Official Title: An Open-Label, Multicenter, Rollover Study to Provide Continued Treatment for Participants With Advanced Malignancies Previously Enrolled in Studies of Pemigatinib

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Statistical Analysis Plan

INCB 54828-801

An Open-Label, Multicenter, Rollover Study to Provide Continued Treatment for Participants With Advanced Malignancies Previously Enrolled in Studies of Pemigatinib

IND Number:	**124,358**
EudraCT Number:	**2021-002207-36**
Sponsor:	**Incyte Corporation** **1801 Augustine Cut-Off** **Wilmington, DE 19803** **United States**
Protocol Version:	**Protocol dated 17 MAY 2021**
CRF Approval Date:	**08 MAR 2023**
SAP Version:	**Original**
SAP Author:	[redacted] [redacted]**, Biostatistics**
Date of Plan:	**15 MAR 2024**

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

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LIST OF ABBREVIATIONS

Abbreviations and Special Terms	Definition
AE	adverse event
CRF	case report form
CTCAE	Common Terminology Criteria for Adverse Events
eCRF	electronic case report form
FAS	full analysis set
MedDRA	Medical Dictionary for Regulatory Activities
PT	preferred term
QD	once daily
SAE	serious adverse event
SAP	statistical analysis plan
SOC	system organ class
Study treatment	refers to pemigatinib monotherapy or combination therapy with pemigatinib
TEAE	treatment-emergent adverse event
WHO	World Health Organization

1. INTRODUCTION

This is a Phase 2, open-label, multicenter, rollover study for participants with advanced malignancies currently enrolled in Incyte-sponsored studies of pemigatinib who are continuing to receive clinical benefit from treatment with pemigatinib (monotherapy or in combination).

Section 2 of the Protocol provide a detailed description of the investigational product, background, study rationale for doses to be examined, and potential risks and benefits of treatment with study treatment.

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in the Study INCB 54828-801 Protocol.

2. STUDY INFORMATION, OBJECTIVE, AND ENDPOINT

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 54828-801 Protocol dated 17 MAY 2021 and CRFs approved 08 MAR 2023. Unless superseded by an amendment, this SAP will be effective for all subsequent Protocol amendments and eCRF versions.

2.2. Study Objective and Endpoint

Table 1 presents the study objective and its endpoint.

Table 1: Objective and Endpoint

Objective	Endpoint
To evaluate the long-term safety and tolerability of pemigatinib.	Frequency and nature of AEs and SAEs as assessed by CTCAE v5.0.

3. STUDY DESIGN

This rollover study allows participants from multiple Protocols, who are receiving clinical benefit from pemigatinib as either monotherapy or combination therapy, to continue to be treated following the completion of the parent study (also referred to as parent Protocol). The population for the rollover study should be consistent with the population defined in each parent Protocol. The primary eligibility criterion for a participant to enter the rollover study is participation in an Incyte-sponsored study (parent Protocol) and receiving ongoing study treatment.

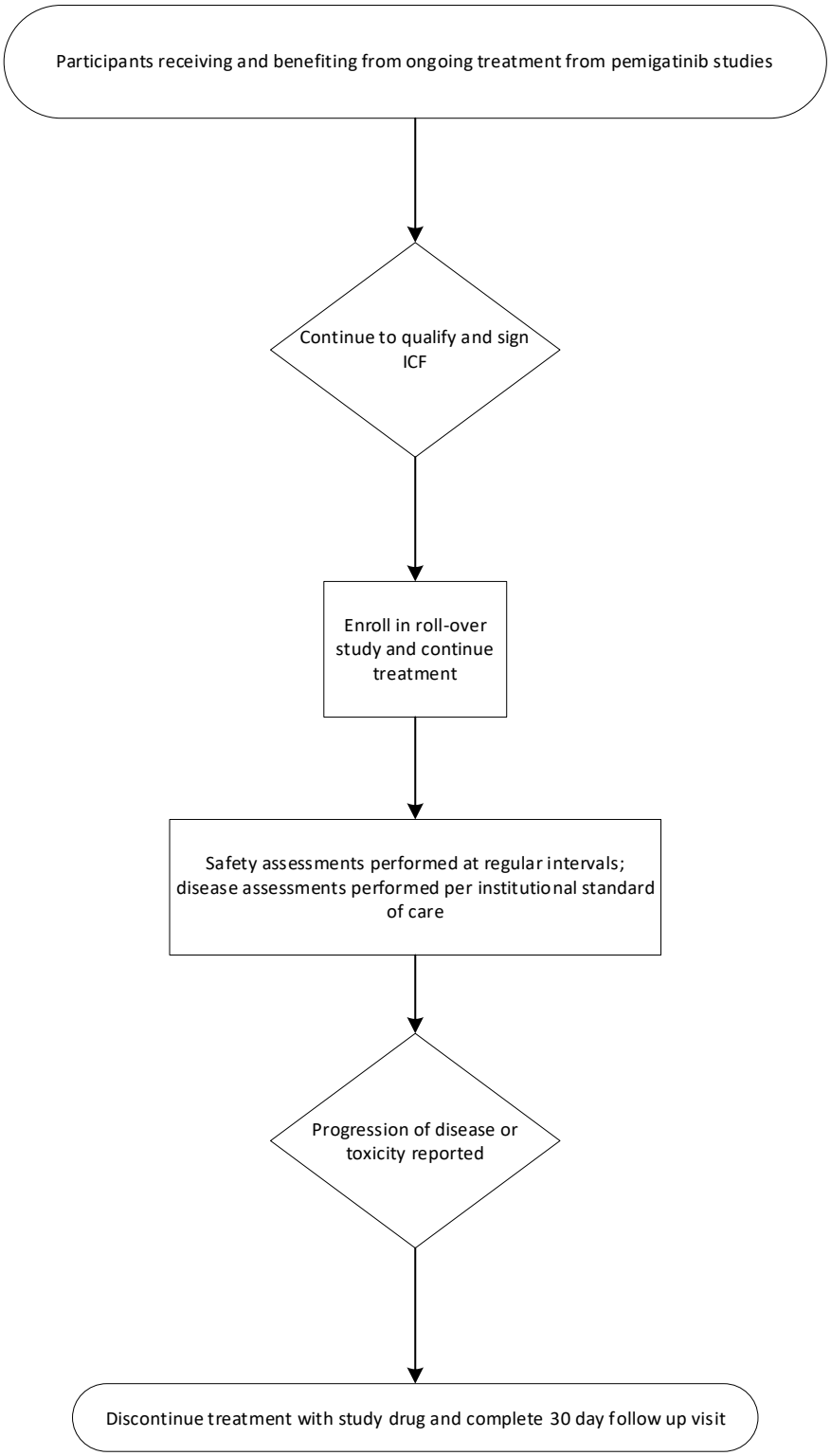
Participants who have enrolled in a prior study (parent Protocol) with pemigatinib as monotherapy or combination therapy and are assessed by the investigator to continue to benefit from ongoing treatment and who cannot access pemigatinib outside of a clinical trial will be eligible.

Disease assessments will be performed per standard of care, with date of progression reported and safety data collected.

Once a participant has rolled over into this study from a parent study, the database for the parent study will be closed and locked, and the parent Protocol study will be considered completed and closed; however, the participant in the rollover study will still be treated as per the plan outlined in the parent Protocol. The parent Protocols include INCB 54828-101 (FIGHT-101); INCB 54828-201 (FIGHT-201); INCB 54828-202 (FIGHT-202); and INCB 54828-207 (FIGHT-207). The study treatments include pemigatinib, INCMGA00012 (INCB 54828-101 only), and pembrolizumab (INCB 54828-101 only).

The study begins when the first participant signs the study informed consent form. The end of the study is defined as the date of the last visit of the last participant in the study. It is estimated that an individual will participate for approximately 12 months. The study is considered completed when the last participant's last visit has occurred. Figure 1 elaborates on the study design.

Figure 1: Study Design Schema



3.1. Randomization

Not applicable.

3.2. Control of Type I Error

This study will only conduct analyses on safety data with regard to AEs. All statistical analyses are exploratory in nature. Control of Type I error is not applicable.

3.3. Sample Size Considerations

Approximately 20 participants will be enrolled from prior (parent) pemigatinib studies.

No formal sample size calculations will be performed for this study.

3.4. Schedule of Assessments

Refer to Protocol dated 17 MAY 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 study treatment (pemigatinib as monotherapy or combination therapy) in the rollover study 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

Participants are continually taking study treatments before Day 1 of this study. Baseline is not applicable in this study.

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 date of last dose is used in deriving variables such as duration of treatment or TEAE flag, a 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 will be used.
- If both the month and day are missing, then the earlier date of 31 DEC of the year or the date that the participant discontinued treatment will be used.
- Otherwise, the date that the participant discontinued treatment will be used as the date of the last dose.

4.1.5. Cycle Length and Duration

Cycle 1 Day 1 is the day that the first dose of study treatment in the rollover study is administered. The scheduled cycle length is 21 days with the first day of each cycle corresponding with the first day of pemigatinib as monotherapy or combination therapy (pembrolizumab or INCMGA00012) administrated in that cycle.

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 as monotherapy or combination therapy.

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

- Before the date of first administration of pemigatinib as monotherapy or combination therapy and is ongoing throughout the rollover study or ends on/after the date of first administration of study treatment.
- On/after the date of first administration of pemigatinib as monotherapy or combination therapy and is ongoing or ends during the course of study treatment 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 as monotherapy or combination therapy. 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; v9.4 or later) will be used for the generation of all tables, listings, and statistical analyses. Descriptive summaries for continuous variables will include, but not be limited to, the number of participants, mean, standard deviation, median, minimum, and maximum. Descriptive summaries for categorical variables will include the number and percentage of participants in each category.

Participants will undergo disease assessments according to the institution's standard of care. Disease assessment details will not be captured, with the exception of documenting the date of disease progression. Analyses of efficacy data will not be performed under this SAP.

5.2. Treatment Groups

This is an open-label, multicenter, rollover study for participants with advanced malignancies currently enrolled in Incyte-sponsored studies of pemigatinib who are continuing to receive clinical benefit from treatment with pemigatinib (as either monotherapy or in combination therapy).

Participants will be summarized by initially assigned dose level and overall monotherapy total (pemigatinib monotherapy 6 mg QD, pemigatinib monotherapy 9 mg QD, pemigatinib monotherapy 13.5 mg QD, pemigatinib monotherapy total, pemigatinib 9 mg QD + pembrolizumab 200 mg) in this study.

5.3. Analysis Populations

5.3.1. Full Analysis Set

The FAS will include all participants who received at least 1 dose of study treatment (ie, pemigatinib as monotherapy or combination therapy) in the rollover study.

The FAS will be used for the summary of participant disposition, as well as the listing and summary of demographics.

5.3.2. Safety Population

The safety population will include all participants who received at least 1 dose of study treatment (ie, pemigatinib as monotherapy or combination therapy).

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 and Baseline Characteristics

The following demographics characteristics will be summarized and listed for the FAS: age (at entry into the rollover study), sex, race, and ethnicity.

6.2. Disposition of Participants

The number and percentage of participants who were treated, who were ongoing with study treatment, who discontinued from study treatment with a primary reason for discontinuation, who were still in the study, and who withdrew from the study with a primary reason for withdrawal will be summarized for the FAS.

6.3. Protocol Deviations

Protocol deviations recorded in this study will be listed, if applicable.

6.4. Exposure

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

- **Duration of treatment with pemigatinib (days):**
  Date of last dose of pemigatinib – date of first dose of pemigatinib + 1
- **Pemigatinib dose modifications:**
  Number of participants who had pemigatinib dose reduction and interruption

6.5. Study Treatment Compliance

Not applicable.

6.6. Prior and Concomitant Medication

Prior medications concomitant medications will be coded using the WHO Drug Dictionary. The prior and concomitant medication will be listed for participants in the safety population by WHO drug class and WHO drug preferred term.

7. SAFETY AND TOLERABILITY

Appendix A provides a list of data displays.

7.1. 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.

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

7.2. Adverse Events

7.2.1. Adverse Event Definitions

Adverse events that are ongoing at the time of rollover from the parent Protocol will be entered on the Adverse Event Form in the eCRF for this study.

A TEAE is any AE either reported for the first time in this Protocol and within 30 days of last dose of study treatment, or any AE ongoing and defined as treatment-emergent from the parent Protocol. 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 tabulated by MedDRA PT and SOC. Severity of AEs will be graded using the National Cancer Institute 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 treatment will be considered to be treatment-related AEs. If the investigator does not specify the relationship of the AE to study drug, the AE will be considered to be treatment-related. The incidence of AEs and treatment-related AEs will be tabulated. Serious TEAEs will also be tabulated. In addition, serious TEAEs and serious AEs will be listed.

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.

7.2.2. Adverse Event Summaries

An overall summary of AEs by dose level 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 who had any TEAEs related to pemigatinib
- Number (%) of participants who temporarily interrupted pemigatinib because of TEAEs
- Number (%) of participants who permanently discontinued from pemigatinib because of TEAEs
- Number (%) of participants who had pemigatinib dose reductions because of TEAEs
- Number (%) of participants who had any TEAEs with a fatal outcome

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

- Summary of TEAEs by MedDRA SOC and PT
- Summary of TEAEs by MedDRA PT in decreasing order of frequency
- Summary of Grade 3 or higher TEAEs by MedDRA SOC and PT
- Summary of serious TEAEs by MedDRA SOC and PT
- Summary of TEAEs with a fatal outcome by MedDRA SOC and PT
- Summary of pemigatinib treatment-related serious TEAEs 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

Listings will be provided for all AEs, SAEs, AEs of Grade 3 and higher, treatment-related AEs, fatal AEs, and AEs leading to interruption, reduction, or discontinuation of study drug. All listings will be presented for the safety population.

8. INTERIM ANALYSES

There are no planned, formal interim analyses for this study.

9. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 2.

Table 2: Statistical Analysis Plan Versions

SAP Version	Date
Original	15 MAR 2024

9.1. Changes to Protocol-Defined Analyses

Not applicable.

9.2. Changes to the Statistical Analysis Plan

Not applicable.

APPENDIX A. PLANNED TABLES, FIGURES, AND LISTINGS

This appendix provides a list of the planned tables, figures, and listings for the clinical study report. Standard tables will follow the conventions in the Standard Safety Tables v1.13. In-text tables are identical in structure and content as appendix tables but follow a Rich Text Format.

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

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Baseline and Demographic Characteristics			
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1.2 Demography and Baseline Characteristics			
1.2.1	Summary of Demographic Characteristics	FAS	X
Safety			
3.1 Dose Exposure			
3.1.1	Summary of Exposure and Duration of Exposure to Pemigatinib	Safety	X
3.2 Adverse Events			
3.2.1	Overall Summary of Treatment-Emergent Adverse Events	Safety	X
3.2.2	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.3	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety	X
3.2.6	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.8	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.15	Summary of Pemigatinib-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.16	Summary of Treatment-Emergent Adverse Events with a Fatal Outcome by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.18	Summary of Treatment-Emergent Adverse Events Leading to Pemigatinib Dose Reduction by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.19	Summary of Treatment-Emergent Adverse Events Leading to Pemigatinib Dose Interruption by MedDRA System Organ Class and Preferred Term	Safety	X
3.2.20	Summary of Treatment-Emergent Adverse Events Leading to Pemigatinib Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term	Safety	X

Listings

Listing No.	Title
2.1 Participant Disposition	
2.1.1	Participant Enrollment and Disposition Status
2.2 Protocol Deviations	
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2.7.5	Treatment-Related Adverse Events
2.7.6	Adverse Events Leading to Interruption, Reduction, or Discontinuation of Study Treatment
2.11 Eye Examinations	
2.11.1	Eye Examination
2.11.2	Optical Coherence Tomography