Oficial Title: A Phase 2, Open-Label, Single-Arm, Multicenter Study to Evaluate the Efficacy and Safety of Pemigatinib in Participants With Advanced Non–Small Cell Lung Cancer With an FGFR Alteration Who Progressed on Previous Therapy (FIGHT-210)

NCT Number: NCT05253807

Document Date: Statistical Analysis Plan Version 1: 20-Oct-2023

Statistical Analysis Plan

INCB 54828-210

A Phase 2, Open-Label, Single-Arm, Multicenter Study to Evaluate the Efficacy and Safety of Pemigatinib in Participants with Advanced Non–Small Cell Lung Cancer With an FGFR Alteration who Progressed on Previous Therapy (FIGHT-210)

IND Number:	**158,139**
EudraCT Number:	**2021-004934-12**
Sponsor:	**Incyte Corporation** **1801 Augustine Cut-Off** **Wilmington, DE 19803** **United States**
Protocol Version:	**Protocol Amendment 1 dated 08 DEC 2021**
CRF Approval Date:	**25 MAR 2022**
SAP Version:	**Original**
SAP Author:	[redacted] [redacted] **Biostatistics**
Date of Plan:	**20 OCT 2023**

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	Definition
AE	adverse event
[redacted]	[redacted]
BOR	best overall response
CFR	Code of Federal Regulations
CI	confidence interval
[redacted]	[redacted]
[redacted]	[redacted]
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
[redacted]	[redacted]
[redacted]	[redacted]
EQ VAS	EuroQoL visual analogue screening
FAS	full analysis set
FDA	Food and Drug Administration
FGFR	fibroblast growth factor receptor
FGFR1-3	fibroblast growth factor receptor 1, 2, or 3
ICR	independent central radiology
KM	Kaplan-Meier
NCI	National Cancer Institute
NE	not evaluable
NSCLC	non–small cell lung cancer
ORR	objective response rate
OS	overall survival
PD	progressive disease
PFS	progression-free survival
[redacted]	[redacted]
PP	per Protocol
PR	partial response
PT	preferred term

Abbreviation	Definition
QoL	quality of life
QTc	QT interval corrected
RECIST	Response Evaluation Criteria in Solid Tumors
SAP	Statistical Analysis Plan
SD	stable disease
TEAE	treatment-emergent adverse event
[redacted]	[redacted]
TNM	tumor nodes metastasis
ULN	upper limit of normal
WHO	World Health Organization

1. INTRODUCTION

This is a Phase 2 open-label, single-arm, multicenter study of pemigatinib in participants with advanced NSCLC with an FGFR alteration who progressed on previous 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 pemigatinib.

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in the Study INCB 54828-210 Protocol.

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 54828-210 Protocol Amendment 1 dated 08 DEC 2021 and CRFs approved 25 MAR 2022. 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 efficacy of pemigatinib in participants in Cohort A	ORR in Cohort A, defined as the proportion of participants who achieve a CR or PR based on RECIST v1.1. Clinical response will be determined by an ICR review.
Secondary	
To evaluate the efficacy of pemigatinib in participants in Cohort B	ORR in Cohort B, defined as the proportion of participants who achieve a CR or PR based on RECIST v1.1. Clinical response will be determined by an ICR review.
To evaluate the efficacy of pemigatinib in Cohort A	• PFS in Cohort A, defined as the time from first dose of study drug until PD (according to RECIST v1.1 as assessed by an ICR review) or death, whichever is first. • DOR in Cohort A, defined as the time from the date of first CR or PR until the date of the first PD (according to RECIST v1.1 as assessed by an ICR review), or death, whichever is first. • OS in Cohort A, defined as the time from first dose of study drug to death of any cause.
To assess safety and tolerability of pemigatinib in all participants	Safety and tolerability, as assessed by the occurrence of TEAEs and treatment-related TEAEs according to NCI CTCAE v5.0, physical examination changes, vital sign changes, laboratory evaluations, and ECGs.

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
Exploratory	
To evaluate the efficacy of pemigatinib in Cohort B	PFS in Cohort B, defined as the time from first dose of study drug until PD (according to RECIST v1.1 as assessed by an ICR review) or death, whichever is first. DOR in Cohort B, defined as the time from the date of first CR or PR until the date of the first PD (according to RECIST v1.1 as assessed by an ICR review), or death, whichever is first. OS in Cohort B, defined as the time from first dose of study drug to death of any cause.
[redacted]	

3. STUDY DESIGN

This is an open-label, monotherapy study of pemigatinib in participants with advanced NSCLC with an FGFR alteration who progressed while on previous therapy. The study includes 2 cohorts, Cohort A and Cohort B, and will enroll approximately 125 participants. Participants will receive pemigatinib 13.5 mg once daily on an intermittent dose schedule (2 weeks on therapy and 1 week off therapy schedule). Full study drug administration information can be found in the Protocol, Section 6.

All potential participants must have documented FGFR1-3 mutations or fusions/rearrangements before enrollment. Acceptable FGFR alterations may be classified as fusion, rearrangement, translocation, mutation, or fluorescent in-situ hybridization-positive.

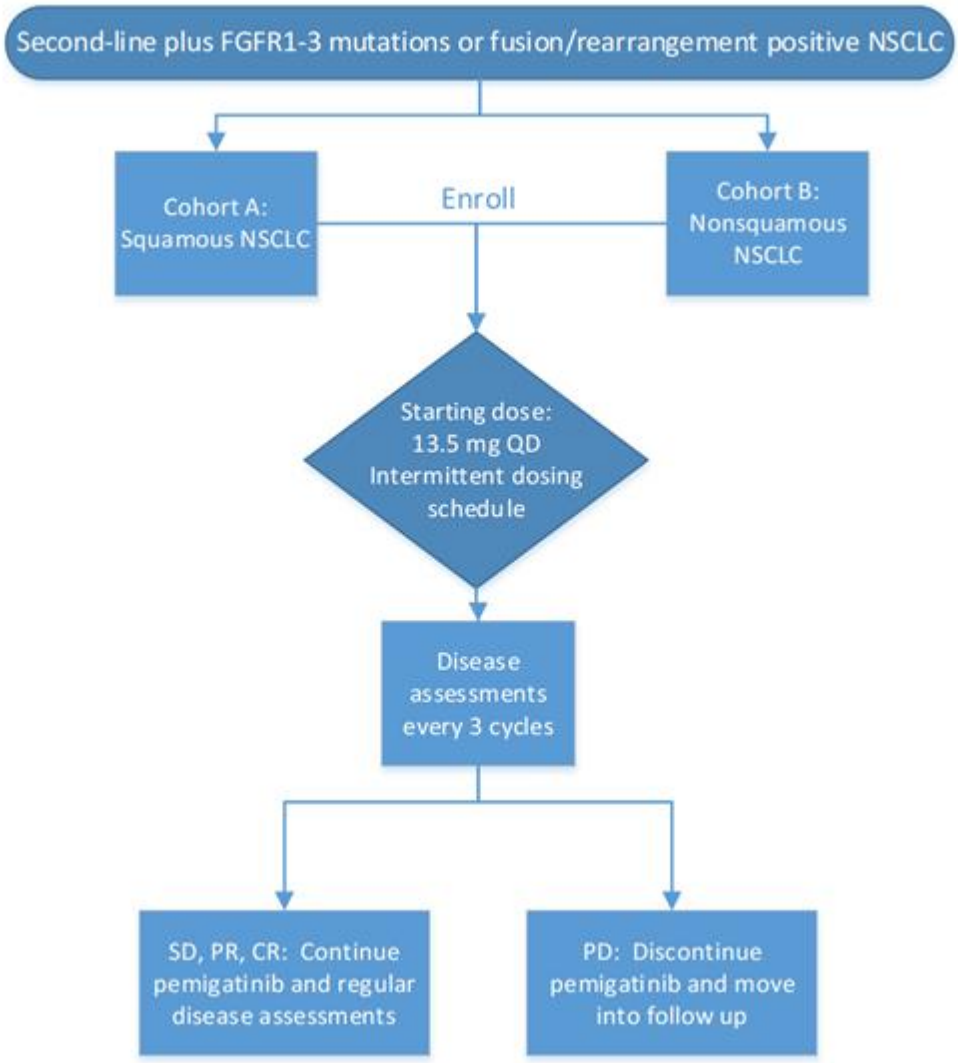
Previous therapies may include targeted therapies, chemotherapeutic agents and immunotherapies, with or without radiotherapy. Participants receiving radiotherapy to target lesion(s) must show progression of the target lesion prior to entry into the study.

Due to the different histology (eg, squamous, nonsquamous, and large cell) and genetic markers (eg, epidermal growth factor receptor mutant), participants enrolled in this study will be assigned to 1 of 2 cohorts as follows:

- Cohort A: Squamous NSCLC with known or likely FGFR1-3 driver mutations outside the kinase domain or fusions/rearrangements ($n \approx 100$).
- Cohort B: Nonsquamous NSCLC with known or likely FGFR1-3 driver mutations outside the kinase domain or fusions/rearrangements, including participants who have relapsed on prior targeted therapy ($n \approx 25$).

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 study drug administration in 21-day cycles until documented disease progression or unacceptable toxicity is reported. See Figure 1 for the study design.

Figure 1: Study Design Scheme



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 125 participants with select FGFR alterations are planned for the final analysis of the primary endpoint of ORR. With the assumed rates of 40% for pemigatinib, a sample size of approximately 100 participants would provide about > 95% probability of having a 95% CI with a lower limit of > 20%.

Up to 25 participants will be enrolled in Cohort B, which will provide > 80% chance of observing at least 3 responders in this cohort if the underlying ORR is 20%.

3.4. Schedule of Assessments

Refer to Protocol Amendment 1 dated 08 DEC 2021 for a full description of all study procedures and assessment schedules for this study.

4. DATA HANDLING DEFINITIONS AND CONVENTIONS

4.1. Scheduled Study Evaluations and Study Periods

4.1.1. Day 1

Day 1 is the date that the first dose of 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 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 assessment are available on the day of the first dose and the time is missing, use the scheduled assessment as baseline.
- If all scheduled assessments are missing on the day of the first dose and an unscheduled assessment is available, use the unscheduled assessment as baseline.

4.1.4. 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 time since diagnosis of cancer, partial cancer 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 date of 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 use the earlier date of the last day of the month 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 pemigatinib is administered. The scheduled cycle length is 21 days. The actual Day 1 of subsequent cycles will correspond with the first day of administration of pemigatinib in that cycle.

4.1.6. Analysis Window

For parameters that will be summarized by visit, the nominal visit, as recorded on the eCRF, 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 study drug administration.
- 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 the first dose of pemigatinib. 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, listings, and statistical analyses.

Interim analyses will not be conducted due to early termination.

5.2. Treatment Groups

This is an open-label, single treatment group study. Participants will be listed by treatment cohort. Cohort determination will be based on the results of histology and genetic markers from central genomics laboratory.

5.3. Analysis Populations

5.3.1. Full Analysis Set

The FAS will include all enrolled participants who received at least 1 dose of pemigatinib. Participants will be analyzed according to the treatment cohort to which they are initially assigned. The FAS will be used for the listings of demographics, baseline characteristics, participant disposition, and analyses of all efficacy data.

5.3.2. Safety Population

The safety population will include all enrolled participants who received at least 1 dose of pemigatinib. All safety analyses will be conducted using the safety population.

6. BASELINE, EXPOSURE, AND DISPOSITION

Appendix A provides a list of data displays.

6.1. Demographics, Baseline Characteristics, and Disease History

6.1.1. Demographics and Baseline Characteristics

The following demographics and baseline characteristics will be listed for the FAS: age, sex, race, ethnicity, weight and height.

6.1.2. Baseline Disease Characteristics

The following baseline disease characteristics will be listed for the FAS: ECOG performance status and baseline phosphate.

6.1.3. Disease History

The time since diagnosis, tumor histology, TNM staging at initial diagnosis, current TNM staging, current stage of disease, current sites of disease, smoking status, and tumor marker test results will be listed for all participants in the FAS.

Time since diagnosis will be calculated as follows:

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

6.1.4. Prior Therapy

The prior systemic cancer therapy regimens will be listed for all participants in the FAS. The component drugs of prior systemic therapy regimens will be coded using the WHO Drug Dictionary. The prior systemic cancer therapy regimen name, component drugs, start and stop dates, purpose of the regimen, best response, reason for discontinuation, and date of relapse/progression will be listed for all participants in the FAS.

The prior radiotherapy type, body site, start and stop dates, total dose, and best response will be listed for all participants in the FAS.

The date and description of the prior surgery/procedure for disease under study will be listed for all participants in the FAS.

6.1.5. Medical History

For participants in the FAS, medical history will be listed. This list will include the medical history event for each body system/organ class as documented on the eCRF.

6.2. Disposition of Participants

The treatment group, that is, if the treatment is ongoing or discontinued, and the primary reason for treatment discontinuation, or if the participant is still in study or withdrawal, and the primary reason for study withdrawal, will be listed for all participants in the FAS.

6.3. Exposure

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

- **Number of treatment cycles:**
  Number of cycles with a nonzero dose of pemigatinib.
- **Duration of treatment with pemigatinib (days):**
  Date of last dose of pemigatinib – date of first dose of pemigatinib + 1
- **Average daily dose of pemigatinib (mg/day):**
  Total actual dose taken (mg) / duration of treatment with pemigatinib (days)

  Total actual dose taken will be calculated based on the information entered on the Drug Accountability eCRF.
- **Pemigatinib dose modifications:**
  Participants who had pemigatinib dose reduction and interruption.

6.4. 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] / [total prescribed dose]

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 eCRF. If there are dispensed drugs that have not been returned yet, the actual dose taken starting from the dispense date of the unreturned drugs will be imputed by the dose taken as reported on the Dosing eCRF.

6.5. Prior and Concomitant Medication

Prior medications and concomitant medications will be coded using the WHO Drug Dictionary. The prior and concomitant medication will be listed for participants in the FAS by WHO drug class and WHO drug preferred term. In the data listing, each medication will be recorded as only prior, only concomitant, or both prior and concomitant.

7. EFFICACY

Appendix A provides a list of data displays.

7.1. Efficacy Hypothesis

Not applicable.

7.2. Analysis of the Primary Efficacy Parameter

7.2.1. Primary Efficacy Analysis

The primary endpoint of the study is ORR in Cohort A. Objective response rate is defined as the proportion of participants who achieve a CR or PR based on RECIST v1.1 (Eisenhauer 2009), as assessed by an ICR review committee. Confirmation of CR and PR is required and documented in the ICR charter. This analysis will be based on the FAS. 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 ORR. The 95% CI for the ORR will be estimated using the Clopper-Pearson method.

7.2.1.1. Response Criteria

Overall disease status will be categorized and listed using RECIST v1.1 (Eisenhauer 2009). Participants will have their overall response evaluated as CR, PR, SD, PD, or NE at each postbaseline radiologic assessment based on changes in target lesions, nontarget lesions, and appearance of new lesions.

7.2.1.2. Objective Response Rates and Best Overall Response

A participant is considered an objective responder if they have a best overall response of CR or PR at any postbaseline visit prior to first PD.

In general, under the RECIST v1.1, BOR is the best response recorded postbaseline prior to and including the first PD, in the order of CR, PR, SD, PD, and NE. The BOR will be determined from response assessments before or on the same day as the new anticancer therapy. If any alternative cancer therapy is taken while on study, any subsequent assessment(s) will be excluded from the BOR determination. A BOR of CR or PR needs to be confirmed; the confirmation method is described in the ICR charter.

In the case of SD, measurements must meet the SD criteria at least once after the date of first dose (ie, a minimum interval of 42 days). Participants who fail to meet this criterion will have either a BOR of PD, if the next available assessment indicates PD, or NE, if there is no additional assessment available.

7.2.2. Subgroup Analyses for Primary Endpoint

Not applicable.

7.3. Analysis of the Secondary Efficacy Parameter

7.3.1. Secondary Endpoints Involving Objective Response Rate

The ORR in Cohort B is defined as the proportion of participants who achieve a CR or a PR based RECIST v1.1 as assessed by an ICR review. Confirmation of CR and PR is required and documented in the ICR charter. This analysis will be based on the FAS. 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 ORR. The 95% CI for the ORR will be estimated using the Clopper-Pearson method.

7.3.2. Progression-Free Survival

Progression-free survival is defined as the time from the date of first dose of pemigatinib (Day 1) to the date of the first documented PD or death due to any cause, whichever is first. Progressive disease will be evaluated according to RECIST v1.1 and assessed by an ICR review. Partial death dates will be handled using the rules described in Section 4.1.4. Participants who are alive without progression, before the analysis cutoff date, will be censored. Censoring for PFS will follow the algorithm outlined in Table 2 based on FDA guidance (FDA 2015, FDA 2018).

Table 2: Evaluation and Censoring of Progression-Free Survival

Situation	Outcome	Date of Progression or Censoring
No baseline tumor assessments	Censored	Day 1
No valid postbaseline response assessments	Censored	Day 1
Progression documented between scheduled response assessments	Progressed	Date of first overall response of PD
No progression	Censored	Date of last valid radiologic assessment (not NE and not missing)
Study discontinuation for undocumented progression	Censored	Date of last valid radiologic assessment (not NE and not missing)
Study discontinuation for toxicity or other reason	Censored	Date of last valid radiologic assessment (not NE and not missing)
New anticancer treatment started	Censored	Date of last valid radiologic assessment (not NE and not missing) on/before starting a new anticancer treatment
Death before first PD 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 radiologic assessment (not NE and not missing)

Progression-free survival data will be analyzed by the KM method in Cohort A. The number of participants who progressed or died and the number of participants censored will be summarized. The KM estimates of median PFS will be presented with its 95% CI. The 95% CI will be calculated using the generalization of Brookmeyer and Crowley's method (1982) with log-log transformation (Klein and Moeschberger 1997).

7.3.3. Duration of Response

For objective responders, DOR is defined as the time from the date that a participant first achieves CR or PR, until the date of first documented disease progression or death, whichever is first. Responses and PD will be evaluated based on RECIST v1.1 by an ICR review. The partial death dates will be handled using the rules described in Section 4.1.4. Participants who are alive without progression before the analysis cutoff date will be censored. Censoring of DOR will follow the same algorithm as the censoring of PFS (see Section 7.3.2).

The DOR data will be analyzed by the KM method in Cohort A. The total number of responders, the number of participants who progressed or died, and the participants censored will be summarized. The KM estimate of median DOR will be presented with its 95% CI. The 95% CI will be calculated using the generalization of Brookmeyer and Crowley's method (1982) with log-log transformation (Klein and Moeschberger 1997).

7.3.4. Overall Survival

Overall survival is defined as the time from the date of first dose of pemigatinib to the date of death due to any cause. Date of death will be determined using Death Report, Survival Follow-up, and Participant Status eCRFs. Participants who are lost to follow-up or still alive at the time of the analysis will be right-censored at the earlier of the date the participant was last known alive and clinical data cutoff date for the analysis. The last known alive date is defined as the later of the last study visit and the date the participant was last known alive from the Survival Follow-up and Participant Status eCRFs. The partial death dates will be handled using the rules described in Section 4.1.4.

The OS will be analyzed by the KM method in Cohort A. The number of participants who died and the number of participants censored will be summarized. The median survival will be estimated using the KM method. The 95% CIs for median survival time will be calculated using the generalization of Brookmeyer and Crowley's method (1982) with log-log transformation (Klein and Moeschberger 1997).

7.4. Analysis of Other Efficacy Parameters

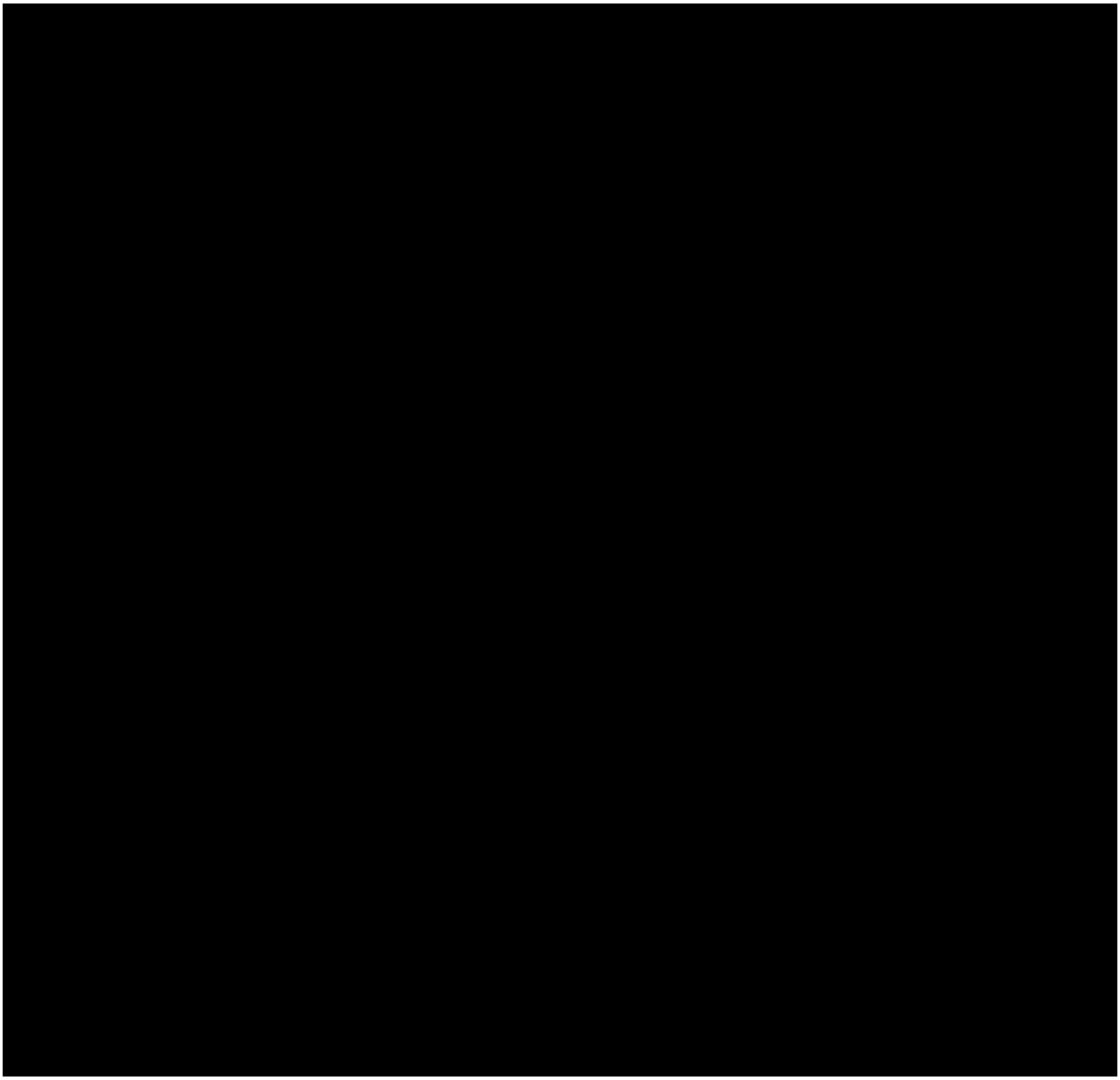
7.4.1. Largest Percentage Reduction in Sum of Diameters of Target Lesions

For each participant in the FAS with measurable target lesions at baseline, target lesion sizes will be measured by sum of diameters. The best percentage change from baseline, defined as the largest decrease in target lesion size for each participant during the study, will be listed.

Per RECIST criteria, target lesions considered "too small to measure" will be assigned a default value of 5 mm for purposes of this analysis. Likewise, target lesions identified as "not present" at postbaseline assessments will be assigned 0 mm for this analysis. In the event a target lesion is unaccounted for in a particular postbaseline timepoint (ie, assessment missing or not evaluable), then the overall sum of diameters for target lesions will not be evaluable for that postbaseline timepoint.

7.5. Analysis of Exploratory Efficacy Variables

The PFS, DOR (ie, per RECIST v1.1 and as assessed by ICR), and OS in Cohort B will be analyzed for the FAS in the same fashion as Cohort A.



7.5.2. Eastern Cooperative Oncology Group Performance Status

The ECOG performance status at scheduled assessment times will be listed by treatment cohorts.

8. SAFETY AND TOLERABILITY

Appendix A provides a list of data displays.

8.1. General Considerations

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

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 treatment until 30 days of the last dose of study treatment. 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 treatment 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 listed by Medical Dictionary for Regulatory Activities PT and system organ class. Severity of AEs will be graded using the NCI CTCAE v5.0. 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 v5.0 criteria, it will be rated on a scale of 1 to 5 as follows: 1 = mild, 2 = moderate, 3 = severe, 4 = life-threatening, and 5 = fatal. All toxicities will be graded based on the worst level reached, not the level they may have reached if they had not been treated. When the intensity of an AE changes over time for a reporting period (eg, between visits), each change in intensity will be reported as an AE until the event resolves.

The subset of AEs considered by the investigator to be related to study drug will be considered to be treatment-related AEs. If the investigator does not specify the relationship of the AE to study drug, the AE will be considered to be treatment-related. The incidence of AEs and treatment-related AEs will be listed. In addition, serious TEAEs and serious AEs will be listed.

Any missing data pertaining to date of onset, causality, or severity of an AE must be queried for resolution. Unresolved missing causality or severity of an AE 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.

8.2.2. Adverse Event Listings

The following listings will be produced:

- Listing of AEs
- Listing of serious AEs
- Listing of Grade 3 or higher AEs
- Listing of AEs with a fatal outcome
- Listing of pemigatinib treatment-related AEs
- Listing of AEs leading to interruption, reduction, or discontinuation of pemigatinib

8.3. Clinical Laboratory Tests

8.3.1. Laboratory Value Definitions

Laboratory values and change from baseline values will be listed. 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 outside of the normal range will be assessed for severity based upon the numerical component of CTCAE v5.0.

8.3.2. Laboratory Value Summaries

All test results and associated normal ranges from central laboratories will be reported in SI units. All tests with numeric values will have a unique unit per test. Any laboratory test results and associated normal ranges from local laboratories will be converted to SI units.

Severity grades will be assigned to laboratory test values based on the numerical component of CTCAE v5.0. CTCAE grades will be reported. Separate lists for abnormally high and abnormally low laboratory values will be provided when the laboratory parameter has both high and low grading criteria.

8.3.3. Potential Hy's Law Events

The participants with elevated alanine transaminase or aspartate transaminase > 3 × ULN range and alkaline phosphatase < 2 × ULN range accompanied by total bilirubin > 2 × ULN range at the same visit will be listed by cohort.

8.4. Vital Signs

Values at each scheduled visit for vital signs, including weight, systolic blood pressure, diastolic blood pressure, pulse, temperature, and respiratory rate, will be listed.

Criteria for clinically notable vital sign abnormalities are defined in Table 4. The abnormal values for participants exhibiting clinically notable vital sign abnormalities will be listed along with their cohort. Alert vital signs are defined as an absolute value outside the defined normal range and percentage change from baseline 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 heart rate (HR), PR, QRS, QT and QTc intervals will be obtained for each participant during the study. Values at each scheduled visit, change, and percent change from baseline will be listed for each ECG parameter. Baseline will be determined as the average of all nonmissing values before the first administration of pemigatinib.

Criteria for clinically notable ECG abnormalities are defined in Table 5. The ECG values will also be considered abnormal if the absolute percentage change from baseline is more than 25% (QRS 30%). Participants exhibiting ECG abnormalities will be listed with study visit and assigned cohort. Abnormal values for participants with alert ECG values, defined as both the absolute value and the percentage change from baseline being outside the defined normal ranges, will be identified and listed.

Table 5: Criteria for Clinically Notable Electrocardiogram Abnormalities

Parameter	High Threshold	Low Threshold
PR	> 220 ms	< 75 ms
HR	> 100 bpm	< 45 bpm
QT	> 500 ms	< 300 ms
QRS	> 120 ms	< 50 ms
QTc	> 460 ms	< 295 ms

9. INTERIM ANALYSIS

Not applicable.

10. 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	20 OCT 2023

10.1. Changes to Protocol-Defined Analyses

A decision was made to terminate study enrollment. At the time of study termination there were fewer than 10 participants enrolled; as a result, an interim futility analysis and a sensitivity analysis will not be conducted. The RECIST-evaluable population and the Per-Protocol population will not be generated for analysis.

10.2. Changes to the Statistical Analysis Plan

Not applicable.

11. REFERENCES

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APPENDIX A. PLANNED TABLES, FIGURES, AND LISTINGS

This appendix provides a list of the planned tables, figures, and listings for the Clinical Study Report. 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
Efficacy			
2.1 Primary Efficacy			
2.1.1	Summary of Best Overall Response and Objective Response Rate – Cohort A	FAS	
2.2 Secondary Efficacy			
2.2.1	Summary of Best Overall Response and Objective Response Rate – Cohort B	FAS	
2.2.2	Summary of Progression-Free Survival – Cohort A	FAS	
2.2.3	Summary of Duration of Response – Cohort A	FAS	
2.2.4	Summary of Overall Survival – Cohort A	FAS	

Listings

Listing No.	Title
2.1 Participant Disposition	
2.1.1	Participant Enrollment and Disposition Status
2.1.2	Participant Inclusion and Exclusion Criteria Violations
2.3 Safety Analyses	
2.3.1	Analysis Populations
2.4 Demographics and Baseline Characteristics (Including Concomitant Medications)	
2.4.1	Demographic and Baseline Characteristics
2.4.2	Disease History
2.4.3	Prior Radiation Treatment
2.4.4	Prior Systemic Therapy
2.4.5	Prior Surgery or Surgical Procedure
2.4.6	Medical History
2.4.7	Prior and Concomitant Medication
2.4.8	Procedures and Nondrug Therapy
2.4.9	Post Therapy
2.5 Drug Compliance	
2.5.1	Study Drug Compliance
2.5.2	Study Drug Administration
2.6 Efficacy	
2.6.1	Deaths
2.6.2	Best Overall Response, Duration of Response, Progression-Free Survival, and Overall Survival
2.6.3	Overall Response Assessment by Visit – RECIST
2.6.4	Response Assessment: Target Lesions – RECIST
2.6.5	Response Assessment: Nontarget Lesions – RECIST
2.6.6	Response Assessment: New Lesions – RECIST
2.6.7	FGFR Status

Listing No.	Title
2.6.8	ECOG Status
[redacted]	[redacted]
[redacted]	[redacted]
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	Treatment-Related Adverse Events
2.7.6	Adverse Events Leading to Interruption, Reduction, or Discontinuation of Pemigatinib
2.8 Laboratory Data	
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	Abnormal Clinical Laboratory Values – Coagulation
2.8.8	Potential Hy's Law Events
2.8.9	Serology Laboratory Test
2.8.10	Pregnancy Test
2.9 Vital Signs	
2.9.1	Vital Signs
2.9.2	Abnormal Vital Sign Values
2.9.3	Alert Vital Sign Values
2.10 ECG	
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 Eye Examinations	
2.11.1	Eye Examination
2.11.2	Optical Coherence Tomography