STATISTICAL ANALYSIS PLAN
PHASE 2

DATE OF PLAN:

17 JAN 2012

BASED ON:

Protocol Amendment 1 on 17 August 2011

CRF Study Design Version 2.1 on 24 October 2011 (by Central Designer™)

STUDY DRUG:

RUXOLITINIB PHOSPHATE TABLETS / *INC 18424*

PROTOCOL NUMBER:

258

STUDY TITLE:

AN OPEN LABEL ASSESSMENT OF SAFETY AND EFFICACY OF RUXOLITINIB (INCB018424) IN SUBJECTS WITH PRIMARY MYELOFIBROSIS, POST ESSENTIAL THROMBOCYTHEMIA-MYELOFIBROSIS AND POST POLYCYTHEMIA VERA-MYELOFIBROSIS WHO HAVE PLATELET COUNTS OF 50 x 10^9/L TO 100 x 10^9/L

SPONSOR:

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

Statistical Analysis Plan Approval

SAP ID:	INCB 18424-258 SAP
SAP Version ID:	Version 1 – Final
Submitter	[redacted], PhD [redacted]
Date Submitted:	13 January 2012
Protocol Version:	17 August 2011 (Amendment 1)
CRF Approval Date:	
☒ Approval of initial SAP	☐ Approval of Amendment of SAP

NOTE:

1) An amendment made prior to the release of unblinded data (eg, treatment assignment received by each subject) for a blinded study or database release for an open-labeled study must be included in an updated SAP.
2) An amendment made to the statistical analyses defined in the SAP which occurs after unblinding or database release must be documented in the final Clinical Study Report.
3) The approvers must ensure that all relevant functions are in agreement with the final SAP.

This document has been reviewed and accepted by:

[redacted]

1/17/2012
Date

17 Jan 2012
Date

17 Jan 2012
Date

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1. LIST OF ABBREVIATIONS

Table 1: List of Abbreviations

Abbreviation	Term
AE	Adverse event
ALB	Albumin (G/L)
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
AUC	Area under the concentration-time curve
$AUC_{(0-\infty)}$	AUC from time zero (pre-dose) extrapolated to infinite time
$AUC_{(0-\tau)}$	AUC from time zero (pre-dose) to time of last observed quantifiable concentration within a subject across all treatments
BLQ	Below limit of quantification
BMI	Body mass index
bid.	Twice daily
BP	Blood pressure
bpm	Beats per minute
BUN	Blood urea nitrogen
°C	Degrees Celsius
Ca	Calcium
Cl	Chloride
CLr	Renal clearance
C_{max}	Maximum observed concentration
CRF	Case report form
CSR	Clinical study report
Ct	Last observed quantifiable concentration
DBP	Diastolic blood pressure
DL	Deciliter
DOB	Date of birth
ECG	Electrocardiogram
^{o}F	Degrees fahrenheit
GCP	Good Clinical Practices

Table 1: List of Abbreviations (Continued)

Abbreviation	Term
GGT	Gamma-glutamyl transferase
HGB	Hemoglobin
In	Inches
IP	Investigational product
IRB	Institutional Review Board
ITT	Intent-to-treat population
IU	International units
K	Potassium
λ_z	Terminal phase rate constant
LDH	Lactate dehydrogenase
LFTs	Liver function tests
LLN	Lower limit of normal
MedDRA	Medical Dictionary for Regulatory Activities Terminology
mg	Milligrams
mL	Milliliter
mmHg	Millimeters of mercury
msec	Milliseconds
Na	Sodium
ng	Nanograms
[redacted]	[redacted]
PET-MF	Post Essential Thrombocythemia-Myelofibrosis
[redacted]	[redacted]
PMF	Primary Myelofibrosis
PP	Per-protocol population
PPV-MF	Post Polycythemia Vera-Myelofibrosis
RBC	Red blood cell count
SAE	Serious adverse event
SAS	Statistical Analysis System
SBP	Systolic blood pressure
SGOT	Serum glutamic oxaloacetic transaminase
SGPT	Serum glutamic pyruvic transaminase

Table 1: List of Abbreviations (Continued)

Abbreviation	Term
$t_{1/2}$	Terminal phase half-life
t_{max}	Time of occurrence of C_{max}
TIBC	Total iron binding capacity
UIBC	Unsaturated iron-binding capacity
ULN	Upper limit of normal
WBC	White blood cell count
WHO	World Health Organization

2. INTRODUCTION

The purpose of this document is to provide a detailed statistical analysis plan (SAP) for the data collected during the conduct of the study protocol (entitled "An open label assessment of safety and efficacy of ruxolitinib (INCB018424) in subjects with primary myelofibrosis (PMF), post essential thrombocythemia-myelofibrosis (PET-MF) and post polycythemia vera-myelofibrosis (PPV-MF) who have platelet counts of 50 x 10^9/L to 100 x 10^9/L", Amendment 1 dated 17 August 2011) which will be analyzed, summarized, and presented in the clinical study report (CSR). The case report form (CRF) version covered by this SAP is Study Design Version 1.6 (dated 28 July 2011, generated by Central Designer™).

Section 4 of the protocol provides a detailed description of the investigational product, target patient population, the rationale for doses to be examined, and the potential risks and benefits of ruxolitinib (INCB018424).

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives and Endpoints

3.1.1. Study Objectives

Primary Objectives:

- To determine the effects of ruxolitinib on spleen volume and symptom burden in patients with PMF, PPV-MF, and PET-MF who have a baseline platelet count of 50 x 10^9/L to 100 x 10^9/L.

- To determine the safety and tolerability of ruxolitinib in subjects with PMF, PPV-MF, and PET-MF who have a baseline platelet count of 50 x 10^9/L to 100 x 10^9/L.

Secondary Objective:

- To determine an appropriate dosing strategy for subjects with low platelets.

3.1.2. Study Endpoints

3.1.2.1. Co-Primary Endpoints

- Correlation of percent change from baseline in spleen volume at Week 24 versus final titrated dose.

- Correlation of percent change from baseline in total symptom score as measured by the modified MFSAF v2.0 diary at Week 24 versus final titrated dose.

3.1.2.2. Safety Endpoint(s)

- Safety and tolerability will be assessed by monitoring the frequency, duration, and severity of adverse events (AEs), performing physical examinations, collecting vital signs, collecting laboratory data for hematology, serum chemistry, coagulation parameters, and urinalysis. In addition, analyses will include:

  – Proportion of subjects with new onset Grade 4 thrombocytopenia events as assessed by CTCAE v4.03;

  – Proportion of subjects with new onset Grade 2 or higher hemorrhage as assessed by CTCAE v4.03.

3.1.2.3. Secondary Endpoints

- Percent change from baseline in spleen volume at Week 24.
- Percent change from baseline in total symptom score as measured by the modified MFSAF v2.0 diary at Week 24.
- Proportion of subjects with ≥ 35% reduction from baseline in spleen volume at Week 24.
- Proportion of subjects with ≥ 10% reduction from baseline in spleen volume at Week 24.
- Proportion of subjects with ≥ 50% improvement from baseline in total symptom score as measured by the modified MFSAF v2.0 diary at Week 24.
- Change and percentage change from baseline in spleen length as measured by palpation at each visit where the parameter is assessed.

3.2. Statistical Hypotheses

The null hypothesis is that the correlation between percent change in spleen volume or total symptom score and final titrated dose is zero. The alternative hypothesis is that the correlation is not zero.

4. STUDY DESIGN

4.1. Overall Description

This is an open label study of 24 weeks duration of ruxolitinib in subjects with PMF, PPV-MF, and PET-MF. The study is comprised of 4 phases (see protocol Section 7.1, Overall Study Design):

Screening: up to 21 days.
Baseline: exactly 7 days.
Treatment Phase: 24 weeks. For subjects receiving benefit from treatment, further participation may continue up to the time of commercial availability of ruxolitinib.
Follow-up Phase: 30 to 37 days after the last dose of ruxolitinib is taken.

All subjects will begin dosing at 5 mg bid ruxolitinib. Doses should be taken morning and evening, approximately 12 hours apart, and without regard to food.

Doses of ruxolitinib may be increased in 5 mg qd increments up to 10 mg bid starting at the Week 4 visit and at subsequent study visits (no more than every 4 weeks) if subjects meet prespecified criteria (refer to protocol Section 8.6, Dose Adjustments).

Doses may not exceed 10 mg bid except in subjects who continue to meet the dose escalation criteria (see Protocol, Section 8.6, Dose Adjustments), and who have, in addition, a PGIC score of minimally worse, much worse, or very much worse while receiving 10 mg bid. Such subjects may continue dose escalation to a maximum dose of 15 mg bid.

Doses may never exceed 15 mg bid, and no dose increases may occur after Week 16.

Subjects will be required to decrease the dose for platelet count $< 35 \times 10^9$/L, and to hold administration for platelet count $< 25 \times 10^9$/L. Subjects will have the option to restart or re-escalate the dose with improving platelet count.

Subjects will be required to interrupt administration for any Grade 2 or higher hemorrhage events. Subjects will be able to restart ruxolitinib administration with resolution of Grade 2 events; restart after a second event requires review and discussion of pertinent data with the sponsor. Restarts of ruxolitinib will only be permitted in some cases of Grade 3 and 4 events, after review and discussion of pertinent data with the sponsor.

Sites will provide information on incidents of Grade 4 thrombocytopenia and Grade 3 and Grade 4 hemorrhage events via FAX to the sponsor within 24 hours of learning of the event. The overall incidence of these events will be continuously monitored by the sponsor, and with ongoing data review, could result in a temporary hold for further enrollment, a reduction in the maximum allowable dose for subjects in the study, or a protocol amendment to modify dose titration rules (see protocol Section 11.7, Study Safety Monitoring).

4.2. Scheduled Visits

Table 2 (source: protocol Table 3) and Table 3 (source: protocol Table 4) on the next pages provide detailed study visits and measurements of safety and efficacy variables defined for this study.

Table 2: List of Assessments

	Screening	Baseline	Day 1	Weeks 1,2, 3,5,6,7,10, 14, 18, 28 and q4 weeks thereafter	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Extension Phase Visits (q12 weeks after Week 24)	End of Treatment or Early Termination Visit (EOT)	Follow-Up 30-37 days after last dose of ruxolitinib or EOT visit
Evaluation/window	Day -28 to -8	Day -7 to -1	Day 1	± 3 days	± 5 days	± 5 days	± 5 days	± 5 days	± 5 days	± 5 days	± 5 days	± 5 days	
Assign Subject Number	X												
Informed consent / Eligibility Criteria	X	X											
Prior Medical & medication history	X	X											
Concomitant medication review		X	X		X	X	X	X	X	X	X	X	X
Transfusion history/status	X	X			X	X	X	X	X	X	X	X	X
Discontinue prior MF therapies	X												
Screening Symptom Form	X												
Record AEs	X	X	X		X	X	X	X	X	X	X	X	X
Physical examination	X	X					X			X	X	X	X
Spleen Palpation	X	X			X	X	X	X	X	X	X	X	X
Vital Signs	X	X			X	X	X	X	X	X	X	X	X
12-lead ECG	X												
BM biopsy	X	X[a]											
MRI of upper and lower abdomen and pelvis		X								X			
Modified MFSAF v2.0		Diary is completed each evening from Day -7 to the Week 24 visit											
Dispense and/or Bring MFSAF v2.0 diary to visit		X	X		X	X	X	X	X	X			
PGIC[b]					X	X	X	X	X	X	X	X	
ECOG status	X	X			X	X	X			X	X	X	
[redacted]													
Dispense reminder card		X	X		X	X	X	X	X	X	X		
Contact IVRS	X		X		X	X	X	X	X	X	X	X	
Administer study drug during visit			X		X								
Dispense study drug			X		X	X	X	X	X	X	X		
Drug accountability assessment					X	X	X	X	X	X	X	X	

[a] If not completed at Screening visit, and biopsy in prior 2 months is not available.
[b] PGIC = Patient Global Impression of Change (protocol Appendix V).

Table 3: Table of Laboratory Assessments

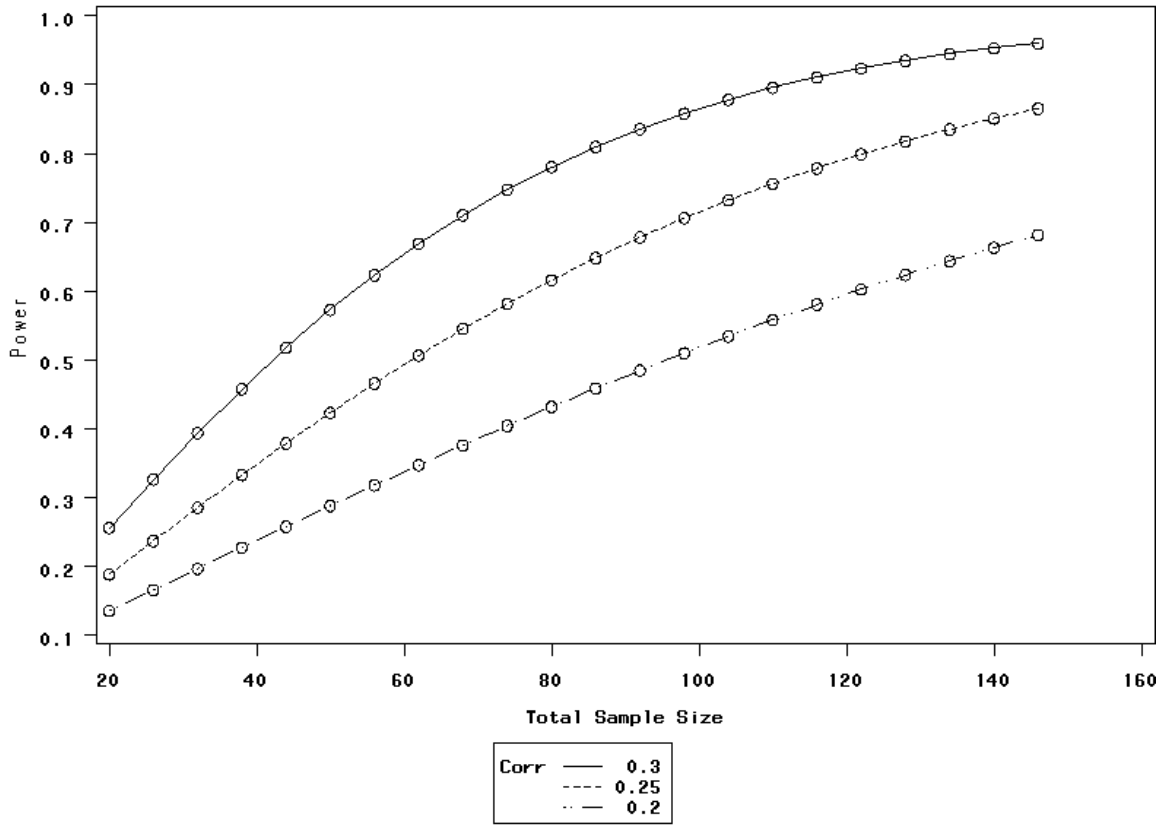
	Screening	Baseline	Day 1	Weeks 1,2, 3,5,6,7,10, 14, 18, 28 and q 4 weeks thereafter	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Extension Phase Visits (q12 weeks after Week 24)	End of Treatment or Early Termination Visit (EOT)	Follow-Up 30 to 37 days after last dose of ruxolitinib or EOT visit
Laboratory Assessment	Day -28 to -8	Day -7 to -1	Day 1	± 3 days	± 5 days	± 5 days	± 5 days	± 5 days	± 5 days	± 5 days	± 5 days	± 5 days	
Serum Chemistry	X	X			X	X	X	X	X	X	X	X	X
Hematology	X	X		X	X	X	X	X	X	X	X	X	X
Coagulation panel	X	X					X			X	X	X	X
Lipid Panel		X			X		X			X	X	X	X
Serum Pregnancy Test[a]	X												X
Urine Pregnancy Test[a]		X			X	X	X	X	X	X	X	X	
Serology for HIV, HBV, HCV	X												
[redacted]													
Urinalysis		X								X	X	X	X

[a] Women of childbearing potential only.

4.3. Sample Size Considerations

Approximately 150 subjects will be enrolled in order to assess (on the efficacy side) the dose-effect correlation (between percent changes from baseline in spleen volume/total symptom score at Week 24 and final titrated dose level). Using an alpha of 5% (2-sided), this sample size gives a power of 96% to reject the null hypothesis of no dose-effect correlation if the true correlation is 0.30. The power is 87% if the true correlation is 0.25, and the power is 69% if the true correlation is 0.20. These calculations are based on Cohen 1988, Formula 12.3.4. SAS procedure POWER is used and the power curves are displayed in Figure 1.

Figure 1: Power and Sample Size Curves for 3 Alternative Hypotheses on the Level of Dose-Effect Correlation



It is noted that the above sample size calculation is based on the rationale that the first primary endpoint (correlation between percent change from baseline in spleen volume at Week 24 by the final titrated dose) is powered following the procedure of the sequential test used for this study (see Section 5.4.2). At the given sample size, power can also be assessed for the second co-primary endpoint (correlation between percent change from baseline in total symptom score at Week 24 by the final titrated dose.

In addition, the mean percent change from baseline in spleen volume measured by MRI, and mean percent change from baseline in total symptom score at Week 24 will each be estimated with a 95% confidence interval. With 150 subjects, the half-length of the 95% confidence

interval of the change from baseline in spleen volume at Week 24 is approximately 3%. This is based on the Phase 3 study (INCB 18424-351), where the standard deviation of the percent change from baseline in spleen volume at Week 24 was 19%.

5. DATA HANDLING DEFINITIONS AND CONVENTIONS

5.1. Scheduled Analyses

In addition to the planned final CSR analysis, interim data reviews by the DMC focused on events of thrombocytopenia and hemorrhage on predefined schedules are planned.

- 28 days after 20 subjects have enrolled.
- 28 days after 40 subjects have enrolled.
- Other reviews can be scheduled only if the DMC deems it necessary that additional data would need to be reviewed to assess safety parameters as specified by the protocol.

Since all interim data reviews are focused on safety only, there is no alpha-spend of the final CSR efficacy analysis.

5.1.1. First DMC Data Review Meeting

When the 20th patient is enrolled, additional screening of subjects will be paused for at least 28 days and up to approximately 42 days. Subjects in screening at that time will be allowed to enroll if they are found to be eligible. During this period, enrolled subjects will be allowed to continue on study per the protocol. At least 28 days from the enrollment of the 20th subject, safety data will be assessed by the DMC and the sponsor. Subjects will be analyzed if they have completed at least 28 days on the study or have discontinued the study because of Grade 4 thrombocytopenia or > Grade 2 hemorrhage. Demographics, baseline characteristics, and dose exposure will be summarized for those subjects. Also AE and laboratory parameters will be analyzed.

5.1.2. Second DMC Data Review Meeting

At least 28 days from the enrollment of the 40th subject, safety data will be assessed by the DMC and the sponsor. Since the first dose escalation opportunity in the study is at Day 28 and the starting dose for all subjects of 5 mg bid will have been adequately assessed for safety at the first safety review after the enrollment of 20 patients, screening will not be suspended following enrollment of the 40th subject. If safety of the 5 mg bid dose is not clear from this first data review, the DMC and the sponsor may mandate a hold on screening at the review that occurs with enrollment of the 40th subject. Subjects will be analyzed when they have completed at least 28 days on the study or discontinued due to Grade 4 thrombocytopenia or > Grade 2 hemorrhage. Demographics, baseline characteristics, and exposure will be summarized for those subjects. Also AE and laboratory parameters will be analyzed.

More details were described in the protocol Section 11.7, Data Safety Monitoring and the corresponding DMC charter.

5.2. Treatment Groups

Subjects will be summarized as 1 group regardless of dose titration. For certain summaries of AEs by dose received (details can be found in the appendix of table shells), subjects will be grouped into the following categories: ≤ 5 mg, > 5 to 10 mg, > 10 to 15 mg, > 15 to 20 mg, > 20 to 25 mg, and > 25 mg based on the final titrated total daily dose (see Section 5.9.3.1).

In addition, for the summary of exposure, final titrated dose groups as defined above may be used as treatment groups and additional efficacy analysis may utilize these dose categories.

5.3. Analysis Populations

5.3.1. Safety Population

All subjects who are enrolled and have taken at least 1 dose of study drug comprise the safety population. The safety population will be used to conduct all safety analyses, including baseline and demographics.

5.3.2. Intent-to-Treat Population

All subjects who are enrolled and have taken at least 1 dose of study drug constitute the intent-to-treat (ITT) population. All efficacy analyses will be conducted using the ITT population. It is noted that the ITT population is effectively identical to the safety population for this study.

5.3.3. Per-Protocol Population

The per-protocol (PP) population includes those subjects in the ITT population who are considered to be sufficiently compliant with the protocol. The PP population will be used for certain supportive sensitivity analysis of efficacy and safety. Derivation rules for PP population can be found in Section 5.9.6.

[redacted]

5.4. Statistical Methodology

5.4.1. General Methodology

Unless otherwise denoted, SAS® procedures (Version 9 or above) will be employed for the generation of all tables, graphs, and statistical analyses. [redacted] 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.

The Safety Population will be used for all safety analyses, and the ITT population will be used for all efficacy analyses. The primary efficacy analysis will also be repeated by using the PP population. [redacted]

5.4.2. Control of Type I Error

All confidence intervals will be 95% and tests will be performed at 2-sided 0.05% level. Because of the exploratory nature of the study analyses, except for tests regarding the coprimary endpoints, no multiplicity adjustment will be performed. To control overall Type I error in testing hypotheses regarding the coprimary endpoints, a sequential testing procedure will be used.

- Step 1 will test the correlation between percent change from baseline in spleen volume at Week 24 and the last titrated dose level, and only if the null hypothesis of no correlation can be rejected, Step 2 will be carried out.

- Step 2 will test the correlation between percent change from baseline in total symptom score at Week 24 and the last titrated dose level. In case Step 1 fails to reject the null hypothesis, the inferential comparison (p-values) of Step 2 will still be generated for descriptive purposes only.

5.5. Baseline Values

A baseline value (for analysis purposes) is the last, non-missing measurement obtained during the screening visit and baseline visit unless otherwise stated, with the exception of laboratory values and the total symptom score. For laboratory assessments, values obtained on Day 1 (see Section 5.6) will be included in deriving baseline as the laboratory values are scheduled to be obtained before on-site administration of study drug. For total symptom scores, different derivation rules will be used (see Section 5.9.2.2).

5.6. Day 1, Study Day, and Study Time Points

Day 1 is the date of first dose of study medication.

The study day at a visit/reporting date will be calculated by the visit/reporting Date – Day 1 + 1. This study day will be subtracted by 1 if it is less than or equal to zero, so that a study day of zero will never occur. A study day of -1 indicates 1 day prior to Day 1.

Other study time points will use nominal weeks, such as Weeks 4, 8, 12, etc, according to the Schedules of Assessments (see Table 2 and Table 3), as recorded on the CRF, regardless of the actual time windows these visits fall into, unless otherwise stated. This is especially true for analyses such as laboratory values and vital sign values where by-study-week summaries are to be generated, as well as for spleen palpation length over time summaries.

Exceptions to the statements about study time points described above include (but are not limited to) spleen volume at Week 24 (see Section 5.9.1), total symptom score at several major study time points (see Section 5.6), and final titrated dose level (see Section 5.9.3.1).

Another exception is related to spleen palpation length analysis. Per study CRF design, if a subject's EOT Visit coincides with a scheduled visit, then in database, only EOT Visit data will be available. So when a subject has spleen palpation length data collected on an "EOT Visit" (or End of Extension Phase Visit, as appropriate and if applicable), an effort will be made to see if the data actually falls into a scheduled visit, such as Weeks 4, 8, 12, 16, 20, 24 (treatment phase), 36, 48, 60, etc (extension phase) by using the window of Week of scheduled visit*7 ± 5 days.

Following the situation described above, if EOT data contain spleen volume measurements and the situation is not resolved by the time of database lock, then similar effort will be made by treating spleen volume data labeled from "EOT Visit" as data collected from unscheduled visit. See Section 5.9.1 for how spleen volume data from unscheduled visits will be used in the analysis.

The situation described above is not an issue of importance to other variables such as laboratory values, since in analyses by time point, "EOT" will be one of the time points to be displayed.

5.7. Concomitant Medications and Partial Dates

Prior medication is defined as any non-study medication started prior to the date of first study drug administration.

Concomitant medication is defined as any non-study medication that is:

- Started before the date of first study drug administration and is ongoing throughout the study or ends on/after the date of first study drug administration;
- Started on/after the date of first study drug administration and is ongoing or ends during the course of study medication.

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 medication. In the listing, it will be indicated whether or not a medication is prior-only, concomitant-only, or both prior and concomitant medication.

The start/stop dates recorded by the Investigator and his/her research staff in the eCRF will be used to identify when a concomitant medication was taken during the study. Any missing start date must be queried for resolution. Unresolved missing start dates will be handled according to the following order of steps.

- If the date is completely missing, the medication will be considered both prior and concomitant.
- If only the day is missing, and the last day of the month is prior the first dose date on Day 1, then the concomitant medication will be considered as starting prior to Day 1, and the incomplete date will be handled as if it is the last day of the month.
- If only the day is missing, and the first day of the month is after the first dose date on Day 1, then the concomitant medication will be considered as starting after Day 1, and the incomplete date will be handled as if it is the first day of the month.
- If only the day is missing, and the month is equal to the month of the first dose date on Day 1, then the missing day will be handled as if it is the first day of the month.
- If both the month and day are missing, and the last day of the year is prior to the first dosing date on Day 1, then the concomitant medication will be considered as starting before Day 1, and the incomplete date will be handled as if it is the last day of the year. Otherwise, the missing date will be handled as if it is the first day of the year.

5.8. Adverse Events and Missing Data

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

Severity of AEs will be described and graded using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE). CTCAE v4.03 is used for this protocol. If the toxicity is not included in the CTCAE v4.03 criteria it will be rated on a 1 to 4 scale as follows: mild = 1; moderate = 2; severe =3; and life-threatening = 4.

An AE will also be assessed by its relationship to study medication as well as by seriousness. These assessments will be directly from data collected on eCRFs and are described in details in the protocol.

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

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

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

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

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

5.9. Variable Definitions and/or Derivation Rules

5.9.1. Spleen Volume Value at Week 24

If Week 24 spleen volume value is obtained in the manner of by-schedule visit, it will be used as the analytic value for study analysis regardless of the actual time window it falls into. However, if the only values available are from unscheduled visits, then the last available value within the window of Day 141 to Day 175 (=168 + 7 days) will be used as Week 24 spleen volume analytic value. When spleen volume data are available for both by-schedule and unscheduled visits (within the window), the value from the scheduled visit will be used.

5.9.2. Total Symptom Score

5.9.2.1. Daily Total Symptom Score

Daily total symptom score is derived as the sum of 6 individual symptom scores (the total score excludes scores for degree of inactivity); this score will be missing if there are any missing individual scores. Observations with an un-resolved missing date will be excluded from analysis.

5.9.2.2. Baseline Total Symptom Score

Baseline value of total symptom score is derived as the average of the prorated daily total symptom score for the 7 days before the first dose on Day 1 (ie, from Day -7 to Day -1). If ≥ 4 daily total symptom score values are missing during this period of time, the baseline total symptom score value is set as missing.

5.9.2.3. Total Symptom Score at Weeks 4, 8, 12, 16, 20, and 24

Week X (where X = 4, 8, 12, 16, 20, and 24) total symptom score is derived as the average of the daily total symptom scores collected from the last 28 consecutive days covering the interval between up to Day (X+n)*7, where n is 1 for Week 24 and 0 otherwise, and Day (X-4)*7 + 1 as presented in Table 4.

Table 4: Windows for Total Symptom Score at Given Study Time Points

Study Time Point	Window	Note
Week 4	Day 1 to Day 28	
Week 8	Day 29 to Day 56	
Week 12	Day 57 to Day 84	
Week 16	Day 85 to Day 112	
Week 20	Day 113 to Day 140	
Week 24	Last 28 days of the window from Day 141 to the last day when daily total symptom score value is available and it is ≤ Day 175.	If the last evaluation day is before Day 168-7 = 161 then total symptom score will be set as missing for Week 24.

Total symptom score for given study time points displayed above will be missing if there are more than 8 values missing in the 28-day window. It should be noted that a score of 0 is not a missing value.

5.9.3. Dosing Level and Compliance

5.9.3.1. Final Titrated Dose Level

The analytic value of the last titrated dose level will be derived as the average of the total daily dose (excluding periods of dose interruption) during the time interval of Day 141 and Day 168, or the last 28 days of available dosing data (for subjects who discontinued treatment early). All available data points in the time interval will be used for this calculation.

5.9.3.2. Last Average Daily Dose Level During the Treatment Period

For subjects who have the analytic value of the last titrated dose level derived, the last average daily dose level during the treatment period will be the same. For subjects who discontinued and do not have last titrated dose level derived, it will be the average of the last 28 days (excluding periods of dose interruption) of treatment. For subjects who discontinued study before Day 28, it is the same as the average daily dose level during the study.

5.9.3.3. Study Drug Compliance

Study drug compliance (%) is calculated as

100 × [total dose taken]/[total dose prescribed]

where total dose taken is calculated as before, and total dose prescribed will be based on the dosing prescription as collected through the CRF pages of EX domain. If prescribed dose collected from EX domain is 0, it also indicates a prescribed dose interruption; in addition, dose reduction or increase as recorded in EX domain are all regarded as investigator-mandated prescriptions on study drug for the subjects to follow.

Study drug compliance will be calculated only for the pre-extension phase of 24 weeks. Based on need of exploratory analysis, compliance for other periods may be derived as well.

Because of the eCRF design, other than calculating study drug compliance, data collected on the EX domain of the eCRF will be used as actual study drug administration information in order to carry out other dose-response type analyses, such as AEs by the dose level before the AE (Section 5.9.3.4). In the case of a serious discrepancy between the prescribed dose and the dose received, additional actions may be taken to modify data entries.

5.9.3.4. Last Dose Level Prior to an Adverse Event

The last dose level prior to an AE is derived as the last non-zero dose (from EX domain) prior to the day an AE occurred. The reason to use "prior to the day" which excludes the day on which an AE occurred is that daily dose is divided into morning and evening doses and no dose administration time is collected on eCRF, making the last dose prior to an AE difficult to verify if "on the same day" dose levels are also included in the derivation.

It is noted that the data collected through the EX domain is treated as actual doses (rather than the prescribed dose schedule, as is the case of deriving compliance, defined earlier). This approach is used throughout when dose-response analyses (for both safety and efficacy) are carried out.

5.9.4. Blood Transfusion Independence at Baseline

Transfusion independence at baseline is defined in 2 ways.

1. It is defined as receiving no transfusions (of red blood cell products) in the 8 weeks before Day 1.

2. It is defined as receiving no transfusions (of red blood cell products) in the 12 weeks before Day 1.

5.9.5. Blood Transfusion Independence at Post-Baseline

Transfusion independence during post-baseline period is defined in 2 ways.

1. It is defined as receiving no transfusions (of red blood cell products) during the final 8 weeks of a subject's participation before the data cutoff date.

2. It is defined as receiving no transfusions (of red blood cell products) during the final 12 weeks of a subject's participation before the data cutoff date.

5.9.6. Derivation of Per-protocol Population

The following process will be followed in deriving the PP population.

- Analysis programming team will generate a study drug compliance listing (by Week 24) and pass it to the clinical team.

- Based on study drug compliance and protocol deviation information from the clinical monitoring database, the clinical team will generate a PP population file indicating the membership of subjects to this population, and pass this file to the analysis programming team.

- Analysis programming team will use the PP population file to set the population indicator in analysis datasets for analysis.

In addition, the clinical team will also generate a source document containing all protocol deviations collected through the clinical monitoring process and pass it to the analysis programming team for generation of the protocol deviation listing.

6. BASELINE, EXPOSURE, AND DISPOSITION VARIABLES AND ANALYSES

6.1. Baseline and Demographics

Descriptive summaries for demographic and baseline characteristics will include, but not limited to, age, age group (≤ 65 vs > 65), sex, race, ethnicity, weight, height, ECOG performance status, transfusion history status, [redacted] history of usage of any and all other drugs used to treat MF, and spleen palpation length. A data listing will be provided.

6.2. Disposition and Enrollment

The number and percentage of subjects enrolled, completed, and withdrawn from the study with a primary reason of withdrawal will be summarized for the safety population. Per study design, disposition is applicable to the following 3 contexts: End of Treatment Phase or Early Termination, End of Extension Phase or Early Termination, and End of Study. Summaries will be provided for each of these 3 contexts and support listing will also be provided.

In addition, a listing for screen failures will be provided and will include information regarding demographics and eligibility status.

6.3. Protocol Deviations

Protocol deviations captured will be listed in subject data listings.

6.4. Exposure

For subjects in the safety population, descriptive statistics will be provided for duration of treatment (defined as days or weeks between first dose and last dose inclusive disregard dose interruptions in between); total patient years of exposure; total dose (mg); average daily dose (mg), which is defined as the total dose divided by duration of treatment; last titrated dose level (mg/day); and last average daily dose. Average daily dose (mg) will also be summarized by the major study time points (ie, during Weeks 1, 4, 8, 12, 16, 20, and 24). A data listing will be provided.

6.5. Study Medication Compliance

Overall compliance (%) will be summarized and a data listing will be provided.

6.6. Medical History

Medical history will be summarized. Summaries will include the number and percentage of subjects with significant medical history for each body system/organ class listed on the CRF page.

6.7. Concomitant Medication

Concomitant medications will be summarized by WHO drug class and WHO drug term. In the data listing, each record will be flagged as whether or not the medication is of prior, concomitant, or both prior and concomitant usage.

Prior medication information will also be reviewed by the clinical monitor to identify anti-cancer medication received by subjects prior to enrollment into the study. Prior anti-cancer medication data will be summarized as well as listed.

6.8. Blood Transfusion Dependency

The proportion of subjects who were blood-transfusion dependent at baseline and at post-baseline will be summarized by baseline platelet count group (50-75 GI/L vs > 75 GI/L). A shift summary including the number and percentage of subjects who changed transfusion status was also produced by baseline platelet count group. In addition, the total units and average monthly units of transfusions will also be summarized by baseline platelet count group.

7. EFFICACY ANALYSES

7.1. Primary Efficacy Endpoints

For the co-primary endpoints (correlation of percent change from baseline in spleen volume at Week 24 versus final titrated dose, and correlation of percent change from baseline in total symptom score at Week 24 versus final titrated dose), the following t-test will be used generate the p-values:

$$T = r \times \sqrt{\frac{n-2}{1-r^2}} \sim t_{n-2} \mid H_0$$

where r is the product-moment (Pearson) correlation coefficient, n is the sample size of paired observations, and $\sim t_{n-2} \mid H_0$ means the test statistic will follow a t-distribution with n-2 degrees of freedom under the null hypothesis.

In addition, correlation estimate and the corresponding approximate 95% confidence intervals will be calculated by using the Fisher's r-to-z transformation. The following SAS codes will be used to generate the all these statistics:

```
ODS OUTPUT  FisherPearsonCorr=correst PearsonCorr=pval;
PROC CORR FISHER PEARSON;
     VAR X Y;
RUN; ***CORREST has point estimate and CI from Fisher z-transformation, and
PVAL has p-value and the raw Pearson correlation coefficient ***;
```

The analysis will be generated for the ITT population. The same analysis will be repeated by using The PP population as a sensitivity analysis (Sensitivity Analysis 1).

An additional sensitivity analysis may be generated in dealing with missing data by using multiple imputation procedures (Sensitivity Analysis 2).

7.2. Secondary Endpoint(s) and Analyses

For the following secondary endpoints, descriptive summaries will be provided for overall as well as for the final titrated dose group:

- Percent change from baseline in spleen volume at Week 24.
- Percent change from baseline in total symptom score at Week 24.
- Proportion of subjects with ≥ 35% reduction from baseline in spleen volume at Week 24.
- Proportion of subjects with ≥ 10% reduction from baseline in spleen volume at Week 24.

- Proportion of subjects with ≥ 50% improvement from baseline in total symptom score at Week 24.

- Change and percentage change from baseline in spleen length as measured by palpation at each visit where the parameter is assessed.

Supporting data listings will also be provided.

8. SAFETY ANALYSES

8.1. Adverse Events

The following summaries will be produced for AEs for the overall subject group:

High Level Summary

- Number (%) of subjects reporting any TEAEs
- Number (%) of subjects reporting any DLT
- Number (%) of subjects reporting any treatment-related AEs
- Number (%) of subjects reporting any SAEs
- Number (%) of subjects reporting any Grade 3 or 4 AEs
- Number (%) of subjects who discontinued study drug because of AEs
- Number (%) of subjects with study drug dose reductions because of AEs
- Number (%) of subjects who died

By MedDRA Term:

- Number (%) of subjects reporting TEAEs by organ class and preferred term
- Number (%) of subjects reporting Grade 3 or 4 TEAEs by organ class and preferred term
- Number (%) of subjects reporting treatment-related AEs by organ class and preferred term
- Number (%) of subjects reporting treatment-emergent SAEs by organ class and preferred term
- Number (%) of subjects reporting treatment-emergent non-serious AEs by organ class and preferred term

In addition, a listing of DLTs will be provided.

These TEAEs occurring in 2 or more subjects in the safety population will be summarized by the Medical Dictionary for Regulatory Activities (MedDRA) preferred term for all causalities as well as for treatment-related causalities.

Proportion of subjects with new onset of Grade 4 thrombocytopenia events based on laboratory data and as measured by CTCAE grades will be summarized. The hazard function of time to onset of Grade 4 thrombocytopenia will be estimated using life table method.

Proportion of subjects with new onset of Grade 2 or higher hemorrhage based on preferred terms included in the Standardized MedDRA Query (SMQ) for "Haemorrhage terms (excluding laboratory terms) (SMQ)" and as measured by CTCAE grades will be summarized. The hazard functions of time to onset will be estimated using life table method.

Proportion of subjects with new onset of Grade 4 anemia based on laboratory data and as measured by CTCAE grades will be summarized. The hazard functions of time to onset will be estimated using life table method.

For the above 3 types of AEs, additional analyses using summary tables as well as data listings may be provided taking into account the blood transfusion status at baseline and post-baseline blood transfusion history.

Selected maximal severity AE summary tables will also be generated by the dose level the subject received.

8.2. Laboratory Values

Clinical laboratory tests including hematology, serum chemistry, coagulation, and urinalysis will be performed for each subject during the study in accordance with the Schedule of Observations (see Table 3). If specific safety issues arise, additional, unscheduled laboratory tests/analyses may be performed at the discretion of the investigator.

All test results and associated normal ranges from central laboratories will be reported in Standard International units (SI unit). All tests with numeric values will have a unique unit per test. Any laboratory results and associated normal ranges from local laboratories will be converted to SI units. When there are multiple laboratory values for a subject's particular test at a given visit, the last non-missing value will be used in the by-visit tabulations and summaries described below.

Numeric laboratory values will be summarized descriptively, and non-numeric test values will be tabulated by study visit using data collected from scheduled visits.

For those tests with available normal ranges, the number and percentage of subjects with the laboratory values being low, normal, or high will be calculated for each test. A shift summary will be produced, which presents the change from baseline as shown in Table 5.

Table 5: Example Shift Summary for Applicable Laboratory Assessments

	At a Post-baseline Visit				
At Baseline	Missing	Low-Only	Normal	High-Only	**Both Low and High**
Missing	N (%)	N (%)	N (%)	N (%)	**N (%)**
Low	N (%)	N (%)	N (%)	N (%)	**N (%)**
Normal	N (%)	N (%)	N (%)	N (%)	**N (%)**
High	N (%)	N (%)	N (%)	N (%)	**N (%)**
Total	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (100%)**

Laboratory test values outside the normal range will be assessed for severity based on severity CTCAE grade or CTCAE grade criteria (where clinical intervention is required for CTCAE grading). Shift tables relative to baseline will be generated using all available data from scheduled and unscheduled visits.

8.3. Vital Signs

Descriptive statistics for measurements, as well as change from baseline values, will be provided for vital signs (blood pressure, heart rate, respiratory rate, and body temperature) at each assessment time. Subjects exhibiting clinically notable vital sign abnormalities will be listed.

A value will be considered an "alert" value if it is outside the established range and shows a change from baseline greater than 25%, according to the high and/or low threshold values listed in Table 6.

Table 6: High and Low Threshold Values for Alert Vital Sign Observations

Parameter	High Threshold	Low Threshold
Systolic blood pressure	> 160 mm Hg	< 85 mm Hg
Diastolic blood pressure	> 100 mm Hg	< 50 mm Hg
Respiratory Rate	> 24 per minute	< 8 per minute
Heart rate	> 100 bpm	< 45 bpm
mm Hg = millimeters of mercury; bpm = beats per minute.		

Alert vital sign data will also be listed.

8.4. Electrocardiograms

Electrocardiogram data collected at the screening visit will be listed. If additional data are collected, they will be listed and may be summarized as appropriate.

9. CLINICAL PHARMACOLOGY/ [redacted]

[redacted]

9.2. Subject Demographic, Clinical Laboratory, and Disease-Related Variables

Subject demographic assessments (age, weight, body mass index, sex, and race), disease-related evaluations (baseline platelet count, tumor type), and clinical laboratory measurements (creatinine clearance, ALB, total bilirubin, alkaline phosphatase, alanine aminotransferase, AST) may be explored as time independent predictors of [redacted] variability.

9.3. Concomitant Medication

CYP3A4 inhibitors and inducers may be may be tested as time dependent variables of [redacted] variability if more than 15% of patients will take them as concomitant medications.

[redacted]

[redacted]

9.5. Pharmacokinetic-Pharmacodynamic Data Analysis

The relationship between PK model predicted concentrations/parameters and pharmacologic, safety, and efficacy read-outs are planned. A longitudinal analysis of platelets (absolute values or change from pre-dose) using predicted PK and baseline platelet values as covariates will be performed to assess platelet change over time. The population PK model will be used to derive estimates of individual steady-state exposure measures for PK-PD analysis.

9.6. Output

A population PK report will be prepared in accordance with guidance of both US and EU regulatory authorities.

10. LIST OF PLANNED TABLES, LISTINGS, AND FIGURES

10.1. Tables

Table Number	Title	Population
Baseline and Demographic Characteristics		
14.1.1	Summary of Subject Enrollment and Exit Status	Safety
14.1.2	Summary of Demographics	Safety
14.1.3	Summary of Baseline Characteristics	Safety
14.1.4	Summary of Medical History by MedDRA System Organ Class and Preferred Term	Safety
14.1.5.1	Summary of Prior Medications	Safety
14.1.5.2	Summary of Concomitant Medications	Safety
14.1.5.3	Summary of Prior Anti-Cancer Treatment	Safety
14.1.6.1	Summary of Change in Status of Blood Component Transfusion Dependency by Baseline Platelet Count Group	Safety
14.1.6.2	Summary of Blood Component Transfusions by Baseline Platelet Count Group	Safety
Efficacy		
14.2.1.1	Summary of Correlations of Final Titrated Dose vs. Percent Change from Baseline in Spleen Volume at Week 24 and vs. Percent Change in Total Symptom Score at Week 24	ITT

Table Number	Title	Population
14.2.1.2	Summary of Correlations of Final Titrated Dose vs. Percent Change from Baseline in Spleen Volume at Week 24 and vs. Percent Change in Total Symptom Score at Week 24: Sensitivity Analysis 1	Per-Protocol
14.2.1.3	Summary of Correlations of Final Titrated Dose vs. Percent Change from Baseline in Spleen Volume at Week 24 and vs. Percent Change in Total Symptom Score at Week 24: Sensitivity Analysis 2	ITT
14.2.2.1	Summary of Spleen Volume Data by Study Week and Final Titrated Dose Group	ITT
14.2.2.2	Summary of Proportion of Subjects with >= 35% Reduction from Baseline in Spleen Volume at Week 24 by Final Titrated Dose Group	ITT
14.2.2.3	Summary of Proportion of Subjects with >= 10% Reduction from Baseline in Spleen Volume at Week 24 by Final Titrated Dose Group	ITT
14.2.3.1	Summary of Total Symptom Score Data by Study Week and Final Titrated Dose Group	ITT
14.2.3.2	Summary of Proportion of Subjects with >= 50% Reduction from Baseline in Total Symptom Score by Study Week and Final Titrated Dose Group	ITT
[redacted]		
14.2.4.1	Summary of Spleen Palpation Length Data by Study Week and Final Titrated Dose Group	ITT
14.2.4.2	Summary of Proportion of Subjects with >= 50% Reduction from Baseline in Spleen Palpation Length by Study Week and Final Titrated Dose Group	ITT
14.2.4.3	Summary of Proportion of Subjects with >= 20% Reduction from Baseline in Spleen Palpation Length by Study Week and Final Titrated Dose Group	ITT
[redacted]		
Safety: Exposure		
14.3.1.1	Summary of Exposure and Duration of Exposure to Study Medication Through Week 24	Safety
14.3.1.2	Summary of Exposure to Ruxolitinib Through Week 4	Safety
14.3.1.3	Summary of Average Daily Dose of Ruxolitinib by Study Week	Safety
Safety: Adverse Events		
14.3.2.1	Overall Summary of Treatment-Emergent Adverse Events by Dose Level Ever Received	Safety
14.3.2.2.1	Summary of Subjects Reporting Treatment-Emergent Adverse Events (All Causalities) by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Safety

Table Number	Title	Population
14.3.2.2.2	Summary of Subjects Reporting Treatment-Emergent Adverse Events (All Causalities) by MedDRA System Organ Class, Preferred Term, and Dose Level Ever Received	Safety
14.3.2.3.1	Summary of Subjects Reporting Treatment-Emergent Adverse Events (All Causalities) by MedDRA Preferred Term (Sorted by Decreasing Frequency) and Maximal Severity	Safety
14.3.2.3.2	Summary of Subjects Reporting Treatment-Emergent Adverse Events (All Causalities) by MedDRA Preferred Term (Sorted by Decreasing Frequency) and Dose Level Ever Received	Safety
14.3.2.3.3	Summary of Subjects Reporting Treatment-Emergent Hemorrhage Adverse Events (All Causalities) by MedDRA Preferred Term and Dose Level Ever Received	Safety
14.3.2.3.4	Summary of Subjects Reporting Treatment-Emergent Hemorrhage Adverse Events (All Causalities) of Grade 3 or Higher by MedDRA Preferred Term and Dose Level Ever Received	Safety
14.3.2.4.1	Summary of Subjects Reporting Treatment-Emergent Treatment-Related Adverse Events (All Causalities) by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Safety
14.3.2.4.2	Summary of Subjects Reporting Treatment-Emergent Treatment-Related Adverse Events (All Causalities) by MedDRA System Organ Class, Preferred Term, and Dose Level Ever Received	Safety
14.3.2.5.1	Summary of Subjects Reporting Treatment-Emergent Serious Adverse Events (All Causalities) by MedDRA System Organ Class, Preferred Term, and Dose Level Ever Received	Safety
14.3.2.6	Summary of Subjects Reporting Treatment-Emergent Adverse Events (All Causalities) Leading to Study Medication Decrease or Interruption by MedDRA System Organ Class, Preferred Term, and Dose Level Ever Received	Safety
14.3.2.7	Summary of Subjects Reporting Treatment-Emergent Adverse Events (All Causalities) Leading to Study Discontinuation by MedDRA System Organ Class, Preferred Term, and Dose Level Ever Received	Safety
14.3.2.8	Summary of Subjects Reporting Treatment-Emergent Adverse Events (All Causalities) Leading to On-Study Death by MedDRA System Organ Class, Preferred Term, and Dose Level Ever Received	Safety
Safety: Laboratory Data		
14.3.3.1.1	Summary of Laboratory Values – Hematology	Safety
14.3.3.1.2	Shift Summary of Laboratory Values in Normal Ranges - Hematology	Safety
14.3.3.2.1	Summary of Laboratory Values – Serum Chemistry	Safety
14.3.3.2.2	Shift Summary of Laboratory Values in Normal Ranges – Serum Chemistry	Safety
14.3.3.3.1	Summary of Laboratory Values – Coagulation	Safety
14.3.3.3.2	Shift Summary of Laboratory Values in Normal Ranges – Coagulation	Safety
14.3.3.4.1	Summary of Laboratory Values – Urinalysis	Safety
14.3.3.4.2	Shift Summary of Laboratory Values in Normal Ranges – Urinalysis	Safety
14.3.3.5.1	Shift Summary of Laboratory Values in CTC Grade - To the Worst Abnormal Value (Tests with One Directional CTC Grade)	Safety

Table Number	Title	Population
14.3.3.5.2	Shift Summary of Laboratory Values in CTC Grade - To the Worst Abnormal Value (Tests with Two Directional CTC Grade)	Safety
14.3.3.6.1	Summary of Subjects with Treatment Emergent Thrombocytopenia of Grade 4 as Derived From Laboratory Data by Dose Level Ever Received	Safety
14.3.3.6.2	Summary of Subjects with Treatment Emergent Anemia of Grade 4 as Derived From Laboratory Data by Dose Level Ever Received	Safety
Safety: Vital Signs		
14.3.4.1	Summary of Systolic Blood Pressure	Safety
14.3.4.2	Summary of Diastolic Blood Pressure	Safety
14.3.4.3	Summary of Heart Rate	Safety
14.3.4.4	Summary of Respiratory Rate	Safety
14.3.4.5	Summary of Body Temperature	Safety

10.2. Figures

Figure Number	Title	Population
14.2.1.1.1	Scatter Plot of Percent Change from Baseline in Spleen Volume at Week 24 vs. Final Titrated Dose Level	ITT
14.2.1.1.2	Scatter Plot of Percent Change from Baseline in Spleen Volume vs. Percent Change in Total Symptom Score at Week 24	ITT
14.2.1.2.1	Mean (95%) Percent Change from Baseline in Spleen Volume at Week 24	ITT
14.2.1.2.2	Median Percent Change from Baseline in Spleen Volume at Week 24 by Final Titrated Dose Group	ITT
14.2.1.3.1	Bar Plot of Percent of Subjects with >= 35% Reduction from Baseline in Spleen Volume at Week 24 by Final Titrated Dose Group	ITT
14.2.1.3.2	Bar Plot of Percent of Subjects with >= 10% Reduction from Baseline in Spleen Volume at Week 24 by Final Titrated Dose Group	ITT
14.2.2.1.1	Scatter Plot of Percent Change from Baseline in Total Symptom Score at Week 24 vs. Final Titrated Dose Level	ITT
14.2.2.2.1	Mean (95%) Percent Change from Baseline in Total Symptom Score at Week 24 by Final Titrated Dose Group	ITT
14.2.2.2.2	Median Percent Change from Baseline in Total Symptom Score at Week 24 by Final Titrated Dose Group	ITT
14.2.2.3.1	Bar Plot of Percent of Subjects with >= 50% Reduction from Baseline in Total Symptom Score at Week 24 by Final Titrated Dose Group	ITT
[redacted]		
14.2.3.1.1	Scatter Plot of Percent Change from Baseline in Spleen Palpation Length at Week 24 vs. Final Titrated Dose Level	ITT
14.2.3.2.1	Mean (95%) Percent Change from Baseline in Spleen Palpation Length at Week 24 by Final Titrated Dose Group	ITT
14.2.3.2.2	Median Percent Change from Baseline in Spleen Palpation Length at Week 24 by Final Titrated Dose Group	ITT

Figure Number	Title	Population
14.2.3.3.1	Bar Plot of Percent of Subjects with >= 50% Reduction from Baseline in Spleen Palpation Length at Week 24 by Final Titrated Dose Group	ITT
14.2.3.3.2	Bar Plot of Percent of Subjects with >= 20% Reduction from Baseline in Spleen Palpation Length at Week 24 by Final Titrated Dose Group	ITT
14.2.3.3.3	Bar Plot of Percent of Subjects with >= 50% Reduction from Baseline in Spleen Palpation Length by Study Week	ITT
14.2.3.3.4	Bar Plot of Percent of Subjects with >= 20% Reduction from Baseline in Spleen Palpation Length at Week 24 by Study Week	ITT
14.3.1.1.1	Subject Laboratory Value over Time: Hemoglobin (G/L)	Safety
14.3.1.1.2	Mean (95% CI) Laboratory Value Over Time: Hemoglobin (G/L)	Safety
14.3.1.2.1	Subject Laboratory Value over Time: Platelet (GI/L)	Safety
14.3.1.2.2	Mean (95% CI) Laboratory Value Over Time: Platelet (GI/L)	Safety
14.3.1.3.1	Subject Laboratory Value over Time: WBC (GI/L)	Safety
14.3.1.3.2	Mean (95% CI) Laboratory Value Over Time: WBC (GI/L)	Safety
14.3.1.4.1	Subject Laboratory Value over Time: Neutrophil (GI/L)	Safety
14.3.1.4.2	Mean (95% CI) Laboratory Value Over Time: Neutrophil (GI/L)	Safety

10.3. Listings

Listing Number	Title	Population
16.2.1.1	Subject Enrollment and Exit Status	Safety
16.2.1.2	Screening Failure Subjects	Safety
16.2.2	Protocol Deviations/Violations	Safety
16.2.3	Data Excluded from [redacted] Efficacy, and/or Safety Analyses	Safety
16.2.4.1	Demographic and Baseline Characteristics	Safety
16.2.4.2.1	Medical History	Safety
16.2.4.2.2	Baseline Disease Stage	Safety
16.2.4.3	Prior and Concomitant Drug Treatments	Safety
16.2.4.4	Prior Myelofibrosis Therapy	Safety
16.2.4.5	Prior Anti-Cancer Treatment	Safety
16.2.6.1	Derived Efficacy Variables – Part I	ITT
16.2.6.2	Derived Efficacy Variables – Part II	ITT
16.2.7.1.1	Study Drug Activities and Dosing Compliance	Safety
16.2.7.2.1	Adverse Events	Safety
16.2.7.2.2	Serious Adverse Events	Safety
16.2.7.2.3	Adverse Event Leading to Study Drug Decrease, Interruption, and Discontinuation	Safety
16.2.7.2.4	Adverse Events of Hemorrhage as Identified by SMQ	Safety
16.2.7.2.5	Adverse Events Leading to Discontinuation from the Study	Safety
16.2.7.2.6	Adverse Events Leading to On-Study Death	Safety
16.2.8.1.1	Clinical Laboratory Values	Safety
16.2.8.1.2	Abnormal Clinical Laboratory Values	Safety
16.2.8.1.3	Selected Hematology Laboratory Data	Safety
16.2.8.1.4	Selected Hematology Laboratory Data for Subjects with Grade 4 Thrombocytopenia or Grade 4 Anemia	Safety

Listing Number	Title	Population
16.2.8.2.1	Vital Signs	Safety
16.2.8.2.2	Abnormal Vital Sign Values	Safety
16.2.8.2.3	Alert Vital Sign Values	
16.2.8.3.1	12-Lead ECG Values	Safety
16.2.8.3.2	Abnormal 12-Lead ECG Values	Safety
16.2.8.4	Physical Examinations	Safety
16.2.8.5	Blood Component Transfusions	Safety
16.2.8.6	Serum Pregnancy Test	Safety
[redacted]		

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12. APPENDICES

APPENDIX A. MEDDRA PREFERRED TERMS INCLUDED IN THE SMQ TO IDENTIFY HEMORRHAGE ADVERSE EVENTS

Name	Code	Level	Scope	Cate-gory	Weight	Status	Add. Ver.	Last Mod. Ver.
Abdominal wall haematoma	10067383	PT	Narrow	A	0	Active	10.1	12
Abdominal wall haemorrhage	10067788	PT	Narrow	A	0	Active	11	12
Abnormal withdrawal bleeding	10069195	PT	Narrow	A	0	Active	12	12
Acute haemorrhagic leukoencephalitis	10058994	PT	Narrow	A	0	Active	9	12
Adrenal haematoma	10059194	PT	Narrow	A	0	Active	9	12
Adrenal haemorrhage	10001361	PT	Narrow	A	0	Active	9	12
Anal haemorrhage	10049555	PT	Narrow	A	0	Active	9	12
Anal ulcer haemorrhage	10063896	PT	Narrow	A	0	Active	9	12
Anastomotic haemorrhage	10056346	PT	Narrow	A	0	Active	9	12
Anastomotic ulcer haemorrhage	10002244	PT	Narrow	A	0	Active	9	12
Aneurysm ruptured	10048380	PT	Narrow	A	0	Active	9	12
Anorectal varices haemorrhage	10068925	PT	Narrow	A	0	Active	12	12
Antepartum haemorrhage	10002667	PT	Narrow	A	0	Active	9	12
Aortic aneurysm rupture	10002886	PT	Narrow	A	0	Active	9	12
Aortic dissection rupture	10068119	PT	Narrow	A	0	Active	11	12
Aortic intramural haematoma	10067975	PT	Narrow	A	0	Active	11	12
Aortic rupture	10060874	PT	Narrow	A	0	Active	9	12
Application site bleeding	10048938	PT	Narrow	A	0	Active	9	12
Application site haematoma	10068317	PT	Narrow	A	0	Active	11.1	12
Arterial haemorrhage	10060964	PT	Narrow	A	0	Active	9	12
Arteriovenous fistula site haematoma	10055150	PT	Narrow	A	0	Active	9	12
Arteriovenous fistula site haemorrhage	10055123	PT	Narrow	A	0	Active	9	12
Arteriovenous graft site haematoma	10055152	PT	Narrow	A	0	Active	9	12
Arteriovenous graft site haemorrhage	10055126	PT	Narrow	A	0	Active	9	12
Astringent therapy	10067372	PT	Narrow	A	0	Active	10.1	12
Atrial rupture	10048761	PT	Narrow	A	0	Active	13	13
Auricular haematoma	10003797	PT	Narrow	A	0	Active	9	12
Basal ganglia haemorrhage	10067057	PT	Narrow	A	0	Active	10	12
Bladder tamponade	10062656	PT	Narrow	A	0	Active	9	12
Bleeding peripartum	10048607	PT	Narrow	A	0	Active	9	12
Bleeding varicose vein	10005144	PT	Narrow	A	0	Active	9	12
Blood blister	10005372	PT	Narrow	A	0	Active	9	12
Blood urine	10005863	PT	Narrow	A	0	Active	9	12
Blood urine present	10018870	PT	Narrow	A	0	Active	9	12
Bloody discharge	10057687	PT	Narrow	A	0	Active	9	12
Bloody peritoneal effluent	10067442	PT	Narrow	A	0	Active	10.1	12
Brain stem haemorrhage	10006145	PT	Narrow	A	0	Active	9	12
Breast haematoma	10064753	PT	Narrow	A	0	Active	9	12
Breast haemorrhage	10006254	PT	Narrow	A	0	Active	9	12
Broad ligament haematoma	10006375	PT	Narrow	A	0	Active	9	12

Name	Code	Level	Scope	Cate-gory	Weight	Status	Add. Ver.	Last Mod. Ver.
Bronchial haemorrhage	10065739	PT	Narrow	A	0	Active	9	12
Carotid aneurysm rupture	10051328	PT	Narrow	A	0	Active	9	12
Catheter site haematoma	10055662	PT	Narrow	A	0	Active	9	12
Catheter site haemorrhage	10051099	PT	Narrow	A	0	Active	9	12
Cephalhaematoma	10008014	PT	Narrow	A	0	Active	9	12
Cerebellar haematoma	10061038	PT	Narrow	A	0	Active	9	12
Cerebellar haemorrhage	10008030	PT	Narrow	A	0	Active	9	12
Cerebral aneurysm ruptured syphilitic	10008076	PT	Narrow	A	0	Active	9	12
Cerebral arteriovenous malformation haemorrhagic	10008086	PT	Narrow	A	0	Active	9	12
Cerebral haematoma	10053942	PT	Narrow	A	0	Active	9	12
Cerebral haemorrhage	10008111	PT	Narrow	A	0	Active	9	12
Cerebral haemorrhage foetal	10050157	PT	Narrow	A	0	Active	9	12
Cerebral haemorrhage neonatal	10008112	PT	Narrow	A	0	Active	9	12
Cerebral haemorrhage traumatic	10008113	PT	Narrow	A	0	Active	9	12
Cerebral microhaemorrhage	10067277	PT	Narrow	A	0	Active	10	12.1
Cervix haematoma uterine	10050020	PT	Narrow	A	0	Active	9	12
Cervix haemorrhage uterine	10050022	PT	Narrow	A	0	Active	9	12
Choroidal haematoma	10068642	PT	Narrow	A	0	Active	11.1	12
Choroidal haemorrhage	10008786	PT	Narrow	A	0	Active	9	12
Chronic gastrointestinal bleeding	10050399	PT	Narrow	A	0	Active	9	12
Ciliary body haemorrhage	10057417	PT	Narrow	A	0	Active	9	12
Coital bleeding	10065019	PT	Narrow	A	0	Active	9	12
Colonic haematoma	10009996	PT	Narrow	A	0	Active	9	12
Conjunctival haemorrhage	10010719	PT	Narrow	A	0	Active	9	12
Contusion	10050584	PT	Narrow	A	0	Active	13	13
Corneal bleeding	10051558	PT	Narrow	A	0	Active	9	12
Cullen's sign	10059029	PT	Narrow	A	0	Active	9	12
Cystitis haemorrhagic	10011793	PT	Narrow	A	0	Active	9	12
Diarrhoea haemorrhagic	10012741	PT	Narrow	A	0	Active	9	12
Disseminated intravascular coagulation	10013442	PT	Narrow	A	0	Active	9	12
Diverticulitis intestinal haemorrhagic	10013541	PT	Narrow	A	0	Active	9	12
Diverticulum intestinal haemorrhagic	10013560	PT	Narrow	A	0	Active	9	12
Duodenal ulcer haemorrhage	10013839	PT	Narrow	A	0	Active	9	12
Duodenitis haemorrhagic	10013865	PT	Narrow	A	0	Active	9	12
Dysfunctional uterine bleeding	10013908	PT	Narrow	A	0	Active	9	12
Ear haemorrhage	10014009	PT	Narrow	A	0	Active	9	12
Ecchymosis	10014080	PT	Narrow	A	0	Active	9	12
Encephalitis haemorrhagic	10014589	PT	Narrow	A	0	Active	9	12
Enterocolitis haemorrhagic	10014896	PT	Narrow	A	0	Active	9	12
Epistaxis	10015090	PT	Narrow	A	0	Active	9	12
Exsanguination	10015719	PT	Narrow	A	0	Active	9	12
Extradural haematoma	10015769	PT	Narrow	A	0	Active	9	12
Extravasation blood	10015867	PT	Narrow	A	0	Active	9	12
Eye haemorrhage	10015926	PT	Narrow	A	0	Active	9	12

Name	Code	Level	Scope	Cate-gory	Weight	Status	Add. Ver.	Last Mod. Ver.
Eyelid bleeding	10053196	PT	Narrow	A	0	Active	9	12
Foetal-maternal haemorrhage	10016871	PT	Narrow	A	0	Active	9	12
Gastric haemorrhage	10017788	PT	Narrow	A	0	Active	9	12
Gastric ulcer haemorrhage	10017826	PT	Narrow	A	0	Active	9	12
Gastric ulcer haemorrhage, obstructive	10017829	PT	Narrow	A	0	Active	9	12
Gastric ulcer perforation	10017835	PT	Narrow	A	0	Active	9	12
Gastric varices haemorrhage	10057572	PT	Narrow	A	0	Active	9	12
Gastritis alcoholic haemorrhagic	10017857	PT	Narrow	A	0	Active	9	12
Gastritis haemorrhagic	10017866	PT	Narrow	A	0	Active	9	12
Gastroduodenal haemorrhage	10053768	PT	Narrow	A	0	Active	9	12
Gastroduodenitis haemorrhagic	10048712	PT	Narrow	A	0	Active	9	12
Gastrointestinal angiodysplasia haemorrhagic	10017929	PT	Narrow	A	0	Active	9	12
Gastrointestinal haemorrhage	10017955	PT	Narrow	A	0	Active	9	12
Gastrointestinal ulcer haemorrhage	10056743	PT	Narrow	A	0	Active	9	12
Genital haemorrhage	10061178	PT	Narrow	A	0	Active	9	12
Gingival bleeding	10018276	PT	Narrow	A	0	Active	9	12
Graft haemorrhage	10063577	PT	Narrow	A	0	Active	9	12
Haemarthrosis	10018829	PT	Narrow	A	0	Active	9	12
Haematemesis	10018830	PT	Narrow	A	0	Active	9	12
Haematochezia	10018836	PT	Narrow	A	0	Active	9	12
Haematoma	10018852	PT	Narrow	A	0	Active	9	12
Haematoma evacuation	10060733	PT	Narrow	A	0	Active	9	12
Haematoma infection	10051564	PT	Narrow	A	0	Active	9	12
Haematomyelia	10066960	PT	Narrow	A	0	Active	10	12
Haematosalpinx	10050468	PT	Narrow	A	0	Active	9	12
Haematospermia	10018866	PT	Narrow	A	0	Active	9	12
Haematotympanum	10063013	PT	Narrow	A	0	Active	9	12
Haematuria	10018867	PT	Narrow	A	0	Active	9	12
Haematuria traumatic	10018871	PT	Narrow	A	0	Active	9	12
Haemobilia	10058947	PT	Narrow	A	0	Active	9	12
Haemophilic arthropathy	10065057	PT	Narrow	A	0	Active	9	12
Haemoptysis	10018964	PT	Narrow	A	0	Active	9	12
Haemorrhage	10055798	PT	Narrow	A	0	Active	9	12
Haemorrhage coronary artery	10055803	PT	Narrow	A	0	Active	9	12
Haemorrhage foetal	10061191	PT	Narrow	A	0	Active	9	12
Haemorrhage intracranial	10018985	PT	Narrow	A	0	Active	9	12
Haemorrhage neonatal	10061993	PT	Narrow	A	0	Active	9	12
Haemorrhage subcutaneous	10018999	PT	Narrow	A	0	Active	9	12
Haemorrhage subepidermal	10019001	PT	Narrow	A	0	Active	9	12
Haemorrhage urinary tract	10055847	PT	Narrow	A	0	Active	9	12
Haemorrhagic anaemia	10052293	PT	Narrow	A	0	Active	9.1	12
Haemorrhagic arteriovenous malformation	10064595	PT	Narrow	A	0	Active	9	12
Haemorrhagic ascites	10059766	PT	Narrow	A	0	Active	9	12

Name	Code	Level	Scope	Cate-gory	Weight	Status	Add. Ver.	Last Mod. Ver.
Haemorrhagic cerebral infarction	10019005	PT	Narrow	A	0	Active	9	12
Haemorrhagic diathesis	10062713	PT	Narrow	A	0	Active	9	12
Haemorrhagic disease of newborn	10019008	PT	Narrow	A	0	Active	9	12
Haemorrhagic disorder	10019009	PT	Narrow	A	0	Active	9	12
Haemorrhagic erosive gastritis	10067786	PT	Narrow	A	0	Active	11	12
Haemorrhagic hepatic cyst	10067796	PT	Narrow	A	0	Active	11	12
Haemorrhagic infarction	10019013	PT	Narrow	A	0	Active	9	12
Haemorrhagic ovarian cyst	10060781	PT	Narrow	A	0	Active	9	12
Haemorrhagic stroke	10019016	PT	Narrow	A	0	Active	9	12
Haemorrhagic transformation stroke	10055677	PT	Narrow	A	0	Active	9	12
Haemorrhagic tumour necrosis	10054096	PT	Narrow	A	0	Active	9	12
Haemorrhagic urticaria	10059499	PT	Narrow	A	0	Active	9	12
Haemorrhoidal haemorrhage	10054787	PT	Narrow	A	0	Active	9	12
Haemostasis	10067439	PT	Narrow	A	0	Active	10.1	12
Haemothorax	10019027	PT	Narrow	A	0	Active	9	12
Henoch-Schonlein purpura	10019617	PT	Narrow	A	0	Active	9	12
Hepatic haemangioma rupture	10054885	PT	Narrow	A	0	Active	9	12
Hepatic haematoma	10019676	PT	Narrow	A	0	Active	9	12
Hepatic haemorrhage	10019677	PT	Narrow	A	0	Active	9	12
Hereditary haemorrhagic telangiectasia	10019883	PT	Narrow	A	0	Active	9	12
Hyphaema	10020923	PT	Narrow	A	0	Active	9	12
Implant site haematoma	10063780	PT	Narrow	A	0	Active	9	12
Implant site haemorrhage	10053995	PT	Narrow	A	0	Active	9	12
Incision site haematoma	10059241	PT	Narrow	A	0	Active	9	12
Incision site haemorrhage	10051100	PT	Narrow	A	0	Active	9	12
Increased tendency to bruise	10021688	PT	Narrow	A	0	Active	9	12
Induced abortion haemorrhage	10052844	PT	Narrow	A	0	Active	9	12
Infusion site haematoma	10065463	PT	Narrow	A	0	Active	9	12
Infusion site haemorrhage	10065464	PT	Narrow	A	0	Active	9	12
Injection site haematoma	10022066	PT	Narrow	A	0	Active	9	12
Injection site haemorrhage	10022067	PT	Narrow	A	0	Active	9	12
Intestinal haemorrhage	10059175	PT	Narrow	A	0	Active	9	12
Intra-abdominal haematoma	10056457	PT	Narrow	A	0	Active	9	12
Intra-abdominal haemorrhage	10061249	PT	Narrow	A	0	Active	9	12
Intracerebral haematoma evacuation	10062025	PT	Narrow	A	0	Active	9	12
Intracranial haematoma	10059491	PT	Narrow	A	0	Active	9	12
Intracranial tumour haemorrhage	10022775	PT	Narrow	A	0	Active	9	12
Intrapartum haemorrhage	10067703	PT	Narrow	A	0	Active	10.1	12
Intraventricular haemorrhage	10022840	PT	Narrow	A	0	Active	9	12
Intraventricular haemorrhage neonatal	10022841	PT	Narrow	A	0	Active	9	12
Iris haemorrhage	10057418	PT	Narrow	A	0	Active	9	12
Lacrimal haemorrhage	10069930	PT	Narrow	A	0	Active	13	13
Large intestinal haemorrhage	10052534	PT	Narrow	A	0	Active	9	12
Large intestinal ulcer haemorrhage	10061262	PT	Narrow	A	0	Active	9	12

Name	Code	Level	Scope	Cate-gory	Weight	Status	Add. Ver.	Last Mod. Ver.
Laryngeal haemorrhage	10065740	PT	Narrow	A	0	Active	9	12
Lip haematoma	10066304	PT	Narrow	A	0	Active	9.1	12
Lip haemorrhage	10049297	PT	Narrow	A	0	Active	9	12
Lower gastrointestinal haemorrhage	10050953	PT	Narrow	A	0	Active	9	12
Majocchi's purpura	10052316	PT	Narrow	A	0	Active	9	12
Mallory-Weiss syndrome	10026712	PT	Narrow	A	0	Active	9	12
Mediastinal haematoma	10049941	PT	Narrow	A	0	Active	9	12
Mediastinal haemorrhage	10056343	PT	Narrow	A	0	Active	9	12
Melaena	10027141	PT	Narrow	A	0	Active	9	12
Melaena neonatal	10049777	PT	Narrow	A	0	Active	9	12
Meningorrhagia	10052593	PT	Narrow	A	0	Active	9	12
Menometrorrhagia	10027295	PT	Narrow	A	0	Active	9	12
Menorrhagia	10027313	PT	Narrow	A	0	Active	9	12
Metrorrhagia	10027514	PT	Narrow	A	0	Active	9	12
Mouth haemorrhage	10028024	PT	Narrow	A	0	Active	9	12
Mucosal haemorrhage	10061298	PT	Narrow	A	0	Active	9	12
Muscle haemorrhage	10028309	PT	Narrow	A	0	Active	9	12
Myocardial haemorrhage	10048849	PT	Narrow	A	0	Active	9	12
Myocardial rupture	10028604	PT	Narrow	A	0	Active	13	13
Naevus haemorrhage	10062955	PT	Narrow	A	0	Active	9	12
Nail bed bleeding	10048891	PT	Narrow	A	0	Active	9	12
Nephritis haemorrhagic	10029132	PT	Narrow	A	0	Active	9	12
Nipple exudate bloody	10029418	PT	Narrow	A	0	Active	9	12
Ocular retrobulbar haemorrhage	10057571	PT	Narrow	A	0	Active	9	12
Oesophageal haemorrhage	10030172	PT	Narrow	A	0	Active	9	12
Oesophageal ulcer haemorrhage	10030202	PT	Narrow	A	0	Active	9	12
Oesophageal varices haemorrhage	10030210	PT	Narrow	A	0	Active	9	12
Oesophagitis haemorrhagic	10030219	PT	Narrow	A	0	Active	9	12
Operative haemorrhage	10030860	PT	Narrow	A	0	Active	9	12
Optic disc haemorrhage	10030919	PT	Narrow	A	0	Active	9	12
Optic nerve sheath haemorrhage	10030941	PT	Narrow	A	0	Active	9	12
Osteorrhagia	10051937	PT	Narrow	A	0	Active	9	12
Ovarian haematoma	10033263	PT	Narrow	A	0	Active	9	12
Ovarian haemorrhage	10065741	PT	Narrow	A	0	Active	9	12
Pancreatic haemorrhage	10033625	PT	Narrow	A	0	Active	9	12
Pancreatitis haemorrhagic	10033650	PT	Narrow	A	0	Active	9	12
Papillary muscle haemorrhage	10059164	PT	Narrow	A	0	Active	9	12
Paranasal sinus haematoma	10069702	PT	Narrow	A	0	Active	13	13
Parathyroid haemorrhage	10059051	PT	Narrow	A	0	Active	9	12
Parotid gland haemorrhage	10051166	PT	Narrow	A	0	Active	9	12
Pelvic haematoma	10054974	PT	Narrow	A	0	Active	9	12
Pelvic haematoma obstetric	10034248	PT	Narrow	A	0	Active	9	12
Pelvic haemorrhage	10063678	PT	Narrow	A	0	Active	9	12
Penile haemorrhage	10034305	PT	Narrow	A	0	Active	9	12
Peptic ulcer haemorrhage	10034344	PT	Narrow	A	0	Active	9	12
Pericardial haemorrhage	10034476	PT	Narrow	A	0	Active	9	12

Name	Code	Level	Scope	Cate-gory	Weight	Status	Add. Ver.	Last Mod. Ver.
Perineal haematoma	10034520	PT	Narrow	A	0	Active	9	12
Periorbital haematoma	10034544	PT	Narrow	A	0	Active	9	12
Perirenal haematoma	10049450	PT	Narrow	A	0	Active	9	12
Peritoneal haematoma	10058095	PT	Narrow	A	0	Active	9	12
Peritoneal haemorrhage	10034666	PT	Narrow	A	0	Active	9	12
Petechiae	10034754	PT	Narrow	A	0	Active	9	12
Pharyngeal haematoma	10068121	PT	Narrow	A	0	Active	11	12
Pharyngeal haemorrhage	10034827	PT	Narrow	A	0	Active	9	12
Pituitary haemorrhage	10049760	PT	Narrow	A	0	Active	9	12
Placenta praevia haemorrhage	10035121	PT	Narrow	A	0	Active	9	12
Pleural haemorrhage	10035601	PT	Narrow	A	0	Active	9	12
Polymenorrhagia	10064050	PT	Narrow	A	0	Active	9	12
Post abortion haemorrhage	10036246	PT	Narrow	A	0	Active	9	12
Post procedural haematoma	10063188	PT	Narrow	A	0	Active	9	12
Post procedural haematuria	10066225	PT	Narrow	A	0	Active	9.1	12
Post procedural haemorrhage	10051077	PT	Narrow	A	0	Active	9	12
Postmenopausal haemorrhage	10055870	PT	Narrow	A	0	Active	9	12
Postpartum haemorrhage	10036417	PT	Narrow	A	0	Active	9	12
Premature separation of placenta	10036608	PT	Narrow	A	0	Active	9	12
Proctitis haemorrhagic	10036778	PT	Narrow	A	0	Active	9	12
Prostatic haemorrhage	10036960	PT	Narrow	A	0	Active	9	12
Pulmonary alveolar haemorrhage	10037313	PT	Narrow	A	0	Active	9	12
Pulmonary haematoma	10054991	PT	Narrow	A	0	Active	9	12
Pulmonary haemorrhage	10037394	PT	Narrow	A	0	Active	9	12
Puncture site haemorrhage	10051101	PT	Narrow	A	0	Active	9	12
Purpura	10037549	PT	Narrow	A	0	Active	9	12
Purpura neonatal	10037557	PT	Narrow	A	0	Active	9	12
Purpura senile	10037560	PT	Narrow	A	0	Active	9	12
Putamen haemorrhage	10058940	PT	Narrow	A	0	Active	9	12
Rectal haemorrhage	10038063	PT	Narrow	A	0	Active	9	12
Rectal ulcer haemorrhage	10038081	PT	Narrow	A	0	Active	9	12
Renal cyst haemorrhage	10059846	PT	Narrow	A	0	Active	9	13
Renal haematoma	10038459	PT	Narrow	A	0	Active	9	12
Renal haemorrhage	10038460	PT	Narrow	A	0	Active	9	12
Respiratory tract haemorrhage	10038727	PT	Narrow	A	0	Active	9	12
Respiratory tract haemorrhage neonatal	10038728	PT	Narrow	A	0	Active	9	12
Retinal haemorrhage	10038867	PT	Narrow	A	0	Active	9	12
Retinopathy haemorrhagic	10051447	PT	Narrow	A	0	Active	9	12
Retroperitoneal haematoma	10058360	PT	Narrow	A	0	Active	9	12
Retroperitoneal haemorrhage	10038980	PT	Narrow	A	0	Active	9	12
Retroplacental haematoma	10054798	PT	Narrow	A	0	Active	9	12
Ruptured cerebral aneurysm	10039330	PT	Narrow	A	0	Active	9	12
Scleral haemorrhage	10050508	PT	Narrow	A	0	Active	9	12
Scrotal haematocoele	10061517	PT	Narrow	A	0	Active	9	12
Scrotal haematoma	10039749	PT	Narrow	A	0	Active	9	12

Name	Code	Level	Scope	Cate-gory	Weight	Status	Add. Ver.	Last Mod. Ver.
Shock haemorrhagic	10049771	PT	Narrow	A	0	Active	9	12
Skin haemorrhage	10064265	PT	Narrow	A	0	Active	9	12
Skin ulcer haemorrhage	10050377	PT	Narrow	A	0	Active	9	12
Small intestinal haemorrhage	10052535	PT	Narrow	A	0	Active	9	12
Small intestinal ulcer haemorrhage	10061550	PT	Narrow	A	0	Active	9	12
Soft tissue haemorrhage	10051297	PT	Narrow	A	0	Active	9	12
Spermatic cord haemorrhage	10065742	PT	Narrow	A	0	Active	9	12
Spinal cord haemorrhage	10048992	PT	Narrow	A	0	Active	9	12
Spinal epidural haemorrhage	10049236	PT	Narrow	A	0	Active	9	12
Spinal haematoma	10048464	PT	Narrow	A	0	Active	9	12
Splenic haematoma	10041646	PT	Narrow	A	0	Active	9	12
Splenic haemorrhage	10041647	PT	Narrow	A	0	Active	9	12
Splenic varices haemorrhage	10068662	PT	Narrow	A	0	Active	11.1	12
Splinter haemorrhages	10041663	PT	Narrow	A	0	Active	9	12
Spontaneous haematoma	10065304	PT	Narrow	A	0	Active	9	12
Stomatitis haemorrhagic	10042132	PT	Narrow	A	0	Active	9	12
Subarachnoid haemorrhage	10042316	PT	Narrow	A	0	Active	9	12
Subarachnoid haemorrhage neonatal	10042317	PT	Narrow	A	0	Active	9	12
Subcutaneous haematoma	10042345	PT	Narrow	A	0	Active	9	12
Subdural haematoma	10042361	PT	Narrow	A	0	Active	9	12
Subdural haematoma evacuation	10042363	PT	Narrow	A	0	Active	9	12
Subdural haemorrhage	10042364	PT	Narrow	A	0	Active	9	12
Subdural haemorrhage neonatal	10042365	PT	Narrow	A	0	Active	9	12
Subgaleal haematoma	10069510	PT	Narrow	A	0	Active	12.1	12.1
Testicular haemorrhage	10051877	PT	Narrow	A	0	Active	9	12
Thalamus haemorrhage	10058939	PT	Narrow	A	0	Active	9	12
Third stage postpartum haemorrhage	10043449	PT	Narrow	A	0	Active	9	12
Thoracic haemorrhage	10062744	PT	Narrow	A	0	Active	9	12
Thrombocytopenic purpura	10043561	PT	Narrow	A	0	Active	9	12
Thrombotic thrombocytopenic purpura	10043648	PT	Narrow	A	0	Active	9	12
Thyroid haemorrhage	10064224	PT	Narrow	A	0	Active	9	12
Tongue haematoma	10043959	PT	Narrow	A	0	Active	9	12
Tongue haemorrhage	10049870	PT	Narrow	A	0	Active	9	12
Tonsillar haemorrhage	10057450	PT	Narrow	A	0	Active	9	12
Tooth socket haemorrhage	10064946	PT	Narrow	A	0	Active	9	12
Tracheal haemorrhage	10062543	PT	Narrow	A	0	Active	9	12
Traumatic haematoma	10044522	PT	Narrow	A	0	Active	9	12
Traumatic haemorrhage	10053476	PT	Narrow	A	0	Active	9	12
Traumatic intracranial haemorrhage	10061387	PT	Narrow	A	0	Active	9	12
Tumour haemorrhage	10049750	PT	Narrow	A	0	Active	9	12
Ulcer haemorrhage	10061577	PT	Narrow	A	0	Active	9	12
Umbilical cord haemorrhage	10064534	PT	Narrow	A	0	Active	9	12
Umbilical haematoma	10068712	PT	Narrow	A	0	Active	11.1	12
Umbilical haemorrhage	10045455	PT	Narrow	A	0	Active	9	12
Upper gastrointestinal haemorrhage	10046274	PT	Narrow	A	0	Active	9	12

Name	Code	Level	Scope	Cate-gory	Weight	Status	Add. Ver.	Last Mod. Ver.
Ureteric haemorrhage	10065743	PT	Narrow	A	0	Active	9	12
Urethral haemorrhage	10049710	PT	Narrow	A	0	Active	9	12
Urinary bladder haemorrhage	10046528	PT	Narrow	A	0	Active	9	12
Urogenital haemorrhage	10050058	PT	Narrow	A	0	Active	9	12
Uterine haematoma	10063875	PT	Narrow	A	0	Active	9	12
Uterine haemorrhage	10046788	PT	Narrow	A	0	Active	9	12
Vaccination site haematoma	10069472	PT	Narrow	A	0	Active	12.1	12.1
Vaccination site haemorrhage	10069475	PT	Narrow	A	0	Active	12.1	12.1
Vaginal haematoma	10046909	PT	Narrow	A	0	Active	9	12
Vaginal haemorrhage	10046910	PT	Narrow	A	0	Active	9	12
Varicose vein ruptured	10046999	PT	Narrow	A	0	Active	9	12
Vascular pseudoaneurysm ruptured	10053949	PT	Narrow	A	0	Active	9	12
Vascular purpura	10047097	PT	Narrow	A	0	Active	9	12
Vascular rupture	10053649	PT	Narrow	A	0	Active	9	12
Venous haemorrhage	10065441	PT	Narrow	A	0	Active	9	12
Ventricle rupture	10047279	PT	Narrow	A	0	Active	13	13
Vessel puncture site haematoma	10065902	PT	Narrow	A	0	Active	9	12
Vessel puncture site haemorrhage	10054092	PT	Narrow	A	0	Active	9	12
Vitreous haemorrhage	10047655	PT	Narrow	A	0	Active	9	12
Vulval haematoma	10047756	PT	Narrow	A	0	Active	9	12
Vulval haematoma evacuation	10047757	PT	Narrow	A	0	Active	9	12
Vulval haemorrhage	10063816	PT	Narrow	A	0	Active	9	12
Wound haemorrhage	10051373	PT	Narrow	A	0	Active	9	12

APPENDIX B. SHELLS FOR POST-TEXT TABLES

Shells for post-text tables are presented starting from next page.

PROTOCOL: INCB 18424-258 (Page 1 of 3)
DRUG/INDICATION: Ruxolitinib/Myelofibrosis VERSION: Final

Table 14.1.1

Summary of Subject Enrollment and Exit Status
(Population: Safety Evaluable Subjects)

Variable	Ruxolitinib (N=xxx)
Number (%) of Subjects Completed Treatment Phase	xxx (xx.x)
Number (%) of Subjects Entered Extension Phase	xxx (xx.x)
Number (%) of Subjects Still on Study	xxx (xx.x)
Number (%) of Subjects Discontinued During Treatment Phase	xxx (xx.x)
Primary Reason of Discontinuation: Treatment Phase	
Death	xxx (xx.x)
Adverse Event	xxx (xx.x)
Consent Withdrawn	xxx (xx.x)
Protocol Deviation	xxx (xx.x)
Disease Progression	xxx (xx.x)
Lost to Follow-up	xxx (xx.x)
Non-Compliance with Study Medication	xxx (xx.x)
Non-Compliance with Study Procedures	xxx (xx.x)
Termination of the Clinical Trial by the Sponsor	xxx (xx.x)
Other	xxx (xx.x)

PROGRAM\OUTPUT: T_DISP.SAS\T_TERM1.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.2.1.1

PROTOCOL: INCB 18424-258 (Page 2 of 3)
DRUG/INDICATION: Ruxolitinib/Myelofibrosis VERSION: Final

Table 14.1.1

Summary of Subject Enrollment and Exit Status
(Population: Safety Evaluable Subjects)

Variable	Ruxolitinib (N=xxx)
Number (%) of Subjects Discontinued During Extension Phase	xxx (xx.x)
Primary Reason of Discontinuation: Extension Phase	
Death	xxx (xx.x)
Adverse Event	xxx (xx.x)
Consent Withdrawn	xxx (xx.x)
Protocol Deviation	xxx (xx.x)
Disease Progression	xxx (xx.x)
Lost to Follow-up	xxx (xx.x)
Non-Compliance with Study Medication	xxx (xx.x)
Non-Compliance with Study Procedures	xxx (xx.x)
Termination of the Clinical Trial by the Sponsor	xxx (xx.x)
Other	xxx (xx.x)

PROGRAM\OUTPUT: T_DISP.SAS\T_TERM1.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.2.1.1

PROTOCOL: INCB 18424-258 (Page 3 of 3)
DRUG/INDICATION: Ruxolitinib/Myelofibrosis VERSION: Final

Table 14.1.1

Summary of Subject Enrollment and Exit Status
(Population: Safety Evaluable Subjects)

Variable	Ruxolitinib (N=xxx)
Number (%) of Subjects Discontinued During the Study	xxx (xx.x)
Primary Reason of Discontinuation: Extension Phase	
Death	xxx (xx.x)
Adverse Event	xxx (xx.x)
Consent Withdrawn	xxx (xx.x)
Protocol Deviation	xxx (xx.x)
Disease Progression	xxx (xx.x)
Lost to Follow-up	xxx (xx.x)
Non-Compliance with Study Medication	xxx (xx.x)
Non-Compliance with Study Procedures	xxx (xx.x)
Termination of the Clinical Trial by the Sponsor	xxx (xx.x)
Other	xxx (xx.x)

PROGRAM\OUTPUT: T_DISP.SAS\T_TERM1.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listing 16.2.1.1

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DRUG/INDICATION: Ruxolitinib/Myelofibrosis VERSION: Final

Table 14.1.2

Summary of Demographics
(Population: Safety Evaluable Subjects)

Variable	Ruxolitinib (N=xxx)
Age (yrs)	
n	xxx
Mean	xx.x
STD	x.xx
Min	xx.x
Median	xx.x
Max	xx.x
<=65 years	xxx (xx.x)
>65 years	xxx (xx.x)
Gender - n (%)	
Male	xxx (xx.x)
Female	xxx (xx.x)
Ethnicity - n (%)	
Hispanic or Latino	xxx (xx.x)
Not Hispanic or Latino	xxx (xx.x)
Race - n (%)	
Black or African American	xxx (xx.x)
White	xxx (xx.x)
Asian	xxx (xx.x)
Native Hawaiian or Pacific Islander	xxx (xx.x)
American-Indian or Alaska Native	xxx (xx.x)
Other	xxx (xx.x)

PROGRAM\OUTPUT: T_DEMOG.SAS\T_DEMOG1.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listings 16.2.4.1

PROTOCOL: INCB 18424-258 (Page 2 of 4)
DRUG/INDICATION: Ruxolitinib/Myelofibrosis VERSION: Final

Table 14.1.2

Summary of Demographics
(Population: Safety Evaluable Subjects)

Variable	Treatment Group Ruxolitinib (N=xxx)
Height at Screening (cm)	
n	xxx
Mean	xx.x
STD	x.xx
Min	xx.x
Median	xx.x
Max	xx.x
Height of Males at Screening (cm)	
n	xxx
Mean	xx.x
STD	x.xx
Min	xx.x
Median	xx.x
Max	xx.x
Height of Females at Screening (cm)	
n	xxx
Mean	xx.x
STD	x.xx
Min	xx.x
Median	xx.x
Max	xx.x

PROGRAM\OUTPUT: T_DEMOG.SAS\T_DEMOG1.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listings 16.2.4.1

PROTOCOL: INCB 18424-258 (Page 3 of 4)
DRUG/INDICATION: Ruxolitinib/Myelofibrosis VERSION: Final

Table 14.1.2

Summary of Demographics
(Population: Safety Evaluable Subjects)

Variable	Treatment Group Ruxolitinib (N=xxx)
Weight at Screening (kg)	
n	xxx
Mean	xx.x
STD	x.xx
Min	xx.x
Median	xx.x
Max	xx.x
Weight of Males at Screening (kg)	
n	xxx
Mean	xx.x
STD	x.xx
Min	xx.x
Median	xx.x
Max	xx.x
Weight of Females at Screening (kg)	
n	xxx
Mean	xx.x
STD	x.xx
Min	xx.x
Median	xx.x
Max	xx.x

PROGRAM\OUTPUT: T_DEMOG.SAS\T_DEMOG1.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listings 16.2.4.1

PROTOCOL: INCB 18424-258 (Page 4 of 4)
DRUG/INDICATION: Ruxolitinib/Myelofibrosis VERSION: Final

Table 14.1.2

Summary of Demographics
(Population: Safety Evaluable Subjects)

Variable	Treatment Group Ruxolitinib (N=xxx)
BMI (kg/m^2)	
n	xxx
Mean	xx.x
STD	x.xx
Min	xx.x
Median	xx.x
Max	xx.x
Resting Systolic Blood Pressure at Screening (mmHg)	
n	xxx
Mean	xx.x
STD	x.xx
Min	xx.x
Median	xx.x
Max	xx.x
Resting Diastolic Blood Pressure at Screening (mmHg)	
n	xxx
Mean	xx.x
STD	x.xx
Min	xx.x
Median	xx.x
Max	xx.x

PROGRAM\OUTPUT: T_DEMOG.SAS\T_DEMOG1.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listings 16.2.4.1

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DRUG/INDICATION: Ruxolitinib/Myelofibrosis VERSION: Final

Table 14.1.3

Summary of Baseline Characteristics
(Population: Safety Evaluable Subjects)

Footnote Page

PROGRAM\OUTPUT: T_DEMOG.SAS\T_DISEASE1.LST DATE(TIME): DDMMMYY(HH:MM)

Note: Baseline = the last measurement prior to 1st dose of study medication.
[1] Year since initial diagnosis = (first dose date - diagnosis date + 1)/365.25.
In case of partial date, first month of the year and/or first day of the month were used where applicable.
[2] ECOG Status: 0=Fully active, able to carry on all pre-disease performance without restriction
1=Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature
2=Ambulatory and capable of all selfcare but unable to carry out any work activities Up and about more than 50% of waking hours
3=Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4=Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5=Dead
Reference: Listings 16.2.4.1 and 16.2.4.2.2

PROTOCOL: INCB 18424-258 (Page 2 of 9)
DRUG/INDICATION: Ruxolitinib/Myelofibrosis VERSION: Final

Table 14.1.3

Summary of Baseline Characteristics
(Population: Safety Evaluable Subjects)

Variable	Ruxolitinib (N=xxx)
Tumor Type - n (%)	
Primary Myelofibrosis	xxx (xx.x)
Post Polycythemia Vera Myelofibrosis	xxx (xx.x)
Post Essential Thrombocythemia Myelofibrosis	xxx (xx.x
Time (year) Since Initial Diagnosis [1]	
n	xxx
Mean	x.x
STD	x.xx
Min	x.x
Median	x.x
Max	xx.x
With History Blood Component Transfusion - n (%)	
Yes	xxx (xx.x)
Previous Hydroxyurea Use (HU) - n (%)	
Yes	xxx (xx.x)

Table 14.1.3

Summary of Baseline Characteristics
(Population: Safety Evaluable Subjects)

Variable	Ruxolitinib (N=xxx)
Fibrosis Grade at Baseline - n (%) [2]	
0	xxx (xx.x)
1	xxx (xx.x)
2	xxx (xx.x)
3	xxx (xx.x)
Platelets at Baseline (GI/L)	
n	xxx
Mean	xxx.x
STD	xxx.xx
Min	xx.x
Median	xxx.x
Max	xxx.x
Hemoglobin at Baseline (G/L)	
n	xxx
Mean	xxx.x
STD	xxx.xx
Min	xx.x
Median	xxx.x
Max	xxx.x

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DRUG/INDICATION: Ruxolitinib/Myelofibrosis VERSION: Final

Table 14.1.3

Summary of Baseline Characteristics
(Population: Safety Evaluable Subjects)

Variable	Ruxolitinib (N=xxx)
Neutrophils at Baseline (GI/L)	
n	xxx
Mean	xxx.x
STD	xxx.xx
Min	xx.x
Median	xxx.x
Max	xxx.x
Leukocytes at Baseline (GI/L)	
n	xxx
Mean	xxx.x
STD	xxx.xx
Min	xx.x
Median	xxx.x
Max	xxx.x
Total Cholesterol at Baseline (MMOL/L)	
n	xxx
Mean	xxx.x
STD	xxx.xx
Min	xx.x
Median	xxx.x
Max	xxx.x

PROTOCOL: INCB 18424-258 (Page 5 of 9)
DRUG/INDICATION: Ruxolitinib/Myelofibrosis VERSION: Final

Table 14.1.3

Summary of Baseline Characteristics
(Population: Safety Evaluable Subjects)

Variable	Ruxolitinib (N=xxx)
Creatinine at Baseline (UMOL/L)	
n	xxx
Mean	xxx.x
STD	xxx.xx
Min	xx.x
Median	xxx.x
Max	xxx.x
Aspartate Aminotransferase at Baseline (U/L)	
n	xxx
Mean	xxx.x
STD	xxx.xx
Min	xx.x
Median	xxx.x
Max	xxx.x
Alanine Aminotransferase at Baseline (U/L)	
n	xxx
Mean	xxx.x
STD	xxx.xx
Min	xx.x
Median	xxx.x
Max	xxx.x

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DRUG/INDICATION: Ruxolitinib/Myelofibrosis VERSION: Final

Table 14.1.3

Summary of Baseline Characteristics
(Population: Safety Evaluable Subjects)

Variable	Ruxolitinib (N=xxx)
Bilirubin at Baseline (UMOL/L)	
n	xxx
Mean	xxx.x
STD	xxx.xx
Min	xx.x
Median	xxx.x
Max	xxx.x
Calcium at Baseline (MMOL/L)	
n	xxx
Mean	xxx.x
STD	xxx.xx
Min	xx.x
Median	xxx.x
Max	xxx.x
Glucose at Baseline (MMOL/L)	
n	xxx
Mean	xxx.x
STD	xxx.xx
Min	xx.x
Median	xxx.x
Max	xxx.x

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DRUG/INDICATION: Ruxolitinib/Myelofibrosis VERSION: Final

Table 14.1.3

Summary of Baseline Characteristics
(Population: Safety Evaluable Subjects)

Variable	Ruxolitinib (N=xxx)
Potassium at Baseline (MMOL/L)	
n	xxx
Mean	xxx.x
STD	xxx.xx
Min	xx.x
Median	xxx.x
Max	xxx.x
Sodium at Baseline (MMOL/L)	
n	xxx
Mean	xxx.x
STD	xxx.xx
Min	xx.x
Median	xxx.x
Max	xxx.x
DIPSS Score	
HIGH RISK (5-6)	xxx (xx.x)
INTERMEDIATE-2 (3-4)	xxx (xx.x)

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Table 14.1.3

Summary of Baseline Characteristics
(Population: Safety Evaluable Subjects)

Variable	Ruxolitinib (N=xxx)
Spleen Volume at Baseline (cm^3)	
n	xxx
Mean	xxx.x
STD	xxx.xx
Min	xx.x
Median	xxx.x
Max	xxx.x
Spleen Palpation Length at Baseline (cm)	
n	xxx
Mean	xxx.x
STD	xxx.xx
Min	xx.x
Median	xxx.x
Max	xxx.x
Total Symptom Score at Baseline	
n	xxx
Mean	xxx.x
STD	xxx.xx
Min	xx.x
Median	xxx.x
Max	xxx.x

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DRUG/INDICATION: Ruxolitinib/Myelofibrosis VERSION: Final

Table 14.1.3

Summary of Baseline Characteristics
(Population: Safety Evaluable Subjects)

Variable	Ruxolitinib (N=xxx)
ECOG at Baseline [3]	
0	xxx (xx.x)
1	xxx (xx.x)
2	xxx (xx.x)
3	xxx (xx.x)
4	xxx (xx.x)
Percent [redacted] at Baseline	
Yes	xxx (xx.x)
No	xxx (xx.x)
Missing	xxx (xx.x)

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Table 14.1.4

Summary of Medical History by MedDRA System Organ Class and Preferred Term
(Population: Safety Evaluable Subjects)

MedDRA System Organ Class Preferred Term	Ruxolitinib (N=xxx)
Subjects With Any Medical History	xxx (xxx.x)
SOC 1	xxx (xxx.x)
Preferred Term 1	xxx (xxx.x)
. . . .	

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

Reference: Listings 16.2.4.2.1

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Table 14.1.5.1

Summary of Prior Medications
(Population: Safety Evaluable Subjects)

ATC Class/WHO Preferred Term	Ruxolitinib (N=xxx)
Subjects With Any Prior Medications	xxx (xxx.x)
WHO Drug Class 1	xxx (xxx.x)
WHO Preferred Term 1	xxx (xxx.x)
WHO Preferred Term 2	xxx (xxx.x)
WHO Preferred Term 3	xxx (xxx.x)
WHO Preferred Term 4	xxx (xxx.x)
WHO Drug Class 2	xxx (xxx.x)
WHO Preferred Term 1	xxx (xxx.x)
WHO Preferred Term 2	xxx (xxx.x)
WHO Preferred Term 3	xxx (xxx.x)
WHO Preferred Term 4	xxx (xxx.x)

PROGRAM\OUTPUT: T_DEMOG.SAS\T_DEMOG1.LST DATE(TIME): DDMMMYY(HH:MM)

Reference: Listings 16.2.4.3

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Table 14.1.5.2

Summary of Concomitant Medications
(Population: Safety Evaluable Subjects)

NOTE TO THE PROGRAMMER: THIS TABLE WILL BE SIMILARLY PROGRAMMED AS Table 14.1.5.1

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Table 14.1.5.3

Summary of Prior Anti-Cancer Treatment
(Population: Safety Evaluable Subjects)

NOTE TO THE PROGRAMMER: THIS TABLE WILL BE SIMILARLY PROGRAMMED AS Table 14.1.5.1

- Reference: Listing 16.2.4.5

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Table 14.1.6.1

Summary of Change in Status of Blood Component Transfusion Dependency by Baseline Platelet Count Group
(Population: Safety Evaluable Subjects)

Pattern of Change in Dependency Status	Time Interval	Baseline Platelet Count Group: 50-75 GI/L N	50-75 GI/L n (%)	>75 GI/L N	>75 GI/L n (%)	Total N	Total n (%)
Depend. to Indep.	8 Weeks before Day 1 to Final 8 Weeks	xx	xx(xx.x)	xx	xx (xx.x)	xx	xx (xx.x)
	12 Weeks before Day 1 to Final 12 Weeks	xx	xx(xx.x)	xx	xx (xx.x)	xx	xx (xx.x)
Indep. to Depend.	8 Weeks before Day 1 to Final 8 Weeks	xx	xx(xx.x)	xx	xx (xx.x)	xx	xx (xx.x)
	12 Weeks before Day 1 to Final 12 Weeks	xx	xx(xx.x)	xx	xx (xx.x)	xx	xx (xx.x)

PROGRAM\OUTPUT: T_xxxxx.SAS\T_xxxx.LST DATE(TIME): ddmmmyyyy(hh:mm)

Note 1: N = # subjects at the beginning of the first interval, and n (%) = # (%) subjects at the end of the second interval. The first interval covered within 8 (or 12) weeks prior to Day 1, and the second interval covered last 8 (or 12) weeks after Day 1. Percents are calculated as n/N*100 for each row of each group.
Note 2: Transfusion dependence is defined as subjects received at least 1 unit of red blood cell product(s) during the given period. Independence is defined as subjects received 0 unit of red blood cell product(s) during the given period.
Reference: xxxx

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Table 14.1.6.2

Summary of Blood Component Transfusions by Baseline Platelet Count Group
(Population: Safety Evaluable Subjects)

	Baseline Platelet Count Group		
Variable	50-75 GI/L (N = xx)	> 75 GI/L (N = xx)	Total (N =xx)
Monthly Units of RBC Transfusion: Baseline			
n			
Mean (Std)			
Median			
Min, Max			
Total Units of RBC Transfusion: Post-Baseline			
n			
Mean (Std)			
Median			
Min, Max			
Monthly Units of RBC Transfusion: Post-Baseline			
n			
Mean (Std)			
Median			
Min, Max			

PROGRAM\OUTPUT: T_xxxxx.SAS\T_xxxx.LST DATE(TIME): ddmmmyyyy(hh:mm)

Note 1: Total units = all units during the treatment phase from Day 1 to the last scheduled visit.
Note 2: Monthly units = total units divided by the treatment duration (in months where 1 month = 30.4375 days).
Reference: Listing xxxxx.

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Table 14.2.1.1

Summary of Correlation of Final Titrated Dose vs. Percent Change from Baseline in Spleen Volume at Week 24
and vs. Percent Change in Total Symptom Score at Week 24
(Population: ITT Subjects)

Variable	Ruxolitinib (N=xxx)
Dose vs. % Chg in Spleen Volume	
Sample size, n	xxx
Pearson correlation coefficient – raw value	x.xxx
p-value from t-test	0.xxx
Estimated corr coeff – Fisher transformation (95% CI)	x.xxx (x.xxx, x.xxx)
Dose vs. % Chg in Total Symptom Score	
Sample size, n	xxx
Pearson correlation coefficient – raw value	x.xxx
p-value from t-test	0.xxx
Estimated corr coeff – Fisher transformation (95% CI)	x.xxx (x.xxx, x.xxx)

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

Note: t-test was based on the raw Pearson correlation coefficient; and 95% confidence interval is based on the Approximation from Fisher's r-to-z transformation.
Reference: Listings 16.2.6.

NOTE TO THE TEAM: if protocol is further amended, we should consistently specify p-value and 95% CI calculation, that they all come from Fisher r-to-z transformation.

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Table 14.2.1.2

Summary of Correlation of Final Titrated Dose vs. Percent Change from Baseline in Spleen Volume at Week 24 and vs. Percent Change in Total Symptom Score at Week 24: Sensitivity Analysis 1
(Population: Per-Protocol Subjects)

NOTE TO THE PROGRAMMER: this table will be similarly programmed as 14.2.1.1.

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Table 14.2.1.3

Summary of Correlation of Final Titrated Dose vs. Percent Change from Baseline in Spleen Volume at Week 24 and vs. Percent Change in Total Symptom Score at Week 24: Sensitivity Analysis 2
(Population: ITT Subjects)

NOTE TO THE PROGRAMMER: this table will be similarly programmed as 14.2.1.1.

- Footnote need to add MI model and procedure for this sensitivity analysis.

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Table 14.2.2.1

Summary of Spleen Volume (cm^3) by Study Week and Final Titrated Dose Group
(Population: ITT Subjects)

Study Week Variable	Total (N=xxx)	Ruxolitinib Final Titrated Dose (mg) Group: < 5 (N=xx)	>5 to 15 (N=xx)	>15 to 25 (N=xx)	>25 (N=xx)
Baseline					
n	xxx	xx	xx	xx	xx
Mean	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Std	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx
Median	xxxx.x	xxxxx.x	xxxx.x	xxxx.x	xxxx.x
Min, Max	(xxxx.x, xxxx.x)	(xxxx.x, xxxx.x)	(xxxx.x, xxxx.x)	(xxxx.x, xxxx.x)	(xxxx.x, xxxx.x)
Week 24: raw					
n	xxx	xx	xx	xx	xx
Mean	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Std	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx
Median	xxxx.x	xxxxx.x	xxxx.x	xxxx.x	xxxx.x
Min, Max	(xxxx.x, xxxx.x)	(xxxx.x, xxxx.x)	(xxxx.x, xxxx.x)	(xxxx.x, xxxx.x)	(xxxx.x, xxxx.x)

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

Reference: Listing 16.2.6.

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DRUG/INDICATION: Ruxolitinib/Myelofibrosis VERSION: Final

Table 14.2.2.1

Summary of Spleen Volume (cm^3) by Study Week and Final Titrated Dose Group
(Population: ITT Subjects)

Study Week Variable	Total (N=xxx)	Ruxolitinib Final Titrated Dose (mg) Group < 5 (N=xx)	 >5 to 15 (N=xx)	 >15 to 25 (N=xx)	 >25 (N=xx)
Week 24: Chg from Baseline					
n	xxx	xx	xx	xx	xx
Mean	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Std	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx
Median	xxxx.x	xxxxx.x	xxxx.x	xxxx.x	xxxx.x
Min, Max	(xxxx.x, xxxx.x)	(xxxx.x, xxxx.x)	(xxxx.x, xxxx.x)	(xxxx.x, xxxx.x)	(xxxx.x, xxxx.x)
p-value from t-test	0.xxxx	0.xxxx	0.xxxx	0.xxxx	0.xxxx
p-value from WRS-test	0.xxxx	0.xxxx	0.xxxx	0.xxxx	0.xxxx
Week 24: %Chg from Baseline					
n	xxx	xx	xx	xx	xx
Mean	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Std	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx
Median	xxxx.x	xxxxx.x	xxxx.x	xxxx.x	xxxx.x
Min, Max	(xxxx.x, xxxx.x)	(xxxx.x, xxxx.x)	(xxxx.x, xxxx.x)	(xxxx.x, xxxx.x)	(xxxx.x, xxxx.x)
p-value from t-test	0.xxxx	0.xxxx	0.xxxx	0.xxxx	0.xxxx
p-value from WRS-test	0.xxxx	0.xxxx	0.xxxx	0.xxxx	0.xxxx

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

Reference: Listing 16.2.6.

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DRUG/INDICATION: Ruxolitinib/Myelofibrosis VERSION: Final

Table 14.2.2.2

Summary of Proportion of Subjects with >= 35% Reduction from Baseline in Spleen Volume at Week 24
by Final Titrated Dose Group
(Population: ITT Subjects)

		Ruxolitinib Final Titrated Dose (mg) Group			
Study Week Variable	Total (N=xxx)	< 5 (N=xx)	>5 to 15 (N=xx)	>15 to 25 (N=xx)	>25 (N=xx)
Week 24: Reduction of >= 35% from Baseline - n (%)					
No	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Yes	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
95% CI for response rate [1]	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
Reasons for not Achieving the reduction of >= 35% - n (%)					
Discontinued prior to Week 24	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Data missing/out of window	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

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

[1]: 95% CI is from exact binomial distribution.
Reference: Listing 16.2.6.

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Table 14.2.2.3

Summary of Proportion of Subjects with >= 10% Reduction from Baseline in Spleen Volume at Week 24
by Final Titrated Dose Group
(Population: ITT Subjects)

NOTE TO THE PROGRAMMER: this table will be programmed similarly to Table 14.2.2.2.

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Table 14.2.3.1

Summary of Total Symptom Score by Study Week and Final Titrated Dose Group
(Population: ITT Subjects)

NOTE TO THE PROGRAMMER: this table will be programmed similarly to Table 14.2.2.1 but Study Weeks will be 0, 4, 8, 12, 16, 20, 24.

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Table 14.2.3.2

Summary of Proportion of Subjects with >= 50% Reduction from Baseline in Total Symptom Score
by Study Week and Final Titrated Dose Group
(Population: ITT Subjects)

NOTE TO THE PROGRAMMER: this table will be similarly program as Table 14.2.2.2 but will not derive/display reason of not achieving a response.

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[redacted]

NOTE TO THE PROGRAMMER: this table will be similarly program as Table 14.2.2.2 but will not derive/display reason of not achieving a response.

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Table 14.2.4.1

Summary of Spleen Palpation Length Data by Study Week and Final Titrated Dose Group
(Population: ITT Subjects)

NOTE TO THE PROGRAMMER: this table will be programmed similarly to Table 14.2.2.1 but Study Weeks will be the nominal weeks where spleen length data are scheduled to be collected.

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Table 14.2.4.2

Summary of Proportion of Subjects with >= 50% Reduction from Baseline in Spleen Palpation Length
by Study Week and Final Titrated Dose Group
(Population: ITT Subjects)

NOTE TO THE PROGRAMMER: this table will be similarly program as Table 14.2.2.2 but will not derive/display reason of not achieving a response.

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Table 14.2.4.3

Summary of Proportion of Subjects with >= 20% Reduction from Baseline in Spleen Palpation Length
by Study Week and Final Titrated Dose Group
(Population: ITT Subjects)

NOTE TO THE PROGRAMMER: this table will be similarly program as Table 14.2.2.2 but will not derive/display reason of not achieving a response.

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Table 14.2.5.1

Summary of Patient Global Impression of Change Score by Study Week and Final Titrated Dose Group
(Population: ITT Subjects)

NOTE TO THE PROGRAMMER: this table will be similarly program as Table 14.2.2.1 but no change and percent change will be derived.

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[redacted]

NOTE TO THE PROGRAMMER: this table will be similarly program as Table 14.2.2.1.

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[redacted]

NOTE TO THE PROGRAMMER: this table will be similarly program as Table 14.2.2.1.

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Table 14.3.1.1

Summary of Exposure and Duration of Exposure to Study Medication Through Week 24 by Final Titrate Dose Level
(Population: Safety Evaluable Subjects)

		Ruxolitinib Final Titrated Dose (mg)			
Variable	Total (N=xxx)	< 5 (N=xx)	>5 to 15 (N=xx)	>15 to 25 (N=xx)	>25 (N=xx)
Duration of Treatment (weeks) [1]					
n	xxx	xx	xx	xx	xx
Mean	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Std	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx
Median	xxxx.x	xxxxx.x	xxxx.x	xxxx.x	xxxx.x
Min, Max	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
<=30 Days	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
31-90 Days	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
91-120 Days	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
121-150 Days	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
>150 Days	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Patient Year [2]	x.xx	x.xx	x.xx	x.xx	x.xx

PROGRAM\OUTPUT: T_xxxx.SAS\T_xxxx.LST DATE(TIME): ddmmmyy(hh:mm)
[1] Duration of treatment is calculated as (last dose date during the treatment period – first dose date +1)/7 disregard interruptions in between.
[2] Patient year is calculated based on duration of treatment.
[3] Average daily dose is calculated as total dose (mg) divided by duration of treatment expressed in days.
[4] Overall compliance is calculated as (total # of tablets consumed)/(total # of tablets expected to be consumed)*100, where total # of tablets expected to be consumed is based on prescribed doses (including interruption) from CRF domain of EX.
Reference: Listing 16.2.7.1.1.

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Table 14.3.1.1

Summary of Exposure and Duration of Exposure to Study Medication Through Week 24 by Final Titrate Dose Level
(Population: Safety Evaluable Subjects)

		Ruxolitinib Final Titrated Dose (mg)			
Variable	Total (N=xxx)	< 5 (N=xx)	>5 to 15 (N=xx)	>15 to 25 (N=xx)	>25 (N=xx)
Average Daily Dose (mg) [3]					
n	xxx	xx	xx	xx	xx
Mean	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Std	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx
Median	xxxx.x	xxxxx.x	xxxx.x	xxxx.x	xxxx.x
Min, Max	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
Last 7 Days Average Daily Dose (mg)					
n	xxx	xx	xx	xx	xx
Mean	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Std	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx
Median	xxxx.x	xxxxx.x	xxxx.x	xxxx.x	xxxx.x
Min, Max	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)

PROGRAM\OUTPUT: T_xxxx.SAS\T_xxxx.LST DATE(TIME): ddmmmyy(hh:mm)
[1] Duration of treatment is calculated as (last dose date during the treatment period – first dose date +1)/7 disregard interruptions in between.
[2] Patient year is calculated based on duration of treatment.
[3] Average daily dose is calculated as total dose (mg) divided by duration of treatment expressed in days.
[4] Overall compliance is calculated as (total # of tablets consumed)/(total # of tablets expected to be consumed)*100, where total # of tablets expected to be consumed is based on prescribed doses (including interruption) from CRF domain of EX.
Reference: Listing 16.2.7.1.1.

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Table 14.3.1.1

Summary of Exposure and Duration of Exposure to Study Medication Through Week 24 by Final Titrate Dose Level
(Population: Safety Evaluable Subjects)

	Ruxolitinib Final Titrated Dose (mg)				
Variable	Total (N=xxx)	< 5 (N=xx)	>5 to 15 (N=xx)	>15 to 25 (N=xx)	>25 (N=xx)
Overall Compliance (%) [4]					
<=50	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
>51-80	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
>80	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

PROGRAM\OUTPUT: T_xxxx.SAS\T_xxxx.LST DATE(TIME): ddmmmyy(hh:mm)
[1] Duration of treatment is calculated as (last dose date during the treatment period – first dose date +1)/7 disregard interruptions in between.
[2] Patient year is calculated based on duration of treatment.
[3] Average daily dose is calculated as total dose (mg) divided by duration of treatment expressed in days.
[4] Overall compliance is calculated as (total # of tablets consumed)/(total # of tablets expected to be consumed)*100, where total # of tablets expected to be consumed is based on prescribed doses (including interruption) from CRF domain of EX.
Reference: Listing 16.2.7.1.1.

Table 14.3.1.2

Summary of Exposure and Duration of Exposure to Study Medication Through Week 4 by Final Titrate Dose Level
(Population: Safety Evaluable Subjects)

NOTE TO THE PROGRAMMER: this table will programmed similarly to Table 14.3.1.1 but present only average daily dose.

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Table 14.3.1.3

Summary of Average Daily Dose of Ruxolitinib by Study Week and Final Titrate Dose Level
(Population: Safety Evaluable Subjects)

		Ruxolitinib Final Titrated Dose (mg)			
Variable	Total (N=xxx)	< 5 (N=xx)	>5 to 15 (N=xx)	>15 to 25 (N=xx)	>25 (N=xx)
Average Daily Dose (mg) for Week 1					
n	xxx	xx	xx	xx	xx
Mean	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Std	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx
Median	xxxx.x	xxxxx.x	xxxx.x	xxxx.x	xxxx.x
Min, Max	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
Average Daily Dose (mg) for Week 2					
. . . .					

PROGRAM\OUTPUT: T_xxxx.SAS\T_xxxx.LST DATE(TIME): ddmmmyy(hh:mm)

Reference: Listing 16.2.7.1.1.

NOTE TO THE PROGRAMMER: Table is continued to Week 48 as long as data is available.

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Table 14.3.2.1

Overall Summary of Treatment-Emergent Adverse Events by Dose Ever Received
(Population: Safety Evaluable Subjects)

Variable	All Subjects (N=23)	Dose Level (mg) Subjects Ever Received				
		<=5 (N=2)	>5 10 (N=23)	>10 15 (N=14)	>15 20 (N=7)	>20 25 (N=1)
Treatment-Emergent Adverse Events (TEAE) Reported	33	1	8	21	3	0 (0.0)
Subjects with a TEAE	10 (43.5)	1 (50.0)	3 (13.0)	5 (35.7)	1 (14.3)	0 (0.0)
Subjects with a Treatment-Related TEAE	2 (8.7)	0 (0.0)	1 (4.3)	1 (7.1)	0 (0.0)	0 (0.0)
Subjects with a Serious TEAE	2 (8.7)	1 (50.0)	0 (0.0)	1 (7.1)	0 (0.0)	0 (0.0)
Subjects with TEAE of Grade 3 or Higher	4 (17.4)	1 (50.0)	1 (4.3)	2 (14.3)	0 (0.0)	0 (0.0)
Subjects with a Dose Increase Due to TEAE	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Subjects with a Dose Reduction Due to TEAE	1 (4.3)	0 (0.0)	0 (0.0)	1 (7.1)	0 (0.0)	0 (0.0)
Subjects with Procedures Performed Due to TEAE	2 (8.7)	0 (0.0)	0 (0.0)	2 (14.3)	0 (0.0)	0 (0.0)
Subjects with a TEAE requiring Concomitant Medication	5 (21.7)	0 (0.0)	1 (4.3)	4 (28.6)	0 (0.0)	0 (0.0)
Subjects with Study Drug Withdrawn Due to TEAE	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Subjects with an TEAE Leading to Discontinuation from the Study	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Subjects with a TEAE Leading to Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

PROGRAM\OUTPUT: T_AESUM1.SAS\T_AE1.LST DATE(TIME): 12DEC11(11:30)

Note 1:TEAEs: AEs that began or worsened from baseline following the first administration of the study drug.
Note 2:Treatment-Related AEs:TEAEs with a possible, probable, definite, or missing casuality.
Note 3:Severity vs CTCAE Grade: Mild=Grade 1, Moderate=Grade 2, Severe=Grade 3, Life-Threatening=Grade 4.
Note 4:For an AE that occurred for more than once to a subject, it is counted in the lowest dose when the highest severity grade is recorded.
Reference: Listings 16.2.7.2.1

NOTE to the reviewer: numbers in the shell is from draft DMC output and is intended to show shell only.

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Table 14.3.2.2.1

Summary of Subjects Reporting Treatment-Emergent Adverse Events (All Causalities) by
MedDRA System Organ Class, Preferred Term, and Maximum Severity
(Population: Safety Evaluable Subjects)

NOTE TO THE PROGRAMMER: shell will following the standard output.

- Reference: 16.2.7.2.1

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Table 14.3.2.2.2

Summary of Subjects Reporting Treatment-Emergent Adverse Events (All Causalities) by MedDRA System Organ Class, Preferred Term, and Dose Level Ever Received
(Population: Safety Evaluable Subjects)

Variable	All Subjects (N=23)	CTCAE Grade 0 (N=2)	>5 10 (N=23)	>10 15 (N=14)	>15 20 (N=7)	>20 25 (N=1)
Number (%) of Subjects With Any TEAEs	10 (43.5)	1 (50.0)	3 (13.0)	5 (35.7)	1 (14.3)	0 (0.0)
Blood and lymphatic system disorders	1 (4.3)	0 (0.0)	0 (0.0)	1 (7.1)	0 (0.0)	0 (0.0)
Anaemia	1 (4.3)	0 (0.0)	0 (0.0)	1 (7.1)	0 (0.0)	0 (0.0)
Gastrointestinal disorders	6 (26.1)	0 (0.0)	0 (0.0)	4 (28.6)	2 (28.6)	0 (0.0)
Abdominal pain	2 (8.7)	0 (0.0)	1 (4.3)	1 (7.1)	0 (0.0)	0 (0.0)
Anorectal discomfort	1 (4.3)	0 (0.0)	0 (0.0)	1 (7.1)	0 (0.0)	0 (0.0)
Diarrhoea	3 (13.0)	0 (0.0)	0 (0.0)	2 (14.3)	1 (14.3)	0 (0.0)
Dry mouth	1 (4.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)
Haemorrhoidal haemorrhage	1 (4.3)	0 (0.0)	0 (0.0)	1 (7.1)	0 (0.0)	0 (0.0)
Nausea	1 (4.3)	0 (0.0)	0 (0.0)	1 (7.1)	0 (0.0)	0 (0.0)
. . . . .						

PROGRAM\OUTPUT: T_AESUM1.SAS\T_AE2.LST DATE(TIME): 12DEC11(11:30)

Note 1:TEAEs: AEs that began or worsened from baseline following the first administration of the study drug.
Note 2:N=the number of subjects who ever took a dose within the dose group, based on which the percent is calculated.
Note 3:For an AE that occurred for more than once to a subject, it is counted in the lowest dose when the highest severity grade is recorded.
Reference: Listings 16.2.7.2.1

NOTE to the reviewer: numbers in the shell is from draft DMC output and is intended to show shell only.

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Table 14.3.2.3.1

Summary of Subjects Reporting Treatment-Emergent Adverse Events (All Causalities) by
MedDRA Preferred Term (Sorted by Decreasing Frequency) and Maximal Severity
(Population: Safety Evaluable Subjects)

NOTE TO THE PROGRAMMER: shell will following the standard output.

- Reference: 16.2.7.2.1

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Table 14.3.2.3.2

Summary of Subjects Reporting Treatment-Emergent Adverse Events (All Causalities) by
MedDRA Preferred Term (Sorted by Decreasing Frequency) and Dose Ever Received
(Population: Safety Evaluable Subjects)

NOTE TO THE PROGRAMMER: shell will following the standard output and table will be similarly programmed as 14.3.2.2.2.

- Reference: 16.2.7.2.1

NOTE: Shells for the following tables are not provided here but they will be programmed similarly to those presented above.

14.3.2.3.2	Summary of Subjects Reporting Treatment-Emergent Adverse Events (All Causalities) by MedDRA Preferred Term (Sorted by Decreasing Frequency) and Dose Level Ever Received	Safety
14.3.2.3.3	Summary of Subjects Reporting Treatment-Emergent Hemorrhage Adverse Events (All Causalities) by MedDRA Preferred Term and Dose Level Ever Received	Safety
14.3.2.3.4	Summary of Subjects Reporting Treatment-Emergent Hemorrhage Adverse Events (All Causalities) of Grade 3 or Higher by MedDRA Preferred Term and Dose Level Ever Received	Safety
14.3.2.4.1	Summary of Subjects Reporting Treatment-Emergent Treatment-Related Adverse Events (All Causalities) by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Safety
14.3.2.4.2	Summary of Subjects Reporting Treatment-Emergent Treatment-Related Adverse Events (All Causalities) by MedDRA System Organ Class, Preferred Term, and Dose Level Ever Received	Safety
14.3.2.5.1	Summary of Subjects Reporting Treatment-Emergent Serious Adverse Events (All Causalities) by MedDRA System Organ Class, Preferred Term, and Dose Level Ever Received	Safety
14.3.2.6	Summary of Subjects Reporting Treatment-Emergent Adverse Events (All Causalities) Leading to Study Medication Decrease or Interruption by MedDRA System Organ Class, Preferred Term, and Dose Level Ever Received	Safety
14.3.2.7	Summary of Subjects Reporting Treatment-Emergent Adverse Events (All Causalities) Leading to Study Discontinuation by MedDRA System Organ Class, Preferred Term, and Dose Level Ever Received	Safety
14.3.2.8	Summary of Subjects Reporting Treatment-Emergent Adverse Events (All Causalities) Leading to On-Study Death by MedDRA System Organ Class, Preferred Term, and Dose Level Ever Received	Safety

NOTE: the following lab tables will be programmed according to standard output.

14.3.3.1.1	Summary of Laboratory Values – Hematology	Safety
14.3.3.1.2	Shift Summary of Laboratory Values in Normal Ranges - Hematology	Safety
14.3.3.2.1	Summary of Laboratory Values – Serum Chemistry	Safety
14.3.3.2.2	Shift Summary of Laboratory Values in Normal Ranges – Serum Chemistry	Safety
14.3.3.3.1	Summary of Laboratory Values – Coagulation	Safety
14.3.3.3.2	Shift Summary of Laboratory Values in Normal Ranges – Coagulation	Safety
14.3.3.4.1	Summary of Laboratory Values – Urinalysis	Safety
14.3.3.4.2	Shift Summary of Laboratory Values in Normal Ranges – Urinalysis	Safety
14.3.3.5.1	Shift Summary of Laboratory Values in CTC Grade - To the Worst Abnormal Value (Tests with One Directional CTC Grade)	Safety
14.3.3.5.2	Shift Summary of Laboratory Values in CTC Grade - To the Worst Abnormal Value (Tests with Two Directional CTC Grade)	Safety

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Table 14.3.3.6.1

Summary of Subjects with Treatment Emergent Thrombocytopenia of Grade 4 as Derived from Laboratory Data
by Last Dose Before Onset
(Population: Safety Evaluable Subjects)

		Dose Level (mg) Subjects Ever Received					
MedDRA Preferred Term	All Subjects (N=xx)	<=5 N=xx	>5 10 N=xx	>10 15 N=xx	>15 20 N=xx	>20 25 N=xx	>25 N=xx
Number (%) of Subjects With Grade 4 Thrombocytopenia [1]	xx (xx.x)	xx xx%	xx xx%	xx xx%	xx xx%	xx xx%	xx xx%

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

Treatment-Emergent AEs: AEs that began or worsened from baseline following the first administration of study drug.
Note: Subjects are counted only once under in the lowest dose group.
Note: N=the number of subjects who ever took a dose within the dose group, based on which the percent is calculated.
Note: AEs that occurred following the date of treatment crossover were not included.
[1] Grade 4 Thrombocytopenia is defined as any occurrence of a treatment emergent hematology lab below 25 GI/L
Reference: Listing 16.2.8.1.4

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Table 14.3.3.6.2

Summary of Subjects with Treatment Emergent Anemia of Grade 4 as Derived from Laboratory Data
by Last Dose Before Onset
(Population: Safety Evaluable Subjects)

NOTE TO THE PROGRAMMER: similarly program this as Table 14.3.3.6.1, just need to update footnote about G4 anemia.

NOTE: the following vital sign tables will be programmed according to standard output.

14.3.4.1	Summary of Systolic Blood Pressure	Safety
14.3.4.2	Summary of Diastolic Blood Pressure	Safety
14.3.4.3	Summary of Heart Rate	Safety
14.3.4.4	Summary of Respiratory Rate	Safety
14.3.4.5	Summary of Body Temperature	Safety

NOTE: the following laboratory tables will be programmed according to standard output.

14.2.1.1	Scatter Plot of Percent Change from Baseline in Spleen Volume at Week 24 vs. Final Titrated Dose Level	ITT
14.2.1.2	Scatter Plot of Percent Change from Baseline in Total Symptom Score at Week 24 vs. Final Titrated Dose Level	ITT
14.2.1.3	Scatter Plot of Percent Change from Baseline in Spleen Volume vs. Percent Change in Total Symptom Score at Week 24	ITT
14.2.2.1	Bar Plot of Percent of Subjects with >= 35% Reduction from Baseline in Spleen Volume at Week 24 by Final Titrated Dose Group	ITT
14.2.2.2	Bar Plot of Percent of Subjects with >= 10% Reduction from Baseline in Spleen Volume at Week 24 by Final Titrated Dose Group	ITT
14.2.2.3.1	Mean (95%) Percent Change from Baseline in Spleen Volume at Week 24	ITT
14.2.2.3.2	Mean (95%) Percent Change from Baseline in Spleen Volume at Week 24 by Final Titrated Dose Group	ITT
14.3.1.1.1	Subject Laboratory Value over Time: Hemoglobin (G/L)	Safety
14.3.1.1.2	Mean (95% CI) Laboratory Value Over Time: Hemoglobin (G/L)	Safety
14.3.1.2.1	Subject Laboratory Value over Time: Platelet (GI/L)	Safety
14.3.1.2.2	Mean (95% CI) Laboratory Value Over Time: Platelet (GI/L)	Safety
14.3.1.3.1	Subject Laboratory Value over Time: WBC (GI/L)	Safety
14.3.1.3.2	Mean (95% CI) Laboratory Value Over Time: WBC (GI/L)	Safety
14.3.1.4.1	Subject Laboratory Value over Time: Neutrophils (GI/L)	Safety
14.3.1.4.2	Mean (95% CI) Laboratory Value Over Time: Neutrophils (GI/L)	Safety