Official Title: A Phase 2, Open-Label, Monotherapy, Multicenter Study to Evaluate the Efficacy and Safety of INCB054828 in Subjects With Myeloid/Lymphoid Neoplasms With FGFR1 Rearrangement

NCT Number: NCT03011372

Document Date: INCB 54828-203 Statistical Analysis Plan 24 FEB 2021

Statistical Analysis Plan

INCB 54828-203

A Phase 2, Open-Label, Monotherapy, Multicenter Study to Evaluate the Efficacy and Safety of INCB054828 in Subjects With Myeloid/Lymphoid Neoplasms With FGFR1 Rearrangement

IND Number:	**131,608**
EudraCT Number:	**2016-002596-10**
Sponsor:	**Incyte Corporation** **1801 Augustine Cut-Off** **Wilmington, DE 19803** **United States**
Protocol Version:	**Protocol Amendment 5 dated 02 JUL 2020**
CRF Approval Date:	**04 SEP 2020**
SAP Version:	**Original**
SAP Author:	[redacted] [redacted] **Biostatistics**
Date of Plan:	**24 FEB 2021**

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

TABLE OF CONTENTS

TITLE PAGE 1
LIST OF ABBREVIATIONS 5
1. INTRODUCTION 6
2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS 6
2.1. Protocol and Case Report Form Version 6
2.2. Study Objectives and Endpoints 6
3. STUDY DESIGN 8
3.1. Randomization 9
3.2. Control of Type I Error 9
3.3. Sample Size Considerations 10
3.4. Schedule of Assessments 10
4. DATA HANDLING DEFINITIONS AND CONVENTIONS 10
4.1. Scheduled Study Evaluations and Study Periods 10
4.1.1. Day 1 10
4.1.2. Study Day 10
4.1.3. Baseline Value 10
4.1.4. Handling of Missing and Incomplete Dates 11
4.1.5. Cycle Length and Duration 11
4.1.6. Analysis Window 11
4.2. Variable Definitions 11
4.2.1. Prior and Concomitant Medication 11
5. STATISTICAL METHODOLOGY 12
5.1. General Methodology 12
5.2. Treatment Groups 12
5.3. Analysis Populations 12
5.3.1. Efficacy Evaluable Population 12
5.3.2. Per Protocol Population 12
5.3.3. Safety Population 13
6. BASELINE, EXPOSURE, AND DISPOSITION VARIABLES AND ANALYSES 13
6.1. Baseline and Demographics, Physical Characteristics, and Disease History 13
6.1.1. Demographics and Baseline Characteristics 13

6.1.2. Disease Characteristics at Initial Diagnosis 13
6.1.3. Disease Characteristics at Screening 13
6.1.4. Prior Therapy 14
6.1.5. Medical History 14
6.2. Disposition of Participants 14
6.3. Protocol Deviations 14
6.4. Exposure 14
6.5. Study Drug Compliance 15
6.6. Prior and Concomitant Medication 15
7. EFFICACY 16
7.1. Efficacy Hypotheses 16
7.2. Analysis of the Primary Efficacy Parameter 16
7.2.1. Primary Efficacy Analysis 16
7.2.2. Sensitivity and Supportive Analyses for Primary Endpoint 16
7.3. Analysis of the Secondary Efficacy Parameter 16
7.4. Analysis of Other Efficacy Parameters 17
7.5. Analysis of Exploratory Efficacy Variables 17
[redacted]
7.5.3. Other Exploratory Variables 19
8. SAFETY AND TOLERABILITY 19
8.1. General Considerations 19
8.2. Adverse Events 19
8.2.1. Adverse Event Definitions 19
8.2.2. Clinically Notable Adverse Events 20
8.2.3. Adverse Event Summaries 20
8.3. Clinical Laboratory Tests 22
8.3.1. Laboratory Value Definitions 22
8.3.2. Laboratory Value Summaries 22
8.3.3. Potential Hy's Law Events 22
8.4. Vital Signs 22
8.5. Electrocardiograms 23
9. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN 24

9.1. Changes to Protocol-Defined Analyses 24
9.2. Changes to the Statistical Analysis Plan....24
10. REFERENCES 25
APPENDIX A. RESPONSE CRITERIA FOR MYELOID/LYMPHOID NEOPLASMS WITH FGFR1 REARRANGEMENT 26
APPENDIX B. MYELOPROLIFERATIVE NEOPLASM SYMPTOM ASSESSMENT FORM (MPN-SAF) 30
APPENDIX C. PLANNED TABLES, FIGURES, AND LISTINGS....32

LIST OF TABLES

Table 1: Objectives and Endpoints 7
Table 2: European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire-C30 Scales 18
Table 3: Clinically Notable Adverse Events Groupings....20
Table 4: Criteria for Clinically Notable Vital Sign Abnormalities....23
Table 5: Criteria for Clinically Notable Electrocardiogram Abnormalities 23
Table 6: Statistical Analysis Plan Versions 24

LIST OF FIGURES

Figure 1: Study Design....9

LIST OF ABBREVIATIONS

Abbreviation	Term
AE	adverse event
BOR	best of response
CCyR	complete cytogenetic response
CHR	complete hematologic response
CI	confidence interval
CR	complete response
CRF	case report form
CTCAE	Common Terminology Criteria for Adverse Events
DOR	duration of response
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	electronic case report form
EORTC QLQ-C30	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30
FDA	Food and Drug Administration
FGF	fibroblast growth factor
FGFR	fibroblast growth factor receptor
MedDRA	Medical Dictionary for Regulatory Activities
MPN-SAF	Myeloproliferative Neoplasm Symptom Assessment Form
NCI	National Cancer Institute
OS	overall survival
PCyR	partial cytogenetic response
PD	progressive disease
PK	pharmacokinetic
PP	per protocol
PR	partial response
PT	preferred term
QD	once daily
QoL	quality of life
SAP	statistical analysis plan
SD	stable disease
SI	international system of units
SOC	system organ class
TEAE	treatment-emergent adverse event
WHO	World Health Organization

1. INTRODUCTION

This is a Phase II, open-label, monotherapy study of pemigatinib in participants with myeloid/lymphoid neoplasms with FGFR1 rearrangement. Section 1 and 3 of the Protocol provide a detailed description of the investigational product, target patient population, rationale for doses to be examined, and potential risks and benefits of treatment with pemigatinib.

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in the Study INCB 54828-203 Protocol.

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 54828-203 Protocol Amendment 5 dated 02 JUL 2020 and CRFs approved 04 SEP 2020. 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	
Evaluate the efficacy of pemigatinib in participants with myeloid/lymphoid neoplasms with FGFR1 rearrangement.	The proportion of participants who achieve CR as determined by investigator assessment according to the response criteria listed in Appendix A.
Secondary	
Evaluate the safety and efficacy of pemigatinib in participants with myeloid/lymphoid neoplasms with FGFR1 rearrangement.	• The proportion of participants who achieve response, defined as a best response of CR or PR, as determined by investigator assessment according to the response criteria listed in Appendix A. • The proportion of participants who achieve a CCyR as assessed by local analysis and investigator evaluation. • The proportion of participants who achieve a PCyR as assessed by local analysis and investigator evaluation. • Duration of CR, defined as the time from first assessment of CR to the earlier of disease progression or death due to any cause. • Duration of response, defined as the time from first assessment of CR or PR to the earlier of disease progression or death due to any cause. • Progression-free survival. • Overall survival. • Safety and tolerability, as assessed by evaluating the frequency, duration, and severity of AEs; through review of findings of physical examinations, changes in vital signs, and ECGs; and through clinical laboratory blood and urine sample evaluations.

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
Exploratory	
[redacted]	

3. STUDY DESIGN

This is an open-label monotherapy study of pemigatinib in participants with myeloid/lymphoid neoplasms with FGFR1 rearrangement. The study will enroll approximately 46 participants.

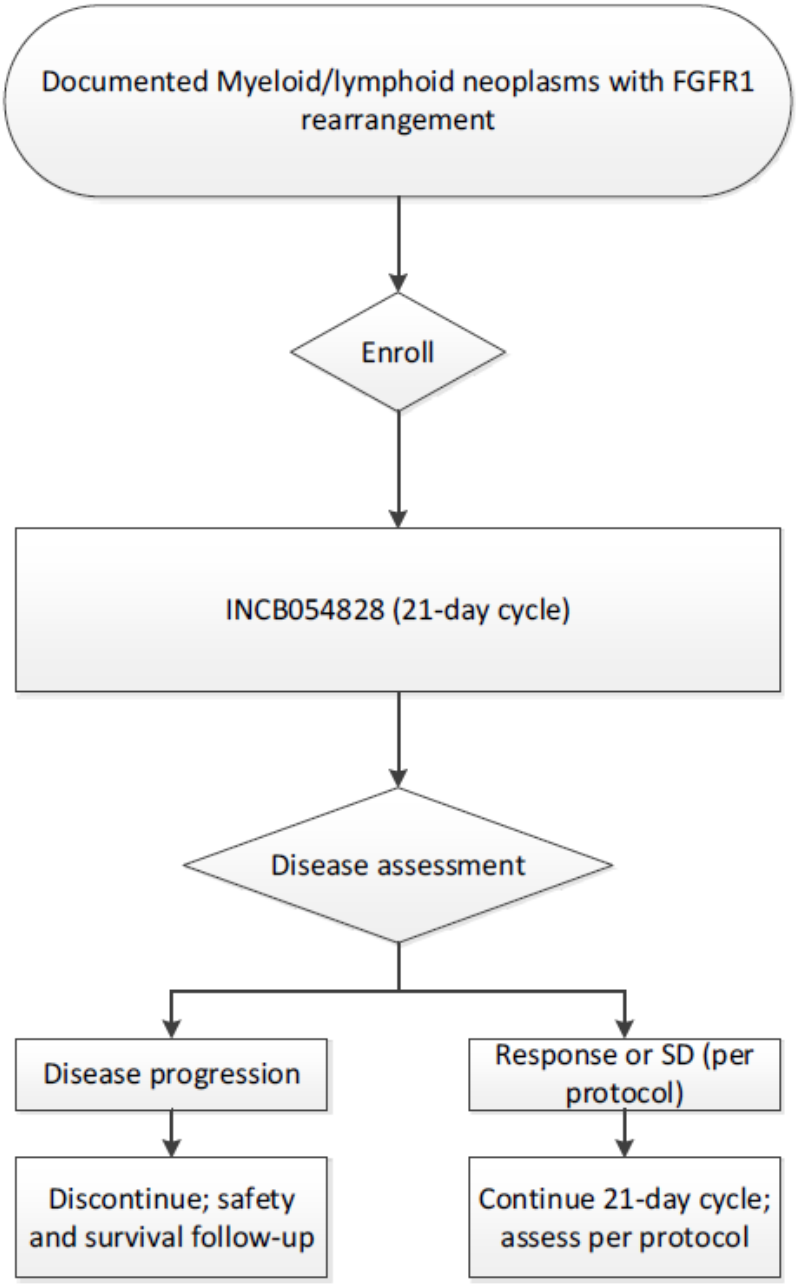
Participants will receive a QD dose of pemigatinib at 13.5 mg on a 2-weeks-on-therapy and 1-week-off-therapy schedule. With Protocol Amendment 3, the administration schedule was adjusted, and newly enrolled participants will receive pemigatinib at 13.5 mg continuous administration (no planned dose hold). Participants receiving treatment under previous versions of the Protocol may be switched to continuous administration after completing at least 3 cycles if there are no ongoing Grade 2 or higher related TEAEs. The written request to switch to continuous administration should be sent to the sponsor's medical monitor.

With Protocol Amendment 4, up-titration of pemigatinib was introduced. In any participant who has not had a serum phosphate level of > 5.5 mg/dL and who meet the criteria in Section 5.4.4 of the Protocol, the investigator will increase the daily dose to 18 mg.

All potential participants must have documentation of an 8p11 translocation known to activate FGFR1 through the site's own cytogenetics laboratory. Once documentation has been provided, the participant will then undergo screening to meet the rest of the inclusion/exclusion criteria. Once a participant has completed screening, the participant will be enrolled.

Treatment will start on Cycle 1 Day 1. Participants will undergo regular safety assessments during treatment as well as regular efficacy assessments. Participants will be allowed to continue administration in 21-day cycles until study treatment withdrawal criteria are met. The overall study design is shown in Figure 1.

Figure 1: Study Design



3.1. Randomization

Not applicable.

3.2. Control of Type I Error

Unless otherwise specified, all CIs provided will be at the 95% confidence level.

3.3. Sample Size Considerations

Approximately 46 participants are planned for the final analysis of the primary endpoint of overall CR rate. With the assumed rates of 35% for the intervention, a sample size of approximately 46 participants would provide > 80% probability to have a 95% CI with lower limit of > 15% assuming 10% lost to follow-up.

3.4. Schedule of Assessments

See Protocol Section 6 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 study drug (pemigatinib) 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 pemigatinib.

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

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

4.1.4. 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, partial diagnosis date will be handled as follows in the calculation:

- If only the day is missing, then use the first day of the month.
- If both the month and day are missing, then use 01 JAN of the year.
- Time since diagnosis will be missing if the diagnosis date is completely missing.

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

- If only the day is missing, then use the earlier date of the last day of the month or the date that the participant discontinued treatment.
- Otherwise, the date that the participant discontinued treatment will be used as the date of the last dose.

For relevant efficacy endpoints, partial date of 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 is earlier than mmyyyy for the death date, then the death date will be set to the first day of the death month.
- Otherwise, a 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 study drug is administered. Scheduled cycle length is 21 days with first day of each cycle corresponding with the first day of pemigatinib administration in that cycle.

4.1.6. Analysis Window

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

4.2. Variable Definitions

4.2.1. Prior and Concomitant Medication

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

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

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

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

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

5. STATISTICAL METHODOLOGY

5.1. General Methodology

Unless otherwise noted, SAS® software (SAS Institute Inc, Cary, NC; v9 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, single treatment group study. Participants will be summarized overall by total only.

5.3. Analysis Populations

5.3.1. Efficacy Evaluable Population

For FDA submission, the efficacy evaluable population includes all enrolled participants with an FGFR1 rearrangement and at least 1 prior systemic therapy who received at least 1 dose of study drug.

For submissions in other regions, the efficacy evaluable population includes all enrolled participants with an FGFR1 rearrangement who received at least 1 dose of study drug.

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

5.3.2. Per Protocol Population

Participants in the efficacy evaluable population who are considered to be sufficiently compliant with the Protocol comprise the PP population.

The following procedures will be performed to identify those participants who are to be excluded from the PP population before the database lock:

- Clinical review of Protocol deviations/violations
- Clinical review of concomitant medications as defined in Section 5.6 of the Protocol
- Clinical review of the dose administration and drug accountability listing

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

5.3.3. Safety Population

The safety population includes all enrolled participants who received at least 1 dose of study drug.

All safety analyses will be conducted on the safety population.

6. BASELINE, EXPOSURE, AND DISPOSITION VARIABLES AND ANALYSES

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

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

6.1.1. Demographics and Baseline Characteristics

The following demographics and baseline characteristics will be summarized for the efficacy evaluable population and safety population: age, sex, race, ethnicity, weight, height, and ECOG performance status.

6.1.2. Disease Characteristics at Initial Diagnosis

Time since initial diagnosis as well as the following disease characteristics at initial diagnosis will be summarized for the efficacy evaluable population and the safety population: specific hematologic malignancy/disease type, the presence of extramedullary disease, fibrotic marrow, organomegaly, blast phase, and whether eosinophilia or monocytosis was present in the peripheral blood.

Time since initial diagnosis will be calculated as:

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

6.1.3. Disease Characteristics at Screening

The following disease characteristics at Screening will be summarized for efficacy evaluable population and safety population: hematologic malignancy/disease type, the presence of extramedullary disease, fibrotic marrow, organomegaly, blast phase, if eosinophilia ($> 0.5 \times 10^9$/L) or monocytosis ($> 0.8 \times 10^9$/L) was present in the peripheral blood, 8p11 abnormality, and additional cytogenetic abnormalities.

Organomegaly is defined as either spleen or liver is palpable at screening; blase phase is defined as bone marrow assessment ≥ 30% at screening; fibrotic marrow is defined as MF-1 or higher on fibrosis grading based on central pathology review at screening.

6.1.4. Prior Therapy

Number of prior systemic cancer therapy regimens will be summarized for all participants in the efficacy evaluable population and safety population. Regimen name, component drugs, start and stop date, best response, reason for discontinuation, and date of relapse/progression will be listed.

Number of participants who received prior radiation will be summarized for the efficacy evaluable population and safety population. Radiotherapy type, body site, start and stop date, number of fractions received, and total dose will be listed.

Participants who had prior surgery or surgical procedure for the malignancies under study will be listed with date and description of the surgery/procedure.

Number of participants who had prior hematopoietic stem cell transplant will be summarized for the efficacy evaluable population and safety population. Transplant date, type, source of cells, line of therapy, best response, and date of relapse/progression will be listed. The regimen name, medication term, dose, and route for prior hematopoietic stem cell transplant will be listed.

6.1.5. Medical History

For participants in the efficacy evaluable population and safety population, medical history will be summarized. 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 Participants

The number and percentage of participants who were enrolled, treated, discontinued from study treatment with a primary reason for discontinuation, and withdrew from the study with a primary reason for withdrawal will be summarized for the efficacy evaluable population and safety population. The number of participants enrolled by country and site will also be provided.

6.3. Protocol Deviations

Protocol deviations will be summarized and listed.

6.4. Exposure

For participants in the safety population, exposure to pemigatinib will be summarized descriptively as the following:

- **Number of treatment cycles:** Number of cycles with a nonzero dose of pemigatinib.
- **Duration of treatment (days):** Date of last dose of pemigatinib – date of first dose of pemigatinib + 1.

- **Average daily dose (mg/day):** Total actual dose taken (mg) / duration of treatment (days).

  Total actual dose taken will be calculated based on the information entered on the Drug Accountability CRF.

Duration of exposure in months will be calculated based on the assumption that each month has 30.4375 days. The number and percentage of participants in each duration category (< 1 month, 1 to < 3 months, 3 to < 6 months, 6 to < 9 months, 9 to < 12 months, 12 to < 15 months, 15 to < 18 months, 18 to < 21 months, 21 to < 24 months, ≥ 24 months as applicable) will be summarized.

Number of participants without dose reduction, with at least 1 dose reduction, with only 1 dose reduction, as well as with more than 1 dose reduction will be summarized.

Number of participants without dose interruption, with at least 1 dose interruption, with only 1 dose interruption, as well as with more than 1 dose interruption will be summarized.

6.5. Study Drug Compliance

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

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

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

The total actual dose taken will be calculated based on information entered on the Drug Accountability CRF. If there is dispensed drug that has not been returned yet, the actual dose taken starting from the dispense date of the unreturned drug will be imputed by the dose taken as reported on the Dosing CRF.

6.6. Prior and Concomitant Medication

Prior medications and concomitant medications will be coded using the WHO Drug Dictionary. Number and percentage of participants in the efficacy evaluable population for each prior and concomitant medications will be summarized by WHO drug class and WHO drug PT.

The number and percentage of participants with concomitant medications of phosphate binder will be summarized by WHO drug class and WHO drug term as follows:

- Phosphate binder includes but is not limited to the following terms: sevelamer, calcium acetate, calcium carbonate, lanthanum, ferric citrate, nicotinamide, tenapanor, aluminum hydroxyide, calcium citrate, and sucroferric oxyhydroxide.

7. EFFICACY

Appendix C provides a list of data displays.

7.1. Efficacy Hypotheses

Not applicable.

7.2. Analysis of the Primary Efficacy Parameter

7.2.1. Primary Efficacy Analysis

The primary endpoint of the study is the proportion of participants who achieve a BOR of CR as determined by investigator assessment according to the response criteria for myeloid/lymphoid neoplasms with FGFR1 rearrangement in Appendix A. This analysis will be based on the efficacy evaluable population. Participants who do not have sufficient baseline or on-study response assessment information to be adequately assessed for response status will be included in the denominators in the calculation of CR rate. The 95% CI for the proportion of participants with CR will be estimated using the Clopper-Pearson method.

7.2.2. Sensitivity and Supportive Analyses for Primary Endpoint

The primary endpoint will be analyzed with the PP population as a sensitivity analysis to the efficacy population.

7.3. Analysis of the Secondary Efficacy Parameter

Secondary efficacy analyses will be conducted for the efficacy evaluable population.

The proportion of participants who achieve response, defined as BOR of CR or PR, as determined by investigator assessment according to the response criteria listed in Appendix A, will be estimated with its 95% CI.

The proportion of participants who achieve BOR of CCyR as assessed by local analysis and investigator evaluation will be estimated with its 95% CI.

The proportion of participants who achieve BOR of PCyR as assessed by local analysis and investigator evaluation will be estimated with its 95% CI.

Duration of CR is defined as the time from first assessment of CR to the earlier of disease progression or death due to any cause. Participants without disease progression or death at the time of analysis will be censored at the date of last response assessment before the cutoff date. Participants who start a new cancer therapy or have stem cell transplant before disease progression will be censored at the date of last response assessment before new cancer therapy start or transplant. Duration of CR will be analyzed by the Kaplan-Meier method. The Kaplan-Meier estimate of median duration of CR will be presented with its 95% CI. The 95% CI will be calculated using the Brookmeyer and Crowley's method (Brookmeyer and Crowley 1982).

Duration of response is defined as the time from first assessment of CR or PR to the earlier of disease progression or death due to any cause. Participants without disease progression or death at the time of analysis will be censored at the date of last response assessment before the cutoff

date. Participants who start a new cancer therapy or have stem cell transplant before disease progression will be censored at the date of last response assessment before new cancer therapy start or transplant. Duration of response will be analyzed by the Kaplan-Meier method. The 95% CI will be calculated using the Brookmeyer and Crowley's method (Brookmeyer and Crowley 1982).

Progression-free survival is defined as the time from the first date of taking study drug until the date of disease progression, as measured by response criteria or until death due to any cause, whichever is earlier. Participants who are still alive without experiencing disease progression at the time of analysis will be censored at the date of the last response assessment before the cutoff date. Participants who start a new cancer therapy or have stem cell transplant before disease progression will be censored at the date of last response assessment before new cancer therapy start or transplant. Progression-free survival data will be analyzed by the Kaplan-Meier method. The 95% CI will be calculated using the Brookmeyer and Crowley's method (Brookmeyer and Crowley 1982).

Overall survival is defined as the time from the first day of taking study drug until death due to any cause. Participants without death observed at the time of the analysis will be censored at last date known to be alive. Overall survival will be analyzed by the Kaplan-Meier method. The 95% CI will be calculated using the Brookmeyer and Crowley's method (Brookmeyer and Crowley 1982).

7.4. Analysis of Other Efficacy Parameters

Proportion of participants who achieve BOR of CR, proportion of participants who achieve BOR of CR or PR, proportion of participants who achieve BOR of CCyR, and proportion of participants who achieve BOR of PCyR as assessed by central review committee will be summarized along with their 95% CI.

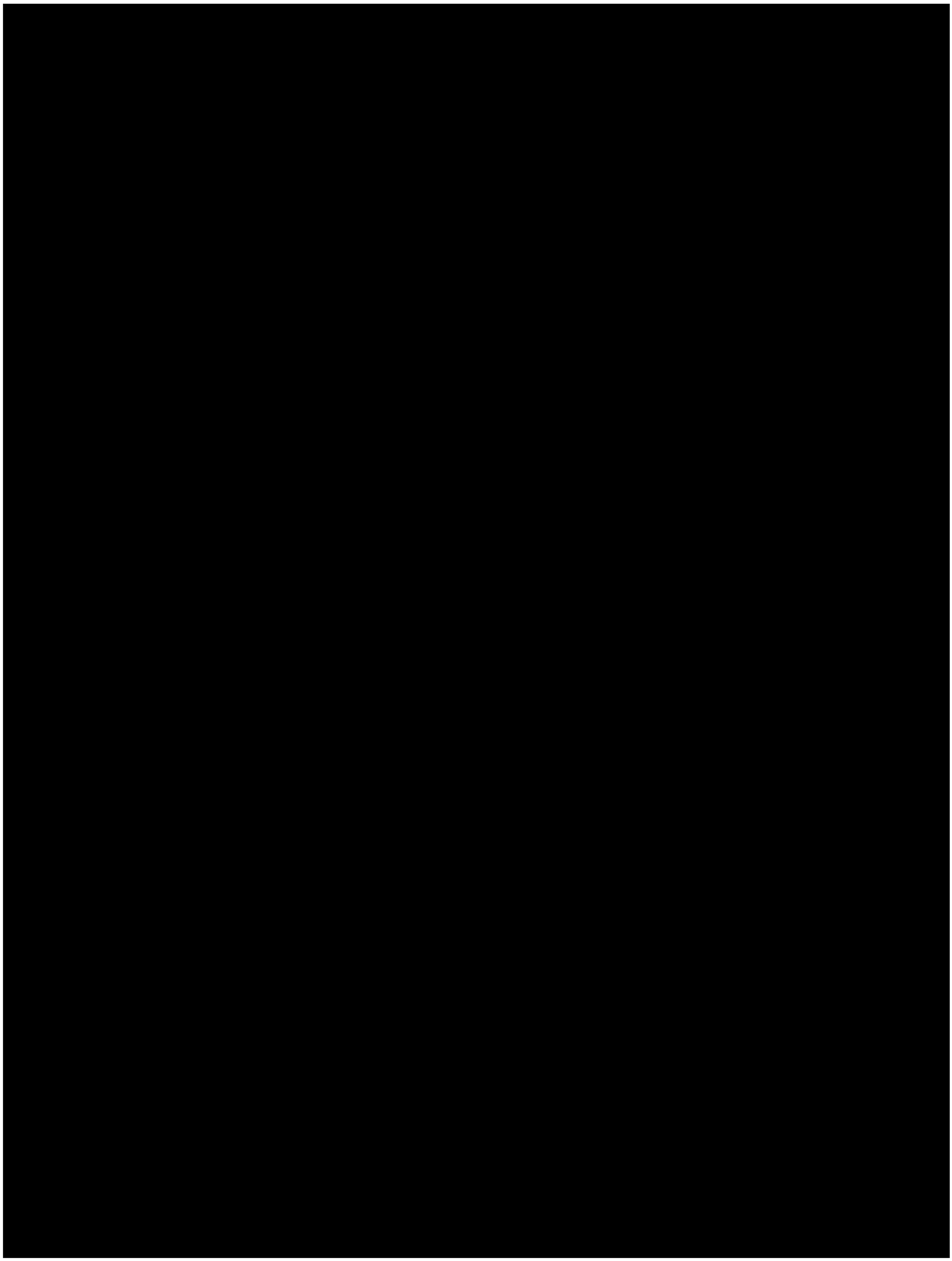
Duration of CR, DOR, and progression-free survival as assessed by central review committee will be analyzed by the Kaplan-Meier method.

For participants who have undergone stem cell transplant after treatment with pemigatinib without disease progression, transplant outcome data will be collected, including rates of graft failure, transplant-related mortality, graft-versus-host disease, and OS. Those data will be summarized (if there are sufficient number of participants who have undergone stem cell transplant, eg, > 10 participants) and listed.

Eastern Cooperative Oncology Group performance status at scheduled assessment times will be summarized.

7.5. Analysis of Exploratory Efficacy Variables

[redacted]



For all other scales, the standardized score will be calculated by the following:

$$(\frac{RawScore - 1}{Range}) \times 100$$

7.5.3. Other Exploratory Variables

[redacted]

8. SAFETY AND TOLERABILITY

Appendix C provides a list of data displays.

8.1. General Considerations

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

Unless otherwise stated, table summaries will be limited to TEAEs.

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 and within 30 days of 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 and in relation to study drug administration.

Adverse events will be tabulated by MedDRA PT and SOC. Severity of AEs will be graded using the NCI CTCAE v4.03. The CTCAE reporting guidelines and grading details are available on the Cancer Therapy Evaluation Program website.

A grading (severity) scale is provided for each AE term. If the toxicity is not included in the CTCAE v4.03 criteria, it will be rated on a scale of 1 to 4 as follows: 1 = mild, 2 = moderate, 3 = severe and 4 = life-threatening. The CTCAE v4.03 severity of Grade 5 will not be used; AEs resulting in death will be graded accordingly using Grades 1 through 4 and have the outcome noted as fatal. When the intensity of an AE changes over time for a reporting period (eg, between visits), each change in intensity will be reported as an AE until the event resolves.

The subset of AEs considered by the investigator to be related to study drug will be considered to be treatment-related AEs. The incidence of AEs and treatment-related AEs will be tabulated. Serious TEAEs will also be tabulated.

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

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

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

8.2.2. Clinically Notable Adverse Events

Specific groupings of clinically notable AEs will be considered and the number of participants with at least 1 event within each grouping will be reported. Such groups consist of AEs for which there is a specific clinical interest in connection with the study drug or AEs that are similar in nature (although not identical). The groups are defined as per Table 3. All clinically notable AEs are defined through reviewing PT according to the current MedDRA v21.1.

Table 3: Clinically Notable Adverse Events Groupings

Categories	Preferred Terms
Serous retinal detachment	Serous retinal detachment, detachment of macular retinal pigment epithelium, detachment of retinal pigment epithelium, retinal detachment, subretinal fluid, chorioretinopathy, retinal pigment epitheliopathy, chorioretinal disorder, retinopathy, maculopathy, retinal disorder, retinal thickening, chorioretinal folds, chorioretinal scar
Nail toxicity	Nail toxicity, nail bed tenderness, nail bed disorder, nail bed bleeding, nail disorder, nail discolouration, nail discomfort, nail dystrophy, nail hypertrophy, nail ridging, nail infection, onychalgia, onychoclasis, onycholysis, onychomadesis, onychomycosis, paronychia, fungal paronychia
Hyperphosphatemia	Hyperphosphataemia, blood phosphorus increased
Hypophosphatemia	Hypophosphataemia, blood phosphorus decreased
Dry eye	Dry eye, meibomian gland dysfunction, lacrimation increased, keratitis, punctate keratitis, pinguecula, pterygium
Eyelash changes	Eyelash changes, growth of eyelashes, trichiasis, trichomegaly
Vision blurred	vision blurred, visual impairment, visual acuity reduced
Vitreous detachment	Vitreous detachment, vitreous floaters

8.2.3. Adverse Event Summaries

An overall summary of AEs will include the following:

- Number (%) of participants reporting any TEAEs
- Number (%) of participants reporting any serious TEAEs
- Number (%) of participants reporting any Grade 3 or higher TEAEs

- Number (%) of participants reporting any TEAEs related to pemigatinib
- Number (%) of participants who temporarily interrupted pemigatinib because of TEAEs
- Number (%) of participants who permanently discontinued pemigatinib because of TEAEs
- Number (%) of participants with pemigatinib dose reductions because of TEAEs
- Number (%) of participants who had a fatal TEAE

The following summaries will be produced by MedDRA term:

- 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 treatment-related TEAEs by MedDRA SOC and PT
- Summary of treatment-related TEAEs by MedDRA PT in decreasing order of frequency
- Summary of Grade 3 or higher treatment-related TEAEs by MedDRA SOC and PT
- Summary of 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 pemigatinib dose reduction by MedDRA SOC and PT
- Summary of TEAEs leading to pemigatinib dose interruption by MedDRA SOC and PT
- Summary of TEAEs leading to discontinuation of pemigatinib by MedDRA SOC and PT
- Summary of sponsor-defined clinically notable TEAEs by category and PT
- Summary of Grade 3 or higher sponsor-defined clinically notable TEAEs by category and PT
- Summary of serious sponsor-defined clinically notable TEAEs by category and PT
- Summary of sponsor-defined clinically notable TEAEs leading to dose reduction by category and PT

- Summary of sponsor-defined clinically notable TEAEs leading to dose interruption by category and PT
- Summary of sponsor-defined clinically notable TEAEs leading to discontinuation of study drug by category 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.

8.3.2. Laboratory Value Summaries

All test results and associated normal ranges will be converted to SI units. All tests with numeric values will have a unique unit per test.

Numeric laboratory values will be summarized descriptively in SI units, and non-numeric test values will be tabulated when necessary. In addition, line graph will be provided for phosphate, creatinine, blood urea nitrogen, calcium, sodium, 1,25-dihydroxyvitamin D, 25-hydroxyvitamin D, and parathyroid hormone.

Severity grades will be assigned to laboratory test values based on the numeric component of CTCAE v4.03. 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. The number of participants who experienced worsening of laboratory abnormalities will be summarized by maximum severity.

8.3.3. Potential Hy's Law Events

The participants with elevated alanine aminotransferase or alanine aminotransferase > 3 × upper limit of normal range and alkaline phosphatase < 2 × upper limit of normal range accompanied by total bilirubin > 2 × upper limit of normal range at the same visit will be listed.

8.4. Vital Signs

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

Criteria for clinically notable vital sign abnormalities are defined in Table 4. The abnormal values for subjects exhibiting clinically notable vital sign abnormalities will be listed. Alert vital signs are defined as an absolute value outside the defined 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 4: Criteria for Clinically Notable Vital Sign Abnormalities

Parameter	High Threshold	Low Threshold
Systolic blood pressure	> 155 mmHg	< 85 mmHg
Diastolic blood pressure	> 100 mmHg	< 40 mmHg
Pulse	> 100 bpm	< 45 bpm
Temperature	> 38ºC	< 35.5ºC
Respiratory rate	> 24 breaths/min	< 8 breaths/min

8.5. Electrocardiograms

Twelve-lead ECGs including RR, PR, QRS, QT, and QTc intervals will be obtained for each participant during the study. Values at each scheduled visit, change from baseline, and percentage change from baseline will be summarized for each ECG parameter. Baseline will be determined as the average of all nonmissing values before the first administration of study drug.

Criteria for clinically notable ECG abnormalities are defined in Table 5. Electrocardiogram values will also be considered abnormal if the absolute percentage change from baseline is more than 25%. Participants exhibiting ECG abnormalities will be listed with study visit. 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 and QTcF values, defined as absolute values > 450 ms, > 500 ms, or change from baseline > 30 ms, will be summarized. The number of participants with clinically significant ECG abnormalities will be summarized.

Table 5: Criteria for Clinically Notable Electrocardiogram Abnormalities

Parameter	High Threshold	Low Threshold
PR	> 220 ms	< 75 ms
RR	> 1330 ms	< 600 ms
QT	> 500 ms	< 300 ms
QRS	> 120 ms	< 50 ms
QTcF	> 450 ms	< 295 ms

QTcF = Fridericia correction.

9. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 6.

Table 6: Statistical Analysis Plan Versions

SAP Version	Date
Original	24 FEB 2021

9.1. Changes to Protocol-Defined Analyses

Efficacy evaluable population is updated to only include participants with FGFR1 rearrangement and with at least 1 prior systemic therapy per health authority request.

9.2. Changes to the Statistical Analysis Plan

Not applicable.

10. REFERENCES

Brookmeyer R, Crowley J. A confidence interval for the median survival time. Biometrics 1982;38:29-41.

APPENDIX A. RESPONSE CRITERIA FOR MYELOID/LYMPHOID NEOPLASMS WITH FGFR1 REARRANGEMENT

Table A1: Response Criteria

Response Subcategory	Response Criteria
CR[a]	Presence of all of the following improvements: 1. Bone marrow: ≤ 5% myeloblasts (including monocytic blast equivalent) and no lymphoblasts, with normal maturation of all cell lines, and return to normal cellularity[b]. 2. Osteomyelofibrosis absent or equal to "mild reticulin fibrosis" (Grade 1 or less fibrosis)[c] 3. Peripheral blood[d] – WBC ≤ 10×10^9 cells/L. – Hgb ≥ 11 g/dL. – Platelets ≥ 100×10^9/L; ≤ 450×10^9/L. – Neutrophils ≥ 1.0×10^9/L. – Blasts = 0%. – Neutrophil precursors reduced to ≤ 2%. – Monocytes ≤ 1×10^9/L. – Eosinophils ≤ 0.5×10^9/L. 4. Extramedullary disease: Complete resolution of extramedullary disease present before therapy (eg, lymphadenopathy), including palpable hepatosplenomegaly. NOTE: Persistent low-level dysplasia is permitted given subjectivity of assignment of dysplasia[b].
PR	Presence of all of the following improvements: 1. Reduction of bone marrow blasts (and blast equivalents) by 50%, but remaining > 5% of cellularity (except in cases with ≤ 5% bone marrow blasts at baseline). 2. Normalization of peripheral blood indices listed in CR Criterion 3. 3. Extra medullary disease response of CMR/CR or PMR/PR (see Table D2).
Progression of disease	Combination of 2 major criteria, 1 major and 2 minor criteria, or 3 minor criteria from following lists: **Major criteria:** • Increase in blast count[a] o < 5% blasts: ≥ 50% increase and to > 5% blasts. o 5%-10% blasts: ≥ 50% increase and to > 10% blasts. o 10%-20% blasts: ≥ 50% increase and to > 20% blasts. o 20%-30% blasts: ≥50% increase and to > 30% blasts. • Evidence of cytogenetic evolution o Re-appearance of a previously present or appearance of a new cytogenetic abnormality in complete cytogenetic remission via classic karyotyping or FISH. o Increase in cytogenetic burden of disease in partical cytogenetic remission by ≥ 50% via classic karyotyping or by ≥ 50% and involving at least 10% (eg, 2/200) of cells via FISH.

Table A1: Response Criteria (Continued)

Response Subcategory	Response Criteria

Progression of disease (continued)	• New or worsening extramedullary disease
	  o Worsening splenomegaly
	  ▪ Progressive splenomegaly that is defined by IWG-MRT: the appearance of a previously absent splenomegaly that is palpable at > 5 cm below the left costal margin or a minimum 100% increase in palpable distance for baseline splenomegaly of 5 to 10 cm or a minimum 50% increase in palpable distance for baseline splenomegaly of > 10 cm.
	  o Extramedullary disease outside of the spleen.
	Minor criteria:
	• Transfusion dependence.[e]
	• Significant loss of maximal response on cytopenias ≥ 50% decrement from maximum remission/response in granulocytes or platelets.
	• Reduction in Hgb by ≥ 1.5g/dL from best response or from baseline as noted on complete blood count.
	• Evidence of clonal evolution (molecular).

Stable disease	Meeting neither progression of disease nor response criteria. Participants with stable disease will be further characterized according to criteria presented in Table A3.
Cytogenetic Response[f]	
Complete (cCyR)	0% 8p11 translocated metaphases as seen on classic karyotyping with minimal of 20 metaphases, or FISH.
Partial (pCyR)	Decrease from baseline of 50% or more 8p11 translocated metaphases as seen on classic karyotyping with minimal of 20 metaphases, or FISH.

CR = complete response; FISH = fluorescence in situ hybridization; Hgb = hemoglobin; IWG-MRT = International Working Group-Myeloproliferative Neoplasms Research and Treatment; PR = partial response; WBC = white blood cell.

[a] Given the current lack of a validated tool to assess complete resolution of symptoms, "CR with resolution of symptoms" (a complete resolution of disease-related symptoms as noted by the MPN-SAF in presence of CR) will be a provisional category of disease response.

[b] Presence of dysplastic changes, which may be interpreted within the scope of normal range of dysplastic changes, may still exist in the presence of CR as allowed in MDS IWG. Marrow should exhibit age-adjusted normocellularity in CR.

[c] The assessment of CR must be confirmed by a minimum of 2 bone marrow assessments only to confirm improvement in fibrosis. If there is no significant fibrosis present on the initial bone marrow biopsy, then a second biopsy is not required to prove resolution of fibrosis. Grading of fibrosis in measurement of treatment response should be according to the European Consensus System.

[d] Resolution of abnormal peripheral blood counts must persist for at least 2 separate analyses over at least 8 weeks. In the case of proliferative disease, CR will include resolution of thrombocytosis to a normal platelet count (150-450 × 10^9/L) and resolution of leukocytosis to WBC ≤ 10 × 10^9 cells/L but ≥ 1.5 × 10^9/L. Hemoglobin should be maintained > 11 g/dL and platelets ≥ 100 × 10^9/L without the support of transfusions. Reduction in myeloid precursors (promyelocytes, myelocytes, metamyelocytes, nucleated red blood cells) to less than appreciable levels (≤ 2%-3%) and/or 1 × 10^9/L monocytosis and/or eosinophils ≤ 0.5 × 10^9/L in the absence of infection, cytokine treatment, or other reactive causes.

[e] Transfusion dependency is defined by a history of at least 2 U of red blood cell transfusions in the past month for a hemoglobin level < 8.5 g/dL that was not associated with clinically overt bleeding. Cytopenias resulting from therapy should not be considered in assessment of progression.

[f] Loss of cytogenetic burden of disease by (via FISH or classic karyotyping) is required to reach complete cytogenetic response. Decrease in the cytogenetic burden of disease must be by ≥ 50% (via FISH or classic karyotyping) to be indicative of a partial cytogenetic response. Given variability of fluorescent probes used in FISH, cytogenetic normalization via FISH will depend on the performance characteristics of the specific probes used.

Table A2: Extramedullary Disease Response Criteria

Assessment	PET-CT Based	CT Based
CMR/CR		
Target	A 5PS score of 1, 2 or 3, w/ or w/o residual mass. Additionally, if screening FDG-PET scan is missing & on-study 5PS score is 1-3, then CMR is possible.	Nodal: < 1.5 cm in LDi. Extra-nodal: Absent.
Non-target		Absent.
New lesions	None.	
PMR/PR		
Target	5PS score of 4 or 5 with reduced FDG uptake compared to baseline and residual masses of any size. Note: Reduced uptake defined as ≥ 25% decrease in $\%\Delta SUV_{max}$.	≥ 50% decrease from baseline in SPD of all target lesions.
Non-target		No increase.
New lesions	None.	
NMR/SD		
Target	5PS score of 4 or 5 with no significant change in FDG uptake compared to baseline and residual masses of any size. Note: "No significant change in uptake" defined as the criteria of PMR/PMD not being met.	< 50% decrease from baseline in SPD of all target lesions. No PD criteria met.
Non-target		No progression.
New lesions	None.	
PMD/PD		
Target	5PS score of 4 or 5 with significant increase in FDG uptake, defined as ≥ 50% increase in the $\%\Delta SUV_{max}$ of the most FDG-avid disease.	Node or lesion must be abnormal with an LDi > 15 mm, an increase by ≥ 50% from nadir PPD, and an increase in LDi or SDi from nadir by: • At least 5 mm for lesions measuring ≤ 20 mm or • At least 10 mm for lesions measuring > 20 mm.
Non-target		Unequivocal progression.
New lesions	New or recurrent markedly diffuse FDG-avid uptake in the liver or spleen.	• Regrowth of previously resolved lesions. • New node > 1.5 cm in any axis. • New extranodal site > 1.0 cm in any axis.

5PS = Deauville 5-point scale; CMR = complete metabolic response; CR = complete response; CT = computed tomography; FDG = fludeoxyglucose; LDi = longest transverse diameter of lesion; NMR = no metabolic response; PD = progressive disease; PET = positron emission tomography; PMD = progressive metabolic disease; PMR = partial metabolic response; PPD = product of perpendicular diameters; PR = partial response; SD = stable disease; SDi = shortest axis perpendicular to LDi; SPD = sum of product of perpendicular diameters of multiple lesions; SUV = standardized uptake value.

Table A3: Characteristics of Stable Disease

Characteristic	Criteria
CHR	Peripheral blood normalization as in CR Criterion 3 (Table A1; peripheral blood response must be verified at ≥ 8 weeks)
Marrow response	• Complete marrow response: Presence of all marrow criteria listed in CR criterion without normalization of peripheral blood indices listed in CR Criterion 2. • Partial marrow response: Bone marrow blasts (and blast equivalents) reduced by 50%, but remaining > 5% of cellularity, or reduction in grading of reticulin fibrosis from baseline on at least 2 bone marrow evaluations spaced at least 2 months apart.
Clinical benefit	Requires 2 of the following in the absence of progression or CR/PR and independent of marrow response (peripheral blood response must be verified at ≥ 8 weeks) to be considered a clinical benefit: Erythroid response: • Hgb increase by ≥ 2.0 g/dL. • TI for > 8 weeks for patients requiring at least 4 packed red blood cell transfusions in the previous 8 weeks. • Only red blood cell transfusions given based on physician's judgment for a pretreatment Hgb of ≤ 8.5 g/dL will count in the red blood cell TI response evaluation.[a] Platelet response: • Transfusion independence when previously requiring platelet transfusions of at least a rate of 4 platelet transfusions in the previous 8 weeks. • Pretreatment ≤ 20×10^9/L: Increase from < 20×10^9/L to > 20×10^9/L and by at least 100%. • Pretreatment > 20×10^9/L but ≤ 100×10^9/L: absolute increase of ≥ 30×10^9/L.[a] Neutrophil response: • Pretreatment ≤ 0.5×10^9/L: At least 100% increase and an absolute increase ≥ 0.5×10^9/L. • Pretreatment > 0.5×10^9/L and ≤ 1.0×10^9/L: At least 50% increase and an absolute increase ≥ 0.5×10^9/L.[a] Eosinophil response: • Normalization if pretreatment > 0.5×10^9/L.[a] Extramedullary disease response: • As defined in Table A2.
Symptom response	Improvement in symptoms as noted by decrease of ≥ 50% as per the MPN-SAF scoring; participants scoring < 20 at baseline were not considered eligible for measuring clinical benefit.

CR = complete response; CHR = complete hematologic response; Hgb = hemoglobin; PR = partial response; TI = transfusion independence.

[a] Resolution of abnormal peripheral blood counts must persist for at least 2 separate analyses over at least 8 weeks. In the case of proliferative disease, CR will include resolution of thrombocytosis to a normal platelet count (150-450 × 10^9/L) and resolution of leukocytosis to WBC ≤ 10×10^9 cells/L but ≥ 1.5×10^9/L. Hemoglobin should be maintained > 11 g/dL and platelets ≥100×10^9/L without the support of transfusions. Clinical benefit may occur when these changes occur in absence of other changes required for CR or marrow response. Platelet and packed red blood cell TI would be considered for clinical benefit, and duration of TI should be monitored. Reduction in myeloid precursors (promyelocytes, myelocytes, metamyelocytes, nucleated red blood cells) to less than appreciable levels (≤ 2%-3%) and/or 1×10^9/L monocytosis in the absence of infection, cytokine treatment, or other reactive causes.

APPENDIX B. MYELOPROLIFERATIVE NEOPLASM SYMPTOM ASSESSMENT FORM (MPN-SAF)

Instructions: Please fill out all questions, as best able, reflecting how these symptoms affected you over the **LAST WEEK** unless directed otherwise. Complete forms until the STOP instruction toward the end of the packet.

Symptom	1 to 10 (0 if absent) ranking* 1 is most favorable and 10 least favorable
Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your fatigue right NOW	(No Fatigue) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your USUAL level of fatigue during past 24 hours	(No Fatigue) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your WORST level of fatigue during past 24 hours	(No Fatigue) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Circle the one number that describes how, during the past 24 hours, fatigue has interfered with your	
• General activity	(Does not Interfere) 0 1 2 3 4 5 6 7 8 9 10 (Completely Interferes)
• Mood	(Does not Interfere) 0 1 2 3 4 5 6 7 8 9 10 (Completely Interferes)
• Walking ability	(Does not Interfere) 0 1 2 3 4 5 6 7 8 9 10 (Completely Interferes)
• Normal work (includes work both outside the home and daily chores)	(Does not Interfere) 0 1 2 3 4 5 6 7 8 9 10 (Completely Interferes)
• Relations with other people	(Does not Interfere) 0 1 2 3 4 5 6 7 8 9 10 (Completely Interferes)
• Enjoyment of life	(Does not Interfere) 0 1 2 3 4 5 6 7 8 9 10 (Completely Interferes)
Abdominal pain	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Abdominal discomfort	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Inactivity	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)

Problems with headaches	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Problems with concentration - Compared to prior to my MPD	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Dizziness/ Vertigo/ Lightheadedness	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Numbness/ Tingling (in my hands and feet)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Difficulty sleeping	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Depression or sad mood	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Problems with sexual desire or Function	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Cough	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Night sweats	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Itching (pruritus)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Bone pain (diffuse not joint pain or arthritis)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
Fever (>100 F)	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Daily)
Unintentional weight loss last 6 months	(Absent) 0 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
What is your overall quality of life?	(As good as it can be) 0 1 2 3 4 5 6 7 8 9 10 (As bad as it can be)

APPENDIX C. PLANNED TABLES, FIGURES, AND LISTINGS

This appendix provides a list of the planned tables, figures, and listings for the Clinical Study Report. Shells are provided in a separate document for tables that are not in the Standard Safety Tables v1.6.

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			
1.1.1	Analysis Populations	Efficacy	X
1.1.2	Summary of Participant Disposition	Efficacy	X
1.1.3	Summary of Number of Participants Enrolled by Country and Site	Efficacy	X
1.1.4	Summary of Protocol Deviations	Efficacy	X
1.2.1	Summary of Demographics and Baseline Characteristics	Efficacy	X
1.3.1	Summary of Disease Characteristics	Efficacy	X
1.3.2	Summary of Prior Cancer Therapy	Efficacy	X
1.4.1	Summary of Prior Medications	Efficacy	X
1.4.2	Summary of Concomitant Medications	Efficacy	X
1.5.1	Summary of General Medical History	Efficacy	X
Efficacy			
2.1.1	Summary of Complete Response Rate and Overall Response Rate	Efficacy	
2.1.2	Summary of Complete Response Rate and Overall Response Rate	Per Protocol	
2.2.1	Summary of Duration of Complete Response	Efficacy	
2.2.2	Summary of Duration of Response	Efficacy	
2.2.3	Summary of Complete Cytogenetic Response Rate and Partial Cytogenetic Response Rate	Efficacy	
2.2.4	Summary of Progression-Free Survival	Efficacy	
2.2.5	Summary of Overall Survival	Efficacy	
2.3.1	Summary of MPN-SAF	Efficacy	
2.3.2	Summary of EORTC QLQ-C30 Score	Efficacy	
2.3.3	Summary of ECOG Status	Efficacy	
Safety			
3.1.1	Summary of Exposure and Duration of Exposure to Pemigatinib	Safety	X
3.1.2	Summary of Study Drug Compliance	Safety	X
3.1.3	Summary of Study Drug Dose Modification	Safety	X
3.2.1	Overall Summary of Treatment-Emergent Adverse Events	Safety	X
3.2.2	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.3	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X
3.2.4	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Safety	X
3.2.5	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.6	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X

Table No.	Title	Population	Standard
3.2.7	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.8	Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X
3.2.9	Summary of Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.10	Summary of Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X
3.2.11	Summary of Grade 3 or Higher Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.12	Summary of Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.13	Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.14	Summary of Treatment-Emergent Adverse Events Leading to Dose Reduction by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.15	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.16	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.17	Summary of Sponsor-Defined Clinically Notable Treatment-Emergent Adverse Events by Category and Preferred Term	Safety	X
3.2.18	Summary of Grade 3 or Higher Sponsor-Defined Clinically Notable Treatment-Emergent Adverse Events by Category and Preferred Term	Safety	X
3.2.19	Summary of Serious Sponsor-Defined Clinically Notable Treatment-Emergent Adverse Events by Category and Preferred Term	Safety	X
3.2.20	Summary of Sponsor-Defined Clinically Notable Treatment-Emergent Adverse Events Leading to Dose Reduction by Category and Preferred Term	Safety	X
3.2.21	Summary of Sponsor-Defined Clinically Notable Treatment-Emergent Adverse Events Leading to Dose Interruption by Category and Preferred Term	Safety	X
3.2.22	Summary of Sponsor-Defined Clinically Notable Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by Category and Preferred Term	Safety	X
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
3.3.1.4	Summary of Laboratory Values - Urinalysis	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

Table No.	Title	Population	Standard
3.3.3.3	Shift Summary of Coagulation Laboratory Values in CTC Grade - to the Worst Abnormal Value	Safety	X
3.3.3.4	Treatment-Emergent Worsening of Laboratory Abnormalities - Hematology	Safety	X
3.3.3.5	Treatment-Emergent Worsening of Laboratory Abnormalities - Chemistry	Safety	X
3.3.3.6	Treatment-Emergent Worsening of Laboratory Abnormalities - Coagulation	Safety	X
3.4.1	Summary of Systolic Blood Pressure	Safety	X
3.4.2	Summary of Diastolic Blood Pressure	Safety	X
3.4.3	Summary of Pulse	Safety	X
3.4.4	Summary of Respiration Rate	Safety	X
3.4.5	Summary of Body Temperature	Safety	X
3.4.6	Summary of Weight	Safety	X
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 QTcF Interval (ms) From 12-Lead ECG	Safety	X
3.5.5	Summary of RR Interval (ms) From 12-Lead ECG	Safety	X
3.5.6	Summary of Outliers of QT and QTcF Interval Values From 12-Lead ECG	Safety	X
3.5.7	Summary of Clinically Significant ECG Abnormality	Safety	X

Figures

Figure No.	Title
4.2 Secondary Efficacy	
4.2.1	Kaplan-Meier Estimates of Duration of Complete Response
4.2.2	Kaplan-Meier Estimates of Duration of Response
4.2.3	Kaplan-Meier Estimates of Progression-Free Survival
4.2.4	Kaplan-Meier Estimates of Overall Survival
4.4 Safety Analyses	
4.6	Line Graph of Selected Laboratory Values by Study Visit

Listings

Listing No.	Title
2.1 Discontinued Participants (Participant Disposition)	
2.1.1	Participant Enrollment and Disposition Status
2.1.2	Participant Inclusion and Exclusion Criteria Violations
2.2.1	Protocol Deviations
2.3.1	Analysis Population
2.4.1	Demographic and Baseline Characteristics

Listing No.	Title
2.4.2	Disease Characteristics
2.4.3	Prior Systemic Therapy
2.4.4	Prior Radiotherapy
2.4.5	Prior Surgery or Surgical Procedure
2.4.6	Prior Stem Cell Transplant
2.4.7	Medical History
2.4.8	Prior and Concomitant Medication
2.4.9	Procedure and Non-drug Therapy
2.4.10	Post Therapy
2.5.1	Study Drug Compliance
2.5.2	Study Drug Administration
2.6.1	Response Criteria for Myeloid/Lymphoid Neoplasms - Investigator
2.6.2	Response Criteria for Myeloid/Lymphoid Neoplasms - Central Review
2.6.3	Bone Marrow
2.6.4	Flow Cytometry
2.6.5	Response Assessment: Target Lesions
2.6.6	Response Assessment: Non-target Lesions
2.6.7	Response Assessment: New Lesions
2.6.8	Investigator Response Criteria for Extramedullary Disease
2.6.9	Results of Central Histopathology Review
2.6.10	Spleen and Liver Examination
2.6.12	5 Point Scale
[redacted]	
2.6.15	Stem Cell Transplant
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	Treatment-Related Adverse Events
2.7.6	Adverse Events Leading to Interruption, Reduction, or Discontinuation of Pemigatinib
2.7.7	Sponsor-Defined Clinically Notable Adverse Events
2.8.1	Clinical Laboratory Values – Hematology
2.8.2	Clinical Laboratory Values – Chemistry
2.8.3	Clinical Laboratory Values – Coagulation
2.8.4	Clinical Laboratory Values – Urinalysis
2.8.5	Abnormal Clinical Laboratory Values– Hematology
2.8.6	Abnormal Clinical Laboratory Values– Chemistry
2.8.7	Potential Hy's Law Events
2.8.8	PK Blood Sampling Times
2.9.1	Vital Signs
2.9.2	Abnormal Vital Sign Values
2.9.3	Alert Vital Sign Values
2.10.1	12-Lead ECG Values
2.10.2	Abnormal 12-Lead ECG Values
2.10.3	Alert 12-Lead ECG Values
2.11.1	Eye Examination

Listing No.	Title
2.11.2	Fundus Photography
2.11.3	Optical coherence tomography
2.11.4	ECOG Performance Score
2.11.5	PRBC/Platelet Transfusions