Statistical Analysis Plan

INCB 52793-101 / NCT02265510

A Phase 1/2, Open-Label, Dose-Escalation, Safety and Tolerability Study of INCB052793 in Subjects With Advanced Malignancies

IND Number:	**134,089**
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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
AML	acute myeloid leukemia
BMI	body mass index
BOR	best overall response
bpm	beats per minute
BSA	body surface area
CI	confidence interval
CR	complete response
CRF	case report form
CRi	complete remission with incomplete hematologic recovery
CT	computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
DLT	dose-limiting toxicity
[redacted]	[redacted]
DSS	Durie Salmon stage
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	electronic case report form
ELN	European LeukemiaNET
FDA	Food and Drug Administration
HMA	hypomethylating agents
HR	heart rate
IPSS-R	International Prognostic Scoring System Risk
ISS	international staging system
IWG	International Working Group
JAK	Janus kinase
MDS	myelodysplastic syndrome
MDS/MPN	myelodysplastic/myeloproliferative neoplasms
MedDRA	Medical Dictionary for Regulatory Activities
MLFS	morphologic leukemia-free state
MM	multiple myeloma
MR	minimal response
MRI	magnetic resonance imaging
MTD	maximum tolerated dose

Abbreviation	Definition
NA	not assessed
ND	not done/not applicable
NE	not evaluable
ORR	objective response rate
OS	overall survival
PAD	pharmacologically active dose
PD	progressive disease
PFS	progression-free survival
PK	pharmacokinetic
PR	partial response
PT	preferred term
QD	once daily
RECIST	Response Evaluation Criteria in Solid Tumors
SAP	Statistical Analysis Plan
sCR	stringent complete response
SD	stable disease
SOC	system organ class
TEAE	treatment-emergent adverse event
TG	treatment group
VGPR	very good partial response
WHO	World Health Organization

1. INTRODUCTION

This is a Phase 1/2, open-label, dose-escalation study of the JAK inhibitor INCB052793 as a monotherapy and combination therapy in subjects with advanced malignancies. The study will be conducted in 2 phases (Phase 1a/1b and Phase 2). Phase 1a will be conducted with INCB052793 monotherapy dose escalation (Part 1) and dose expansion (Part 2). Phase 1b will comprise treatment cohorts in which INCB052793 will be administered in combination with gemcitabine and *nab*-paclitaxel in select solid tumors (Cohort A); dexamethasone, carfilzomib, bortezomib, lenalidomide, and pomalidomide/dexamethasone in subjects with MM (Cohorts B, C, D, E, and G, respectively); azacitidine in subjects with AML or MDS (Cohort F), and INCB050465 in subjects with lymphoma (Cohort H), each including both a dose escalation (Part 1) and an optional dose expansion (Part 2). Phase 2 will include 2 treatment cohorts in which subjects with AML and high-risk MDS who failed prior therapy with HMA will receive azacitidine in combination with INCB052793 (Cohort I) or in combination with itacitinib (Cohort J).

Section 1 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 INCB052793, gemcitabine, *nab*-paclitaxel, dexamethasone, carfilzomib, bortezomib, lenalidomide, pomalidomide, azacitidine, INCB050465, and itacitinib.

This study was prematurely terminated for lack of efficacy. Cohorts A, C, D, E, G, and H were never opened to enrollment.

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in the Protocol. The scope of this plan includes the final analyses that are planned and will be executed by the Department of Biostatistics or designee, and the analyses of PK data. [redacted]

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 52793-101 Protocol Amendment 9 dated 02 MAY 2017 and CRFs approved 01 NOV 2017. Unless superseded by an amendment, this SAP will be effective for all subsequent Protocol amendments and CRF versions.

2.2. Study Objectives

2.2.1. Primary Objectives

- Phase 1a: To assess the safety and tolerability of INCB052793 in subjects with advanced malignancies and select doses for further evaluation.
- Phase 1b: To assess the safety and tolerability of INCB052793 in combination with standard therapies and the novel phosphatidylinositol 3-kinase δ inhibitor INCB050465 in subjects with advanced malignancies.
- Phase 2: To evaluate the efficacy of INCB052793 in combination with azacitidine and of itacitinib in combination with azacitidine in subjects with AML and high-risk MDS who have failed prior therapy with HMA, based on ORR.

2.2.2. Secondary Objectives

- To assess preliminary efficacy by assessing the ORR in subjects with advanced malignancies.
- To assess the safety and tolerability of INCB052793 in combination in azacitidine and of itacitinib in combination with azacitidine in subjects with AML and high-risk MDS who have failed prior therapy with HMA.
- To assess the PK of INCB052793 as monotherapy administered in the fasted state and the effect of food on the PK of INCB052793.
- To assess the PK of INCB052793 when administered in combination with standard therapies and INCB050465 in subjects with advanced malignancies, to assess the PK of INCB050465 when administered in combination with INCB052793, and to assess the PK of itacitinib when administered in combination with azacitidine.

2.3. Study Endpoints

2.3.1. Primary Endpoints

- Phase 1a and 1b: Safety and tolerability of INCB052793 monotherapy and in combination with standard therapies in select malignancies as assessed by summary of clinical laboratory assessments, 12-lead ECGs, and AEs.
- Phase 2: ORR, defined as the proportion of subjects who achieve CR, CRi, PR, or hematologic improvement using the appropriate disease-specific criteria.

2.3.2. Secondary Endpoints

- Response rates in those subjects with measurable disease as determined by investigator assessment of response.
- Safety and tolerability of INCB052793 in combination with azacitidine and of itacitinib in combination with azacitidine in subjects with AML and high-risk MDS who have failed prior therapy with HMA, assessed by summary of clinical laboratory assessments, 12-lead ECGs, and AEs.
- Pharmacokinetics of INCB052793 and itacitinib (Phase 1a, Phase 1b, and Phase 2) will be summarized.
- For Phase 1a Part 2 expansion portion (TGA and TGB), C_{max}, T_{max}, and $AUC_{0\text{-}t}$ for Cycle 1 Day 1 and C_{max}, T_{max}, C_{min}, $AUC_{0\text{-}t}$, and $AUC_{0\text{-}\tau}$ for Cycle 1 Day 15, or C_{max}, T_{max}, C_{min}, $AUC_{0\text{-}t}$, and $AUC_{0\text{-}\tau}$ for Cycle 2 Day 1 in the case of food-effect evaluation.

[redacted]

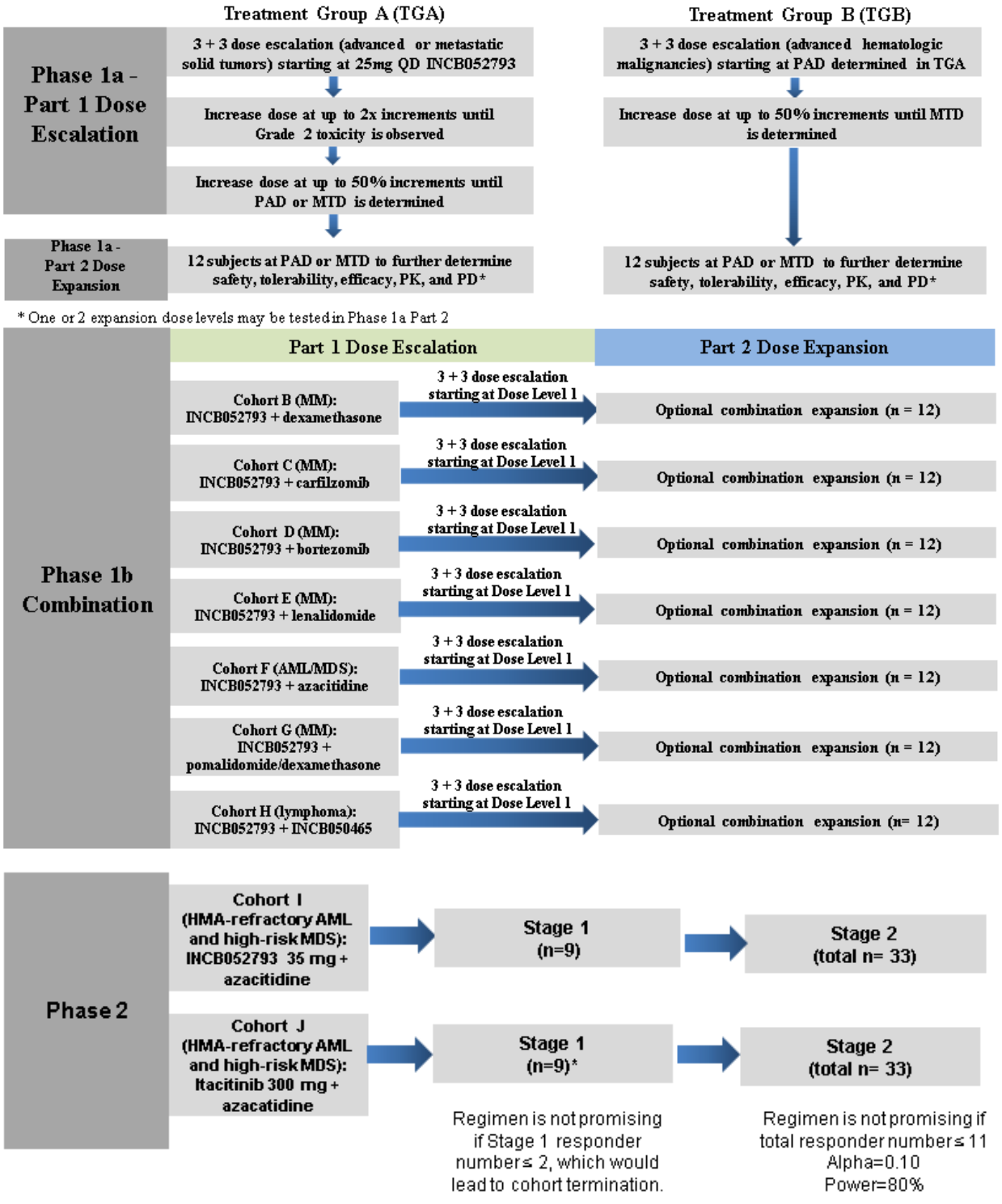
3. STUDY DESIGN

This is a Phase 1/2, open-label, dose-escalation study of the JAK inhibitor INCB052793 as a monotherapy and combination therapy in subjects with advanced malignancies. The study will be conducted in 2 phases (Phase 1a/1b and Phase 2). Phase 1a will be conducted with INCB052793 monotherapy dose escalation (Part 1) and dose expansion (Part 2). Phase 1b will comprise treatment cohorts in which INCB052793 will be administered in combination with dexamethasone in subjects with MM (Cohort B) and azacitidine in subjects with AML or MDS (Cohort F), each including both a dose escalation (Part 1) and an optional dose expansion (Part 2). Phase 2 will include 2 treatment cohorts in which subjects with AML and high-risk MDS who failed prior therapy with HMA will receive azacitidine in combination with INCB052793 (Cohort I) or in combination with itacitinib (Cohort J). Cohort I and Cohort J will use a Simon 2-stage design (1989) to evaluate the efficacy of the combination regimens. If an insufficient number of responders are observed in the cohort at Stage 1, further enrollment in the cohort will be terminated.

This study was prematurely terminated for lack of efficacy. Cohorts A, C, D, E, G, and H were never opened to enrollment.

The study design is shown in Figure 1. Details of the study design are in Section 4 of the Protocol.

Figure 1: Study Design



3.1. Randomization

Not applicable.

3.2. Control of Type I Error

For the primary efficacy endpoint in Phase 2, the 1-sided Type I error will be controlled at 0.10 for each individual cohort expansion. Note that this level of significance does not account for the multiple expansion cohorts. For other endpoints, CIs will be reported at a 95% confidence level.

3.3. Sample Size Considerations

3.3.1. Sample Size in Phase 1a

In Part 1 of Phase 1a of the study, a standard 3 + 3 dose escalation design will be used in 2 disease-specific treatment groups: TGA and TGB. Based on the design, within each treatment group, a minimum of 3 and up to 6 subjects will be enrolled at each dose level. The total sample size in Part 1 of Phase 1a will depend on the frequency of DLTs and the number of dose levels tested before the MTD or PAD is reached. During the 3 + 3 dose escalation part, the probabilities of dose escalation from that dose level for various DLT rates are given in Table 1.

Table 1: Probability of Dose Escalation for Specific Dose-Limiting Toxicity Rates During 3 + 3 Dose Escalation

True DLT Rate	Probability of Dose Escalation
10%	90.6%
20%	70.9%
30%	49.4%
40%	30.9%
50%	17.2%
60%	8.2%

Part 2 of Phase 1a will be the dose expansion part for TGA and TGB and up to 12 subjects may be enrolled in each expansion cohort. With 12 subjects enrolled, there is > 85% chance of observing at least 1 responder if the true underlying response rate is 15%.

Phase 1a of the study will enroll up to 36 subjects.

3.3.2. Sample Size in Phase 1b

In Part 1 of Phase 1b of the study, the standard 3 + 3 dose escalation design will be used in Cohorts B and F. Based on the design, within each cohort, a minimum of 3 and up to 6 subjects will be enrolled at each dose level. The total sample size in Part 1 of Phase 1b will depend on the frequency of DLTs and the number of dose levels tested before the MTD or PAD is reached. During the 3 + 3 dose escalation part, the probabilities of dose escalation from that dose level for various DLT rates are given in Table 1.

Part 2 of Phase 1b will be the dose expansion part for each cohort and up to 12 subjects may be enrolled in each expansion cohort. With 12 subjects enrolled, there is > 85% chance of observing at least 1 responder if the true underlying response rate is 15%.

Phase 1b of the study will enroll up to 39 subjects.

3.3.3. Sample Size in Phase 2

Phase 2 will include 2 treatment cohorts: Cohort I and Cohort J. A Simon 2-stage design (1989) will be used to evaluate the efficacy of combination regimens in these cohorts. Let p_0 denote the historical response rate, and p_1 denote the target response rate. Using a 1-sided Type I error of 0.10 and power of 80%, with the assumption that $p_0 = 26\%$ and $p_1 = 46\%$, each cohort will enroll an initial number of subjects ($n_1 = 9$) at Stage 1. If ≤ 2 subjects have responses among these 9 subjects, it will be concluded that the true response rate is unlikely to be greater than or equal to the target rate, and no more subjects will be enrolled in that cohort. Otherwise, if at least 3 subjects have responses, 24 additional subjects will be treated in Stage 2 to estimate the response rate. At the end of Stage 2, if ≤ 11 subjects have responded among the total of 33 subjects, the efficacy improvement of the combination regimen will not be statistically significant.

Up to 66 subjects will be enrolled for Cohort I and Cohort J in Phase 2.

3.4. Schedule of Assessments

Refer to Protocol Amendment 9 dated 02 MAY 2017 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

For monotherapy (Phase 1a), Day 1 is the date that the first dose of INCB052793 is administered to the subjects.

For combination therapy (Phase 1b and Phase 2), Day 1 is the date that the first dose of study treatment (INCB052793, dexamethasone, azacitidine, or itacitinib) is administered to the subjects.

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

For monotherapy (Phase 1a), baseline is the last nonmissing measurement obtained before the first administration of INCB052793, unless otherwise defined.

For combination therapy (Phase 1b and Phase 2), baseline is the last nonmissing measurement obtained before the first administration of INCB052793 and dexamethasone for Cohort B; INCB052793 and azacitidine for Cohort F and Cohort I; or itacitinib and azacitidine for Cohort J.

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

4.1.4. Handling of Missing and Incomplete Data

In general, values for missing data will not be imputed unless methods for handling missing data are specified in this section or relevant sections.

When calculating time since diagnosis of cancer, partial cancer diagnosis date will be handled as follows:

- If only the day is missing, then the imputed day will be the first of the month.
- If both the month and day are missing, then the imputed day and month will be 01 JAN.
- No imputation will be done if the date is completely missing.

Missing or partial date of last dose will be handled as follows:

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

For relevant efficacy endpoints, partial date of death will be imputed as follows:

- 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

Dexamethasone will be administered as open-label commercial product at a starting dose of 40 mg administered orally weekly on Days 1, 8, 15, and 22 of each 28-day cycle.

Azacitidine will be administered as an open-label commercial product at a starting dose of 75 mg/m^2 subcutaneously for 5 days, followed by 2 days of no treatment, then 75 mg/m^2 for 2 days of each 28-day treatment cycle. Intravenous administration is permitted if subcutaneous administration is not tolerated.

Itacitinib will be administered at a starting dose of 300 mg administered orally QD.

For monotherapy (Phase 1a), Cycle 1 Day 1 is the day that the first dose of INCB052793 is administered. Scheduled cycle length is 21 days. Actual Day 1 of subsequent cycles will correspond with the first day of administration of INCB052793 in that cycle.

For combination therapy (Phase 1b and Phase 2), Cycle 1 Day 1 is the day that first dose of INCB052793 and dexamethasone is administered for Cohort B; INCB052793 and azacitidine is administered for Cohort F and Cohort I; or itacitinib and azacitidine is administered for Cohort J. Scheduled cycle length is 28 days. Actual Day 1 of subsequent cycles will correspond with the first day of administration of dexamethasone or azacitidine in that cycle.

In the event that treatment cycles become out of sync with the originally planned schedule and cycle length is different from scheduled cycle length, the date of the Day 1 of subsequent cycles recorded on the eCRF will be used as the Day 1 of the subsequent cycles.

4.2. Variable Definitions

4.2.1. Body Mass Index

Body mass index will be calculated as follows:

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

4.2.2. Body Surface Area

Body surface area will be calculated based on the Mosteller (1987) formula as follows:

BSA (m^2) = {[weight (kg) × height (cm)] / 3600}^{½}.

4.2.3. Prior and Concomitant Medication

Prior medication is defined as any nonstudy medication started before the first dose of INCB052793 (Phase 1a); INCB052793 and dexamethasone for Cohort B; INCB052793 and azacitidine for Cohort F and Cohort I; or itacitinib and azacitidine for Cohort J.

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

- Before the date of first administration of INCB052793 (Phase 1a); INCB052793 and dexamethasone for Cohort B; INCB052793 and azacitidine for Cohort F and Cohort I; or itacitinib and azacitidine for Cohort J and is ongoing throughout the study or ends on/after the date of first study medication administration.
- On/after the date of first administration of INCB052793 (Phase 1a); INCB052793 and dexamethasone for Cohort B; INCB052793 and azacitidine for Cohort F and Cohort I; or itacitinib and azacitidine for Cohort J and is ongoing or ends during the course of study medication 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 study treatment (ie, INCB052793, dexamethasone, azacitidine, or itacitinib). 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; v9.4 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 subjects in each category.

Interim analyses are planned for this study as defined in Section 9.

5.2. Treatment Groups

This is a Phase 1/2, open-label, dose-escalation study. The efficacy endpoints will be summarized by the appropriate disease subtype. All other data, including baseline characteristics, disposition, and safety, will be summarized overall and by treatment group based on the dose regimen initially assigned. In the event that several dose regimens tested are deemed substantially below the MTD, these doses may be combined for summary purposes.

5.3. Analysis Populations

5.3.1. Efficacy/Safety Evaluable Population

The efficacy/safety evaluable population includes all subjects enrolled in the study who received at least 1 dose of study treatment. All efficacy analyses will be conducted using the efficacy evaluable population. All demographics, baseline characteristics, disease history, subject disposition, and safety analyses will be conducted using the safety evaluable population.

Specific analysis populations to be used for analysis by cancer type may include the following subgroups:

- Solid tumor efficacy/safety evaluable population
- Lymphoma efficacy/safety evaluable population
- AML efficacy/safety evaluable population
- MDS efficacy/safety evaluable population
- MDS/MPN efficacy/safety evaluable population
- MM efficacy/safety evaluable population

5.3.2. Dose Escalation Tolerability Evaluable Populations

The dose escalation tolerability evaluable population includes all subjects enrolled in the dose escalation part of Phase 1a who received at least 17 of 21 days of study medication or who discontinued treatment due to an adverse event in the DLT monitoring period and all subjects enrolled in the dose escalation part of Phase 1b who received at least 75% of planned study medication or who discontinued treatment due to an adverse event in the DLT monitoring period.

5.3.3. Pharmacokinetic Evaluable Populations

The PK evaluable population includes all subjects who received at least 1 dose of study treatment and provided at least 1 postdose sample (1 PK measurement). The study pharmacokineticist will review data listings of study drug administration and sample records to identify subjects to be excluded from PK analyses.

6. BASELINE, EXPOSURE, AND DISPOSITION VARIABLES AND ANALYSES

Appendix A provides a list of planned tables, figures, and listings. Sample data displays are included in a separate document.

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

6.1.1. Demographics

The following demographics will be summarized and listed for the safety evaluable population: age, sex, race, ethnicity, height, weight, BMI, and BSA.

6.1.2. Baseline Disease Characteristics and Disease History

Baseline disease characteristics and disease history will be summarized and listed for all subjects in the safety evaluable population.

For all subjects, baseline ECOG performance status will be summarized and listed.

For subjects with solid tumors, time since initial diagnosis and solid tumor cancer type will be summarized and listed.

For subjects with lymphoma, time since initial diagnosis, disease subtype, results from cytogenetic testing, Ann Arbor staging, presence of B-symptoms at baseline, and International Prognostic Index results will be summarized and listed.

For subjects with AML, time since initial diagnosis, AML disease category, WHO classification, ELN risk classification, and FLT3 status will be summarized and listed.

For subjects with MDS, time since initial diagnosis, WHO classification, IPSS-R group, and IPSS-R prognostic variables will be summarized and listed.

For subjects with MDS/MPN, time since initial diagnosis, MDS/MPN disease type, and presence of extramedullary disease will be summarized and listed.

For subjects with MM, time since initial diagnosis, initial DSS, initial ISS stage, current DSS, current ISS stage, myeloma type, light chain, and light chain type will be summarized and listed.

Time since diagnosis will be calculated as:

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

6.1.3. Prior Therapy

Prior therapy will be summarized and listed for all subjects in the safety evaluable population.

Number of subjects who received prior systemic cancer therapy and the number of prior systemic cancer therapy regimens for each subject will be summarized. In addition, the number of subjects with each prior systemic cancer therapy will be summarized by drug class and preferred term. 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.

Number of subjects who received prior radiation will be summarized. Radiotherapy type, location of administration, start and stop dates, total dose, and best response will be listed.

Number of subjects who had prior surgery or surgical procedure for disease under study will be summarized. The date and description of the surgery/procedure will be listed.

Number of subjects who had hematopoietic stem cell transplant will be summarized. Date of transplant, type of transplant, source of cells, line of therapy, best response, and the medication used with the transplant will be listed.

6.1.4. Medical History

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

6.2. Disposition of Subjects

The number and percentage of subjects who were treated, were receiving ongoing treatment, discontinued study treatment with a primary reason for discontinuation, and withdrew from the study with a primary reason for withdrawal will be summarized and listed for the safety evaluable population.

6.3. Protocol Deviations

Protocol deviations recorded on the eCRF will be summarized by deviation category and presented in the subject data listings.

6.4. Exposure

For subjects in the safety evaluable population, exposure to INCB052793, dexamethasone, azacitidine, and itacitinib will be summarized descriptively as indicated in the following sections.

6.4.1. Exposure for INCB052793

- **Duration of treatment (days):** Date of last dose of INCB052793 – date of first dose of INCB052793 + 1.
- **Average reported daily dose of INCB052793 (mg/day):** Total reported INCB052793 dose (mg) / duration of treatment with INCB052793 (days).
- **Dose modifications for INCB052793:** Number of subjects who had INCB052793 dose reduction and interruption will be summarized.

6.4.2. Exposure for Itacitinib

- **Duration of treatment (days):** Date of last dose of itacitinib – date of first dose of itacitinib + 1.
- **Average reported daily dose of itacitinib (mg/day):** Total reported itacitinib dose (mg) / duration of treatment with itacitinib (days).
- **Dose modifications for itacitinib:** Number of subjects who had itacitinib dose reduction and interruption will be summarized.

6.4.3. Exposure for Dexamethasone

- **Duration of treatment (days):** Date of last dose of dexamethasone – date of first dose of dexamethasone + 1.
- **Average reported daily dose of dexamethasone (mg/day):** Total reported dexamethasone dose (mg) / duration of treatment with dexamethasone (days).
- **Dose modifications for dexamethasone:** Number of subjects who had dexamethasone dose reduction and interruption will be summarized.

6.4.4. Exposure for Azacitidine

- **Number of cycles**: Number of cycles with a nonzero dose of azacitidine.
- **Relative dose intensity of azacitidine (%):** 100 × [total actual dose] / [total assigned dose].

  Total actual dose (mg/m^2) administered is the sum of the BSA-adjusted cumulative dose of azacitidine that has been administered to the subject.

  Total assigned dose (mg/m^2) is the total dose expected if the subject had taken all doses as initially assigned. Let S be the study day of the last date that the subject is exposed to azacitidine. Let D be the assigned dose level of 75 mg/m^2. The total assigned dose is defined as:

  Total assigned dose (mg/m^2) $= D \times (\lceil S / 28 \rceil + \lceil (S-1) / 28 \rceil + \lceil (S-2) / 28 \rceil + \lceil (S-3) / 28 \rceil + \lceil (S-4) / 28 \rceil + \lceil (S-7) / 28 \rceil + \lceil (S-8) / 28 \rceil)$

  where $\lceil . \rceil$ assigns the smallest integer not less than the argument.
- **Azacitidine dose modifications:** Number of subjects who had azacitidine dose reduction and interruption will be summarized.

6.5. Study Drug Compliance

For subjects in the safety evaluable population, overall compliance (%) for INCB052793 or itacitinib will be calculated for all subjects 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.

6.6. Prior and Concomitant Medication

Prior medications and concomitant medications will be coded using the WHO Drug Dictionary. Number and percentage of subjects in the safety evaluable population with each prior and concomitant mediations will be summarized by WHO drug class and WHO drug preferred term.

7. EFFICACY

Appendix A provides a list of planned tables, figures, and listings. Sample data displays are included in a separate document.

7.1. General Considerations

All efficacy analyses will be performed using the efficacy evaluable population. If there are fewer than 5 subjects for a disease subtype, efficacy data may be presented in data listings only.

Due to study termination, only the primary and secondary efficacy endpoints will be analyzed.

7.2. Efficacy Hypotheses

Not applicable.

7.3. Analysis of the Efficacy Parameter

7.3.1. Solid Tumors

7.3.1.1. Response Assessment

Tumor assessment for subjects with solid tumors will be performed using RECIST v1.1 (Eisenhauer et al 2009). The investigator's assessment will be used to determine responses and will be logged into the eCRF.

Response status per the investigator's assessment for solid tumors will be recorded at each response assessment visit as CR, PR, SD, PD, NE, or NA.

7.3.1.2. Best Overall Response and Objective Response Rate

Best overall response for subjects with solid tumors is the best response recorded before and including the first PD, in the order of CR, PR, SD, PD, and NE. In the case of SD, measurements must meet the SD criterion at least once on or after Day 42. Subjects who fail to meet this criterion will have a BOR of PD if the next available assessment after the initial assessment indicates PD or a BOR of NE if there are no additional assessments available.

A subject is considered a responder if the subject has a BOR of CR or PR.

Objective response rate is the proportion of responders. Subjects 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 calculations of ORR.

Best overall response will be summarized descriptively. Objective response rate will be estimated with 95% CIs. Confidence intervals will be calculated based on the exact method for binomial distributions.

7.3.2. Lymphoma

7.3.2.1. Response Assessment

Disease assessment for subjects with lymphoma will be performed following Response Criteria for Lymphoma – The Lugano Classification (Cheson et al 2014). The investigator's assessment will be used to determine responses and will be logged into the eCRF.

Response status per investigator's assessment by CT/MRI and/or PET for lymphoma will be recorded at each response assessment visit as Complete Radiologic Response/Complete Metabolic Response, Partial Remission/Partial Metabolic Response, SD/No Metabolic Response, PD/Progressive Metabolic Disease, NE, or ND.

7.3.2.2. Best Overall Response and Objective Response Rate

Best overall response for subjects with lymphoma is the best response recorded before and including the first PD/Progressive Metabolic Disease, in the order of Complete Radiologic Response/Complete Metabolic Response, Partial Remission/Partial Metabolic Response, SD/No Metabolic Response, PD/Progressive Metabolic Disease, and NE. In the case of SD/No Metabolic Response, measurements must meet the SD/No Metabolic Response criterion at least once on or after Day 42. Subjects who fail to meet this criterion will have a BOR of PD/Progressive Metabolic Disease if the next available assessment after the initial assessment indicates PD/Progressive Metabolic Disease or a BOR of NE if there are no additional assessments available.

A subject is considered a responder if the subject has a BOR of Complete Radiologic Response/Complete Metabolic Response or Partial Remission/Partial Metabolic Response.

Objective response rate is the proportion of responders. Subjects 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 calculations of ORR.

Best overall response will be summarized descriptively. Objective response rate will be estimated with 95% CIs. Confidence intervals will be calculated based on the exact method for binomial distributions.

7.3.3. Acute Myeloid Leukemia

7.3.3.1. Response Assessment

Disease assessment for subjects with AML will be performed following the IWG Response Criteria for AML (Cheson et al 2003). The investigator's assessment will be used to determine responses and will be logged into the eCRF.

Response status per investigator's assessment for AML will be recorded at each response assessment as complete remission, CRi, partial remission, MLFS, SD, or treatment failure.

7.3.3.2. Best Overall Response and Objective Response Rate

For subjects with AML, BOR is the best response recorded before and including the first treatment failure, in the order of complete remission, CRi, partial remission, MLFS, SD, and treatment failure.

A subject is considered a responder if the subject has a BOR of complete remission, CRi, or partial remission.

Objective response rate is defined as the proportion of responders. Subjects 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 calculations of ORR.

Best overall response will be summarized descriptively. Objective response rate will be estimated with 95% CIs. Confidence intervals will be calculated based on the exact method for binomial distributions.

7.3.4. Myelodysplastic Syndrome

7.3.4.1. Response Assessment

Disease assessment for subjects with MDS will be performed following the IWG Response Criteria for MDS (Cheson et al 2006). The investigator's assessment will be used to determine responses and will be logged into the eCRF.

Response status per investigator's assessment for MDS will be recorded at each response assessment as complete remission, partial remission, marrow complete remission, SD, treatment failure, disease progression, disease transformation, or relapse after complete remission or partial remission.

7.3.4.2. Best Overall Response and Objective Response Rate

For subjects with MDS, BOR is the best response recorded before and including the first progression, which consists of treatment failure, disease progression, disease transformation, and relapse after complete remission or partial remission, in the order of complete remission, partial remission, marrow complete remission, SD, and progression.

A subject is considered a responder if the subject has a BOR of complete remission, partial remission, or marrow complete remission.

Objective response rate is defined as the proportion of responders. Subjects 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 calculations of ORR.

Best overall response will be summarized descriptively. Objective response rate will be estimated with 95% CIs. Confidence intervals will be calculated based on the exact method for binomial distributions.

7.3.5. Myelodysplastic Syndrome/Myeloproliferative Neoplasms

7.3.5.1. Response Assessment

Disease assessment for subjects with MDS/MPN will be performed following the International Consortium Proposal of Uniform Response Criteria for MDS/MPN in Adults (Savona et al 2015). The investigator's assessment will be used to determine responses and will be logged into the eCRF.

Response status will be recorded at each response assessment visit as complete remission, partial remission, marrow response, clinical benefit, SD, and disease progression.

7.3.5.2. Best Overall Response and Objective Response Rate

For subjects with MDS/MPN, BOR is the best response recorded before and including the first PD in the order of complete remission, partial remission, marrow response, clinical benefit, SD, and disease progression.

A subject is considered a responder if the subject has a BOR of complete remission, partial remission, or marrow response.

Objective response rate is defined as the proportion of responders. Subjects 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 calculations of ORR.

Best overall response will be summarized descriptively. Objective response rate will be estimated with 95% CIs. Confidence intervals will be calculated based on the exact method for binomial distributions.

7.3.6. Multiple Myeloma

7.3.6.1. Response Assessment

Disease assessment for subjects with MM will be performed following the International Uniform Response Criteria for Multiple Myeloma (Durie et al 2006) and Criteria for Evaluating Disease Response and Progression in Patients With Multiple Myeloma Treated by High-Dose Therapy and Haemopoietic Stem Cell Transplantation (Blade et al 1998), which is for assessing MR only. The investigator's assessment will be used to determine responses and will be logged into the eCRF.

Response status per investigator's assessment for MM will be recorded at each response assessment visit as sCR, CR, VGPR, PR, MR, SD, PD, or relapse.

7.3.6.2. Best Overall Response and Objective Response Rate

Best overall response for MM is the best response recorded before and including the first progression, which consists of PD and relapse, in the order of sCR, CR, VGPR, PR, MR, SD, and PD.

A subject is considered a responder if they have a best overall response of sCR, CR, VGPR, or PR.

Objective response rate is the proportion of responders. Subjects 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 calculations of ORR.

Best overall response will be summarized descriptively. Objective response rate will be estimated with 95% CIs. Confidence intervals will be calculated based on the exact method for binomial distributions.

7.4. Analysis of Other Efficacy Variables

7.4.1. Eastern Cooperative Oncology Group Performance Status

Eastern Cooperative Oncology Group Performance status will be listed.

7.5. Pharmacokinetic Analyses

Pharmacokinetic analysis of INCB052793, including C_{max}, T_{max}, C_{min}, $AUC_{0\text{-}t}$, $AUC_{0\text{-}\tau}$ and Cl/F, will be performed on samples collected at the specified timepoints. The parameters will be calculated from the blood plasma concentrations of INCB052793 using standard noncompartmental (model-independent) PK methods and commercial software. The PK parameters will be summarized by descriptive statistics by part and cohort.

The log-transformed PK parameters will be compared among the dose levels by using a 1-factor ANOVA. Dose-dependent parameters (C_{max} and AUC) will be normalized to the lowest common dose before statistical comparisons. C_{max} and AUC will be evaluated using a power model, for example, $AUC = \alpha \cdot (dose\beta)$ or, equivalently, $\log(AUC) = \log(\alpha) + \beta \cdot \log(dose)$, where linear dose proportionality is accepted if β is not significantly different from 1. Attainment of steady-state will be assessed separately for each cohort by comparing trough plasma concentrations on Days 8 and 15.

For the food-effect assessment, the log-transformed PK parameters will be compared between the fed and fasted treatments using an ANOVA for a 1-way crossover design. The geometric mean relative bioavailability and 90% CIs will be calculated for comparing C_{max} and AUC between the fed (test) and fasted (reference) treatments. Population PK methods may be employed if there are a sufficient number of plasma PK samples.

8. SAFETY AND TOLERABILITY

Appendix A provides a list of planned tables, figures, and listings. Sample data displays are included in a separate document.

8.1. General Considerations

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

Unless otherwise stated, table summaries will be limited to AEs occurring within 30 days of the last administration of study drug.

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 first dose of study treatment (until 30 days after 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 in relation to study treatment administration.

Adverse events will be tabulated by MedDRA PT and SOC. Severity of AEs will be graded using the NCI CTCAE v4.03 (2010). The CTCAE reporting guidelines and grading details are available on the Cancer Therapy Evaluation Program website.

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

Any missing onset date, 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. Dose-Limiting Toxicities

Subjects with DLTs and the type of DLT will be listed.

8.2.3. Maximum Tolerated Dose

The MTD will be defined as 1 dose level below that at which one-third or more of subjects in a particular cohort experience DLTs.

8.2.4. Adverse Event Summaries

An overall summary of AEs by treatment group will include:

- Number (%) of subjects reporting any TEAEs
- Number (%) of subjects reporting any serious TEAEs
- Number (%) of subjects reporting any Grade 3 or 4 TEAEs
- Number (%) of subjects reporting any TEAEs related to INCB052793/itacitinib
- Number (%) of subjects reporting any TEAEs related to dexamethasone/azacitidine
- Number (%) of subjects who temporarily interrupted INCB052793/itacitinib because of TEAEs
- Number (%) of subjects who temporarily interrupted dexamethasone/azacitidine because of TEAEs
- Number (%) of subjects who permanently discontinued INCB052793/itacitinib because of TEAEs
- Number (%) of subjects who permanently discontinued dexamethasone/azacitidine because of TEAEs
- Number (%) of subjects with INCB052793/itacitinib dose reductions because of TEAEs
- Number (%) of subjects with dexamethasone/azacitidine dose reductions because of TEAEs
- Number (%) of subjects who had a fatal TEAE

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

- Summary of TEAEs by SOC and PT
- Summary of TEAEs by PT in decreasing order of frequency
- Summary of TEAEs by SOC, PT, and maximum severity
- Summary of Grade 3 or 4 TEAEs by SOC and PT
- Summary of Grade 3 or 4 TEAEs by PT in decreasing order of frequency
- Summary of INCB052793 treatment-related TEAEs by SOC and PT
- Summary of INCB052793 treatment-related TEAEs by PT in decreasing order of frequency
- Summary of Grade 3 or 4 INCB052793 treatment-related TEAEs by SOC and PT
- Summary of itacitinib treatment-related TEAEs by SOC and PT
- Summary of itacitinib treatment-related TEAEs by PT in decreasing order of frequency

- Summary of Grade 3 or 4 itacitinib treatment-related TEAEs by SOC and PT
- Summary of dexamethasone/azacitidine treatment-related TEAEs by SOC and PT
- Summary of dexamethasone/azacitidine treatment-related TEAEs by PT in decreasing order of frequency
- Summary of Grade 3 or 4 dexamethasone/azacitidine treatment-related TEAEs by SOC and PT
- Summary of TEAEs with a fatal outcome by SOC and PT
- Summary of serious TEAEs by SOC and PT
- Summary of serious TEAEs by PT in descending order of frequency
- Summary of INCB052793 treatment-related serious TEAEs by SOC and PT
- Summary of Itacitinib treatment-related serious TEAEs by SOC and PT
- Summary of dexamethasone/azacitidine treatment-related serious TEAEs by SOC and PT
- Summary of TEAEs leading to INCB052793 dose reduction by SOC and PT
- Summary of TEAEs leading to itacitinib dose reduction by SOC and PT
- Summary of TEAEs leading to dexamethasone/azacitidine dose reduction by SOC and PT
- Summary of TEAEs leading to INCB052793 dose interruption by SOC and PT
- Summary of TEAEs leading to itacitinib dose interruption by SOC and PT
- Summary of TEAEs leading to dexamethasone/azacitidine dose interruption by SOC and PT
- Summary of TEAEs leading to discontinuation of INCB052793 by SOC and PT
- Summary of TEAEs leading to discontinuation of itacitinib by SOC and PT
- Summary of TEAEs leading to discontinuation of dexamethasone/azacitidine by SOC and PT
- Summary of Grade 3 or 4 TEAEs during the DLT monitoring period by SOC and PT

8.3. Clinical Laboratory Tests

8.3.1. Laboratory Value Definitions

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

Laboratory test values will be assessed for severity based on the numerical component of CTCAE v4.03.

8.3.2. Laboratory Value Summaries

Any laboratory test results and associated normal ranges from local laboratories will be converted to SI units. When there are multiple laboratory nonmissing values for a subject's particular test at a scheduled visit, the laboratory value with the smallest laboratory sequence number will be used in by-visit summaries.

Numeric laboratory values will be summarized descriptively in SI units, and non-numeric test values will be tabulated when necessary. In addition, line graphs will be provided for hemoglobin, platelet counts, white blood cell counts, neutrophils, and lymphocytes.

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 subjects in the baseline category.

8.4. Vital Signs

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

Normal ranges for vital sign values are defined in Table 2. The abnormal values for subjects exhibiting vital sign abnormalities will be listed along with their assigned dose level. Alert vital signs are defined as an absolute value outside the defined normal range and percentage change from baseline greater than 25%. The values for subjects exhibiting alert vital sign abnormalities will be listed.

Table 2: Normal Ranges for Vital Sign Values

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	> 38°C	< 35.5°C
Respiratory rate	> 24 breaths/min	< 8 breaths/min

8.5. Electrocardiograms

Twelve-lead ECGs including PR, QRS, QT, QTcF, QTcB, and RR intervals will be obtained for each subject during the study. Values at each scheduled timepoint, change, 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 treatment.

Normal ranges for ECG values are defined in Table 3. Electrocardiogram values will also be considered abnormal if the absolute percentage change from baseline is more than 25% (30% for QRS interval). Subjects exhibiting ECG abnormalities will be listed with study visit and assigned dose level. Abnormal values for subjects 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.

Table 3: Normal Ranges for Electrocardiogram Values

Parameter	High Threshold	Low Threshold
PR	> 220 ms	< 75 ms
QRS	> 120 ms	< 50 ms
QT	> 500 ms	< 300 ms
QTcF, QTcB	> 460 ms	< 295 ms
RR	> 1330 ms	< 600 ms

QTcB = Bazett's correction; QTcF = Fridericia's correction.

9. INTERIM ANALYSES

9.1. Overview of Interim Analyses

For Cohort I and Cohort J, a stopping rule for futility is planned for each cohort when 9 subjects have been treated and evaluated for response or have permanently discontinued study treatment because of disease progression, withdrawal of consent, or death. Further enrollment in that cohort will be terminated for futility if ≤ 2 of the 9 subjects responded based on assessments provided by investigator.

10. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 4.

Table 4: Statistical Analysis Plan Versions

SAP Version	Date
Original	28 MAY 2019

10.1. Changes to Protocol-Defined Analyses

Due to study termination, only primary and secondary efficacy endpoints will be analyzed. Cohorts A, C, D, E, G, and H were never opened to enrollment.

Interim analyses of the primary efficacy endpoint are planned for Stage 1 subjects in Cohorts I and J.

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. Standard tables will follow the conventions in the Standard Safety Tables v1.3. Shells are provided for nonstandard tables in a separate document.

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
1.1.1	Analysis Populations	Safety Evaluable
1.1.2	Summary of Subject Disposition	Safety Evaluable
1.1.4	Summary of Protocol Deviations	Safety Evaluable
1.2.1	Summary of Demographic and Baseline Characteristics	Safety Evaluable
1.3.1.1	Summary of Baseline Disease Characteristics and Disease History for Subjects with Solid Tumors	Safety Evaluable
1.3.1.2	Summary of Baseline Disease Characteristics and Disease History for Subjects With Lymphoma	Safety Evaluable
1.3.1.3	Summary of Baseline Disease Characteristics and Disease History for Subjects With AML	Safety Evaluable
1.3.1.4	Summary of Baseline Disease Characteristics and Disease History for Subjects With MDS	Safety Evaluable
1.3.1.5	Summary of Baseline Disease Characteristics and Disease History for Subjects With MDS/MPN	Safety Evaluable
1.3.1.6	Summary of Baseline Disease Characteristics and Disease History for Subjects With MM	Safety Evaluable
1.3.2	Summary of Prior Cancer Therapy	Safety Evaluable
1.3.3	Summary of Prior Cancer Medication by Drug Class and Preferred Term	Safety Evaluable
1.4.1	Summary of Prior Medications	Safety Evaluable
1.4.2	Summary of Concomitant Medications	Safety Evaluable
1.5.1	Summary of General Medical History	Safety Evaluable
2.1.1	Summary of Best Overall Response for Subjects With Solid Tumors	Efficacy Evaluable
2.1.2	Summary of Best Overall Response for Subjects With Lymphoma	Efficacy Evaluable
2.1.3	Summary of Best Overall Response by IWG Response Criteria for Subjects With AML	Efficacy Evaluable
2.1.4	Summary of Best Overall Response by IWG Response Criteria for Subjects With MDS	Efficacy Evaluable
2.1.5	Summary of Best Overall Response for Subjects with MDS/MPN	Efficacy Evaluable
2.1.6	Summary of Best Overall Response by International Uniform Response Criteria for Subjects With MM	Efficacy Evaluable
3.1	Summary of Exposure and Compliance	Safety Evaluable
3.2.1	Overall Summary of Treatment-Emergent Adverse Events	Safety Evaluable
3.2.2	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety Evaluable
3.2.3	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety Evaluable
3.2.4	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Safety Evaluable
3.2.5	Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety Evaluable

Table No.	Title	Population
3.2.6	Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety Evaluable
3.2.7	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety Evaluable
3.2.8	Summary of Serious Treatment-Emergent Adverse Events by Preferred Term in Decreasing Order of Frequency	Safety Evaluable
3.2.9.1	Summary of INCB052793 Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety Evaluable
3.2.9.2	Summary of Itacitinib Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety Evaluable
3.2.9.3	Summary of Dexamethasone or Azacitidine Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety Evaluable
3.2.10.1	Summary of INCB052793 Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety Evaluable
3.2.10.2	Summary of Itacitinib Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety Evaluable
3.2.10.3	Summary of Dexamethasone or Azacitidine Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety Evaluable
3.2.11.1	Summary of Grade 3 or 4 INCB052793 Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety Evaluable
3.2.11.2	Summary of Grade 3 or 4 Itacitinib Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety Evaluable
3.2.11.3	Summary of Grade 3 or 4 Dexamethasone or Azacitidine Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety Evaluable
3.2.12.1	Summary of INCB052793 Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety Evaluable
3.2.12.2	Summary of Itacitinib Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety Evaluable
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3.2.14.1	Summary of Treatment-Emergent Adverse Events Leading to INCB052793 Dose Reduction by MedDRA System Organ Class and Preferred Term	Safety Evaluable
3.2.14.2	Summary of Treatment-Emergent Adverse Events Leading to Itacitinib Dose Reduction by MedDRA System Organ Class and Preferred Term	Safety Evaluable
3.2.14.3	Summary of Treatment-Emergent Adverse Events Leading to Dexamethasone or Azacitidine Dose Reduction by MedDRA System Organ Class and Preferred Term	Safety Evaluable
3.2.15.1	Summary of Treatment-Emergent Adverse Events Leading to INCB052793 Dose Interruption by MedDRA System Organ Class and Preferred Term	Safety Evaluable
3.2.15.2	Summary of Treatment-Emergent Adverse Events Leading to Itacitinib Dose Interruption by MedDRA System Organ Class and Preferred Term	Safety Evaluable
3.2.15.3	Summary of Treatment-Emergent Adverse Events Leading to Dexamethasone or Azacitidine Dose Interruption by MedDRA System Organ Class and Preferred Term	Safety Evaluable
3.2.16.1	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of INCB052793 by MedDRA System Organ Class and Preferred Term	Safety Evaluable

Table No.	Title	Population
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3.2.17	Summary of Grade 3 or 4 Treatment-Emergent Adverse Events During the DLT Monitoring Period by MedDRA System Organ Class and Preferred Term	Safety Evaluable
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3.3.4	Shift Summary of Chemistry Laboratory Values in CTC Grade – to the Worst Abnormal Value	Safety Evaluable
3.3.5	Summary of Laboratory Values – Coagulation	Safety Evaluable
3.3.6	Shift Summary of Coagulation Laboratory Values in CTC Grade – to the Worst Abnormal Value	Safety Evaluable
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3.4.3	Summary of Pulse	Safety Evaluable
3.4.4	Summary of Respiratory Rate	Safety Evaluable
3.4.5	Summary of Body Temperature	Safety Evaluable
3.4.6	Summary of Body Weight	Safety Evaluable
3.5.1	Summary of PR Interval (ms) From 12-Lead ECG	Safety Evaluable
3.5.2	Summary of QRS Interval (ms) From 12-Lead ECG	Safety Evaluable
3.5.3	Summary of QT Interval (ms) From 12-Lead ECG	Safety Evaluable
3.5.4	Summary of QTcB Interval (ms) From 12-Lead ECG	Safety Evaluable
3.5.5	Summary of QTcF Interval (ms) From 12-Lead ECG	Safety Evaluable
3.5.6	Summary of RR Interval (ms) From 12-Lead ECG	Safety Evaluable
3.5.7	Summary of Outliers of QT and QTcB/QTcF Interval Values From 12-Lead ECG	Safety Evaluable

Figures

Figure No.	Title
4.4.1	Line Graph of Selected Laboratory Values by Study Visit

Listings

Listing No.	Title
2.1.1	Subject Enrollment and Disposition Status
2.1.2	Subject Inclusion and Exclusion Criteria Violations
2.2.1	Protocol Deviations
2.3.1	Analysis Populations
2.4.1	Demographic and Baseline Characteristics
2.4.2	Baseline Disease Characteristics and Disease History
2.4.3	Prior Radiation Treatment
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2.6.1	Deaths
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2.7.7.1	Adverse Events Leading to Interruption, Reduction, or Discontinuation of INCB052793
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2.8.1	Clinical Laboratory Values - Hematology
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2.10.1	12-Lead ECG Values
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2.11.1	Body Weight

Signature Manifest

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[redacted]	[redacted]	28 May 2019, 02:44:19 PM	Approved
[redacted]	[redacted]	29 May 2019, 03:41:21 PM	Approved
[redacted]	[redacted]	29 May 2019, 04:22:01 PM	Approved
[redacted]	[redacted]	30 May 2019, 12:35:32 PM	Approved