Official Title: A Phase 2 Study of Itacitinib, for the Prevention of Cytokine Release Syndrome Induced by Immune Effector Cell Therapy

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Statistical Analysis Plan

INCB 39110-211

A Phase 2 Study of Itacitinib for the Prevention of Cytokine Release Syndrome Induced by Immune Effector Cell Therapy

IND Number:	[redacted]
Sponsor:	**Incyte Corporation** **1801 Augustine Cut-Off** **Wilmington, DE 19803**
Protocol Version:	**Protocol Amendment 4 dated 08 DEC 2022**
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SAP Version:	**Amendment 1**
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Date of Plan:	**08 MAY 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	Term
AE	adverse event
ALL	acute lymphoblastic leukemia
ALP	alkaline phosphatase
ALT	alanine aminotransferase
ASBMT	American Society for Blood and Marrow Transplantation
AST	aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical
[redacted]	[redacted]
BID	twice daily
BMI	body mass index
CAR	chimeric antigen receptor
CI	confidence interval
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
CNS	central nervous system
CR	complete response
CRF	case report form
CRi	complete response with incomplete blood count recovery
CRS	cytokine release syndrome
CTCAE v5.0	Common Terminology Criteria for Adverse Events version 5.0
DLBCL	diffuse large B-cell lymphoma
DSMB	Data Safety Monitoring Board
EAS	efficacy evaluable analysis set
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	electronic case report form
EOS	end of study
EOT	end of treatment
ICANS	immune effector cell–associated neurotoxicity syndrome
ICE	immune effector cell–associated encephalopathy
ICF	informed consent form
IEC	immune effector cell
IRB	institutional review board

Abbreviation	Term
MCL	mantle cell lymphoma
MedDRA	Medical Dictionary for Regulatory Activities
MIPI	Mantle Cell Lymphoma International Prognostic Index
[redacted]	[redacted]
NCCN	National Comprehensive Cancer Network
NCI	National Cancer Institute
[redacted]	[redacted]
[redacted]	[redacted]
PT	preferred term
QD	once daily
QTcB	QT interval corrected by Bazett
QTcF	QT interval corrected by Fridericia
SAP	Statistical Analysis Plan
SoA	schedule of activities
SOC	system organ class
TEAE	treatment-emergent adverse event
[redacted]	[redacted]
[redacted]	[redacted]
ULN	upper limit of normal
WHO	World Health Organization

1. INTRODUCTION

INCB 39110-211 is a Phase 2 study designed to assess the safety and efficacy of oral administration of itacitinib to participants planning to receive IEC therapy for any approved hematologic indication. This study will be conducted in 2 parts. In Part 1, participants are administered itacitinib 200 mg QD (open label). In Part 2, participants are randomized to receive either itacitinib 200 mg BID or placebo. According to Protocol Amendment 4, the study treatment itacitinib/placebo will begin on Day –3 (pre-IEC) and continue through Day 26 (study treatment period). Immune effector cell therapy will be administered on Day 0 (IEC infusion day). Protocol-defined assessments will be conducted on Days –3, –1, 0, 1, 3, 5, 7, 14, 21, and 28. Additional post-therapy follow-up visits will be conducted at Day 90 and Day 180 (90 and 180 days after IEC). End of study is met at Day 180 (6 months after IEC).

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in the INCB 39110-211 Protocol. The scope of this plan includes the interim and final analyses that are planned and will be executed by the Department of Biostatistics or designee. [redacted]

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 39110-211 Protocol Amendment 4 dated 08 DEC 2022 and the CRF was approved on 10 JUN 2022. Unless superseded by an amendment, this SAP will be effective for all subsequent Protocol amendments and CRF versions.

2.2. Study Objectives and Endpoints

Table 1 presents the objectives and endpoints.

Table 1: Objectives and Endpoints

Objectives	Endpoints
Primary	
To evaluate the efficacy of itacitinib as a preventative treatment for CRS associated with IEC therapy.	Efficacy, as determined by the proportion of participants who develop ≥ Grade 2 CRS by Day 14 using ASBMT CRS Consensus Grading.
Secondary	
To evaluate the proportion of participants with ICANS regardless of CRS, after IEC therapy.	Incidence and severity of ICANS, as determined by the proportion of participants with ICANS by Day 28, after IEC therapy using the ICANS Consensus Grading.

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
Secondary (continued)	
To evaluate the onset and episode of ICANS using the ICANS Consensus Grading, regardless of CRS, by Day 28.	Time to onset and duration of ICANS using the ICANS Consensus Grading, regardless of CRS, by Day 28.
To evaluate the duration of all grades of CRS, by Day 28.	Time to onset and duration of all grades of CRS by Day 28 using ASBMT CRS Consensus Grading.
To evaluate the proportion of participants who develop any grade of CRS within 48 hours after IEC therapy.	Proportion of participants with any grade of CRS at 48 hours, after IEC therapy using ASBMT CRS Consensus Grading.
To evaluate the proportion of participants who develop ≥ Grade 2 CRS by Day 28 of administration after first IEC therapy.	Proportion of participants with ≥ Grade 2 CRS by Day 28, after first IEC therapy.
To characterize the safety of itacitinib, before and after IEC therapy, excluding CRS and ICANS.	Safety of itacitinib assessed by the incidence of all AEs except CRS and ICANS, by collecting laboratory data, performing physical examinations, and collecting vital signs beginning at Day –3 and through the duration of safety follow-up.
	≥ Grade 3 cytopenias ongoing by Day 30.
To evaluate the number of and length of hospital admissions for CRS and ICANS.	Number of hospital admissions and duration of stay for participants with CRS and/or ICANS by EOS.
To assess intervention for CRS and ICANS.	Proportion of participants who were treated with tocilizumab for CRS.
	Proportion of participants requiring more than 1 dose of dexamethasone (or equivalent) for ICANS.
[redacted]	

Table 1: Objectives and Endpoints (Continued)

[redacted]

3. STUDY DESIGN

3.1. Overall Study Design

This is a 2-part Phase 2 study designed to assess the safety and efficacy of oral administration of itacitinib for the prevention of CRS in male or female participants planning to receive IEC therapy for any approved hematologic indication.

- In Part 1, approximately 62 participants older than 12 years will be administered itacitinib 200 mg QD (open label). Based on the Protocol-defined analysis in Protocol Amendment 2, 10 participants with ALL will be included.
- In Part 2, approximately 46 evaluable participants older than 18 years will be randomized to receive either itacitinib 200 mg BID or placebo.

This study includes a 14-day screening period after apheresis. Apheresis will be per institutional standard of care. Conditioning chemotherapy will be administered at the discretion of the investigator.

Participants will be administered study drug beginning at Day −3 to Day −1 before IEC infusion. Immune effector cell therapy will be administered on Day 0 along with study drug. Participants will continue to receive study drug through Day 26 to complete a 30-day study treatment period.

During the treatment period, Protocol-defined assessments will be conducted on Day –3, Day –1, Day 0 (IEC infusion day), Day 1, Day 3, Day 5, Day 7, Day 14, Day 21, and Day 28. Restaging of hematologic disease will be conducted per institutional guidelines. Completers are defined as participants who complete 30 days of itacitinib administration (Day –3 to Day 26). An EOT assessment will be conducted at Day 28 ± 2 days. Additional post-therapy follow-up visits will be conducted 30 days after the last dose of itacitinib and 90 and 180 days after IEC infusion. End of study is met at Day 180.

Safety will be monitored beginning at screening and will continue through to a 30-day post-treatment safety follow-up visit.

Hematologic disease assessments should be conducted as indicated in the SoA. The date of the assessment as well as the results should be recorded in the eCRF.

A planned interim analysis for CRS futility will be conducted when 24 participants in Part 1 are treated with an approved IEC therapy and complete the Day 28 (EOT) visit. The study may be stopped for futility at the interim analysis if the conditional power based on interim results is lower than 20%, which is equivalent to more than 17 out of 24 participants experiencing ≥ Grade 2 CRS by Day 14.

See Figure 1 and Figure 2 for the study design.

Figure 1: Study Design Schema Part 1

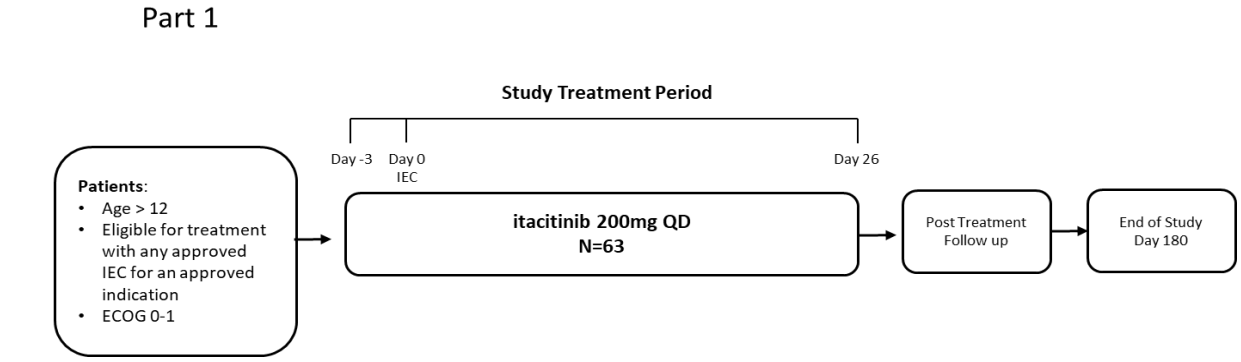
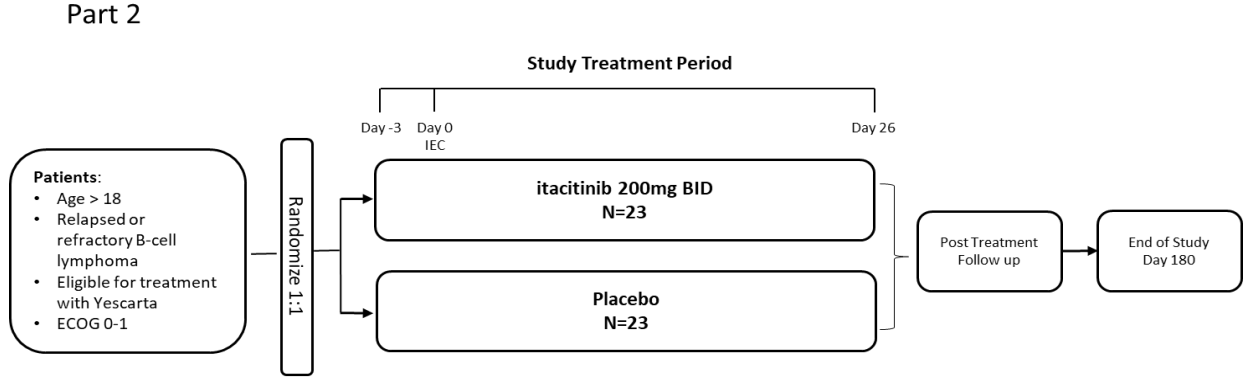


Figure 2: Study Design Schema Part 2



3.1.1. Treatment Discontinuation

Participants **must** be withdrawn from study treatment for the following reasons:

- The participant becomes pregnant.
- Consent is withdrawn.
  Note: Consent withdrawn means that the participant has explicitly indicated that they do not want to be followed any longer; in this case no further data, except data in public domain, may be solicited from or collected on the participant. Participants may choose to discontinue study treatment and remain in the study to be followed for progression and survival.
- Further participation would be injurious to the participant's health or well-being, in the investigator's medical judgment.
- Unacceptable toxicity.
- The study is terminated by the sponsor.
- The study is terminated by the local health authority and/or IRB.

3.1.2. Study Duration

The study begins when the first participant signs the ICF. The end of the study is expected to occur when the last participant reaches their 180-day (6-month) follow-up visit.

Completers (of treatment) are defined as participants who complete 30 days of itacitinib administration (Day –3 to Day 26). A participant is considered to have completed the study if he/she has completed all periods of the study including the 6-month follow-up for which a disease assessment is required.

3.2. Randomization

Part 1: Not applicable.

Part 2: The planned 46 participants will be randomized 1:1 to receive either itacitinib or placebo, resulting in 23 participants in each cohort.

3.3. Control of Type I Error

For Part 1, analysis of CRS rate, 2-sided 95% exact confidence level by Clopper-Pearson method will be reported (Clopper and Pearson 1934).

For Part 2, the analysis of the primary efficacy endpoint, a 2-sample t test with 1-sided Type I error of 0.05 will be conducted to test the difference between the 2 treatment groups. Two-sided 95% CIs will be reported, for the primary efficacy endpoint for each treatment group and the difference between the 2 treatment groups.

3.4. Sample Size Considerations

Part 1 is a single-arm open-label study. The sample size calculation is based on the primary endpoint of ≥ Grade 2 CRS rate by Day 14. It was considered that 60% ≥ Grade 2 CRS by Day 14 is clinically relevant in this setting. Based on a target rate of 60%, a sample size of 62 will provide 90% power to exclude a higher limit of 79% of a 2-sided 95% CI. The sample size calculation is based on an EAS (see Section 5.3 for definition).

Table 2 represents CRS rates and CIs for a sample size of 62.

Table 2: Cytokine Release Syndrome Rates and 95% Confidence Intervals

Sample Size	Number of CRS	CRS Rate (%)	95% CI (%)
62	36	58.1	44.8, 70.5
62	38	61.3	48.1, 73.4
62	40	64.5	51.3, 76.3
62	42	67.7	54.7, 79.1
62	44	71.0	58.1, 81.8

Part 2 is a randomized expansion of the study; itacitinib 200 mg BID versus placebo.

As in Part 1, the primary endpoint is Grade ≥ 2 CRS rate by Day 14. Assuming Grade ≥ 2 CRS rate in the placebo arm is 50% (Nastoupil et al 2020) and is 20% in the treatment arm (~30%

change in CRS rate), a sample size of 23 evaluable participants per group would provide 70% power based on a 1-sided Type I error rate of 5%. Sufficient number of participants will be enrolled to yield 23 evaluable participants in each group.

A Bayesian interpretation for the selection and impact of the sample size can be provided in terms posterior probabilities. As the response rate based on CRS rate has a binomial (n, p) distribution with s number of responders out of n participants, it is common to use a conjugate Beta (a, b) prior which leads to a Beta(a + s, b + n − s) posterior distribution. For this exercise, we assume a noninformative Beta(1,1) (~ Uniform(0,1) prior).

Table 3 presents scenarios of Bayesian posterior probability of demonstrating a treatment difference (≥ 30%) by Day 14 in CRS rates, between the itacitinib 200 mg BID group and the placebo group, under various CRS rates assumption (number and percentage of participants experiencing > = Grade 2 CRS).

Table 3: Bayesian Posterior Probability of Demonstrating a Treatment Difference

N[a] (%) 200 BID Group	N[b] (%) Placebo	Posterior Probability[c]
2 (8.7)	9 (39.1)	43.7
	12 (52.5)	79.4
	14 (60.9)	93.4
5 (21.7)	9 (39.1)	13.9
	12 (52.5)	45.9
	14 (60.9)	67.9
7 (30.4)	9 (39.1)	4.7
	12 (52.5)	22.7
	14 (60.9)	44.7

[a] Number of participants with CRS ≥ Grade 2, out of 23 participants, in the 200 mg BID group.
[b] Number of participants with CRS ≥ Grade 2, out of 23 participants, in the placebo group.
[c] Bayesian posterior probability that the itacitinib group has at least 30% improvement over placebo, based on CRS ≥ Grade 2.

Based on the scenarios presented in Table 3, if we assume observed CRS rates (CRS ≥ Grade 2) of 2/23 (8.7%) and 12/23 (52.2%) in the itacitinib and placebo groups, respectively, then a Bayesian calculation is expected to yield a posterior probability of 79.4% of seeing an reduction of at least 30% in the itacitinib group.

3.5. Schedule of Assessments

Refer to Protocol Amendment 4 dated 08 DEC 2022 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. Study Drug

Itacitinib and placebo are the study drugs in this study.

4.1.2. Study Treatment

Itacitinib, placebo, and IEC therapy are all considered as the study treatments in this study.

4.1.3. Day 1

Day 1 is the date of first dose of itacitinib/placebo, which is given 3 days to 1 day before IEC infusion.

4.1.4. 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.

4.1.5. Baseline Value

Baseline is the last nonmissing assessment obtained before the first administration of study drug for safety analysis. For efficacy endpoints related to IEC therapy, the last nonmissing assessment prior to IEC therapy may be taken as baseline depending on the specific analysis to be conducted.

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.

4.1.6. 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.

Missing or partial disease 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 first day of the month or the date that the participant discontinued treatment.
- Otherwise, the date that the participant discontinued treatment will be used as the date of the last dose.

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

- If mmyyyy for the last contact date = mmyyyy for the death date, then the death date will be set to the day after the last contact date.
- If mmyyyy for the last contact 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.

For prior and concomitant medications:

The start/stop dates recorded in the eCRF by the investigator and his or her research staff will be used to identify when a concomitant medication was taken during the study. Any missing start date must be queried for resolution. Unresolved missing start dates will be handled as follows:

- If the date is completely missing, the medication will be considered both prior and concomitant.
- If only the day is missing, and the last day of the month is before the first dose date on Day 1, then the concomitant medication will be considered as starting before Day 1, and the incomplete date will be imputed as the last day of the month.
- If only the day is missing, and the first day of the month is on or after the first dose date on Day 1, then the concomitant medication will be considered as starting after Day 1, and the incomplete date will be imputed as the first day of the month.
- If only the day is missing, and the month is equal to the month of the first dose date on Day 1, then the incomplete date will be imputed as the first day of the month.
- If both the month and day are missing, and the last day of the year is before the first dose date on Day 1, then the concomitant medication will be considered as starting before Day 1, and the incomplete date will be imputed as if it is the last day of the year. Otherwise, if the last day of the year is on or after the first dose date Day 1, the incomplete date will be imputed as if it is the first day of the year.

- If the imputed start date through the above procedure is after the stop date recorded in the eCRF, then the imputed start date will be set equal to the stop date.

4.1.7. On-Treatment Assessment/Event

Safety data can be summarized for itacitinib and IEC therapy, respectively. For itacitinib, on-treatment assessment/event is defined as any assessment/event obtained in the following time interval:

Date of first administration of study drug through the date of last administration of study drug + 30 days.

Adverse events that begin or worsen after informed consent should be recorded in the Adverse Events eCRF.

If the last date of study drug is missing, on-treatment assessments/events include any assessment/event recorded in the database that occurred after the start date of study drug.

For IEC therapy, any safety data reported after IEC therapy would be considered as on-treatment assessment/event without cutoff.

To simplify data reporting, any safety data collected after Day 1 will be presented in summary table. Data listings will include all assessments/events, and those which are not on-treatment assessments/events to itacitinib will be flagged.

4.2. Variable Definitions

The following variables will only be calculated.

4.2.1. Body Mass Index

Body mass index will be calculated as follows:

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

4.2.2. Prior and Concomitant Medication

Prior medication is defined as any non-study medication started before the first dose of itacitinib.

Concomitant medication is defined as any non-study medication that is started accordingly:

- Before the date of first administration of itacitinib 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 itacitinib and is ongoing or ends during the course of study drug administration.

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

For the purposes of analysis, all medications will be considered concomitant medications unless the medications can unequivocally be defined as not concomitant, that is, if the start date and end date are all missing, then the medication is considered as concomitant medication.

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, figures, and statistical analyses. Descriptive summaries for continuous variables will include, but not be limited to, the number of observations, mean, standard deviation, median, minimum, and maximum. Descriptive summaries for categorical variables will include the number and percentage of participants in each category.

Interim analyses are planned for this study as defined in Section 10.

5.2. Treatment Groups

In Part 1, all participants will take itacitinib. Participants may receive any of the 3 IECs approved for hematologic indications at the time of study conduct. Thus, the treatment groups in this study are as the following:

- Itacitinib 200 mg QD + Kymriah® (tisagenlecleucel)
- Itacitinib 200 mg QD + Yescarta® (axicabtagene ciloleucel)
- Itacitinib 200 mg QD + Tecartus® (brexucabtagene autoleucel)

In this part, 3 different disease populations are planned to be enrolled in this study (ie, B-cell lymphoma, MCL, and ALL).

In Part 2, the participants will be randomized 1:1 into 2 groups (ie, itacitinib 200 mg BID and placebo). The study population will include participants who are receiving Yescarta for relapsed or refractory large B-cell lymphoma or follicular lymphoma. Thus, the treatment groups in this part are as the following:

- Itacitinib 200 mg BID + Yescarta (axicabtagene ciloleucel)
- Placebo + Yescarta (axicabtagene ciloleucel)

For all summary tables, results from Parts 1 and 2 will be displayed in the same table for each analysis, unless otherwise specified. This will apply for all analyses in this study. For analysis purpose, efficacy and safety will be presented separately for Part 1 and Part 2 by treatment group. Specific analysis such as disease history and baseline characteristics and response of underlying disease will be summarized by treatment group and disease population. Further split or combination may be considered in analysis.

5.3. Analysis Populations

Table 4 presents the populations for analysis.

Table 4: Analysis Populations

Population	Description
Safety population	The safety population includes all enrolled participants who received at least 1 dose of study drug. All safety analyses will be conducted using the safety population.
Efficacy evaluable analysis set (EAS)	The EAS includes all participants who have received at least 1 dose of study drug and have received IEC therapy. All efficacy analyses will be conducted using EAS.
[redacted]	[redacted]

6. BASELINE, EXPOSURE, AND DISPOSITION VARIABLES AND ANALYSES

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

Unless otherwise specified, for Part 1 of the study, the information specified in this section will be summarized by treatment group as well as overall using the safety population. [redacted] For Part 1 of the study, if any of the subgroups include less than 10% of the overall sample size for that part, the information for that subgroup will only be listed. For Part 2 of the study, the information will be summarized by treatment group using the safety population.

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

6.1.1. Demographics and Baseline Characteristics

Demographics and baseline characteristics will be listed in detail. The following will be summarized using safety population: age, sex, race, ethnicity, body weight, height, BMI, and ECOG status, all at baseline. Qualitative data will be summarized by contingency tables while quantitative data will be summarized by descriptive summary statistics.

6.1.2. Baseline Disease Characteristics and Disease History

Baseline disease characteristics will be separately summarized in participants with ALL, B-cell lymphoma, and MCL. According to data collected in the eCRF, the following information will be summarized for participants with ALL: time since diagnosis, which is from diagnosis date to the first dose date of study drug; CNS status; morphology % blast; marrow morphology category; number of prior lines of therapy; and whether or not prior radiation was given. For participants with B-cell lymphoma, the following information will be summarized: time since diagnosis, which is from diagnosis date to the first dose date of study drug; B-cell lymphoma disease type; NCCN prognostic index; DLBCL type and subtype; number of prior lines of therapy; Philadelphia chromosome status; and whether or not prior radiation was given. For participants with MCL, the following information will be summarized time since diagnosis, which is from diagnosis date to the first dose date of study treatment; number of prior systemic treatment regimens; current Ann Arbor staging; whether or not current B-symptoms are present; current MIPI risk category; prior radiation therapy; and prior surgery. Tumor marker information may be summarized if sufficient data are collected.

6.1.3. Prior Therapy

For prior medication therapy, the number and percentage of participants who received each drug will be summarized by WHO drug class and preferred name. The term for the medication/therapy taken; the start and stop dates; best response; reason for discontinuation; date of relapse/progression; and the route, collected on the prior therapy page of the CRF, will be listed.

For prior radiotherapy, the radiotherapy type; the start and stop dates; the reason for regimen; the number of fractions received; total dose; and best response, collected on the prior radiotherapy page of the CRF, will be listed.

6.1.4. Medical History

Medical history will be summarized for all participants in the safety population. This summary will be presented by primary SOC and PTs.

6.2. Disposition of Participants

The number and percentage of participants who are on treatment, who discontinued any study drug with a primary reason for discontinuation, who are on study, and who withdrew from the study with a primary reason for study withdrawal will be summarized for all participants in the safety population.

6.3. Protocol Deviations

Protocol deviations recorded on the eCRF will be presented in the participant data listings and summarized descriptively.

6.4. Exposure

For participants in the safety population, exposure to itacitinib, placebo, and IEC therapy will be summarized descriptively as follows:

- **Total dose administered of study drug (mg):** total actual study drug taken (mg)
- **Average daily dose of study drug (dose intensity) (mg):** Total dose administered (mg) / duration of treatment
- **Duration of treatment of study drug (days):** Date of last dose of study drug – date of first dose of study drug + 1
- **Total cell count of IEC and CAR-positive viable T cells** will be summarized for IEC therapy

6.5. Study Drug Compliance

Overall compliance (%) for itacitinib will be calculated for all participants as follows:

Overall compliance (relative dose intensity) (%) = 100% × (total dose administered) / (intended dose)

Intended dose is defined as the sum of the doses prescribed by the investigator accounting both for planned dose reductions as well as those reductions or increases mandated by the investigator.

For IEC infusions, compliance calculations are not applicable. Infusion information collected in eCRF may be listed as needed, including any temporary infusion interruption.

6.6. Prior and Concomitant Medication

Prior medications and concomitant medications will be coded using the WHO Drug Dictionary and summarized by ATC drug class and WHO drug term. Results will be summarized as number and percentage of participants with prior and concomitant medications by ATC class and WHO drug class in the safety population. For the summary of concomitant medication, only medications starting on or after the first dose of study drug will be included. Medications with missing start/end dates will be considered as concomitant medication in the summary. Other medications will be provided in the listing.

7. EFFICACY

A list of planned tables, figures, and listings is provided in Appendix A.

7.1. General Considerations

Unless otherwise specified, for Part 1 of the study, all efficacy analyses will be summarized by treatment group as well as overall using the EAS. For Part 1 of the study, if any of the subgroup includes less than 10% of the overall sample size for that part, the information for this subgroup will only be listed. For Part 2 of the study, all efficacy analyses will be summarized by treatment group using the EAS.

7.2. Analysis of the Primary Efficacy Parameter

7.2.1. Primary Efficacy Analysis

The primary endpoint of the study is CRS rate by Day 14, defined as the percentage of participants experiencing ≥ Grade 2 CRS by Day 14 after IEC therapy.

In Part 1, the CRS rate will be calculated for each treatment group as follows:

$$CRS\ rate = \frac{x}{n}$$

where *n* is the number of efficacy evaluable participants, and *x* is the number of efficacy evaluable participants who experience ≥ Grade 2 CRS by Day 14.

The exact 95% CI (2-sided) will be calculated using the Clopper-Pearson method (Clopper and Pearson 1934), as the following:

$$\left(B\left(\frac{\alpha}{2}; x, n-x+1\right), B\left(1-\frac{\alpha}{2}; x+1, n-x\right)\right)$$

where *B (p; v, w)* is the *p*th percentile from a beta distribution with shape parameters *v* and *w*, and α is 5%.

In Part 2, the CRS rate and the associated 95% CI will also be calculated for each treatment group, itacitinib 200 mg BID and placebo, in the same way as the analysis for Part 1. The primary efficacy endpoint analysis will be the comparison of the percentage of efficacy evaluable participants experiencing ≥ Grade 2 CRS by Day 14 between the 2 treatment groups. The CRS rates will be compared using a 1-sided Z-test at the significance level of 0.05, and a 95% CI (2-sided) for the difference in the CRS rate will be calculated. The following statistical hypothesis will be tested for the primary efficacy endpoint analysis:

$$H_0: CRS_A \geq CRS_B \text{ versus } H_1: CRS_A < CRS_B$$

where CRS_A and CRS_B will be the CRS rates for itacitinib 200 mg BID and placebo, respectively. The Z-test for the difference between the 2 treatment groups will be based on the following test statistic:

$$z = \frac{\widehat{CRS}_A - \widehat{CRS}_B}{\sqrt{\widehat{CRS}(1-\widehat{CRS})\left(\frac{1}{n_1}+\frac{1}{n_2}\right)}}$$

where n_1 and n_2 are the numbers of efficacy evaluable participants for itacitinib 200 mg BID and placebo, respectively, and

$$\widehat{CRS}_A = \frac{x_1}{n_1}$$

$$\widehat{CRS}_B = \frac{x_2}{n_2}$$

$$\widehat{CRS} = \frac{x_1 + x_2}{n_1 + n_2}$$

where x_1 and x_2 are the number of efficacy evaluable participants experiencing CRS ≥ Grade 2 by Day 14 for the treatment group, itacitinib 200 mg BID and placebo, respectively.

For the 1-sided test specified above, the p-value will be calculated as the probability of $Z \leq z$, where Z is the random variable for the standard normal distribution. If the p-value is smaller than or equal to the significance level at 0.05, the null hypothesis will be rejected. It could be concluded that the ≥ Grade 2 CRS rate by Day 14 after Yescarta for itacitinib 200 mg BID is significantly lower than that for placebo.

The 95% CI (2-sided) of the difference in the CRS rate between the 2 treatment groups can be calculated as follows:

$$\widehat{CRS}_A - \widehat{CRS}_B \pm 1.96 * \sqrt{\frac{\widehat{CRS}_A(1-\widehat{CRS}_A)}{n_1} + \frac{\widehat{CRS}_B(1-\widehat{CRS}_B)}{n_2}}.$$

7.2.1.1. Handling of Missing Data in Primary Analysis

For the primary analysis, if a participant drops out of the study prior to reaching Day 14 after IEC without experiencing a CRS event of ≥ Grade 2, the participant will be considered as not experiencing ≥ Grade 2 CRS by Day 14. See Section 7.2.1.2 for the sensitivity analysis that is planned in this regard.

7.2.1.2. Sensitivity Analysis

A sensitivity analysis will be performed on the primary efficacy endpoint. For this analysis, participants who dropped out of the study prior to reaching Day 14 after IEC without experiencing any CRS event of ≥ Grade 2 will be excluded. If there is no participant in this situation, the sensitivity analysis will not be performed. The same method for the primary efficacy endpoint analysis specified in Section 7.2.1 will be used for this analysis, except that no hypothesis testing will be conducted here.

7.2.1.3. Supportive Analysis

A supportive analysis will be conducted by comparing the itacitinib 200 mg QD dose in Part 1 with the placebo group in Part 2, using a 95% CI (2-sided), for participants with B-cell lymphoma and treated with Yescarta as the IEC therapy. For the itacitinib 200 mg QD treatment group, only participants with B-cell lymphoma and treated with Yescarta from Part 1 will be considered; whereas all participants in the placebo treatment group from Part 2 are considered for this analysis. This analysis is performed in the same way as the primary efficacy endpoint analysis for Part 2, except that no hypothesis testing is conducted.

As another supportive analysis, comparison between the itacitinib 200 mg QD dose from Part 1 and the itacitinib 200 mg BID treatment group from Part 2 will be conducted in the same way as the analysis specified above, for participants with B-cell lymphoma and treated with Yescarta as the IEC therapy, except that no hypothesis testing is conducted.

7.3. Analysis of the Secondary Efficacy Parameters

7.3.1. Immune Effector Cell-Associated Neurotoxicity Syndrome Incidence

Incidence of ICANS, defined as the percentage of participants experiencing ICANS by Day 28 (over the first 28-day period) after IEC therapy, will be summarized and presented together with its exact 95% CI (2-sided). The 95% CIs will be calculated in the same way as for the CRS rate in Section 7.2.1.

There will be no missing data imputation in calculation of ICE score or ICANS grading. In addition, ICANS incidence will be provided separately for each IEC therapy.

7.3.2. Onset and Duration of Immune Effector Cell-Associated Neurotoxicity Syndrome

Time to first onset of ICANS from date of IEC infusion is summarized within the first 28 days. Participants without ICANS will be considered as missing and not included in the summary.

The duration of ICANS is defined as the number of days where a participant has a non-zero ICANS grade. Duration of ICANS by Day 28 after IEC as the secondary analysis will be summarized. For investigational purpose, duration of all ICANS including events after Day 28 may also be conducted.

For ICANS that occurs prior to or on Day 30, refer to the information collected on the ICANS assessment log of the CRF; for ICANS that occur after Day 30, refer to the information collected on the ICANS page of the CRF.

Summary statistics including mean, median, standard deviation, minimum, and maximum will be provided for time to first onset of ICANS and duration of ICANS.

7.3.3. Onset and Duration of Cytokine Release Syndrome

Time to first onset of CRS from date of IEC infusion will be summarized within the first 28 days. Participants without CRS will be considered as missing in the summary.

Duration of CRS is defined as the number of days where a participant has a CRS event. Duration of multiple occurrence of CRS within each participant will be added together regardless of grading. The duration of CRS by Day 28 as the secondary analysis will be summarized. For investigational purposes, a summary of the overall duration may be conducted..

Summary statistics including mean, median, standard deviation, minimum, and maximum are provided for time to first onset of CRS and duration of CRS by treatment group.

7.3.4. Cytokine Release Syndrome-Free Survival

The CRS-free survival analysis will be performed using the Kaplan-Meier method, with the following events considered as the events of interest:

- CRS of ≥ Grade 2
- Death
- Initiation of tocilizumab with the indication of CRS treatment
- Initiation of corticosteroids with the indication of CRS treatment

For participants who experience any of the events of interest mentioned above, the time-to-event variable will be calculated as the number of days from IEC therapy to the first occurrence of the events of interest. For participants who do not experience any of the events of interest, they will be treated as censored observations, and the time-to-event variable will be calculated as the number of days from Day 0 to the date of the last available CRS assessment by Day 28. The numbers of participants who do and do not experience any of the events of interest will be summarized. The median CRS-free survival in days, and the CRS-free survival rates on Days 7, 14, 21, and 28 will be included in the summary.

7.3.5. Occurrence of Cytokine Release Syndrome Within 48 Hours

Percentage of participants who developed CRS within 48 hours of IEC infusion as well as the maximum grade of CRS will be summarized, using the same method as for the analysis of the CRS rate specified in Section 7.2.1.

7.3.6. Cytokine Release Syndrome Rate Within 28 Days

Percentage of participants who developed CRS within 28 days of IEC infusion as well as the maximum grade of CRS will be summarized, using the same method as for the analysis of the CRS rate specified in Section 7.2.1.

7.3.7. Intervention for CRS and ICANS

To assess intervention for CRS, the use of tocilizumab and corticosteroid for CRS treatment will be summarized. All use of tocilizumab and corticosteroid are listed including ICANS as the indication.

[redacted]

9. SAFETY AND TOLERABILITY

A list of planned tables, figures, and listings is provided in Appendix A.

9.1. General Considerations

The clinical safety data (eg, vital signs, ECGs, routine laboratory tests, physical examinations, and AEs) will be summarized using descriptive statistics (eg, mean, frequency) using the safety population. The safety analyses will be performed separately for different treatment groups. Specific safety analyses may also be summarized by underlying disease as needed. 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.

Safety summaries are also presented by the 2 dose groups and placebo for all the safety endpoints that are described below.

9.2. Adverse Events

9.2.1. Adverse Event Definitions

A TEAE is any AE either reported for the first time or worsening of a pre-existing event after the first dose of study drug. Analysis of AEs (as discussed below) will be limited to TEAEs, but data listings will include all AEs regardless of their timing in relation to study drug administration.

Adverse events will be tabulated by MedDRA PT and SOC. 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.

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

In addition, serious TEAEs will also be tabulated.

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.

- If the stop/resolution date is before the first dose administration date on Day 1, then the AE will be considered as not being treatment-emergent.
- If both the month and day are missing, and the last day of the year is before the first dose administration date on Day 1, then the AE will not be considered treatment-emergent.

- If only the day is missing, and the last day of the month is before the first dose administration date on Day 1, then the AE will not be considered treatment-emergent.
- If only the day is missing, and the first day of the month is after the first dose administration date on Day 1, then the AE will be considered treatment-emergent.

9.2.2. Adverse Event Summaries

An overall summary of AEs by treatment group will include the following:

- Number (%) of participants who had any TEAEs
- Number (%) of participants who had any serious TEAEs
- Number (%) of participants who had any Grade 3 or higher TEAEs
- Number (%) of participants who had any TEAEs related to study drug
- Number (%) of participants who had any serious TEAEs related to study drug
- Number (%) of participants who had any Grade 3 or higher TEAEs related to study drug
- Number (%) of participants who temporarily interrupted study drug because of TEAEs
- Number (%) of participants who permanently discontinued study drug because of TEAEs
- Number (%) of participants who had study drug dose reductions because of TEAEs
- Number (%) of participants who had a fatal TEAE
- Number (%) of participants who had any AEs related to IEC therapy

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 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 TEAEs by SOC and PT
- Summary of ≥ Grade 3 TEAEs by PT in decreasing order of frequency
- Summary of ≥ Grade 3 TEAEs by SOC, PT, and maximum severity
- Summary of serious TEAEs by SOC and PT
- Summary of serious TEAEs by PT in decreasing order of frequency
- Summary of study drug treatment-related TEAEs by SOC and PT
- Summary of study drug treatment-related TEAEs by SOC, PT, and maximum severity

- Summary of IEC therapy treatment-related TEAEs by SOC and PT
- Summary of IEC therapy treatment-related TEAEs by SOC, PT, and maximum severity
- Summary of treatment-related ≥ Grade 3 study drug TEAEs by SOC and PT
- Summary of treatment-related ≥ Grade 3 IEC therapy TEAEs by SOC and PT
- Summary of study drug treatment-related serious TEAEs by SOC and PT
- Summary of IEC therapy treatment-related serious TEAEs by SOC and PT
- Summary of TEAEs with a fatal outcome by SOC and PT
- Summary of TEAEs leading to study drug dose interruptions by SOC and PT
- Summary of TEAEs leading to IEC therapy interruptions by SOC and PT
- Summary of TEAEs leading to study drug dose reduction by SOC and PT
- Summary of TEAEs leading to withdrawal of study drug
- Summary of Deaths

9.3. Eastern Cooperative Oncology Group Performance Status

ECOG performance status at scheduled assessment times are summarized by treatment group and in overall population. The changes in ECOG status from the baseline may also be summarized.

9.4. Clinical Laboratory Tests

9.4.1. Laboratory Value Definitions

Laboratory values and change from baseline values will be summarized descriptively by visit. Baseline will be determined according to Table 5. If there are multiple values that meet the criteria for baseline, Table 5 may be referred to as tiebreaker to delineate which value will be defined as baseline.

Table 5: Baseline Laboratory Identification

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

Laboratory test values outside the normal range will be assessed for severity based on CTCAE grade or similar criteria where clinical intervention is required for CTCAE grading. The incidence of abnormal laboratory values and shift tables relative to baseline will be tabulated.

9.4.2. Laboratory Value Summaries

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

SI units. For test results that will be summarized with available normal ranges, the number and percentage of participants with the laboratory values being low (but never high), normal, high (but never low), and both low and high will be calculated for each test. This shift summary may be produced for each test for the safety population. The denominator for the percentage calculation will use the number of participants in the baseline category (ie, low, high, normal, missing) as the denominator for the percentage in each of the categories during the treatment period. For numeric laboratory values, baseline value, postbaseline value, change from baseline, and percentage change from baseline will be summarized by visit.

Shift tables will be presented showing change in CTC grade from baseline to worst postbaseline grade. Separate summaries for abnormally high and abnormally low laboratory values will be provided when the laboratory parameter has both high and low grading criteria. The denominator for the percentage calculation will be the number of participants in the baseline category.

The following summaries will be produced for laboratory data (by laboratory parameter) reported on treatment. All laboratory assessments will be listed, and those collected later than 30 days after the last treatment/exposure date will be flagged in the listings.

- Number and percentage of participants with worst postbaseline CTC grade (regardless of the baseline status) will be summarized. Each participant will be counted only for the worst grade observed after baseline.
- Shift tables using CTC grades comparing baseline with the worst postbaseline value will be produced for hematology, chemistry, and some other laboratory parameters with CTC grades.
- For laboratory parameters where CTC grades are not defined, shift tables to the worst postbaseline value will be produced using the low/normal/high classifications based on laboratory reference ranges.
- Number and percentage of participants meeting categorical liver function test criteria, including ALT, AST, and ALT or AST ($\geq 3 \times, 5 \times, 8 \times, 10 \times, 20 \times$ ULN); total bilirubin ($\geq 1 \times, 2 \times$ ULN); ALP ($\geq 1.5 \times, 2 \times, 3 \times, 5 \times, 8 \times, 10 \times$ ULN); combined categories of ALT/AST and total bilirubin (eg, ALT/AST $\geq 3 \times$ ULN and total bilirubin $\geq$ ULN); combined categories of ALT/AST total bilirubin; and ALP (ALT or AST $\geq 3 \times$ ULN and total bilirubin $\geq 2 \times$ ULN and ALP $< 2 \times$ ULN at the same visit; potential drug induced liver injury). The worst values observed postbaseline for each participant will be used for each of the categories.

9.5. Vital Signs

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

Normal ranges for vital sign values are defined in Table 6. The abnormal values for participants exhibiting vital sign abnormalities will be listed along with their assigned treatment group. Alert vital signs are defined as an absolute value outside the defined normal range and percentage change greater than 25%. Note that the definition of alert vital signs does not apply for body

temperature. The abnormal values for participants exhibiting alert vital sign abnormalities will be listed.

Table 6: 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	≤ 38ºC	≥ 35.5ºC
Respiratory rate	≤ 24 breaths/min	≥ 8 breaths/min

9.6. Electrocardiograms

Twelve-lead ECGs including PR, QT, QRS, QTcB, and QTcF intervals will be obtained for each participant during the study. Baseline will be determined as the last nonmissing ECG measurements taken on or before the first administration of study drug.

Normal ranges for ECG values are defined in Table 7. ECG values will also be considered abnormal if the absolute percentage change from baseline is more than 25%. Participant exhibiting ECG abnormalities will be listed with study visit and assigned treatment group. Abnormal values for participant with alert ECG values, defined as both the absolute value and the percentage change from baseline being outside normal ranges, will be identified and listed. Outliers of QT, QTcB, and QTcF values, defined as absolute values > 450 ms, > 500 ms, or change from baseline > 30 ms, will be summarized.

Table 7: Normal Ranges for Electrocardiogram Intervals

Parameter	High Threshold	Low Threshold
PR	≤ 220 ms	≥ 75 ms
QT	≤ 500 ms	≥ 300 ms
QRS	≤ 120 ms	≥ 50 ms
QTcF, QTcB	≤ 460 ms	≥ 295 ms

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

In addition to ECG, echocardiogram may also be conducted, and data collected will be summarized and listed as appropriate.

9.7. Cytopenias Ongoing by Day 30

All the cytopenias ≥ Grade 3 by Day 30 will be summarized. The laboratory tests on neutrophils, hemoglobin, and platelets will be included. [redacted]

10. INTERIM ANALYSES

For Part 1, an interim analysis is planned after approximately 24 participants are dosed with IEC therapy and complete the Day 28 (EOT) visit. The results from the interim analysis will be reviewed by the DSMB. The primary intent of this analysis is to minimize unnecessary exposure to itacitinib in the event of futility of treating CRS. The study may be stopped for futility at the interim analysis if the conditional power based on interim results is lower than 20%, which is equivalent to more than 17 out of 24 participants experiencing ≥ Grade 2 CRS by Day 14. More than 24 participants may be available in EAS at the time of interim analysis, and the stopping boundary will be re-evaluated at the time of the analysis. [redacted] Enrollment will continue while the analysis is being conducted.

No interim analysis is planned for Part 2.

11. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 8.

Table 8: Statistical Analysis Plan Versions

SAP Version	Date
Original	06 JAN 2021
Amendment 1	08 MAY 2023

[redacted]

11.2. Changes to the Statistical Analysis Plan

11.2.1. Amendment 1

The primary purpose of SAP Amendment 1 is to implement Protocol Amendments 3 and 4 by adding the analyses for the randomized placebo-controlled Part 2 of the study using a 200 mg BID regimen.

Other minor updates include:

- Replaced previous IND number with a new IND number.
- Revised Section 7.2.1 to provide explanation of calculations.
- Additional analyses were added to Section 7.2.1 and Section 7.3.
- Liver function test criteria was updated to align with the new version of standard.
- Format changes were applied to Appendix A. Additional tables and listings were added.
- In Appendix A, ECG tables were deleted due to data collection, the corresponding listings will still be created.
- Editorial changes have been made for better clarity and accuracy.

12. REFERENCES

Clopper C, Pearson ES. The use of confidence or fiducial limits illustrated in the case of the binomial. Biometrika 1934;26:404-413.

Nastoupil LJ, Jain MD, Feng L, et al. Standard-of-care axicabtagene ciloleucel for relapsed or refractory large B-cell lymphoma: results from the US Lymphoma CAR T consortium. J Clin Oncol 2020;38:3119-3128.

APPENDIX A. PLANNED TABLES, FIGURES, AND LISTINGS

This appendix provides a list of the planned tables, figures, and listings for the Clinical Study Report. 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
Baseline and Demographic Characteristics		
1.1 Disposition		
1.1.1	Analysis Populations	Enrolled
1.1.2	Summary of Participant Disposition	Safety
1.1.3	Summary of Number of Participants Enrolled by Site	Enrolled
1.1.4	Summary of Protocol Deviations	Safety
1.2 Demography and Baseline Characteristics		
1.2.1	Summary of Demographics and Baseline Characteristics	Safety
1.3 Baseline Disease Characteristics (refine per data collection)		
1.3.1	Summary of Underlying Disease History and Baseline Disease Characteristics for B-Cell Lymphoma	Safety
1.3.2	Summary of Underlying Disease History and Baseline Disease Characteristics for Mantle Cell Lymphoma	Safety
1.3.3	Summary of Underlying Disease History and Baseline Disease Characteristics for Acute Lymphoblastic Leukemia	Safety
1.3.4	Summary of Cancer Types	Safety
1.3.5	Summary of Prior Therapy	Safety
1.4 Prior Medication and Concomitant Medication (refine per data collection)		
1.4.1	Summary of Prior Medications	Safety
1.4.2	Summary of Concomitant Medications	Safety
1.5 Others		
1.5.1	Summary of General Medical History	Safety
1.5.2	Summary of Death	
2 Efficacy (add subgroup analysis as needed)		
2.1.1	Summary of CRS Rate by Day 14 After IEC Therapy	EAS
2.1.1.1	Sensitivity Analysis: Summary of CRS Rate by Day 14 After IEC Therapy – Excluding Participants Who Drop Out of the Study Prior to Day 14 Without Experiencing ≥ Grade 2 CRS	EAS
2.2.1	Summary of ICANS Rate by Day 28 After IEC Therapy	EAS
2.2.2.1	Summary of Onset and Duration of ICANS by Day 28 After IEC Therapy	EAS
2.2.2.2	Summary of Onset and Duration of ICANS During the Lifetime of the Study	EAS
2.2.3.1	Summary of Onset and Duration of CRS by Day 28 After IEC Therapy	EAS
2.2.3.2	Summary of Onset and Duration of CRS During the Lifetime of the Study	EAS
2.2.4.1	Summary of CRS-Free Survival by Day 28 After IEC Therapy	EAS
2.2.4.2	Summary of CRS Rate Within 48 Hours and by Day 28 After IEC Therapy	EAS
2.2.4.3	Summary of Tocilizumab and Corticosteroid Use for CRS Treatment	EAS
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Table No.	Title	Population
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	E[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
Safety		
3.1 Dose Exposure		
3.1.1	Summary of Exposure to Study Drug	Safety
3.1.2	Summary of Exposure to IEC Therapy	EAS
3.2 Adverse Events		
3.2.1.1	Overall Summary of Treatment-Emergent Adverse Events	Safety
3.2.2.1	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety
3.2.3.1	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety
3.2.4.1	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Safety
3.2.5.1	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety
3.2.6.1	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Safety
3.2.7.1	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety
3.2.8.1	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety
3.2.9.1	Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Safety
3.2.10.1	Summary of Study Drug Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety
3.2.11.1	Summary of Study Drug Treatment-Related Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Safety
3.2.12.1	Summary of IEC Therapy Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety
3.2.13.1	Summary of IEC Therapy Treatment-Related Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Safety
3.2.14.1	Summary of Grade 3 or Higher Study Drug Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Safety
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3.2.16.1	Summary of Study Drug Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety
3.2.17.1	Summary of IEC Therapy Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Safety
3.2.18.1	Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term	Safety
3.2.19.1	Summary of Treatment-Emergent Adverse Events Leading to Study Drug Dose Interruption by MedDRA System Organ Class and Preferred Term	Safety

Table No.	Title	Population
3.2.20.1	Summary of Treatment-Emergent Adverse Events Leading to IEC Therapy Interruption by MedDRA System Organ Class and Preferred Term	Safety
3.2.21.1	Summary of Treatment-Emergent Adverse Events Leading to Study Drug Dose Reduction by MedDRA System Organ Class and Preferred Term	Safety
3.2.22.1	Summary of Treatment-Emergent Adverse Events Leading to Withdrawal of Study Drug	Safety
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3.3.1.1	Summary of Laboratory Hematology Values	Safety
3.3.1.2	Summary of Laboratory Chemistry Values	Safety
3.3.1.3	Summary of Laboratory Coagulation Values	Safety
3.3.1.4	Summary of Laboratory Urinalysis Values	Safety
3.3.1.5	Summary of Laboratory Lipid Values	Safety
3.3.2.1	Shift Summary of Hematology Laboratory Values to the Worst Abnormal Value	Safety
3.3.2.2	Shift Summary of Chemistry Laboratory Values to the Worst Abnormal Value	Safety
3.3.2.3	Shift Summary of Coagulation Laboratory Values to the Worst Abnormal Value	Safety
3.3.3.1	Shift Summary of Hematology Laboratory Values in CTC Grade to the Worst Abnormal Value	Safety
3.3.3.2	Shift Summary of Chemistry Laboratory Values in CTC Grade to the Worst Abnormal Value	Safety
3.3.3.3	Shift Summary of Coagulation Laboratory Values in CTC Grade to the Worst Abnormal Value	Safety
3.3.3.4	Treatment-Emergent Worsening of Laboratory Abnormalities - Hematology	Safety
3.3.3.5	Treatment-Emergent Worsening of Laboratory Abnormalities - Chemistry	Safety
3.3.3.6	Treatment-Emergent Worsening of Laboratory Abnormalities - Coagulation	Safety
3.3.6	Summary of Liver Chemistry	Safety
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3.4.2	Summary of Diastolic Blood Pressure	Safety
3.4.3	Summary of Pulse	Safety
3.4.4	Summary of Respiration Rate	Safety
3.4.5	Summary of Body Temperature	Safety
3.4.6	Summary of Weight	Safety
[redacted]		
[redacted]	[redacted]	[redacted]
[redacted]		
[redacted]	[redacted]	[redacted]

Figures

Figure No.	Title
Efficacy (Lab figures may be added as needed)	
4.1.1	Kaplan-Meier Estimates of CRS-Free Survival by Study Part and Treatment Group

Listings

Listing No.	Title
2.1 Discontinued Participants (Participant Disposition)	
2.1.1	Participant Enrollment and Disposition Status

Listing No.	Title
2.1.2	Participant Inclusion and Exclusion Criteria Violations
2.2 Protocol Deviations	
2.2	Protocol Deviations
2.3 Data Excluded From [redacted] Efficacy, and/or Safety Analyses	
2.3	Analysis Populations
2.4 Demography and Baseline (Including Prior and Concomitant Medications)	
2.4.1	Demographic and Baseline Disease Characteristics
2.4.2	Underlying Disease History and Baseline Disease Characteristics for B-Cell Lymphoma
2.4.2.1	Underlying Disease History and Baseline Disease Characteristics for Mantle Cell Lymphoma
2.4.2.2	Underlying Disease History and Baseline Disease Characteristics for Acute Lymphoblastic Leukemia
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2.5 Drug Exposure	
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2.5.4	IEC Therapy Administration
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2.6.1.2	CRS Assessments After Day 30 After IEC Therapy
2.6.2.1	ICANS Assessments by Day 30 After IEC Therapy and at Post-Treatment Follow-Up
2.6.2.2	ICANS Assessments After Day 30 After IEC Therapy
2.6.3	All Response Assessment in Lymphoma
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2.6.5	Use of Tocilizumab and Corticosteroid
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2.7.3	Fatal Adverse Events
2.7.4	Adverse Events Leading to Study Drug Interruption, Reduction, or Withdrawal
2.7.5	Study Drug Treatment-Related Adverse Events
2.7.7	Adverse Events ≥ Grade 3
2.8 Laboratory Data (update per data collection)	
2.8.1	Clinical Laboratory Values – Hematology
2.8.2	Clinical Laboratory Values – Chemistry
2.8.3	Clinical Laboratory Values – Urinalysis
2.8.4	Clinical Laboratory Values – Coagulation
2.8.5	Clinical Laboratory Values – Lipid
2.8.6.1	Abnormal Clinical Laboratory Values – Hematology
2.8.6.2	Abnormal Clinical Laboratory Values – Chemistry
2.8.6.3	Abnormal Clinical Laboratory Values – Urinalysis
2.8.6.4	Abnormal Clinical Laboratory Values – Coagulation
2.8.6.5	Abnormal Clinical Laboratory Values – Lipid
2.8.7	Clinical Laboratory Values – Pregnancy

Listing No.	Title
2.8.10	Clinical Laboratory Values – Liver Chemistry
[redacted]	[redacted]
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 Electrocardiograms	
2.10.1	ECG Values
2.10.2	Abnormal ECG Values
2.11 Physical Examinations	
2.11.1	Physical Examinations
2.11.2	ECOG Performance Status