 months of follow-up as of the cutoff date or discontinued earlier).

Summary statistics and 95% CI will be provided by cohort. The primary comparisons in Part 1 expansion will involve only the 2 itacitinib groups (Treatment Groups A and B) and the corticosteroids-only group (Treatment Group D) as a result of Protocol Amendment 8, in which Treatment Group C (300 mg BID + corticosteroids) was discontinued. Data from Treatment Group C will be presented only as summary statistics and will not be subjected to any statistical comparison.

Pairwise Cochran-Mantel-Haenszel tests will be conducted for Month 6 response rate for each of the 2 itacitinib groups (Treatment Groups A and B) and the corticosteroids-only group (Treatment Group D) as an exploratory analysis.

The secondary endpoints discussed below will be summarized by Treatment Groups A, B, and D using the ITT population for efficacy-related endpoints and all groups for safety-related endpoints.

7.3.2. Time to Response

Time to response is defined as the interval from randomization to first response (CR or PR) before initiation of new therapy. In the time to response analysis, participants without a response after randomization will be censored at either study withdrawal, initiation of new systemic anti-GVHD therapy, death, relapse, or last response assessment prior to or on the cutoff date, whichever is earliest. Time to response will be summarized for participants who achieve a response using the Kaplan-Meier method. Median time to response and a 95% CI will be estimated.

7.3.3. Duration of Response

Duration of response is defined as the interval between the date of initial documentation of response (CR or PR) and the date of cGVHD progression per NIH response criteria, initiation of new systemic cGVHD therapy, or death. Participants experiencing relapse of underlying hematologic relapse will be censored at the date of relapse.

Duration of response will be summarized for participants who achieve a response. Duration of response will be assessed using the Kaplan-Meier method for participants who achieve a response. Median duration and a 95% CI will be estimated. Participants who are still responding at the time of database lock or discontinuation will be right-censored at the time of last valid response assessment.

7.3.4. Best Overall Response

Best overall response for each participant is defined as best response during the course of the study (best in the categories of CR or PR), including responses at unscheduled visits. Participants without a BOR (ie, participants not achieving a response of either CR or PR) in the treatment phase will be considered as nonresponders for BOR in the responder analysis. Number and percentage of participants in each best response category will be tabulated by treatment group.

7.3.5. Overall Survival

Overall survival is defined as the interval between the date of randomization and the date of death due to any cause. Date of death will be determined using the Death Report, the Survival Follow-Up, and the Subject Status CRFs. The Kaplan-Meier method will be used to estimate the survival time distribution and the median survival, if it is applicable. Participants with no observed death or loss to follow-up will be treated as censored at their last date known to be alive. The 95% CI will be calculated using Brookmeyer and Crowley's method (1982). Summary statistics will be provided.

7.3.6. Nonrelapse Mortality Rate

Nonrelapse mortality is defined as the time from date of randomization to date of death not preceded by underlying disease relapse/recurrence. Underlying disease relapse/recurrence is considered a competing event. If a participant is not known to have died or experienced the competing event, then NRM will be censored at the latest date the participant was known to be event-free (on or before the cutoff date). Cumulative incidence of NRM and derived probabilities at Months 3, 6, and 12 will be estimated, considering underlying disease relapse/recurrence as a competing event.

7.3.7. Relapse Rate of Malignant and Nonmalignant Hematologic Diseases

Relapse rate of malignant and nonmalignant hematologic diseases is defined as the proportion of participants whose underlying disease relapses. Relapse rate of malignant and nonmalignant hematologic diseases will be provided with a 95% CI. The CI will be calculated based on the exact method for binomial distributions. Cumulative incidence rate and summary statistics will be provided.

7.3.8. Time to Primary Hematologic Disease Relapse

Time to primary hematologic disease relapse is defined as the interval between the date of randomization and the date of relapse. Time to the relapse will be assessed using Kaplan-Meier method. Median time to relapse and a 95% CI will be estimated. Summary statistics will be provided.

7.3.9. Other Efficacy Analyses

The proportion of participants with ≥ 50% reduction in daily corticosteroid dose at Day 180 will be summarized. Corticosteroid dose on study Day 1 will be defined as the starting dose as appropriate.

The proportion of participants successfully tapered off all corticosteroids at Day 180 will be summarized.

Both time to failure-free survival and average biweekly weight-standardized steroid up to Month 6 will be plotted.

8. PHARMACOKINETIC ANALYSES [redacted]

Appendix G provides a list of planned tables and figures for the PK and PK/pharmacodynamic analyses.

8.1. Pharmacokinetic Analyses

In participants with full profiles (ie, in Part 1 and Part 1 expansion), the PK parameters of C_{max}, T_{max}, C_{min}, $AUC_{0\text{-}t}$, and Cl/F will be calculated from the blood plasma concentrations of itacitinib using standard noncompartmental (model-independent) PK methods. Pharmacokinetic calculations will be performed using commercial software such as WinNonlin® (Pharsight Corporation, Mountain View, CA).

Exposure/response analyses may be performed using model-based AUCs or using observed trough values (C_{min}).

[redacted]

9. SAFETY AND TOLERABILITY

Appendix A provides a list of planned tables and listings.

9.1. General Considerations

All safety analyses will be conducted for the safety population and summarized by treatment group. 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 participants.

In order to accommodate the changes proposed in Protocol Amendment 8 that resulted in discontinuation of Treatment Group C (300 mg BID) and subsequent dose reduction of ongoing participants in Treatment Group C to 400 mg QD, safety tables (specifically AEs) will be presented for the 300 mg BID group with participants who are subject to dose reduction and censored at the date of switching to the lower dose (400 mg QD). An overall summary including both dose groups (participants included before and after the dose reduction) will also be presented.

9.2. Adverse Events

9.2.1. Adverse Event Definitions

A TEAE is either an AE reported for the first time or worsening of a pre-existing condition after first dose of study drug until 30 days after the last dose of study drug. Analysis of AEs will be limited to TEAEs, but data listings will include all AEs, regardless of their timing in relation to study drug administration.

Adverse events will be tabulated by MedDRA PT and SOC. Severity of AEs will be described and graded using the 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, then it will be rated on a scale of 1 to 5 as follows: 1 = mild, 2 = moderate, 3 = severe, 4 = life-threatening, and 5 = death due to AE. All toxicities will be graded based on the worst level reached, not the level they may have reached if they had not been treated. When the intensity of an AE changes over time for a reporting period (eg, between visits), 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. Unresolved missing values will be handled according to the following rules:

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

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

9.2.2. Dose-Limiting Toxicities

Evaluation of DLTs was performed in Part 1 and in Part I expansion for the safety run-in population (first 10 participants) enrolled in Treatment Groups B and C. The toxicity of itacitinib will be monitored continuously for each treatment group using the Bayesian approach of Thall et al (1995, 1996) as extended by Thall and Sung (1998). Dose-limiting toxicities are defined in Table 5. The DLTs will be summarized on the first 28 days of study treatment.

Table 5: Definitions of Dose-Limiting Toxicity

Toxicity	Definition
Nonhematologic	• Any ≥ Grade 3 nonhematologic toxicity that can be reasonably attributed to study treatment. ≥ Grade 3 nonhematologic toxicities that may be related to underlying GVHD (eg, nausea, vomiting, diarrhea, rash, dry eye) will not be considered as DLTs. • Any ≥ Grade 3 clinical chemistry laboratory abnormalities that are considered clinically significant and related to study treatment. Transient abnormal laboratory values without associated clinically significant signs and symptoms, manageable with adequate medical care, and not leading to hospitalization will not be considered as DLTs.
Hematologic	• Grade 4 neutropenia lasting more than 7 days or a ≥ 90% decrease in absolute neutrophil count from baseline that can reasonably be attributed to study treatment. • Platelet count < 10×10^9/L related to study treatment that does not recover to at least 20×10^9/L after 2 weeks with no requirement for platelet transfusion in the preceding 3 days.

Historical data on similar patients show a toxicity rate of 25%. The probability of toxicity for the historical data is modeled by beta distribution (Beta [25, 75]). The prior probability of toxicity for the experimental regimen is also modeled by beta distributions (Beta [0.5, 1.5]), which have the same means as the corresponding beta distributions for the historical data. Denoting the historical probability of toxicity rate by p(TOX,H), the following decision criteria will be applied:

Stop if Prob{p(TOX,H) + δTOX < p(TOX,E)| data} > 0.95, where δTOX = 0

Participants from each treatment group will be monitored according to the following nonbinding stopping boundaries for toxicity in Table 6. If a boundary is reached, the sponsor and external DMC will investigate and decide on the most appropriate action.

Table 6: Toxicity Stopping Boundaries

# Participants (Inclusive)	Maximum Allowable Number of Toxicities (Inclusive)
1-2	No limit
3-4	3
5-6	4
7-9	5
10-11	6
12-14	7
15-17	8
18-19	9
20	9

9.2.3. Adverse Event Summaries

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

- Number (%) of participants reporting any TEAEs
- Number (%) of participants reporting any serious TEAEs
- Number (%) of participants reporting any Grade 3 and higher TEAEs
- Number (%) of participants reporting any DLTs
- Number (%) of participants reporting any TEAEs related to itacitinib
- Number (%) of participants who temporarily interrupted itacitinib because of TEAEs
- Number (%) of participants with itacitinib dose reductions because of TEAEs
- Number (%) of participants who permanently discontinued itacitinib because of TEAEs
- Number (%) of participants reporting any TEAEs related to corticosteroid
- Number (%) of participants who temporarily interrupted corticosteroid because of TEAEs
- Number (%) of participants with corticosteroid dose reductions because of TEAEs
- Number (%) of participants who permanently discontinued corticosteroid because of TEAEs
- Number (%) of participants who had a fatal TEAE

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

- Number (%) of participants reporting TEAEs by SOC and PT
- Number (%) of participants reporting TEAEs by PT in decreasing order of frequency
- Number (%) of participants reporting TEAEs by SOC, PT, and maximum severity

- Number (%) of participants reporting itacitinib treatment-related TEAEs by SOC and PT
- Number (%) of participants reporting itacitinib treatment-related TEAEs by PT in decreasing order of frequency
- Number (%) of participants reporting itacitinib treatment-related, Grade 3 or higher TEAEs by SOC and PT
- Number (%) of participants reporting any Grade 3 or higher TEAEs by SOC and PT
- Number (%) of participants reporting any Grade 3 or higher TEAEs by SOC and PT in decreasing order of frequency
- Number (%) of participants reporting serious TEAEs by SOC and PT
- Number (%) of participants reporting serious TEAEs by SOC and PT in decreasing order of frequency
- Number (%) of participants reporting itacitinib treatment-related, serious TEAEs by SOC and PT
- Number (%) of participants reporting TEAEs leading to itacitinib dose interruption by SOC and PT
- Number (%) of participants reporting TEAEs leading to itacitinib dose reduction by SOC and PT
- Number (%) of participants reporting TEAEs leading to discontinuation of itacitinib by SOC and PT
- Number (%) of participants reporting corticosteroid treatment-related TEAEs by SOC and PT
- Number (%) of participants reporting corticosteroid treatment-related TEAEs by PT in decreasing order of frequency
- Number (%) of participants reporting corticosteroid treatment-related, Grade 3 or higher TEAEs by SOC and PT
- Number (%) of participants reporting corticosteroid treatment-related, serious TEAEs by SOC and PT
- Number (%) of participants reporting TEAEs leading to corticosteroid dose interruption by SOC and PT
- Number (%) of participants reporting TEAEs leading to corticosteroid dose reduction by SOC and PT
- Number (%) of participants reporting TEAEs leading to discontinuation of corticosteroids by SOC and PT
- Number (%) of participants reporting fatal TEAEs by SOC and PT

9.2.4. Clinically Notable Adverse Events Based on Customized MedDRA Queries

There are 9 categories of clinically notable TEAEs (ie, categories of erythropenia [anemia], neutropenia, thrombocytopenia, CMV infections, EBV infections, hyperlipidemia, QT prolongation, thromboembolic events, fungal infections) that, in particular, are of scientific and medical interest specific to itacitinib and the GVHD population. The lists of MQs are in Appendix B through Appendix F.

Within each category, the number and percentage of participants with at least 1 event occurring during treatment tabulated by MedDRA PT will be summarized. Summaries of clinically notable AEs based on customized MQs will be provided by category, PT, and the maximum severity.

9.3. Analyses for the Data Monitoring Committee

All safety data will be closely monitored. An external DMC will perform a full review of safety, efficacy, tolerability, and PK data. The primary purpose of the DMC is to provide a recommendation on an appropriate dose of itacitinib for Part 2.

Details of the efficacy evaluation will be included in the internal DMC charter. All safety information, including the AE data from the replaced participants, will be reviewed during this review process.

9.4. Clinical Laboratory Tests

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

Laboratory data will be classified based on CTCAE grade. The incidence of abnormal laboratory values and shift tables relative to baseline will be tabulated.

9.5. Vital Signs

Descriptive statistics and mean change from baseline will be summarized for vital signs (ie, blood pressure, pulse, respiratory rate, and body temperature) at each assessment time. Vital sign results will be reviewed for abnormalities (see Table 7), and participants exhibiting vital sign abnormalities will be listed. A value will be considered an "alert" value if it is outside the established range and shows a > 25% change from baseline. The values for participants exhibiting alert vital sign abnormalities will be listed.

Table 7: Criteria for 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	> 38°C	< 35.5°C
Respiratory rate	> 24 breaths/min	< 8 breaths/min

9.6. Electrocardiograms

Electrocardiograms will be performed at screening and end of treatment. Electrocardiograms that are identified as abnormal and clinically meaningful compared with the screening assessment should be reported as AEs. No summary of electrocardiogram data is planned.

10. INTERIM ANALYSES

Preplanned analyses of safety will be provided to an independent DMC as specified in the DMC charter.

11. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 8.

Table 8: Statistical Analysis Plan Versions

SAP Version	Date
Original	06 NOV 2019
Amendment 1	03 MAR 2022

11.1. Changes to Protocol-Defined Analyses

Note that the ITT population is equivalent to the safety analysis set as defined in the Protocol.

11.2. Changes to the Statistical Analysis Plan

The changes reflected in this version of the SAP include the title of the study as well as Part 1 expansion details described in Protocol Amendment 7 (addition of Part 1 expansion) and Protocol Amendment 8 (closure of the BID treatment group). More specifically:

- Section 1 was updated to align with Protocol Amendment 8, which includes all details related to Part 1 expansion.
- Section 2 was updated to include all endpoints related to Part 1 expansion.
- Section 3 was updated to include the study design for Part 1 expansion.
- Section 4 was updated to include information on the corticosteroids-only group.
- Section 5 was updated to include clarifications on study populations.
- Section 6 was updated to include primary hematologic disease and transplant characteristics and to update information on exposure.
- Section 7 was updated with detailed descriptions of the efficacy endpoints to align with Protocol Amendment 8.
- Section 9 was updated to include a paragraph on the changes in Treatment Group C as outlined in Protocol Amendment 8.
- Appendix A was updated to include all tables/listings/figures intended for Part 1 expansion.

12. REFERENCES

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APPENDIX A. PLANNED TABLES 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 v1.4. In-text tables are identical in structure and content to appendix tables but follow a Rich Text Format.

Efficacy will use the safety analysis set as described in Section 5.3.

Tables

Table No.	Title	Population
1.1.1.1	Analysis Populations – Part 1 Expansion	Safety
1.1.1.2	Analysis Populations – Part 1 and Part 1 Expansion	Safety
1.1.2.1	Summary of Participant Disposition – Part 1 Expansion	Safety
1.1.2.2	Summary of Participant Disposition – Part 1 and Part 1 Expansion	Safety
1.1.3.1	Summary of Protocol Deviations – Part 1 Expansion	Safety
1.1.3.2	Summary of Protocol Deviations – Part 1 and Part 1 Expansion	Safety
1.2.1.1	Summary of Demographics – Part 1 Expansion	Safety
1.2.1.2	Summary of Demographics – Part 1 and Part 1 Expansion	Safety
1.3.1.1.1	Summary of Baseline Disease Characteristics for Cancer History – Part 1 Expansion	Safety
1.3.1.1.2	Summary of Baseline Disease Characteristics for Cancer History – Part 1 and Part 1 Expansion	Safety
1.3.1.2.1	Summary of Baseline Disease Characteristics for GVHD – Part 1 Expansion	Safety
1.3.1.2.2	Summary of Baseline Disease Characteristics for GVHD – Part 1 and Part 1 Expansion	Safety
1.3.2.1	Summary of Allogeneic Hematopoietic Stem Cell Transplant History – Part 1 Expansion	Safety
1.3.2.2	Summary of Allogeneic Hematopoietic Stem Cell Transplant History – Part 1 and Part 1 Expansion	Safety
1.3.2.3	Summary of Karnofsky Scale	Safety
1.3.3.1	Summary of Prior Anticancer Therapy – Part 1 Expansion	Safety
1.3.3.2	Summary of Prior Anticancer Therapy – Part 1 and Part 1 Expansion	Safety
1.4.1.1	Summary of Prior Medications – Part 1 Expansion	Safety
1.4.1.2	Summary of Prior Medications – Part 1 and Part 1 Expansion	Safety
1.4.2.1	Summary of Concomitant Medications – Part 1 Expansion	Safety
1.4.2.2	Summary of Concomitant Medications – Part 1 and Part 1 Expansion	Safety
1.5.1.1	Summary of General Medical History – Part 1 and Part 1 Expansion	Safety
1.5.1.2	Summary of Conditioning and Prophylaxis Therapy – Part 1 and Part 1 Expansion	Safety
2.2.1	Summary of Overall Response Rate at Months 3, 6, and 12	Safety
2.2.2	Summary of Nonrelapse Mortality Rate	Safety
2.2.3	Summary of Duration of Response	Safety
2.2.4	Summary of Time to Response	Safety
2.2.5	Summary of Relapse Rate of Malignant and Nonmalignant Hematologic Diseases	Safety
2.2.6	Summary of Time to Primary Hematologic Disease Relapse	Safety
2.2.7	Summary of Overall Survival	Safety
2.2.8	Summary of Best Overall Response	Safety
2.2.8.1	Summary of Best Overall Response by GVHD Organ Involved	Safety

Table No.	Title	Population
2.2.8.2	Summary of Best Overall Response for Skin Sclerotic Findings Subgroup	Safety
2.2.9	Summary of Failure-Free Survival	Safety
2.2.11	Summary of Number of Participants With ≥ 50% Reduction in Daily Corticosteroid Dose at Day 180	Safety
2.2.12	Summary of Participants Successfully Tapered Off All Corticosteroids at Day 180	Safety
2.2.13	Summary of Number of Participants With ≥ 50% Reduction in Daily Corticosteroid Dose by (4-Week) Time Interval Up to Month 6	Safety
2.2.14	Summary of Participants Successfully Tapered Off All Corticosteroids by (4-Week) Time Interval Up to Month 6	Safety
3.1.1	Summary of Itacitinib Exposure, Duration of Exposure, and Dose Adjustment	Safety
3.1.2	Summary of Itacitinib Compliance	Safety
3.1.3	Summary of Corticosteroid Exposure, Duration of Exposure, and Dose Adjustment	Safety
3.2.1	Overall Summary of Treatment-Emergent Adverse Events	Safety
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
3.2.4	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Safety
3.2.5	Summary of Itacitinib Treatment-Related, Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety
3.2.6	Summary of Itacitinib Treatment-Related, Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety
3.2.7	Summary of Itacitinib Treatment-Related, Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class, and Preferred Term	Safety
3.2.8	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety
3.2.9	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in Decreasing Order of Frequency	Safety
3.2.10	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety
3.2.11	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in Decreasing Order of Frequency	Safety
3.2.12	Summary of Itacitinib Treatment-Related, Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety
3.2.13	Summary of Treatment-Emergent Adverse Events Leading to Itacitinib Dose Interruption by MedDRA System Organ Class and Preferred Term	Safety
3.2.14	Summary of Treatment-Emergent Adverse Events Leading to Itacitinib Dose Reduction by MedDRA System Organ Class and Preferred Term	Safety
3.2.15	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Itacitinib by MedDRA System Organ Class and Preferred Term	Safety
3.2.16	Summary of Corticosteroid Treatment-Related, Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety
3.2.17	Summary of Corticosteroid Treatment-Related, Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety
3.2.18	Summary of Corticosteroid Treatment-Related, Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety

Table No.	Title	Population
3.2.19	Summary of Treatment-Emergent Adverse Events Leading to Corticosteroid Dose Interruption by MedDRA System Organ Class and Preferred Term	Safety
3.2.20	Summary of Treatment-Emergent Adverse Events Leading to Corticosteroid Dose Reduction by MedDRA System Organ Class and Preferred Term	Safety
3.2.21	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Corticosteroid by MedDRA System Organ Class and Preferred Term	Safety
3.2.22	Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term	Safety
3.2.23	Overall Summary of Treatment-Emergent Clinically Notable Hematologic Events by Customized MQs	Safety
3.2.24	Summary of Clinically Notable Treatment-Emergent Hematologic Events by Customized MQs, Preferred Term, and Maximum Severity	Safety
3.2.25	Overall Summary of Treatment-Emergent CMV Infection Events by Customized MedDRA Queries	Safety
3.2.26	Summary of Treatment-Emergent CMV Infection Events by Customized MedDRA Queries, Preferred Term, and Maximum Severity	Safety
3.2.27	Overall Summary of Treatment-Emergent EBV Infection Events by Customized MedDRA Queries	Safety
3.2.28	Summary of Treatment-Emergent EBV Infection Events by Customized MedDRA Queries, Preferred Term, and Maximum Severity	Safety
3.2.29	Overall Summary of Treatment-Emergent Hyperlipidemia Events by Customized MedDRA Queries	Safety
3.2.30	Summary of Treatment-Emergent Hyperlipidemia Events by Customized MedDRA Queries, Preferred Term, and Maximum Severity	Safety
3.2.31	Summary of Grade 3 or Higher Treatment-Emergent Infections by MedDRA System Organ Class and Preferred Term	Safety
3.2.32	Summary of Treatment-Emergent CMV Infection Events by MedDRA System Organ Class and Preferred Term	Safety
3.2.33	Summary of Treatment-Emergent QT Prolongation Events by Customized MedDRA Queries, Preferred Term, and Maximum Severity	Safety
3.2.34	Overall Summary of Treatment-Emergent Thromboembolic Events by Customized MedDRA Queries	Safety
3.2.35	Summary of Treatment-Emergent Thromboembolic Events by Customized MedDRA Queries, Preferred Term, and Maximum Severity	Safety
3.2.36	Overall Summary of Treatment-Emergent Fungal Infection Events (MedDRA High Level Group Term) by Customized MedDRA Queries	Safety
3.2.37	Summary of Treatment-Emergent Fungal Infection Events (MedDRA High Level Group Term) by Customized MedDRA Queries, Preferred Term, and Maximum Severity	Safety
3.3.1.1	Summary of Laboratory Values – Hematology	Safety
3.3.1.2	Shift Summary of Hematology Laboratory Values in CTCAE Grade – to the Worst Abnormal Value	Safety
3.3.2.1	Summary of Laboratory Values – Chemistry	Safety
3.3.2.2	Shift Summary of Chemistry Laboratory Values in CTCAE Grade – to the Worst Abnormal Value	Safety
3.3.3.1	Summary of Laboratory Values - Coagulation	Safety
3.4.1	Summary of Systolic Blood Pressure	Safety
3.4.2	Summary of Diastolic Blood Pressure	Safety

Table No.	Title	Population
3.4.3	Summary of Pulse	Safety
3.4.4	Summary of Respiratory Rate	Safety
3.4.5	Summary of Body Temperature	Safety
3.4.6	Summary of Body Weight	Safety

Figures

Figure No.	Title
4.2.1	Kaplan-Meier Plot of Time to Failure-Free Survival
4.3.1	Average Biweekly Weight-Standardized Steroid Up to Month 6

Listings

Listing No.	Title
2.1.1	Participant Enrollment and Disposition Status
2.4.7	Posttherapy Medications
2.6.8	Deaths
2.7.7	Adverse Events Leading to Interruption, Reduction, or Discontinuation of Itacitinib
99.2.1	Protocol Deviations by Deviation Coded Term

APPENDIX B. CLINICALLY NOTABLE HEMATOLOGIC EVENTS

This appendix provides a list of 3 categories of clinically notable treatment-emergent hematologic events based on customized MQs.

Adverse Event Category	Preferred Term	Code
Anemia	Anaemia macrocytic	10002064
	Aplasia pure red cell	10002965
	Aplastic anaemia	10002967
	Erythroblast count decreased	10058505
	Erythropenia	10015287
	Hypoplastic anaemia	10021074
	Microcytic anaemia	10027538
	Red blood cell count decreased	10038153
	Anaemia	10002034
	Haematocrit decreased	10018838
	Haemoglobin decreased	10018884
	Leukoerythroblastic anaemia	10053199
	Normochromic normocytic anaemia	10029783
Neutropenia	Agranulocytosis	10001507
	Band neutrophil count decreased	10057950
	Febrile neutropenia	10016288
	Granulocyte count decreased	10018681
	Granulocytopenia	10018687
	Neutropenia	10029354
	Neutropenic infection	10059482
	Neutropenic sepsis	10049151
	Neutrophil count decreased	10029366
Thrombocytopenia	Acquired amegakaryocytic thrombocytopenia	10076747
	Platelet count decreased	10035528
	Thrombocytopenia	10043554
	Plateletcrit decreased	10064784

APPENDIX C. HEMATOLOGIC INFECTION EVENTS

Adverse Event Group	Preferred Term	Code
EBV infections	Epstein-Barr virus positive mucocutaneous ulcer	10079386
	Epstein-Barr viraemia	10065110
	Epstein-Barr virus associated lymphoma	10071441
	Epstein-Barr virus associated lymphoproliferative disorder	10068349
	Epstein-Barr virus infection	10015108
	Hepatitis infectious mononucleosis	10019781
	Infectious mononucleosis	10021914
	Oral hairy leukoplakia	10030979
	Post transplant lymphoproliferative disorder	10051358
	X-linked lymphoproliferative syndrome	10068348
	Epstein-Barr virus test positive	10064545
	Epstein-Barr virus antibody positive	10052324
Cytomegaloviral infections	Congenital cytomegalovirus infection	10010430
	Cytomegalovirus chorioretinitis	10048843
	Cytomegalovirus colitis	10048983
	Cytomegalovirus duodenitis	10049014
	Cytomegalovirus enteritis	10049074
	Cytomegalovirus enterocolitis	10049015
	Cytomegalovirus gastritis	10049016
	Cytomegalovirus gastroenteritis	10051349
	Cytomegalovirus gastrointestinal infection	10052817
	Cytomegalovirus gastrointestinal ulcer	10075619
	Cytomegalovirus hepatitis	10011830
	Cytomegalovirus infection	10011831
	Cytomegalovirus mononucleosis	10011834
	Cytomegalovirus mucocutaneous ulcer	10065036
	Cytomegalovirus myelomeningoradiculitis	10065621
	Cytomegalovirus myocarditis	10056261
	Cytomegalovirus nephritis	10079095
	Cytomegalovirus oesophagitis	10049018
	Cytomegalovirus pancreatitis	10049566
	Cytomegalovirus pericarditis	10056721
	Cytomegalovirus syndrome	10056262
	Cytomegalovirus urinary tract infection	10051350
	Cytomegalovirus viraemia	10058854
	Encephalitis cytomegalovirus	10014586
	Disseminated cytomegaloviral infection	10049075
	Pneumonia cytomegaloviral	10035676
	Cytomegalovirus test positive	10051620

APPENDIX D. HYPERLIPIDEMIA EVENTS

Preferred Term	Code	Level	Scope	Category	Weight	Status	Addition Version	Last Modified Version
Acquired lipoatrophic diabetes	10073667	PT	Narrow	A	0	Active	16.1	16.1
Acquired mixed hyperlipidaemia	10071236	PT	Narrow	A	0	Active	18.0	18.0
Apolipoprotein B/Apolipoprotein A-1 ratio increased	10065516	PT	Narrow	A	0	Active	13.0	13.0
Autoimmune hyperlipidaemia	10071577	PT	Narrow	A	0	Active	14.1	14.1
Blood cholesterol abnormal	10005423	PT	Narrow	A	0	Active	8.1	8.1
Blood cholesterol esterase increased	10071304	PT	Narrow	A	0	Active	14.1	14.1
Blood cholesterol increased	10005425	PT	Narrow	A	0	Active	8.1	8.1
Blood triglycerides abnormal	10005837	PT	Narrow	A	0	Active	8.1	8.1
Blood triglycerides increased	10005839	PT	Narrow	A	0	Active	8.1	8.1
Diabetic dyslipidaemia	10070901	PT	Narrow	A	0	Active	14.0	14.0
Dyslipidaemia	10058108	PT	Narrow	A	0	Active	8.1	8.1
High density lipoprotein abnormal	10020051	PT	Narrow	A	0	Active	8.1	8.1
High density lipoprotein decreased	10020060	PT	Narrow	A	0	Active	8.1	8.1
Hypercholesterolaemia	10020603	PT	Narrow	A	0	Active	8.1	8.1
Hyperlipidaemia	10062060	PT	Narrow	A	0	Active	8.1	8.1
Hypertriglyceridaemia	10020869	PT	Narrow	A	0	Active	8.1	8.1
Hypo HDL cholesterolaemia	10068961	PT	Narrow	A	0	Active	12.0	12.0
Intermediate density lipoprotein increased	10064236	PT	Narrow	A	0	Active	8.1	8.1
LDL/HDL ratio increased	10049030	PT	Narrow	A	0	Active	13.0	13.0
Lipids abnormal	10024588	PT	Narrow	A	0	Active	8.1	8.1
Lipids increased	10024592	PT	Narrow	A	0	Active	8.1	8.1
Lipoprotein (a) abnormal	10054023	PT	Narrow	A	0	Active	8.1	8.1
Lipoprotein (a) increased	10054009	PT	Narrow	A	0	Active	8.1	8.1
Lipoprotein abnormal	10081355	PT	Narrow	A	0	Active	21.1	21.1
Lipoprotein increased	10081354	PT	Narrow	A	0	Active	21.1	21.1
Low density lipoprotein abnormal	10024901	PT	Narrow	A	0	Active	8.1	8.1
Low density lipoprotein increased	10024910	PT	Narrow	A	0	Active	8.1	8.1

Preferred Term	Code	Level	Scope	Category	Weight	Status	Addition Version	Last Modified Version
Non-high-density lipoprotein cholesterol increased	10063967	PT	Narrow	A	0	Active	8.1	8.1
Remnant-like lipoprotein particles increased	10073041	PT	Narrow	A	0	Active	16.0	16.0
Total cholesterol/HDL ratio abnormal	10058633	PT	Narrow	A	0	Active	8.1	8.1
Total cholesterol/HDL ratio increased	10058630	PT	Narrow	A	0	Active	8.1	8.1
Very low density lipoprotein abnormal	10047352	PT	Narrow	A	0	Active	8.1	8.1
Very low density lipoprotein increased	10047361	PT	Narrow	A	0	Active	8.1	8.1

APPENDIX E. QT PROLONGATION EVENTS

Preferred Term	Code	Level	Scope	Category	Weight	Status	Addition Version	Last Modified Version
Electrocardiogram QT interval abnormal	10063748	PT	Narrow	A	0	Active	7.1	7.1
Electrocardiogram QT prolonged	10014387	PT	Narrow	A	0	Active	7.1	7.1
Long QT syndrome	10024803	PT	Narrow	A	0	Active	7.1	7.1
Long QT syndrome congenital	10057926	PT	Narrow	A	0	Active	7.1	7.1
Torsade de pointes	10044066	PT	Narrow	A	0	Active	7.1	7.1
Ventricular tachycardia	10047302	PT	Narrow	A	0	Active	7.1	7.1

APPENDIX F. THROMBOEMBOLIC EVENTS

Group	Preferred Term	Code	Level	Scope	Category	Weight	Status	Addition Version	Last Modified Version
Arterial	Acute aortic syndrome	10074337	PT	Narrow	A	0	Active	17.0	17.0
	Acute myocardial infarction	10000891	PT	Narrow	A	0	Active	10.0	10.0
	Amaurosis	10001902	PT	Narrow	A	0	Active	10.0	10.0
	Amaurosis fugax	10001903	PT	Narrow	A	0	Active	10.0	10.0
	Angioplasty	10002475	PT	Narrow	A	0	Active	16.0	16.0
	Aortic bypass	10057617	PT	Narrow	A	0	Active	10.0	10.0
	Aortic embolus	10002897	PT	Narrow	A	0	Active	10.0	10.0
	Aortic surgery	10061651	PT	Narrow	A	0	Active	10.0	10.0
	Aortic thrombosis	10002910	PT	Narrow	A	0	Active	10.0	10.0
	Aortogram abnormal	10057794	PT	Narrow	A	0	Active	10.0	10.0
	Arterectomy	10071026	PT	Narrow	A	0	Active	14.0	14.0
	Arterectomy with graft replacement	10003140	PT	Narrow	A	0	Active	10.0	10.0
	Arterial angioplasty	10081731	PT	Narrow	A	0	Active	21.1	21.1
	Arterial bypass occlusion	10077766	PT	Narrow	A	0	Active	19.0	19.0
	Arterial bypass operation	10056418	PT	Narrow	A	0	Active	10.0	10.0
	Arterial bypass thrombosis	10077765	PT	Narrow	A	0	Active	19.0	19.0
	Arterial graft	10061655	PT	Narrow	A	0	Active	10.0	10.0
	Arterial occlusive disease	10062599	PT	Narrow	A	0	Active	10.0	10.0
	Arterial stent insertion	10061657	PT	Narrow	A	0	Active	10.0	10.0
	Arterial therapeutic procedure	10052949	PT	Narrow	A	0	Active	10.0	10.0
	Arterial thrombosis	10003178	PT	Narrow	A	0	Active	10.0	10.0
	Arteriogram abnormal	10061659	PT	Narrow	A	0	Active	10.0	10.0
	Arteriogram carotid abnormal	10003195	PT	Narrow	A	0	Active	10.0	10.0
	Arteriotomy	10078636	PT	Narrow	A	0	Active	19.1	19.1
	Atherectomy	10063025	PT	Narrow	A	0	Active	10.0	10.0
	Atherosclerotic plaque rupture	10076604	PT	Narrow	A	0	Active	18.1	18.1
	Atrial appendage closure	10079735	PT	Narrow	A	0	Active	20.1	20.1
	Atrial appendage resection	10080843	PT	Narrow	A	0	Active	21.0	21.0
	Basal ganglia infarction	10069020	PT	Narrow	A	0	Active	12.0	12.0
	Basilar artery occlusion	10048963	PT	Narrow	A	0	Active	10.0	10.0
	Basilar artery thrombosis	10063093	PT	Narrow	A	0	Active	10.0	10.0
	Blindness transient	10005184	PT	Narrow	A	0	Active	10.0	10.0
	Brachiocephalic artery occlusion	10069694	PT	Narrow	A	0	Active	13.0	13.0
	Capsular warning syndrome	10067744	PT	Narrow	A	0	Active	10.1	10.1
	Carotid angioplasty	10071260	PT	Narrow	A	0	Active	14.1	14.1
	Carotid arterial embolus	10007684	PT	Narrow	A	0	Active	10.0	10.0
	Carotid artery bypass	10053003	PT	Narrow	A	0	Active	10.0	10.0
	Carotid artery occlusion	10048964	PT	Narrow	A	0	Active	10.0	10.0
	Carotid artery stent insertion	10066102	PT	Narrow	A	0	Active	10.0	10.0
	Carotid artery thrombosis	10007688	PT	Narrow	A	0	Active	10.0	10.0
	Carotid endarterectomy	10007692	PT	Narrow	A	0	Active	10.0	10.0
	Cerebellar artery occlusion	10053633	PT	Narrow	A	0	Active	10.0	10.0
	Cerebellar artery thrombosis	10008023	PT	Narrow	A	0	Active	10.0	10.0
Arterial	Cerebral artery embolism	10008088	PT	Narrow	A	0	Active	10.0	10.0
	Cerebral artery occlusion	10008089	PT	Narrow	A	0	Active	10.0	10.0

Group	Preferred Term	Code	Level	Scope	Category	Weight	Status	Addition Version	Last Modified Version
	Cerebral artery stent insertion	10081893	PT	Narrow	A	0	Active	22.0	22.0
	Cerebral artery thrombosis	10008092	PT	Narrow	A	0	Active	10.0	10.0
	Cerebral hypoperfusion	10065384	PT	Narrow	A	0	Active	10.0	10.0
	Cerebrovascular insufficiency	10058842	PT	Narrow	A	0	Active	10.0	10.0
	Cerebrovascular stenosis	10061751	PT	Narrow	A	0	Active	10.0	10.0
	Coeliac artery occlusion	10069696	PT	Narrow	A	0	Active	13.0	13.0
	Coronary angioplasty	10050329	PT	Narrow	A	0	Active	16.0	16.0
	Coronary arterial stent insertion	10052086	PT	Narrow	A	0	Active	10.0	10.0
	Coronary artery bypass	10011077	PT	Narrow	A	0	Active	10.0	10.0
	Coronary artery embolism	10011084	PT	Narrow	A	0	Active	10.0	10.0
	Coronary artery occlusion	10011086	PT	Narrow	A	0	Active	10.0	10.0
	Coronary artery reocclusion	10053261	PT	Narrow	A	0	Active	10.0	10.0
	Coronary artery surgery	10011090	PT	Narrow	A	0	Active	10.0	20.1
	Coronary artery thrombosis	10011091	PT	Narrow	A	0	Active	16.0	16.0
	Coronary endarterectomy	10011101	PT	Narrow	A	0	Active	10.0	10.0
	Coronary revascularisation	10049887	PT	Narrow	A	0	Active	10.0	10.0
	Coronary vascular graft occlusion	10075162	PT	Narrow	A	0	Active	17.1	17.1
	Embolia cutis medicamentosa	10058729	PT	Narrow	A	0	Active	10.0	10.0
	Embolism arterial	10014513	PT	Narrow	A	0	Active	10.0	13.1
	Endarterectomy	10014648	PT	Narrow	A	0	Active	10.0	10.0
	Femoral artery embolism	10068365	PT	Narrow	A	0	Active	11.1	11.1
	Hepatic artery embolism	10019635	PT	Narrow	A	0	Active	10.0	10.0
	Hepatic artery occlusion	10051991	PT	Narrow	A	0	Active	10.0	10.0
	Hepatic artery thrombosis	10019636	PT	Narrow	A	0	Active	10.0	10.0
	Hypothenar hammer syndrome	10063518	PT	Narrow	A	0	Active	10.0	10.0
	Iliac artery embolism	10021338	PT	Narrow	A	0	Active	10.0	10.0
	Iliac artery occlusion	10064601	PT	Narrow	A	0	Active	10.0	10.0
	Intra-aortic balloon placement	10052989	PT	Narrow	A	0	Active	10.0	10.0
	Intraoperative cerebral artery occlusion	10056382	PT	Narrow	A	0	Active	10.0	10.0
	Ischaemic cerebral infarction	10060840	PT	Narrow	A	0	Active	10.0	10.0
	Ischaemic stroke	10061256	PT	Narrow	A	0	Active	10.0	10.0
	Lacunar infarction	10051078	PT	Narrow	A	0	Active	10.0	10.0
	Leriche syndrome	10024242	PT	Narrow	A	0	Active	13.1	13.1
	Mesenteric arterial occlusion	10027394	PT	Narrow	A	0	Active	17.0	17.0
	Mesenteric arteriosclerosis	10065560	PT	Narrow	A	0	Active	10.0	10.0
	Mesenteric artery embolism	10027395	PT	Narrow	A	0	Active	10.0	10.0
	Mesenteric artery stenosis	10027396	PT	Narrow	A	0	Active	10.0	10.0
	Mesenteric artery stent insertion	10071261	PT	Narrow	A	0	Active	14.1	14.1
	Mesenteric artery thrombosis	10027397	PT	Narrow	A	0	Active	10.0	10.0
	Myocardial infarction	10028596	PT	Narrow	A	0	Active	10.0	10.0
	Myocardial necrosis	10028602	PT	Narrow	A	0	Active	10.0	17.0
	Ophthalmic artery thrombosis	10081144	PT	Narrow	A	0	Active	21.1	21.1
	Papillary muscle infarction	10033697	PT	Narrow	A	0	Active	10.0	10.0
	Penile artery occlusion	10068035	PT	Narrow	A	0	Active	11.0	11.0
Arterial	Percutaneous coronary intervention	10065608	PT	Narrow	A	0	Active	10.0	10.0
	Peripheral arterial occlusive disease	10062585	PT	Narrow	A	0	Active	10.0	10.0

Group	Preferred Term	Code	Level	Scope	Category	Weight	Status	Addition Version	Last Modified Version
	Peripheral arterial reocclusion	10069379	PT	Narrow	A	0	Active	12.1	12.1
	Peripheral artery angioplasty	10057518	PT	Narrow	A	0	Active	10.0	10.0
	Peripheral artery bypass	10072561	PT	Narrow	A	0	Active	15.1	15.1
	Peripheral artery occlusion	10057525	PT	Narrow	A	0	Active	10.0	19.0
	Peripheral artery stent insertion	10072562	PT	Narrow	A	0	Active	15.1	15.1
	Peripheral artery surgery	10082470	PT	Narrow	A	0	Active	22.0	22.0
	Peripheral artery thrombosis	10072564	PT	Narrow	A	0	Active	15.1	15.1
	Peripheral embolism	10061340	PT	Narrow	A	0	Active	10.0	10.0
	Peripheral endarterectomy	10072560	PT	Narrow	A	0	Active	15.1	15.1
	Popliteal artery entrapment syndrome	10071642	PT	Narrow	A	0	Active	14.1	14.1
	Post procedural myocardial infarction	10066592	PT	Narrow	A	0	Active	10.0	10.0
	Postinfarction angina	10058144	PT	Narrow	A	0	Active	10.0	10.0
	Precerebral artery occlusion	10036511	PT	Narrow	A	0	Active	10.0	10.0
	Precerebral artery thrombosis	10074717	PT	Narrow	A	0	Active	17.0	17.0
	Profundaplasty	10078867	PT	Narrow	A	0	Active	20.0	20.0
	Pulmonary artery occlusion	10078201	PT	Narrow	A	0	Active	19.1	19.1
	Pulmonary artery therapeutic procedure	10063731	PT	Narrow	A	0	Active	10.0	10.0
	Pulmonary artery thrombosis	10037340	PT	Narrow	A	0	Active	10.0	10.0
	Pulmonary endarterectomy	10072893	PT	Narrow	A	0	Active	16.0	16.0
	Pulmonary tumour thrombotic microangiopathy	10079988	PT	Narrow	A	0	Active	20.1	20.1
	Renal artery angioplasty	10057493	PT	Narrow	A	0	Active	15.1	15.1
	Renal artery occlusion	10048988	PT	Narrow	A	0	Active	10.0	10.0
	Renal artery thrombosis	10038380	PT	Narrow	A	0	Active	10.0	10.0
	Renal embolism	10063544	PT	Narrow	A	0	Active	10.0	10.0
	Retinal artery embolism	10038826	PT	Narrow	A	0	Active	10.0	10.0
	Retinal artery occlusion	10038827	PT	Narrow	A	0	Active	10.0	10.0
	Retinal artery thrombosis	10038831	PT	Narrow	A	0	Active	10.0	10.0
	Silent myocardial infarction	10049768	PT	Narrow	A	0	Active	12.1	12.1
	Spinal artery embolism	10049440	PT	Narrow	A	0	Active	10.0	10.0
	Spinal artery thrombosis	10071316	PT	Narrow	A	0	Active	14.1	14.1
	Splenic artery thrombosis	10074600	PT	Narrow	A	0	Active	17.0	17.0
	Splenic embolism	10068677	PT	Narrow	A	0	Active	11.1	11.1
	Stress cardiomyopathy	10066286	PT	Narrow	A	0	Active	10.0	10.0
	Subclavian artery embolism	10042332	PT	Narrow	A	0	Active	10.0	10.0
	Subclavian artery occlusion	10069695	PT	Narrow	A	0	Active	13.0	13.0
	Subclavian artery thrombosis	10042334	PT	Narrow	A	0	Active	10.0	10.0
	Thromboembolectomy	10064958	PT	Narrow	A	0	Active	10.0	10.0
	Thrombotic microangiopathy	10043645	PT	Narrow	A	0	Active	10.0	10.0
	Thrombotic thrombocytopenic purpura	10043648	PT	Narrow	A	0	Active	10.0	10.0
	Transient ischaemic attack	10044390	PT	Narrow	A	0	Active	10.0	10.0
	Truncus coeliacus thrombosis	10062363	PT	Narrow	A	0	Active	10.0	10.0
	Vascular pseudoaneurysm thrombosis	10078269	PT	Narrow	A	0	Active	19.1	19.1

Group	Preferred Term	Code	Level	Scope	Category	Weight	Status	Addition Version	Last Modified Version
Arterial	Vertebral artery occlusion	10048965	PT	Narrow	A	0	Active	10.0	10.0
	Vertebral artery thrombosis	10057777	PT	Narrow	A	0	Active	10.0	10.0
	Visual acuity reduced transiently	10047532	PT	Narrow	A	0	Active	10.0	10.0
Venous	Axillary vein thrombosis	10003880	PT	Narrow	A	0	Active	10.0	10.0
	Brachiocephalic vein occlusion	10076837	PT	Narrow	A	0	Active	18.1	18.1
	Brachiocephalic vein thrombosis	10063363	PT	Narrow	A	0	Active	10.0	19.1
	Budd-Chiari syndrome	10006537	PT	Narrow	A	0	Active	10.0	10.0
	Catheterisation venous	10052698	PT	Narrow	A	0	Active	10.0	10.0
	Cavernous sinus thrombosis	10007830	PT	Narrow	A	0	Active	10.0	10.0
	Central venous catheterisation	10053377	PT	Narrow	A	0	Active	10.0	10.0
	Cerebral venous sinus thrombosis	10083037	PT	Narrow	A	0	Active	22.1	22.1
	Cerebral venous thrombosis	10008138	PT	Narrow	A	0	Active	10.0	10.0
	Compression garment application	10079209	PT	Narrow	A	0	Active	20.0	20.0
	Deep vein thrombosis	10051055	PT	Narrow	A	0	Active	10.0	10.0
	Deep vein thrombosis postoperative	10066881	PT	Narrow	A	0	Active	10.0	10.0
	Embolism venous	10014522	PT	Narrow	A	0	Active	10.0	10.0
	Hepatic vein embolism	10078810	PT	Narrow	A	0	Active	20.0	20.0
	Hepatic vein occlusion	10058991	PT	Narrow	A	0	Active	10.0	10.0
	Hepatic vein thrombosis	10019713	PT	Narrow	A	0	Active	10.0	10.0
	Homans' sign positive	10051031	PT	Narrow	A	0	Active	14.0	14.0
	Iliac vein occlusion	10058992	PT	Narrow	A	0	Active	10.0	10.0
	Inferior vena cava syndrome	10070911	PT	Narrow	A	0	Active	14.0	14.0
	Inferior vena caval occlusion	10058987	PT	Narrow	A	0	Active	10.0	10.0
	Jugular vein embolism	10081850	PT	Narrow	A	0	Active	22.0	22.0
	Jugular vein occlusion	10076835	PT	Narrow	A	0	Active	18.1	18.1
	Jugular vein thrombosis	10023237	PT	Narrow	A	0	Active	10.0	10.0
	Mahler sign	10075428	PT	Narrow	A	0	Active	17.1	17.1
	May-Thurner syndrome	10069727	PT	Narrow	A	0	Active	13.0	13.0
	Mesenteric vein thrombosis	10027402	PT	Narrow	A	0	Active	10.0	10.0
	Mesenteric venous occlusion	10027403	PT	Narrow	A	0	Active	17.0	17.0
	Obstetrical pulmonary embolism	10029925	PT	Narrow	A	0	Active	10.0	10.0
	Obstructive shock	10073708	PT	Narrow	A	0	Active	16.1	16.1
	Ophthalmic vein thrombosis	10074349	PT	Narrow	A	0	Active	17.0	17.0
	Ovarian vein thrombosis	10072059	PT	Narrow	A	0	Active	15.0	15.0
	Paget-Schroetter syndrome	10050216	PT	Narrow	A	0	Active	10.0	10.0
	Pelvic venous thrombosis	10034272	PT	Narrow	A	0	Active	10.0	10.0
	Penile vein thrombosis	10034324	PT	Narrow	A	0	Active	10.0	10.0
	Peripheral vein occlusion	10083103	PT	Narrow	A	0	Active	22.1	22.1
	Peripheral vein thrombus extension	10082853	PT	Narrow	A	0	Active	22.1	22.1
	Phlebectomy	10048874	PT	Narrow	A	0	Active	10.0	10.0
	Portal vein cavernous transformation	10073979	PT	Narrow	A	0	Active	16.1	16.1
	Portal vein embolism	10082030	PT	Narrow	A	0	Active	22.0	22.0
	Portal vein occlusion	10058989	PT	Narrow	A	0	Active	10.0	10.0
	Portal vein thrombosis	10036206	PT	Narrow	A	0	Active	10.0	10.0
	Portosplenomesenteric venous thrombosis	10077623	PT	Narrow	A	0	Active	19.0	19.0

Group	Preferred Term	Code	Level	Scope	Category	Weight	Status	Addition Version	Last Modified Version
	Post procedural pulmonary embolism	10063909	PT	Narrow	A	0	Active	10.0	10.0
Venous	Post thrombotic syndrome	10048591	PT	Narrow	A	0	Active	10.0	10.0
	Postoperative thrombosis	10050902	PT	Narrow	A	0	Active	10.0	10.0
	Postpartum venous thrombosis	10036300	PT	Narrow	A	0	Active	10.0	10.0
	Pulmonary embolism	10037377	PT	Narrow	A	0	Active	10.0	10.0
	Pulmonary infarction	10037410	PT	Narrow	A	0	Active	10.0	10.0
	Pulmonary microemboli	10037421	PT	Narrow	A	0	Active	10.0	10.0
	Pulmonary thrombosis	10037437	PT	Narrow	A	0	Active	10.0	10.0
	Pulmonary vein occlusion	10068690	PT	Narrow	A	0	Active	11.1	11.1
	Pulmonary veno-occlusive disease	10037458	PT	Narrow	A	0	Active	10.0	10.0
	Pulmonary venous thrombosis	10037459	PT	Narrow	A	0	Active	10.0	10.0
	Renal vein embolism	10038547	PT	Narrow	A	0	Active	10.0	10.0
	Renal vein occlusion	10056293	PT	Narrow	A	0	Active	10.0	10.0
	Renal vein thrombosis	10038548	PT	Narrow	A	0	Active	10.0	10.0
	Retinal vein occlusion	10038907	PT	Narrow	A	0	Active	10.0	10.0
	Retinal vein thrombosis	10038908	PT	Narrow	A	0	Active	10.0	10.0
	Septic pulmonary embolism	10083093	PT	Narrow	A	0	Active	22.1	22.1
	SI QIII TIII pattern	10068479	PT	Narrow	A	0	Active	11.1	11.1
	Splenic vein occlusion	10068122	PT	Narrow	A	0	Active	11.0	11.0
	Splenic vein thrombosis	10041659	PT	Narrow	A	0	Active	10.0	10.0
	Subclavian vein occlusion	10079164	PT	Narrow	A	0	Active	20.0	20.0
	Subclavian vein thrombosis	10049446	PT	Narrow	A	0	Active	10.0	10.0
	Superior sagittal sinus thrombosis	10042567	PT	Narrow	A	0	Active	10.0	10.0
	Superior vena cava occlusion	10058988	PT	Narrow	A	0	Active	10.0	17.0
	Superior vena cava syndrome	10042569	PT	Narrow	A	0	Active	10.0	14.0
	Thrombophlebitis	10043570	PT	Narrow	A	0	Active	10.0	10.0
	Thrombophlebitis migrans	10043581	PT	Narrow	A	0	Active	10.0	10.0
	Thrombophlebitis neonatal	10043586	PT	Narrow	A	0	Active	10.0	10.0
	Thrombophlebitis superficial	10043595	PT	Narrow	A	0	Active	14.1	14.1
	Thrombosed varicose vein	10043605	PT	Narrow	A	0	Active	10.0	10.0
	Thrombosis corpora cavernosa	10067270	PT	Narrow	A	0	Active	10.0	10.0
	Transverse sinus thrombosis	10044457	PT	Narrow	A	0	Active	10.0	10.0
	Vena cava embolism	10047193	PT	Narrow	A	0	Active	10.0	10.0
	Vena cava filter insertion	10048932	PT	Narrow	A	0	Active	10.0	10.0
	Vena cava filter removal	10074397	PT	Narrow	A	0	Active	17.0	17.0
	Vena cava thrombosis	10047195	PT	Narrow	A	0	Active	10.0	10.0
	Venogram abnormal	10047209	PT	Narrow	A	0	Active	10.0	10.0
	Venoocclusive disease	10062173	PT	Narrow	A	0	Active	10.0	10.0
	Venoocclusive liver disease	10047216	PT	Narrow	A	0	Active	10.0	10.0
	Venous angioplasty	10077826	PT	Narrow	A	0	Active	19.0	19.0
	Venous occlusion	10058990	PT	Narrow	A	0	Active	10.0	10.0
	Venous operation	10062175	PT	Narrow	A	0	Active	10.0	10.0
	Venous recanalisation	10068605	PT	Narrow	A	0	Active	11.1	11.1
	Venous repair	10052964	PT	Narrow	A	0	Active	17.1	17.1
	Venous stent insertion	10063389	PT	Narrow	A	0	Active	10.0	10.0
	Venous thrombosis	10047249	PT	Narrow	A	0	Active	10.0	10.0

Group	Preferred Term	Code	Level	Scope	Category	Weight	Status	Addition Version	Last Modified Version
	Venous thrombosis in pregnancy	10067030	PT	Narrow	A	0	Active	10.0	10.0
Venous	Venous thrombosis limb	10061408	PT	Narrow	A	0	Active	10.0	10.0
	Venous thrombosis neonatal	10064602	PT	Narrow	A	0	Active	10.0	10.0
	Visceral venous thrombosis	10077829	PT	Narrow	A	0	Active	19.0	19.0

APPENDIX G. PLANNED TABLES AND FIGURES FOR PHARMACOKINETIC AND PHARMACOKINETIC/PHARMACODYNAMIC ANALYSIS

Tables

Table No.	Title
Table 1	Summarization of the Pharmacokinetic Parameters by Dose at Day 1
Table 2	Summarization of the Pharmacokinetic Parameters by Dose at Day 7
Table 3	Summarization of the Pharmacokinetic Parameters by Dose at Day 28

Figures

Figure No.	Title
Figure 1	Mean (± SE) Concentration-Time Profiles by Dose at Day 1
Figure 2	Boxplots of C_{max}, C_{min}, and AUC on Day 7 by NRM at 6 Months
Figure 3	Boxplots of C_{max}, C_{min}, and AUC on Day 7 by Overall Response at 6 Months
Figure 4	Boxplots of C_{max}, C_{min}, and AUC on Day 7 by Chronic GVHD Grading at 6 Months
Figure 5	Boxplots of C_{max}, C_{min}, and AUC on Day 7 by Chronic GVHD Liver Staging at Day 7
Figure 6	Boxplots of C_{max}, C_{min}, and AUC on Day 28 by Chronic GVHD Liver Staging at Day 28
Figure 7	Boxplots of C_{max}, C_{min}, and AUC on Day 7 by Chronic GVHD GI Staging at Day 7
Figure 8	Boxplots of C_{max}, C_{min}, and AUC on Day 28 by Chronic GVHD GI Staging at Day 28

Pharmacokinetic tables and/or figures may be modified or additional PK tables and/or figures may be created as needed based on study findings. For example, plots may be modified to indicate participants taking potent CYP3A4 inhibitors and those who are not, or plots may be modified to highlight a participant who had a particular safety finding.