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Statistical Analysis Plan

INCB 00928-104

A Phase 1/2 Open-Label, Multicenter Study of INCB000928 Administered as a Monotherapy or in Combination With Ruxolitinib in Participants With Anemia Due to Myeloproliferative Disorders

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SAP Author:	[redacted] [redacted]**, Biostatistics**
Date of Plan:	**17 APR 2025**

This study is being conducted in compliance with Good Clinical Practice, including the archiving of essential documents.

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LIST OF ABBREVIATIONS

Abbreviation	Term
AE	adverse event
AUC_{0-t}	area under the plasma concentration-time curve from time 0 to the last quantifiable measurable plasma concentration
BM	bone marrow
BMI	body mass index
BOIN	Bayesian optimal interval
CI	confidence interval
CR	complete response
C_{max}	maximum concentration
CRF	case report form
CSR	Clinical Study Report
CT	computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
DLT	dose-limiting toxicity
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	electronic case report form
EOT	end of treatment
FAS	full analysis set
HR	heart rate
Hgb	hemoglobin
IWG-MRT	International Working Group-Myeloproliferative Neoplasms Research and Treatment
JAK	Janus kinase
LFS	leukemia-free survival
MedDRA	Medical Dictionary for Regulatory Activities
MF	myelofibrosis
MPN-SAF	Myeloproliferative Neoplasm Symptom Assessment Form
MRI	magnetic resonance imaging
MTD	maximum tolerated dose
MUGA	multigated acquisition
NA	not applicable
NCI	National Cancer Institute
ORR	objective response rate
PD	pharmacodynamic(s)
PET-MF	post–essential thrombocythemia myelofibrosis

Abbreviation	Term
PFS	progression-free survival
PK	pharmacokinetic(s)
PMF	primary myelofibrosis
PPV-MF	post–polycythemia vera myelofibrosis
PR	partial response
pRBC	packed red blood cell
PRO	patient-reported outcome
PT	preferred term
QTcB	QT interval corrected using Bazett's formula
QTcF	QT interval corrected using Fridericia's formula
RBC	red blood cell
RDE	recommended dose for expansion
RNA	ribonucleic acid
SAE	serious adverse event
SAP	Statistical Analysis Plan
SOC	system organ class
sTfR	soluble transferrin receptor
TD	transfusion-dependent (transfusion dependency)
TEAE	treatment-emergent adverse event
TGA	Treatment Group A
TGB	Treatment Group B
TGC	Treatment Group C
TI	transfusion-independent (transfusion independency)
t_{max}	time to maximum plasma concentration
TSS	total symptom score
ULN	upper limit of normal
US	United States
WHO	World Health Organization

1. INTRODUCTION

This is a Phase 1/2, open-label, dose-finding study to evaluate the safety and tolerability, PK, PD, and efficacy of INCB000928 administered as monotherapy and in combination with ruxolitinib in participants with MF who are TD or presenting with symptomatic anemia. This study will consist of 2 parts. Part 1 is the dose-escalation stage for INCB000928 monotherapy and INCB000928 + ruxolitinib combination therapy. Part 2 is the dose-expansion stage for INCB000928 monotherapy and INCB000928 + ruxolitinib combination therapy. Section 2 of the Protocol provides a detailed description of the investigational product, target patient population, rationale for doses to be examined, and potential risks and benefits of treatment with INCB000928.

This study was terminated early owing to a strategic decision and Part 2 will not be conducted.

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in the INCB 00928-104 Protocol.

Pharmacokinetic analysis will be conducted by the Incyte pharmacokineticist, and the details of the analysis methodology and results will be included in the CSR.

The details of the analysis methodology of biomarkers and PD and results will be reported separately.

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 00928-104 Protocol Amendment 8 dated 05 DEC 2023 and CRFs approved 13 SEP 2024. Unless superseded by an amendment, this SAP will be effective for all subsequent Protocol amendments and eCRF versions.

2.2. Study Objectives and Endpoints

Table 1 presents the objectives and endpoints.

Table 1: Objectives and Endpoints

Objectives	Endpoints
Primary	
To determine the safety and tolerability of INCB000928 administered as monotherapy (TGA) or in combination with ruxolitinib (TGB and TGC).	• Frequency and severity of AEs and SAEs, including changes in vital signs, ECGs, physical examinations, and clinical blood and urine laboratory parameters. • Identification of the DLTs, MTD, and RDE.
Secondary	
To determine the efficacy of INCB000928 administered as monotherapy (TGA) or in combination with ruxolitinib (TGB and TGC).	• Anemia response, defined as follows (modified from Tefferi et al [2013] definitions): – An Hgb increase of 1.5 g/dL relative to baseline for any "rolling" 12-week period (84 days with each assessment meeting this requirement) during the first 24 weeks of treatment if TI at baseline **OR** – Achieving TI for any "rolling" 12-week period (absence of any RBC transfusion over any 84-day period) during the first 24 weeks of treatment if TD at baseline. • Duration of anemia response, defined as follows: – The interval from the first onset of anemia response to the earliest date of loss of anemia response that persists for at least 4 weeks or death from any cause (for the TI participants at baseline) **OR** – Duration of RBC-TI period for participants achieving RBC-TI for at least 12 consecutive weeks during the first 24 weeks of treatment (for the TD participants at baseline). • Mean change from baseline in the Hgb value over 12-week treatment periods. • Rate of RBC transfusion through Weeks 24 and 48, defined as the average number of RBC units per participant-month during the treatment period.

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
Secondary (continued)	
To determine the efficacy of INCB000928 administered as monotherapy (TGA) or in combination with ruxolitinib (TGB and TGC). (continued)	**For TGB and TGC participants only:** • Splenic volume response rate at Week 24, defined as the proportion of participants achieving a ≥ 35% reduction in spleen volume at Week 24 relative to baseline as measured by MRI or CT scan. • Spleen length response, defined as the proportion of participants achieving a ≥ 50% reduction in spleen length at any visit relative to baseline as measured by palpation. • ORR, defined as the proportion of participants with CR or PR (including the morphologic effects of the combination of INCB000928 with ruxolitinib on BM) according to Tefferi et al (2013) definitions. • PFS, defined as the interval from the first dose of study treatment until the first documented progression or death according to Tefferi et al (2013) definitions. • LFS, defined as the interval from the first dose of study treatment until the first documented leukemia transformation or death from any cause.
To evaluate the PK of INCB000928 administered as monotherapy (TGA) or in combination with ruxolitinib (TGB and TGC).	• PK parameters: C_{max}, t_{max}, and AUC_{0-t} for INCB000928 alone, for ruxolitinib alone, or for the combination of INCB000928 with ruxolitinib, as applicable.
To evaluate the effect of INCB000928 administered as monotherapy (TGA) or in combination with ruxolitinib (TGB and TGC) on hepcidin level, iron homeostasis, and erythropoiesis.	• Blood levels of hepcidin • Iron homeostasis parameters • Erythropoiesis parameters
Exploratory	
[redacted]	

3. STUDY DESIGN

This is a Phase 1/2, open-label, dose-finding study to evaluate the safety and tolerability, PK, PD, and efficacy of INCB000928 administered as monotherapy and in combination with ruxolitinib in participants with MF who are TD or presenting with symptomatic anemia. This study was planned to consist of 2 parts.

Part 1 consists of dose escalation using a BOIN design (Liu and Yuan 2015) to determine the MTD and/or RDE(s) for the following 3 treatment groups:

- TGA: INCB000928 administered as monotherapy in participants with TD or symptomatic anemia due to PMF, PPV-MF, or PET-MF who were previously treated with JAK inhibitors for at least 12 weeks and are resistant, refractory, or lost response to a JAK inhibitor, or are intolerant, or are not eligible to receive a JAK inhibitor treatment.
- TGB: INCB000928 administered in a combination regimen with ruxolitinib in participants with TD or symptomatic anemia due to PMF, PPV-MF, or PET-MF who have been on a stable dose of ruxolitinib for at least 12 weeks.
- TGC: INCB000928 administered in a combination regimen with ruxolitinib in JAK inhibitor treatment-naive MF participants with TD or symptomatic anemia due to PMF, PPV-MF, or PET-MF, with an indication for ruxolitinib initiation for MF-related symptoms.

Once monotherapy doses have been evaluated in at least 3 participants, dose escalation in TGB will start. Dose escalation/de-escalation in TGB will continue with the same rules as for TGA and will not exceed the MTD determined in TGA. After the TGB starting dose is cleared, TGC may start at the highest dose of INCB000928 that has been shown to be safe and tolerable in TGB. The dose escalation/de-escalation in TGC will continue with the same rules applied to TGA and TGB. In each treatment group, up to approximately 40 evaluable participants will be treated in the dose-escalation stage, and the dose-escalation procedure may be stopped if the number of evaluable participants treated at any dose level is greater than 9. The dose-escalation and dose-expansion stages will be conducted in an independent and parallel fashion in TGA (as applicable), TGB, and TGC; different RDE(s) may be defined in the different treatment groups.

The sponsor, in consultation with participating investigators, may elect to explore alternative administration schedules or expand dose cohorts deemed tolerable, in order to obtain supplemental PK, PD, and safety data.

Alternative dose levels or administration schedules (such as twice a day) may be explored. In that situation, the total daily dose of the alternative administration schedule(s) explored will not exceed 2-fold of the prior total daily dose or the MTD, as applicable. Alternative dose schedules for dose-escalation cohorts will be communicated to sites prior to cohort enrollment.

Part 2 is the expansion stage of TGA, TGB, and TGC but will not be conducted because this study was terminated early owing to a strategic decision. Each of the respective RDE(s) identified in the dose-escalation stages will be evaluated as follows:

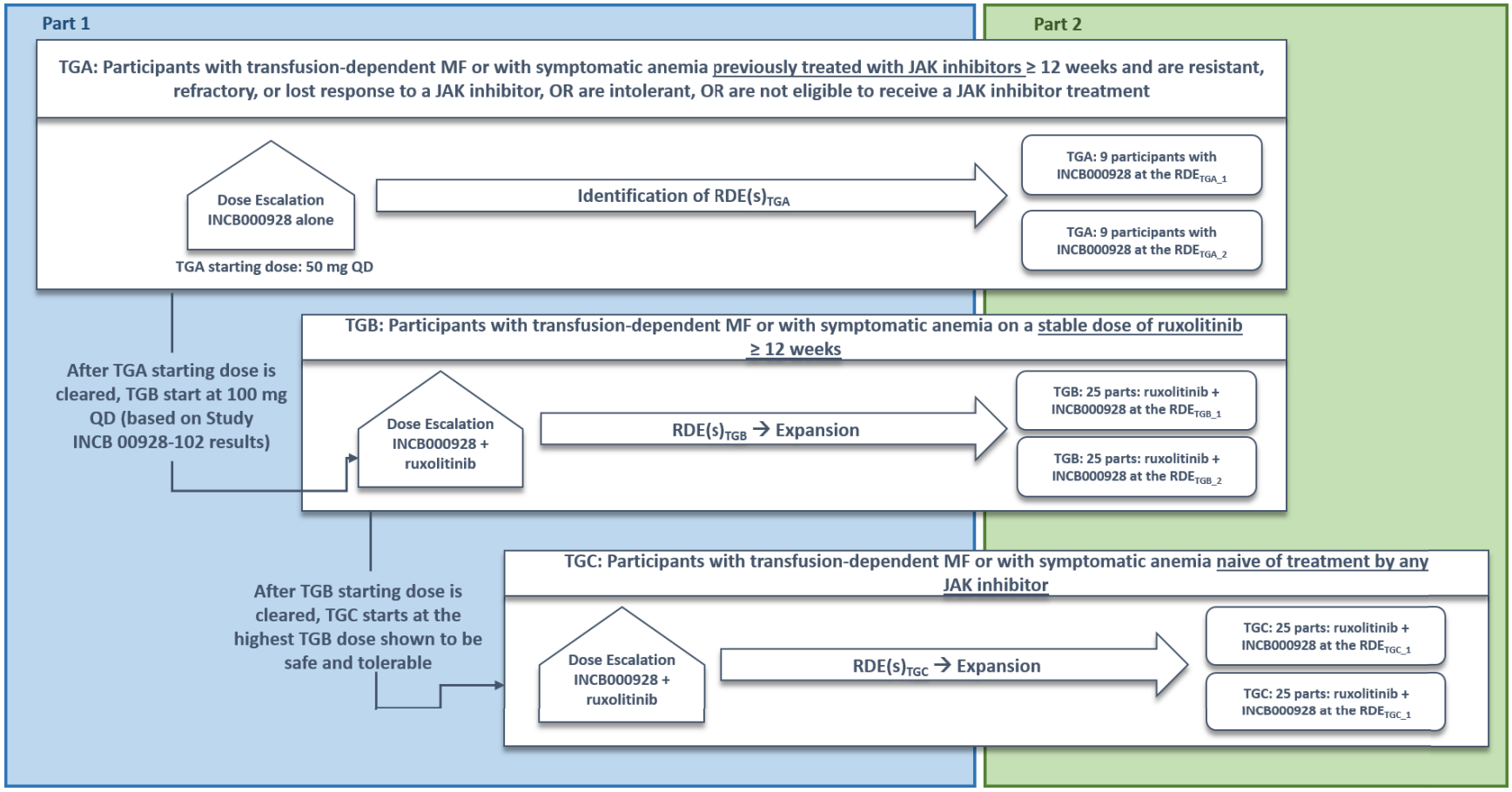
- Independently between treatment groups
- At least 9 evaluable participants at each RDE in TGA
- At least 25 evaluable participants at each RDE in TGB
- At least 25 evaluable participants at each RDE in TGC
- In the event that more than 1 RDE is explored in a treatment group, the participants in that treatment group will be randomly allocated to 1 of the RDEs
- Further evaluation of the safety, efficacy, PK, and PD of the RDE will be performed

Additional participants may be included at the sponsor's discretion in TGB and TGC to ensure that at least 30%, or 10 TD participants, are included in each of the TGB and TGC dose-expansion cohorts.

If an RDE cohort in TGA, TGB, or TGC does not include any Japanese participants, 1 Japanese participant will be enrolled in the cohort.

Figure 1 presents a schematic representation of the study design.

Figure 1: Study Design Schema



QD = once daily.
Note: This study was terminated early owing to a strategic decision and Part 2 will not be conducted.

3.1. Randomization

For Part 1, randomization is not applicable.

For Part 2, in the event that more than 1 RDE is explored in a treatment group, the participants in that treatment group will be randomly allocated to 1 of the RDEs. This study was terminated early owing to a strategic decision and Part 2 will not be conducted.

3.2. Control of Type I Error

Not applicable. All statistical analyses are exploratory in nature; for the other endpoints, CIs will be reported at a 95% confidence level.

3.3. Sample Size Considerations

3.3.1. Part 1 – Dose-Escalation Stages of Treatment Groups A, B, and C

In each of the dose-escalation stages (TGA, TGB, and TGC), a BOIN design (Liu and Yuan 2015) will be used to determine the MTD. The cohort size will be 3. In each treatment group, up to approximately 40 evaluable participants will be treated in the dose-escalation stage, and the dose-escalation procedure may be stopped if the number of evaluable participants treated at any dose level is greater than 9. The target DLT is 0.28. The value of 0.6×0.28 is the highest DLT rate that is deemed subtherapeutic. The lowest DLT rate deemed overly toxic is 1.4×0.28, meaning that if the participants have a DLT rate of $\leq 0.6 \times 0.28$, dose escalation is required; if the participants have a DLT rate of $\geq 1.4 \times 0.28$, dose de-escalation is required. An equal prior probability of the hypothesis being true is assigned to each of the hypotheses. The value of 0.95 is selected for the cutoff to eliminate an overly toxic dose for safety.

Table 2 will be used to guide dose escalation/de-escalation decisions.

Table 2: Decision Boundaries

Number of Participants Treated at Current Dose	1	2	3	4	5	6	7	8	9
Escalate if Number of Participants With DLT(s) is ≤	0	0	0	0	1	1	1	1	1
De-Escalate if Number of Participants With DLT(s) is ≥	1	1	2	2	2	3	3	3	4
Unacceptable Toxicity if Number of Participants With DLT(s) is ≥	NA	NA	3	3	4	4	4	5	5

If the number of participants with DLT(s) specified in the last row on Table 2 is reached, that dose level and any higher dose levels will be eliminated. If the number of participants with DLT(s) is between the escalation and de-escalation boundaries specified in the second and third rows in Table 2, another 3 evaluable participants will be enrolled in the current dose-level cohort. The exact number of participants treated in each dose-escalation stage will depend on the number of participants required per dose level and on the number of dose levels studied.

At the end of the dose-escalation part of the study, the estimated MTD is the dose at which the observed DLT rate is closest to the target DLT rate of 28% using an isotonic method that takes the assumption of a monotonic dose-toxicity relationship into account.

Assuming the true DLT is 28% and the number of dose levels to be tested is 5, Table 3 provides the operating characteristics of BOIN design with a maximum number of cohorts of 13 and an early stopping rule of 9 evaluable participants at each dose level for the 4 scenarios in Table 4.

Table 3: Operating Characteristics of Bayesian Optimal Interval Design

	Scenario			
	1	**2**	**3**	**4**
Average participants treated at MTD	8	7	6	5
Total participants treated	14	18	21	22
Correct selection (%)	57.6	43.0	39.3	36.0
Risk of overdosing (%)	33.3	27.2	27.0	24.0
Risk of underdoing (%)	9.1	29.8	33.7	40.0

Table 4: Four Scenarios for the Simulation of Bayesian Optimal Interval Design

	DLTs for 5 Dose Levels				
Scenario	**Dose 1**	**Dose 2**	**Dose 3**	**Dose 4**	**Dose 5**
1	0.28	0.35	0.45	0.55	0.65
2	0.15	0.28	0.35	0.45	0.55
3	0.05	0.15	0.28	0.35	0.45
4	0.05	0.10	0.15	0.28	0.35

3.3.2. Integration of Japan and Japanese Safety Run-In Cohort

Since Japan will join the study later than the US and Europe, the first 3 participants in Japan will be enrolled in a Japanese safety run-in cohort in TGA, and the initial dose level for these participants will be the highest dose level already demonstrated to be safe and tolerable in TGA in the US and Europe.

The management of the Japanese safety run-in cohort will be performed as follows:

- In the absence of any DLT in these 3 participants, and if the PK parameters are comparable between Japanese and Western sites, the next participants enrolled in Japan will be enrolled in the same cohort as in the US/Europe. The dose-escalation algorithm as described in Section 3.3.1 will apply globally.
- If at least 1 of the 3 participants enrolled in the Japanese safety run-in cohort presents a DLT, or if the PK parameters between Japanese and Western sites are determined to be different by the study team, then the BOIN design will apply for Japan, and an independent dose finding will be conducted in this country as described in Section 3.3.1.

3.4. Schedule of Assessments

Refer to Protocol Amendment 8 dated 05 DEC 2023 for a full description of all study procedures and assessment schedules for this study.

4. DATA HANDLING DEFINITIONS AND CONVENTIONS

4.1. Scheduled Study Evaluations and Study Periods

4.1.1. Day 1

Day 1 is the date that the first dose of INCB000928 is administered to the participants.

4.1.2. Study Day

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

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

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

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

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

4.1.3. Baseline Value

Baseline is the last nonmissing measurement obtained before the first administration of INCB000928, unless otherwise defined below.

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

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

Baseline Hgb will be measured up to 12 weeks before Cycle 1 Day 1 to Cycle 1 Day 1 (Day −84 to Day 1). The baseline Hgb will be defined as the average of all eligible Hgb assessments. The Hgb values within the window from the date of received RBC transfusion + 1 day to the date of received RBC transfusion + 14 days that do not trigger another transfusion will be excluded. The eligible Hgb values for baseline will be calculated based on the information entered in the Transfusion History eCRF and Local Labs – HGB eCRF.

Baseline 12-lead ECG will be determined as the average of all nonmissing values for each ECG parameter before the first administration of INCB000928. If there are multiple records for each test at the same visit, those records will be averaged for analysis.

4.1.4. Handling of Missing and Incomplete Dates

In general, values for missing dates will not be handled unless methods for handling missing dates are specified in this section or relevant sections. The original reported dates collected on the eCRF should be used in all relevant listings. The following rules will be used for handling partial dates for analyses requiring dates.

When calculating the time since diagnosis of disease, a partial disease diagnosis date will be handled as follows in the calculation:

- If only the day is missing, then the first day of the month will be used.
- If both the month and day are missing, then 01 JAN of the year will be used.
- If the diagnosis date is completely missing, then the time since diagnosis will not be calculated.

When calculating the exposure duration of ruxolitinib prior to the study treatment, a partial date of exposure of the first and last dose will be handled as follows:

- If only the day is missing, then the first day of the month will be used.
- If both the month and day are missing, then 01 JAN of the year will be used.
- If the exposure date is completely missing, then the date will not be calculated.
- The imputed date of exposure should before Cycle 1 Day 1.

When the date of the last dose is used in deriving variables such as duration of treatment or TEAE flag, a missing or partial date of the last dose will be handled as follows:

- If only the day is missing, then the earlier date of the last day of the month or the date that the participant discontinued treatment will be used.
- If both the month and day are missing, then the earlier date of 31 DEC of the year or the date that the participant discontinued treatment will be used.
- Otherwise, the date that the participant discontinued treatment will be used as the date of the last dose.

For relevant efficacy endpoints, a partial date of the death date will be handled as follows in the calculation:

- If mmyyyy for the last known alive date = mmyyyy for the death date, then the death date will be set to the day after the last known alive date.
- If mmyyyy for the last known alive date < mmyyyy for the death date, then the death date will be set to the first day of the death month.
- Otherwise, the partial death date will not be imputed.

4.1.5. Cycle Length and Duration

Cycle 1 Day 1 is the day that the first dose of INCB000928 is administered. The scheduled cycle length is 28 days. The actual Day 1 of subsequent cycles will correspond with the first day of administration of INCB000928 for that particular cycle; thus, treatment cycles may become out

of sync with the originally planned schedule, and the cycle length may be different from 28 days. The date of the Day 1 of subsequent cycles recorded on the eCRF will be used as the Day 1 of the subsequent cycles.

4.2. Variable Definitions

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

4.2.1. Body Mass Index

Body mass index will be calculated as follows:

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

4.2.2. Prior and Concomitant Medication

Prior medication is defined as any nonstudy medication started before the first dose of INCB000928.

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

- Before the date of first administration of INCB000928 and is ongoing throughout the study or ends on/after the date of first study drug administration.
- On/after the date of first administration of INCB000928 and is ongoing or ends during the course of study.

A prior medication could also be classified as "both prior and concomitant medication" if the end date is on or after first dose of INCB000928.

In the listing, it will be indicated whether a medication is only prior, only concomitant, or both prior and concomitant.

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

5. STATISTICAL METHODOLOGY

5.1. General Methodology

Unless otherwise noted, SAS® software (SAS Institute Inc, Cary, NC; v9 or later) will be used for the generation of all tables, graphs, and statistical analyses. Descriptive summaries for continuous variables will include but not be limited to the number of observations, mean, standard deviation, median, minimum, and maximum. Descriptive summaries for categorical variables will include the number and percentage of participants in each category.

5.2. Treatment Groups

This is an open-label, dose-finding study to evaluate the safety and tolerability, PK, PD, and efficacy of INCB000928 administered as monotherapy and in combination with ruxolitinib in participants with MF who are TD or presenting with symptomatic anemia. Data will be summarized by treatment group and INCB000928 dose level based on the dose regimen initially assigned unless otherwise noted. In the event that several dose regimens tested are deemed substantially below the MTD, these doses may be combined for summary purposes.

For the Japanese cohorts, data will be summarized by treatment group and dose level separately from Western sites for selected tables. If the safety profile and the PK parameters are determined to be similar to the Western countries, analyses of pooled data for the Japanese and Western participants will be summarized by treatment group and dose level in addition to the separate summary of Japanese cohorts.

5.3. Analysis Populations

5.3.1. All-Screened Population

The all-screened population will include all participants who signed the informed consent form.

5.3.2. Full Analysis Set

The FAS will include all participants who received at least 1 dose of INCB000928 or ruxolitinib, as applicable. Participants will be analyzed according to the treatment to which they have been initially assigned.

The FAS will be used for the summary of demographics, baseline characteristics, participant disposition, and analyses of all efficacy data.

5.3.3. Safety Population

The safety population will include all participants who received at least 1 dose of INCB000928 or ruxolitinib, as applicable. Treatment groups for this population will be determined according to the actual treatment the participant received regardless of assigned study drug treatment.

All safety analyses will be conducted using the safety population.

5.3.4. Dose-Limiting Toxicity Evaluable Population

The DLT evaluable population will include all non-backfill participants eligible for dose-escalation evaluation that meet the following criteria:

- Participants who are observed for at least the first treatment cycle (ie, 28 days).
- Participants who receive at least 75% of doses of study treatment at the level assigned to that cohort (ie, 21 days of treatment) or have a DLT during the first study treatment cycle (ie, 28 days).
- Participants who do not receive any strong or potent cytochrome P450 3A4/5 inhibitor or inducer during the first study treatment cycle (DLT-assessment period).
- Participants who do not have a dose reduction of ruxolitinib during the first study treatment cycle (DLT-assessment period).

6. BASELINE, EXPOSURE, AND DISPOSITION

Appendix A provides a list of data displays. Sample data displays are included in a separate document.

6.1. Demographics, Baseline Characteristics, and Disease History

6.1.1. Demographics and Baseline Characteristics

The following demographics and baseline characteristics will be summarized for the FAS by treatment group and dose level: age, sex, race, ethnicity, weight, height, and BMI.

6.1.2. Baseline Disease Characteristics

The following baseline disease characteristics will be summarized and listed for the FAS by treatment group and dose level: ECOG performance status, the time since diagnosis to Day 1, current MF disease type, prognostic factors, risk level as defined by the Dynamic International Prognostic Scoring System, whether a prior splenic irradiation was performed, whether the participant was ineligible or did they not respond to available therapies for anemia, categorization of a prior therapy for MF, whether an antianemic treatment received, categorization of a prior antianemic therapy, whether a prior radiation was performed, and whether prior surgery was performed. For TGB and TGC, the starting daily dose of ruxolitinib will be summarized and listed by treatment group and dose level.

6.1.3. Disease History

Time since diagnosis will be calculated as follows:

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

Transfusion dependency at baseline will also be summarized and listed for the FAS by treatment group and dose level. Transfusion-dependent participants are defined according to Section 7.2.1.1. Participants who do not satisfy TD criteria at baseline will be TI participants.

The transfusion date, blood component, reason for RBC/platelet transfusion, quantity, and unit will be listed.

For TGB, the duration of treatment with ruxolitinib prior to study treatment will be summarized and listed by treatment group and dose level.

Duration of treatment with ruxolitinib prior to study treatment will be calculated as follows:

> Prior exposure duration of ruxolitinib (days) = date of last dose of ruxolitinib prior to treatment – date of first dose of prior ruxolitinib prior to treatment + 1.

The duration of treatment with ruxolitinib prior to study treatment only includes the period prior to study treatment. The days exposed to a stable dose of ruxolitinib for TGB participants before Day 1 will not be included. Participants may have more than 1 ruxolitinib dose exposure period prior to study treatment; the duration of treatment with ruxolitinib prior to study treatment will include the days from all available exposure period(s). Prior exposure duration of ruxolitinib will be calculated based on the information entered into the PTHERAPY eCRF.

6.1.4. Prior Therapy

The number of prior systemic anticancer therapy regimens will be summarized for all participants in the FAS by treatment group and dose level. The component drugs of prior systemic therapy regimens will be coded using the WHO Drug Dictionary. The number and percentage of participants who received each drug will be summarized by WHO drug class and WHO drug PT. The regimen name, dose, unit, frequency, route, start and stop dates, and reason for discontinuation will be listed.

The number of participants who received prior antianemic treatments will be summarized for all participants in the FAS by treatment group and dose level. The component drugs of prior systemic therapy regimens will be coded using the WHO Drug Dictionary. The number and percentage of participants who received each drug will be summarized by WHO drug class and WHO drug PT. The regimen name, dose, unit, frequency, route, start and stop dates, and reason for discontinuation will be listed.

The number of participants who received prior radiation will be summarized for the FAS by treatment group and dose level. The radiotherapy type, body site, start and stop dates, total dose, reason for regimen, best response, number or fractions received, and total dose will be listed.

The number of participants who had prior surgery or surgical procedure for the malignancies under study will be summarized for the FAS by treatment group and dose level. The date and description of the surgery/procedure will be listed.

6.1.5. Medical History

For participants in the FAS, medical history will be summarized by assigned treatment group and dose level. This summation will include the number and percentage of participants with significant medical history for each body system/organ class as documented on the eCRF.

6.2. Disposition of Participant

The number and percentage of participants who were treated, who were ongoing on study treatment, who discontinued study treatment with a primary reason for discontinuation, who

were still in the study, and who withdrew from the study with a primary reason for withdrawal will be summarized for the FAS by treatment group and dose level. The number of participants enrolled by country and/or site will also be provided by treatment group and dose level.

6.3. Protocol Deviations

Protocol deviations provided by iCore will be summarized and listed.

6.4. Exposure

- **Duration of treatment with INCB000928 (days)**: date of last dose of INCB000928 – date of first dose of INCB000928 + 1.
- **Average daily dose of INCB000928 (mg/day)**: total actual INCB000928 dose taken (mg) / duration of treatment with INCB000928 (days).

  Total actual dose of INCB000928 taken will be calculated based on the information entered into the Dosing eCRF.
- **INCB000928 dose modifications**: number of participants who had INCB000928 dose reductions, escalations, and interruptions.

  INCB000928 dose escalations will include participants who received intraparticipant dose escalation, meaning they received a dose of INCB000928 higher than their initial prescribed dose.

  INCB000928 dose modifications will be based on the information entered into the Dosing eCRF.
- **Duration of treatment with ruxolitinib (days)**: date of last dose of ruxolitinib − date of first dose of ruxolitinib + 1.

  The duration of ruxolitinib only includes the period starting from Day 1. The days exposed to a stable dose of ruxolitinib before Day 1 and the days after the date of last dose of INCB000928 will not be included.
- **Average daily dose of ruxolitinib (mg/day)**: total actual ruxolitinib dose taken (mg) / duration of treatment with ruxolitinib (days).

  The total actual ruxolitinib dose taken will only include the dose taken starting from Day 1. The stable dose of ruxolitinib received before Day 1 and the dose received after the date of the last dose of INCB000928 will not be included. Total actual ruxolitinib dose taken will be calculated based on the information entered into the Dosing eCRF.
- **Ruxolitinib dose modifications**: number of participants who had ruxolitinib dose reductions, escalations, and interruptions.

  Ruxolitinib dose modifications will be based on the information entered into the Dosing eCRF.

6.5. Study Drug Compliance

For participants in the safety population, overall compliance (%) for INCB000928 will be calculated for all participants as follows:

compliance (%) = 100 × (total dose actually taken / total prescribed dose).

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

The total dose actually taken will be calculated based on information entered into the Dosing eCRF.

6.6. Prior and Concomitant Medication

Prior medications and concomitant medications will be coded using the WHO Drug Dictionary. The number and percentage of participants in the FAS for each prior and concomitant medication will be summarized by WHO drug class and WHO drug PT.

7. EFFICACY

Appendix A provides a list of data displays. Sample data displays are included in a separate document.

7.1. General Considerations

Unless otherwise stated, the FAS will be used in all efficacy analyses.

This study was terminated early owing to a strategic decision. The analyses described in Sections 7.2.5, 7.2.6, 7.2.7, 7.2.8, 7.2.9, and 7.3 will not be performed.

7.2. Analysis of the Secondary Efficacy Parameters

7.2.1. Proportion of Participants With Anemia Response

Hemoglobin values and RBC transfusions at baseline will be recorded for at least 12 weeks before Cycle 1 Day 1. The collection of Hgb values and RBC transfusions is mandatory only during the 8 weeks before Cycle 1 Day 1. Baseline Hgb value will be determined according to Section 4.1.3.

The proportions of participants with anemia response will be estimated as described below for the TGA, TGB, and TGC FAS.

7.2.1.1. Proportion of Participants With Anemia Response for Transfusion-Dependent Participants at Baseline

Transfusion-dependent participants at baseline are defined as participants who received at least 4 units of RBC transfusions during the 28 days immediately preceding Cycle 1 Day 1 or received at least 4 units of RBC transfusions in the 8 weeks immediately preceding Cycle 1 Day 1, for an Hgb level of < 8.5 g/dL, in the absence of bleeding or treatment-induced anemia. In addition, the most recent transfusion episode must have occurred in the 28 days before Cycle 1 Day 1.
For TD participants at baseline, anemia response is defined as achieving RBC-TI for any "rolling" 12-week period (absence of any RBC transfusion over any 84-day period) during the first 24 weeks of treatment. At least 3 separate Hgb assessments with 28 ± 6 days between each measurement are required during this 84-day window. The proportion of participants achieving RBC-TI will be estimated along with its 95% CI. The response rate will be estimated with its 95% CI by treatment group and dose level for participants who have been on treatment for at least 84 days or discontinued from treatment before 12 weeks. The CI will be calculated by exact binomial distribution.

Red blood cell transfusions will be recorded during the study period and up to 30 days after the last dose exposed to INCB000928. If a participant completes the safety follow-up period or starts a new anticancer treatment before the end of a 12-week (84-day) window, then information as to whether the participant received an RBC transfusion will be missing. The participant will not be considered as having achieved anemia response during this 12-week period.

For participants who remain on study for more than 12 weeks, additional 12-week windows (eg, Days 2-85, Days 3-86) will be derived for the first 24 weeks of treatment.

7.2.1.2. Proportion of Participants With Anemia Response for Transfusion-Independent Participants at Baseline

Participants who do not satisfy TD criteria at baseline will be TI participants at baseline. For TI participants at baseline, anemia response is defined as an Hgb increase of 1.5 g/dL relative to baseline for any "rolling" 12-week period (84 days with each assessment meeting this requirement) during the first 24 weeks of treatment. Any postbaseline Hgb assessment(s) within the window from the date of received RBC transfusion + 1 day to the date of received RBC transfusion + 14 days are not eligible to determine the anemia response and will be excluded. At least 3 separate Hgb assessments with 28 ± 6 days between each measurement are required during this 84-day window. The proportion of participants with anemia response will be estimated along with its 95% CI by treatment group and dose level for participants who have been on treatment for at least 84 days or discontinued from treatment before 12 weeks. The CI will be calculated by exact binomial distribution. A valid baseline Hgb value is required for participants to be included in the calculation of anemia response rate. Baseline Hgb value will be determined according to Section 4.1.3.

For TI participants at baseline, for each 12-week period that the participant was on study, the Hgb value will be recorded according to schedule of assessments in the Protocol. If a participant completes the safety follow-up or starts a new anticancer treatment before the end of a 12-week (84-day) window, this 12-week period and thereafter will be excluded from the analysis.

For participants who remain on study for more than 12 weeks, additional 12-week windows (eg, Days 2-85, Days 3-86) will be derived for the first 24 weeks of treatment.

7.2.2. Duration of Anemia Response

The duration of anemia response will be estimated as described below for participants in FAS TGA, TGB, and TGC. The estimate of median duration of anemia response and its 95% CI will be calculated using the Kaplan-Meier method when the number of responders is > 5 per treatment group.

7.2.2.1. Duration of Anemia Response for Transfusion-Dependent Participants at Baseline

For TD participants at baseline, duration of anemia response is defined as the interval from the first onset of RBC-TI period to the date of the first available RBC transfusion after the first RBC-TI period or death due to any cause, whichever occurs first, among the participants who achieve anemia response.

If loss of RBC-TI or death is not observed before the date of analysis, the duration will be censored at the last assessment of Hgb prior to a new anticancer treatment or new antianemic treatment date, whichever is earlier.

Kaplan-Meier estimates of median duration of response and its 95% CIs will be provided. The 95% CI will be calculated using the generalization of Brookmeyer and Crowley's (1982) method with log-log transformation (Klein and Moeschberger 1997).

7.2.2.2. Duration of Anemia Response for Transfusion-Independent Participants at Baseline

For TI participants at baseline, duration of anemia response is defined as the interval from the first onset of anemia response during the first 24 weeks of treatment to the earliest date of loss of anemia response that persists for at least 4 weeks or death from any cause, whichever is earlier, among the TI participants who achieved anemia response. The loss of anemia response for TI participants at baseline is defined as the Hgb increase relative to baseline is < 1.5 g/dL and the Hgb increase < 1.5 g/dL is confirmed by a second measurement at least 4 weeks apart with no measurement in between with Hgb ≥ 1.5 g/dL relative to baseline.

If loss of anemia response or death is not observed before the date of analysis, the duration will be censored at the last assessment of Hgb prior to a new anticancer treatment or new antianemic treatment date, whichever is earlier.

Kaplan-Meier estimates of median duration with 95% CIs will be provided. The 95% CI will be calculated using the generalization of Brookmeyer and Crowley's (1982) method with log-log transformation (Klein and Moeschberger 1997).

7.2.3. Mean Change From Baseline in Hemoglobin Value

Mean change from baseline in Hgb value, defined as the largest increase from baseline in the mean Hgb values over any rolling 12-week treatment period during the first 24 weeks of treatment, will be summarized for FAS participants who remain on study for more than 12 weeks during the first 24 weeks of treatment and with at least 1 valid Hgb assessment by treatment group and by dose level descriptively. Any postbaseline Hgb assessment(s) within the window from the date received RBC transfusion + 1 day to the date received RBC transfusion + 14 days will not be considered a valid value and will be excluded.

The Hgb baseline value will be defined according Section 4.1.3 and the 12-week treatment period will be defined according to the algorithm provided in Section 7.2.1.

Missing values will not be imputed.

7.2.4. Rate of Packed Red Blood Cell Transfusion Through Weeks 24 and 48

Rate of pRBC transfusion through Weeks 24 and 48 is defined as the average number of pRBC units per participant-month during the treatment period. The pRBC transfusion(s) between Week 24 and Week 48 up to the last available transfusion record prior to a new anticancer treatment will be included in the analysis. This endpoint will be summarized by treatment group and by dose level descriptively.

The average number of pRBC units through Weeks 24 and 48 will be calculated as follows:

> Rate of pRBC units through Weeks 24 and 48 = total pRBC units received through Weeks 24 and 48 / (days the participant is on treatment during Weeks 24 and 48 / 30.4375).

7.2.5. Splenic Volume Response Rate at Week 24 for Participants in Treatment Groups B and C in Part 2

Splenic volume response rate at Week 24, defined as the proportion of participants achieving a ≥ 35% reduction in spleen volume at Week 24 relative to baseline as measured by MRI or CT scan will be estimated with its 95% CI.

Spleen volume will be measured by MRI (or by CT for applicable participants). The baseline spleen volume will be measured during screening (Day −56 to Day 1); the last nonmissing value during this period will be used if there are multiple values measured during this time.

The Week 24 spleen volume will be measured during the Cycle 6 visit (± 2 weeks of Day 168); if there are more than 1 assessment measured within this window, the assessment measured closest to Day 168 will be used.

Missing value will not be imputed.

A participant will be included in the splenic volume response analysis if the participant was in the TGB or TGC FAS in Part 2 with a baseline spleen volume measurement and has any of the following:

- Week 24 spleen volume measurement.
- Been on treatment for at least 171 days but with no Week 24 spleen volume measurement.
- Discontinued treatment before Cycle 6 visit.

A participant will be considered as having achieved ≥ 35% reduction of the spleen volume from baseline to Week 24 if the participant had both baseline and Week 24 spleen volume measurements, and the percentage change from baseline was not missing and was less than or equal to −35%.

A participant that has been on treatment for at least 171 days but with a missing Week 24 spleen volume will be considered as a nonresponder for the ≥ 35% reduction of the spleen volume. Participants who discontinued treatment before Cycle 6 visit will be considered as having not achieved the ≥ 35% reduction of the spleen volume.

A waterfall plot of percentage change from baseline in spleen volume at Week 24 will be provided.

7.2.6. Spleen Length Response for Participants in Treatment Groups B and C in Part 2

Spleen length response, defined as the proportion of participants achieving a ≥ 50% reduction in spleen length at any visit relative to baseline as measured by palpation, will be estimated with its 95% CI.

The baseline spleen length will be measured during screening and before the first administration of INCB000928 (Day −56 to Day 1); the last nonmissing value during this period will be used if there are multiple values measured during this time.

The Week 4 spleen length will be measured within ± 1 week of Day 28; if there are more than 1 assessment measured during this window, the assessment closest to Day 28 will be used.

Missing value will not be imputed.

A participant will be included in the spleen length analysis if the participant is in the TGB or TGC FAS in Part 2 with a baseline spleen length measurement and has any of the following:

- At least 1 postbaseline spleen length measurement.
- Been on treatment for at least 30 days but with no postbaseline spleen length measurement.
- Discontinued treatment before Cycle 2 Day 1 visit.

A participant will be considered as having achieved ≥ 50% reduction of the spleen length from baseline if the participant had both baseline and at least 1 postbaseline measurement with the percentage change from baseline ≤ −50%.

A participant that has been on treatment for at least 30 days but with no spleen length measurement will be considered as a nonresponder. Participants who discontinued treatment before the Cycle 2 Day 1 visit will be considered as having not achieved the ≥ 50% reduction of the spleen volume.

Spleen length measurements, change and percentage change in spleen length from baseline for every available 4-week period (eg, Week 8, Week 12, etc) to last visit prior to EOT , and at EOT will be summarized by treatment group and dose level.

7.2.7. IWG-MRT Consensus Criteria for Participants in Treatment Groups B and C in Part 2

The IWG-MRT provides criteria for response to treatment in MF. Recently published response criteria developed by the IWG on MF will be used in this study (Tefferi et al 2013). Overall response assessment will be graded according to the IWG-MRT consensus criteria for treatment response in PMF, PPV-MF, and PET-MF. The criteria for response assessment according to IWG-MRT is provided in Appendix B.

The IWG-MRT assessment will be performed at baseline and every sixth cycle at the end of the cycle starting at Cycle 6. The number of participants with the best responses including CR, PR, clinical improvement, stable disease, and progressive disease according to investigator-reported IWG-MRT consensus criteria will be summarized. The number of participants with relapse, anemia response, spleen response, and symptom response will also be summarized. Objective response rate, defined as the proportion of participants with CR or PR, will be calculated with its 95% CI. The CI will be calculated by exact binomial distribution.

Missing values will not be imputed. A participant will be included in the ORR analysis if the participant is in the TGB or TGC FAS in Part 2 with a baseline measurement and has any of the following:

- ≥ 1 postbaseline IWG-MRT assessment.
- Been on treatment for at least 171 days.
- Discontinues treatment.

7.2.8. Progression-Free Survival for Participants in Treatment Groups B and C in Part 2

Progression-free survival is defined as the interval from the first dose of study treatment until the first documented progression or death according to Tefferi et al (2013) definitions. Partial death dates will be handled using the rules described in Section 4.1.4. Censoring for PFS will follow the algorithm outlined in Table 5. The population for this analysis is the FAS.

The total number of participants whose disease progressed or who died and the number of participants censored will be summarized. Kaplan-Meier estimation of median PFS with 95% CI will be summarized. The 95% CI will be calculated using the generalization of Brookmeyer and Crowley's (1982) method with log-log transformation (Klein and Moeschberger 1997).

Table 5: Evaluation and Censoring of Progression-Free Survival

Situation	Outcome	Date of Progression or Censoring
No baseline assessments	Censored	Date of Day 1
No valid postbaseline response assessments	Censored	Date of Day 1
Progression documented between scheduled response assessments	Progressed	Date of first overall response of progressive disease
No progression	Censored	Date of last valid IWG-MRT assessment
Treatment discontinuation for undocumented progression	Censored	Date of last valid IWG-MRT assessment
Treatment discontinuation for toxicity or other reason	Censored	Date of last valid IWG-MRT assessment
New anticancer treatment started	Censored	Date of last valid IWG-MRT assessment on/before starting a new anticancer treatment
Death before first progressive response assessment	Progressed	Date of death
Death between adequate response assessments	Progressed	Date of death
Death or progression after 2 or more missed assessments	Censored	Date of last valid IWG-MRT assessment

7.2.9. Leukemia-Free Survival for Participants in Treatment Groups B and C in Part 2

Leukemia-free survival is defined as the interval from the first dose of study treatment until the first documented leukemia transformation or death from any cause. If the participant does not have leukemia transformation or death before the time of analysis, the participant will be censored at the time of analysis or EOT whichever is earlier. Leukemia-free survival will be analyzed using the FAS for TGB and TGC in Part 2.

The total number of participants who received leukemia transformation or death and number of participants censored will be summarized. The Kaplan-Meier estimation of median LFS will be summarized with its 95% CI. The 95% CI will be calculated using the generalization of

Brookmeyer and Crowley's (1982) method with log-log transformation (Klein and Moeschberger 1997).

7.3. Analysis of Exploratory Efficacy Variables

8. SAFETY AND TOLERABILITY

Appendix A provides a list of data displays. Sample data displays are included in a separate document.

8.1. General Considerations

Summary tables may be replaced with listings when appropriate. For instance, an AE frequency table may be replaced with a listing if it only contains a few unique PTs reported on relatively few participants.

This study was terminated early owing to a strategic decision and Part 2 will not be conducted. The analyses described below for Part 2 will not be performed.

8.2. Adverse Events

8.2.1. Adverse Event Definitions

A TEAE is any AE either reported for the first time or worsening of a pre-existing event after the first dose of study drug until 30 days after the last dose of study drug. Analysis of AEs (as discussed below) will be limited to TEAEs, but data listings will include all AEs regardless of their timing in relation to study drug administration. For purposes of analysis, all AEs will be considered TEAEs unless the AE can unequivocally be defined as not treatment-emergent.

Adverse events will be tabulated by MedDRA PT and SOC. Severity of AEs will be graded using the NCI CTCAE v5. The CTCAE reporting guidelines and grading details are available on the Cancer Therapy Evaluation Program website.

The subset of AEs considered by the investigator to be related to study drug will be considered to be treatment-related AEs. If the investigator does not specify the relationship of the AE to study

drug, the AE will be considered to be treatment-related. The incidence of AEs and treatment-related AEs will be tabulated. In addition, serious TEAEs will also be tabulated.

8.2.2. Dose-Limiting Toxicities

Dose-limiting toxicities that occur in the DLT-assessment period among the DLT evaluable population will be summarized by treatment group and dose level. The DLT incidence rate along with an 80% Bayesian credible interval based on a prior distribution of Beta(1,1) will be provided for each dose level using the DLT evaluable set. The participants with DLTs and the type of DLT will be listed by dose level.

8.2.3. Adverse Event Summaries

An overall summary of AEs by treatment group and INCB000928 dose level for Part 1 and Part 2 will include the following:

- Number (%) of participants who had any TEAEs
- Number (%) of participants who had any DLTs
- Number (%) of participants who had any serious TEAEs
- Number (%) of participants who had any Grade 3 or higher TEAEs
- Number (%) of participants who had any TEAEs related to INCB000928
- Number (%) of participants who had any TEAEs related to ruxolitinib
- Number (%) of participants who had any serious TEAEs related to INCB000928
- Number (%) of participants who had any serious TEAEs related to ruxolitinib
- Number (%) of participants who had any Grade 3 or higher TEAEs related to INCB000928
- Number (%) of participants who had any Grade 3 or higher TEAEs related to ruxolitinib
- Number (%) of participants who temporarily interrupted INCB000928 because of TEAEs
- Number (%) of participants who temporarily interrupted ruxolitinib because of TEAEs
- Number (%) of participants who permanently discontinued INCB000928 because of TEAEs
- Number (%) of participants who permanently discontinued ruxolitinib because of TEAEs
- Number (%) of participants who had INCB000928 dose reductions because of TEAEs
- Number (%) of participants who had ruxolitinib dose reductions because of TEAEs
- Number (%) of participants who had any fatal TEAEs

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

- Summary of TEAEs by MedDRA SOC and PT
- Summary of TEAEs by MedDRA PT in decreasing order of frequency
- Summary of TEAEs by MedDRA SOC, PT, and maximum severity
- Summary of Grade 3 or higher TEAEs by MedDRA SOC and PT
- Summary of Grade 3 or higher TEAEs by MedDRA PT in decreasing order of frequency
- Summary of serious TEAEs by MedDRA SOC and PT
- Summary of serious TEAEs by MedDRA PT in decreasing order of frequency
- Summary of INCB000928 treatment-related TEAEs by MedDRA SOC and PT
- Summary of ruxolitinib treatment-related TEAEs by MedDRA SOC and PT
- Summary of INCB000928 treatment-related TEAEs by MedDRA PT in decreasing order of frequency
- Summary of ruxolitinib treatment-related TEAEs by MedDRA PT in decreasing order of frequency
- Summary of Grade 3 or higher INCB000928 treatment-related TEAEs by MedDRA SOC and PT
- Summary of Grade 3 or higher ruxolitinib treatment-related TEAEs by MedDRA SOC and PT
- Summary of INCB000928 treatment-related serious TEAEs by MedDRA SOC and PT
- Summary of ruxolitinib treatment-related serious TEAEs by MedDRA SOC and PT
- Summary of TEAEs with a fatal outcome by MedDRA SOC and PT
- Summary of TEAEs leading to INCB000928 dose reduction by MedDRA SOC and PT
- Summary of TEAEs leading to ruxolitinib dose reduction by MedDRA SOC and PT
- Summary of TEAEs leading to INCB000928 dose interruption by MedDRA SOC and PT
- Summary of TEAEs leading to ruxolitinib dose interruption by MedDRA SOC and PT
- Summary of TEAEs leading to discontinuation of INCB000928 by MedDRA SOC and PT
- Summary of TEAEs leading to discontinuation of ruxolitinib by MedDRA SOC and PT

8.3. Clinical Laboratory Tests

8.3.1. Laboratory Value Definitions

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

Laboratory test values will be assessed for severity based on the numerical component of CTCAE v5.

8.3.2. Laboratory Value Summaries

All test results and associated normal ranges from local laboratories will be reported in SI units. Any laboratory test results and associated normal ranges from local laboratories will be converted to SI units.

When there are multiple nonmissing laboratory values for a participant's particular test within a visit window, the convention described in Table 6 will be used to determine the record used for by-visit tabulations and summaries.

Table 6: Identification of Records for Postbaseline By-Visit Summaries

Priority	Laboratory Visit	Proximity to Visit Window	Tiebreaker
1	Scheduled	In-window	Use smallest laboratory sequence number
2	Unscheduled	In-window	
3	Scheduled	Out-of-window	

Numeric laboratory values will be summarized descriptively in SI units, and nonnumerical test values will be tabulated when necessary. In addition, line graphs will be provided for Hgb, iron metabolism, and erythropoiesis by study visit.

For test results that will be summarized with available normal ranges, the number and percentage of participants with laboratory values being low (but never high), normal, high (but never low), and both low and high will be calculated for each test. This shift summary will be produced for each test for the safety population. The denominator for the percentage calculation will use the number of participants in the baseline category (ie, low, high, normal, missing) as the denominator for the percentage in each of the categories during the study.

Severity grades will be assigned to laboratory test values based on the numerical component of CTCAE v5. Shift tables will be presented showing change in CTCAE grade from baseline to worst grade postbaseline. Separate summaries for abnormally high and abnormally low laboratory values will be provided when the laboratory parameter has both high and low grading criteria. The denominator for the percentage calculation will be the number of participants in the baseline category.

In cases where differentials of hematology parameters are obtained without corresponding absolute count data, efforts will be made to investigate if the conversion to an absolute value will

lead to additional abnormalities. This will be discussed with the clinical team regarding appropriate documentation and action.

8.3.3. Hy's Law Events

Participants with elevated alanine aminotransferase or aspartate aminotransferase ≥ 3 × ULN range concurrent with total bilirubin > 2 × ULN without findings of cholestasis (serum alkaline phosphatase < 2 × ULN) will be listed by treatment group and dose level. The elevations need to be at the same time or within a specified timeframe.

8.4. Vital Signs

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

Normal ranges for vital sign values are defined in Table 7. For participants exhibiting vital sign abnormalities, the abnormal values will be listed along with their assigned treatment group. Alert vital signs are defined as an absolute value outside the defined normal range and percentage change greater than 25%. Note that the definition of alert vital signs does not apply for body temperature and weight. The abnormal values for participants exhibiting alert vital sign abnormalities will be listed.

Table 7: Normal Ranges for Vital Sign Values

Parameter	High Threshold	Low Threshold
Systolic blood pressure	≤ 155 mm Hg	≥ 85 mm Hg
Diastolic blood pressure	≤ 100 mm Hg	≥ 40 mm Hg
Pulse	≤ 100 bpm	≥ 45 bpm
Temperature	≤ 38°C	≥ 35.5°C
Respiratory rate	≤ 24 breaths/min	≥ 8 breaths/min

8.5. Electrocardiograms

Twelve-lead ECGs including HR and PR, RR, QT, QRS, QTcB, and QTcF intervals will be obtained for each participant during the study. Values at each scheduled visit, change, and percentage change from baseline will be summarized for each ECG parameter. Baseline will be determined according to the algorithm provided in Section 4.1.3. If there are multiple postbaseline records for each test at the same visit and/or timepoint, those records will be averaged for analysis. Upon implementation of Protocol Amendment 7, triplicate 12-lead ECGs were added. Triplicate 12-lead ECGs will be averaged per visit per timepoint; the averaged values will be summarized with 12-lead ECGs for each test at the same visit and/or timepoint.

Normal ranges for ECG values are defined in Table 8. Electrocardiogram values will also be considered abnormal if the absolute percentage change from baseline is more than 25% (30% for QRS interval). Participants exhibiting ECG abnormalities will be listed with study visit and assigned treatment group. Abnormal values for participants with alert ECG values, defined as both the absolute value and the percentage change from baseline being outside normal ranges, will be identified and listed. Outliers of QT, QTcB, and QTcF values, defined as absolute values > 450 milliseconds, > 500 milliseconds, or change from baseline > 30 milliseconds, will be summarized.

Table 8: Normal Ranges for Electrocardiogram Intervals

Parameter	High Threshold	Low Threshold
HR	≤ 100 bpm	≥ 45 bpm
PR	≤ 220 ms	≥ 75 ms
RR	≤ 1330 ms	≥ 600 ms
QT	≤ 500 ms	≥ 300 ms
QRS	≤ 120 ms	≥ 50 ms
QTcB, QTcF	≤ 450 ms	≥ 295 ms

Electrocardiogram abnormalities, both at baseline and postbaseline visits, will be tabulated by treatment group and dose level. Incidences of abnormalities and a description of the abnormality will be listed with study visit and assigned treatment group.

The abnormal MUGA results will be listed.

8.6. Tolerability

Tolerability of study drug treatment will be assessed by summarizing the number of participants with treatment dose interruption, treatment dose reduction, and treatment discontinuation due to an AE. Reasons for dose interruption, dose reduction, and discontinuation will be listed.

9. INTERIM ANALYSES

No formal interim analyses are planned. Safety data will be monitored continuously in order to determine dosing in subsequent cohorts, per the algorithm in Protocol Amendment 8, Section 4.1.1. A data monitoring committee will be formed to review study data at least every 6 months until study termination, before Part 2 enrollment starts, after 50% of participants are enrolled in Part 2, and after all participants are enrolled in Part 2. This study was terminated early owing to a strategic decision and Part 2 will not be conducted.

10. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 9.

Table 9: Statistical Analysis Plan Versions

SAP Version	Date
Original	11 DEC 2020
Amendment 1	21 JUL 2021
Amendment 2	17 APR 2025

10.1. Changes to Protocol-Defined Analyses

Modifications were made to the protocol-defined analyses given that this will be an abbreviated CSR because this study was terminated early owing to a strategic decision.

The hypothesis testing for the proportion of participants with an anemia response for TGB and TGC will not be conducted because it is not applicable for this Phase 1/2 study, which is a dose-finding study, and the primary endpoints will evaluate safety and tolerability. Therefore, the Type I error control will not be applicable.

The endpoint language in the Protocol referring to "Frequency and severity of AEs and SAEs," "Identification of DLTs, MTD, and RDE" is not correct. The endpoint should specify participant-level data to be analyzed, such as "DLTs" and "TEAEs." In future protocols, this language will be updated to better reflect the participant-level data for the analyses.

Clarity was provided for mean change from baseline in Hgb value that it will only be performed during the first 24 weeks of treatment.

10.2. Changes to the Statistical Analysis Plan

10.2.1. Amendment 1

Since Japan will join the study later than the US and Europe, Section 3.3.2 was added to integrate the Japanese participants. The treatment group assignment for the Japanese participants was added in Section 5.2.

Other minor updates include:

- [redacted]

10.2.2. Amendment 2

The following clarifications and modification have been added in the SAP:

- Sections 1, 3, 3.1, 3.3, 7.1, 8.1, 9, and 10.1 and Appendix A were updated to reflect that this study was terminated early owing to a strategic decision.
- Sections 3, 3.1, 3.2, 3.3.1, 7.2.1, 7.2.5, 7.2.6, 7.2.7, 7.2.8, 7.2.9, and 7.3.1 and Figure 1 were updated to reflect Protocol Amendment 7 changes to add TGC and

indicate that dose expansion will be performed in 1 or more RDE for each treatment group.

- Section 3 was updated to reflect Protocol Amendment 7 and the percentage of TD participants to be enrolled in TGB and TGC.
- Sections 4.1.3, 7.2.1, 7.2.1.2, and 7.2.3 were updated to clarify that Hgb assessed within a 14-day washout window of an RBC transfusion will be excluded from baseline and efficacy analysis related to Hgb.
- Sections 4.1.3 and 8.5 were updated to reflect the changes of updated ECG schedules and the addition of triplicate ECGs per Protocol Amendment 7.
- Section 5.3.1 was added to clarify that the all-screened population will include all participants who signed the informed consent form.
- Section 5.3.4 was updated to indicate that participants in a backfill cohort will not be included in the DLT evaluable population.
- Sections 4.1.4 and 6.1.3 were updated to add the duration of ruxolitinib prior to study treatment for TGB participants was added.
- Section 6.4 was updated to clarify that the treatment duration of ruxolitinib and the average daily dose of ruxolitinib will only use the data on or after Day 1 through the date of last dose of INCB000928. Information on INCB000928 and ruxolitinib dose modifications was added.
- Section 6.5 was updated to clarify that the total dose actually taken for drug compliance will be the sum of the doses prescribed by the investigator accounting for dose modifications on the Dosing eCRF.
- Sections 7.2.5 and 7.2.6 were updated to reflect the change to the screening period from 28 to 56 days per Protocol Amendment 8.
- Section 8.3.3 and Appendix A were updated to clarify that Hy's law events will be listed and that the elevations will need to be at the same time or within a specified timeframe.
- Other minor, administrative updates have been incorporated throughout the SAP and are noted in the redline version of the amendment.

11. REFERENCES

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Thiele J, Kvasnicka HM, Facchetti F, Franco V, van der Walt J, Orazi A. European consensus on grading bone marrow fibrosis and assessment of cellularity. Haematologica 2005;90:1128-1132.

APPENDIX A. PLANNED TABLES, FIGURES, AND LISTINGS

This appendix provides a list of the planned tables, figures, and listings for the CSR. Shells are provided in a separate document for tables that are not in the Standard Safety Tables v1.13.

The lists of tables, figures, and listings are to be used as guidelines. Modifications of the lists that do not otherwise affect the nature of the analysis will not warrant an amendment to the SAP.

Tables

Table No.	Title	Population	Standard
Baseline and Demographic Characteristics			
1.1 Disposition			
1.1.1	Analysis Populations	FAS	X
1.1.2	Summary of Participant Disposition	FAS	X
1.1.3	Summary of Number of Participants Enrolled by Country and Site	FAS	X
1.1.4	Summary of Protocol Deviations	FAS	X
1.2 Demography and Baseline Characteristics			
1.2.1	Summary of Demographics and Baseline Characteristics	FAS	X
1.3 Baseline Disease Characteristics			
1.3.1	Summary of Baseline Disease Characteristics	FAS	
1.4 Prior Medication and Concomitant Medication			
1.4.1	Summary of Prior Medications	FAS	X
1.4.2	Summary of Concomitant Medications	FAS	X
1.4.3	Summary of Prior Systemic Cancer Therapy by WHO Drug Class and Preferred Term	FAS	X
1.4.4	Summary of Prior Antianemic Treatment by WHO Drug Class and Preferred Term	FAS	X
1.5 Others			
1.5.1	Summary of General Medical History	FAS	X
Efficacy			
2.2 Secondary Efficacy			
2.2.1.1	Summary of Anemia Response Through Week 24	FAS	
2.2.2.1	Summary of the Largest Increase From Baseline in Mean Hgb Values Over Any Rolling 12-Week Treatment Period During the First 24 Weeks	FAS	
2.2.2.2	Rate of pRBC Transfusion Through Weeks 24 and 48	FAS	
Safety			
3.1 Dose Exposure			
3.1.1	Summary of Exposure and Duration of Exposure to INCB000928	Safety	X
3.1.2	Summary of Exposure and Duration of Exposure to Ruxolitinib	Safety	X
3.1.3	Summary of Study Drug Compliance of INCB000928	Safety	X
3.2 Adverse Events			
3.2.1	Overall Summary of Treatment-Emergent Adverse Events	Safety	X
3.2.2	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.3	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X

Table No.	Title	Population	Standard
3.2.4	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Safety	X
3.2.6	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.7	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X
3.2.8	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.9	Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X
3.2.10.1	Summary of INCB000928 Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.10.2	Summary of Ruxolitinib Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.11.1	Summary of INCB000928 Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X
3.2.11.2	Summary of Ruxolitinib Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X
3.2.14.1	Summary of Grade 3 or Higher INCB000928 Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.14.2	Summary of Grade 3 or Higher Ruxolitinib Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.15.1	Summary of INCB000928 Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.15.2	Summary of Ruxolitinib Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.16	Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.18.1	Summary of Treatment-Emergent Adverse Events Leading to INCB000928 Dose Reduction by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.18.2	Summary of Treatment-Emergent Adverse Events Leading to Ruxolitinib Dose Reduction by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.19.1	Summary of Treatment-Emergent Adverse Events Leading to INCB000928 Dose Interruption by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.19.2	Summary of Treatment-Emergent Adverse Events Leading to Ruxolitinib Dose Interruption by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.20.1	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of INCB000928 by MedDRA System Organ Class and Preferred Term	Safety	X

Table No.	Title	Population	Standard
3.2.20.2	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Ruxolitinib by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.24	Summary of DLT	DLT Evaluable	
3.2.25	Summary of Tolerability	Safety	
3.3 Laboratory			
3.3.1.1	Summary of Laboratory Values - Hematology	Safety	X
3.3.1.2	Summary of Laboratory Values - Chemistry	Safety	X
3.3.1.3	Summary of Laboratory Values - Coagulation	Safety	X
3.3.3.1	Shift Summary of Hematology Laboratory Values in CTC Grade - to the Worst Abnormal Value	Safety	X
3.3.3.2	Shift Summary of Chemistry Laboratory Values in CTC Grade - to the Worst Abnormal Value	Safety	X
3.3.3.3	Shift Summary of Coagulation Laboratory Values in CTC Grade - to the Worst Abnormal Value	Safety	X
3.3.9	Summary of Ferritin Values Up to Cycle 7 Day 1	Safety	X
3.4 Vital Signs			
3.4.1	Summary of Systolic Blood Pressure	Safety	X
3.4.2	Summary of Diastolic Blood Pressure	Safety	X
3.4.3	Summary of Pulse	Safety	X
3.4.4	Summary of Respiratory Rate	Safety	X
3.4.5	Summary of Body Temperature	Safety	X
3.4.6	Summary of Weight	Safety	X
3.5 ECG			
3.5.1	Summary of PR Interval (ms) From 12-Lead ECG	Safety	X
3.5.2	Summary of QRS Interval (ms) From 12-Lead ECG	Safety	X
3.5.3	Summary of QT Interval (ms) From 12-Lead ECG	Safety	X
3.5.4	Summary of QTcB Interval (ms) From 12-Lead ECG	Safety	X
3.5.5	Summary of QTcF Interval (ms) From 12-Lead ECG	Safety	X
3.5.6	Summary of RR Interval (ms) From 12-Lead ECG	Safety	X
3.5.7	Summary of Heart Rate (bpm) From 12-Lead ECG	Safety	X
3.5.8	Summary of Outliers of QT, QTcB, and QTcF Interval Values (ms) From 12-Lead ECG	Safety	X
3.5.9	Summary of Clinically Significant ECG Abnormality	Safety	X

Figures

Figure No.	Title
4.6 Laboratory Data	
4.6.1	Line Graph of Selected Laboratory Values (Hemoglobin, Iron Metabolism, Erythropoiesis) by Study Visit
4.6.2	Line Graph of Hemoglobin Change From Baseline to Week 48 for Transfusion-Independent Participants at Baseline by Treatment Group
4.6.3.1	Swim Plot of pRBC Transfusions for Transfusion-Dependent Participants at Baseline
4.6.3.2	Swim Plot of pRBC Transfusions for Transfusion-Independent Participants at Baseline

Listings

Listing No.	Title
2.1 Discontinued Participants (Participant Disposition)	
2.1.1	Participant Enrollment and Disposition Status
2.2 Protocol Deviations	
2.2.1	Protocol Deviations
2.2.2	Participant Inclusion and Exclusion Criteria Violations
2.3 Data Excluded From PK, Efficacy, and/or Safety Analyses	
2.3.1	Analysis Population
2.4 Demographic and Baseline Characteristics (Including Prior and Concomitant Medications)	
2.4.1	Demographic and Baseline Characteristics
2.4.2	Disease History
2.4.3	Medical History
2.4.4	Prior and Concomitant Medication
2.4.5	Prior Radiation Treatment
2.4.6	Prior Systemic Therapy
2.4.7	Prior Antianemic Treatment
2.4.8	Prior Surgery or Surgical Procedure
2.5 Drug Compliance	
2.5.1.1	Study Drug Dosing Changes of INCB000928
2.5.1.2	Study Drug Dosing Changes of Ruxolitinib
2.5.2.1	Study Drug Administration of INCB000928
2.5.2.2	Study Drug Administration of Ruxolitinib
2.6 Efficacy (and/or PK Data)	
2.6.1	Deaths
2.6.2	RBC/Platelet Transfusion
2.6.8	ECOG Status
2.6.9	Anemia Response
2.7 Adverse Events	
2.7.1	Adverse Events
2.7.2	Serious Adverse Events
2.7.3	Grade 3 and Higher Adverse Events
2.7.4	Fatal Adverse Events
2.7.5	Adverse Events Leading to Reduction of INCB000928 or Ruxolitinib
2.7.6	Adverse Events Leading to Interruption of INCB000928 or Ruxolitinib
2.7.7	Adverse Events Leading to Discontinuation of INCB000928 or Ruxolitinib
2.7.10	Dose-Limiting Toxicities
2.7.11	Treatment-Related Adverse Events
2.8.1 Laboratory Data	
2.8.1.1	Clinical Laboratory Values - Hematology
2.8.1.1.1	Abnormal Laboratory Values - Hematology
2.8.1.2	Clinical Laboratory Values - Chemistry
2.8.1.2.1	Abnormal Laboratory Values - Chemistry
2.8.1.4	Clinical Laboratory Values - Coagulation
2.8.1.4.1	Abnormal Laboratory Values - Coagulation

Listing No.	Title
2.8.1.6	Ferritin Values Up to Cycle 7 Day 1
2.8.1.8	Hy's Law Events
2.8.2 Vital Signs	
2.8.2.1	Vital Signs
2.8.2.2	Abnormal Vital Sign Values
2.8.2.3	Alert Vital Sign Values
2.8.3 ECG	
2.8.3.1	12-Lead ECG Values
2.8.3.2	Abnormal 12-Lead ECG Values
2.8.3.3	Alert 12-Lead ECG Values
2.8.3.4	Abnormal MUGA Assessments
2.11 Physical Examination	
2.11.1	Physical Examinations

APPENDIX B. IWG-MRT CRITERIA

Response Categories	Required Criteria (for All Response Categories, Benefit Must Last for ≥ 12 Weeks to Qualify as a Response)
CR	Bone marrow[a]: Age-adjusted normocellularity; < 5% blasts; ≤ Grade 1 MF[b] and
	Peripheral blood: Hemoglobin ≥ 100 g/L and < UNL; neutrophil count ≥ 1 × 10^9/L and < UNL;
	Platelet count ≥ 100 × 10^9/L and < UNL; < 2% immature myeloid cells[c] and
	Clinical: Resolution of disease symptoms; spleen and liver not palpable; no evidence of EMH
PR	Peripheral blood: Hemoglobin ≥ 100 g/L and < UNL; neutrophil count ≥ 1 × 10^9/L and < UNL; platelet count ≥ 100 × 10^9/L and < UNL; < 2% immature myeloid cells[c] and
	Clinical: Resolution of disease symptoms; spleen and liver not palpable; no evidence of EMH or
	Bone marrow:[a] Age-adjusted normocellularity; < 5% blasts; ≤ Grade 1 MF[b]; and peripheral blood: hemoglobin ≥ 85 g/L but < 100 g/L and < UNL; neutrophil count ≥ 1 × 10^9/L and < UNL; platelet count ≥ 50 × 10^9/L but < 100 × 10^9/L and < UNL; < 2% immature myeloid cells[c] and
	Clinical: Resolution of disease symptoms; spleen and liver not palpable; no evidence of EMH
CI	The achievement of anemia, spleen or symptoms response without progressive disease or increase in severity of anemia, thrombocytopenia, or neutropenia[d]
Anemia response	Transfusion-independent patients: a ≥ 20 g/L increase in hemoglobin level[e]
	Transfusion-dependent patients: becoming transfusion-independent[f]
Spleen response[g]	A baseline splenomegaly that is palpable at 5-10 cm, below the LCM, becomes not palpable[h] or
	A baseline splenomegaly that is palpable at > 10 cm, below the LCM, decreases by ≥ 50%[h]
	A baseline splenomegaly that is palpable at < 5 cm, below the LCM, is not eligible for spleen response
	A spleen response requires confirmation by MRI or CT showing ≥ 35% spleen volume reduction
Symptoms response	A ≥ 50% reduction in the MPN-SAF TSS[i]
Progressive disease[j]	Appearance of a new splenomegaly that is palpable at least 5 cm below the LCM or
	A ≥ 100% increase in palpable distance, below LCM, for baseline splenomegaly of 5-10 cm or
	A 50% increase in palpable distance, below LCM, for baseline splenomegaly of > 10 cm or
	Leukemic transformation confirmed by a bone marrow blast count of ≥ 20% or
	A peripheral blood blast content of ≥ 20% associated with an absolute blast count of ≥ 1 × 10^9/L that lasts for at least 2 weeks
Stable disease	Belonging to none of the above-listed response categories
Relapse	No longer meeting criteria for at least CI after achieving CR, PR, or CI, or
	Loss of anemia response persisting for at least 1 month or
	Loss of spleen response persisting for at least 1 month

CI = clinical improvement; CR = complete response; CT = computed tomography; EMH = extramedullary hematopoiesis; LCM = left costal margin; MF = myelofibrosis; MPN-SAF TSS = Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score; MRI = magnetic resonance imaging; PR = partial response; PRBC = packed red blood cell; UNL = upper normal limit.

[a] Baseline and post-treatment bone marrow slides are to be interpreted at 1 sitting by a central review process. Cytogenetic and molecular responses are not required for CR assignment.

[b] Grading of MF is according to the European classification (Thiele et al 2005). It is underscored that the consensus definition of a CR bone marrow is to be used only in those patients in which all other criteria are met, including resolution of leukoerythroblastosis. It should also be noted that it was a particularly difficult task for the working group to reach a consensus regarding what represents a complete histologic remission.

[c] Immature myeloid cells constitute blasts + promyelocytes + myelocytes + metamyelocytes + nucleated red blood cells. In splenectomized patients, < 5% immature myeloid cells is allowed.

[d] See above for definitions of anemia response, spleen response, and progressive disease. Increase in severity of anemia constitutes the occurrence of new transfusion dependency or a ≥ 20 g/L decrease in hemoglobin level from pretreatment

baseline that lasts for at least 12 weeks. Increase in severity of thrombocytopenia or neutropenia is defined as a 2-grade decline, from pretreatment baseline, in platelet count or absolute neutrophil count, according to the CTCAE version 4.0. In addition, assignment to CI requires a minimum platelet count of $\geq 25{,}000 \times 10^9$/L and absolute neutrophil count of $\geq 0.5 \times 10^9$/L.

[e] Applicable only to patients with baseline hemoglobin of < 100 g/L. In patients not meeting the strict criteria for transfusion dependency at the time of study enrollment (see as follows), but have received transfusions within the previous month, the pretransfusion hemoglobin level should be used as the baseline.

[f] Transfusion dependency before study enrollment is defined as transfusions of at least 6 units of PRBCs, in the 12 weeks prior to study enrollment, for a hemoglobin level of < 85 g/L, in the absence of bleeding or treatment-induced anemia. In addition, the most recent transfusion episode must have occurred in the 28 days prior to study enrollment. Response in transfusion-dependent patients requires absence of any PRBC transfusions during any consecutive "rolling" 12-week interval during the treatment phase, capped by a hemoglobin level of ≥ 85 g/L.

[g] In splenectomized patients, palpable hepatomegaly is substituted with the same measurement strategy.

[h] Spleen or liver responses must be confirmed by imaging studies where a ≥ 35% reduction in spleen volume, as assessed by MRI or CT, is required. Furthermore, a ≥ 35% volume reduction in the spleen or liver, by MRI or CT, constitutes a response regardless of what is reported with physical examination.

[i] Symptoms are evaluated by the MPN-SAF TSS. The MPN-SAF TSS is assessed by the patients themselves and this includes fatigue, concentration, early satiety, inactivity, night sweats, itching, bone pain, abdominal discomfort, weight loss, and fevers. Scoring is from 0 (absent/as good as it can be) to 10 (worst imaginable/as bad as it can be) for each item. The MPN-SAF TSS is the summation of all the individual scores (0-100 scale). Symptoms response requires ≥ 50% reduction in the MPN-SAF TSS.

[j] Progressive disease assignment for splenomegaly requires confirmation by MRI or CT showing a ≥ 25% increase in spleen volume from baseline. Baseline values for both physical examination and imaging studies refer to pretreatment baseline and not to posttreatment measurements.