Official Title: A Phase 1b/2a Basket Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Efficacy of Combination Therapy With the Anti-CD19 Monoclonal Antibody Tafasitamab and the PI3K Inhibitor Parsaclisib in Adult Participants With Relapsed/Refractory Non-Hodgkin Lymphoma or Chronic Lymphocytic Leukemia (topMIND)

NCT Number: NCT04809467

Document Date: INCMOR 0208-101 Statistical Analysis Plan 31 MAR 2022

Statistical Analysis Plan

INCMOR 0208-101

A Phase 1b/2a Basket Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Efficacy of Combination Therapy With the Anti-CD19 Monoclonal Antibody Tafasitamab and the PI3Kδ Inhibitor Parsaclisib in Adult Participants With Relapsed/Refractory Non-Hodgkin Lymphoma or Chronic Lymphocytic Leukemia (topMIND)

IND Number:	**121,474**
EudraCT Number:	**2020-005591-35**
Sponsor:	**Incyte Corporation** **1801 Augustine Cut-Off** **Wilmington, DE 19803** **United States**
Protocol Version:	**Protocol Amendment 1 dated 08 OCT 2021**
CRF Approval Date:	**12 MAY 2021**
SAP Version:	**Original**
SAP Author:	[redacted] [redacted]**, Biostatistics**
Date of Plan:	**31 MAR 2022**

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

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

Abbreviation	Term
ADA	anti-drug antibody
ADI	actual dose intensity
AE	adverse event
ALT	alanine aminotransferase
AST	aspartate aminotransferase
AUC_t	area under the single-dose serum concentration-time curve extrapolated to time "t"
CI	confidence interval
CLL	chronic lymphocytic leukemia
C_{max}	maximum observed plasma or serum concentration
C_{min}	minimum observed plasma or serum concentration
CMR	complete metabolic response
CMV	cytomegalovirus
CR	complete response
CRF	case report form
CRR	complete response rate
CRS	cytokine release syndrome
CTCAE	Common Terminology Criteria for Adverse Events
C_{trough}	trough concentration (pre-dose)
DLBCL	diffuse large B-cell lymphoma
DLT	dose-limiting toxicity
DNA	deoxyribonucleic acid
DOR	duration of response
ECG	electrocardiogram
ECI	events of clinical interest
ECOG	Eastern Cooperative Oncology Group
eCRF	electronic case report form
FAS	full analysis set
FDA	Food and Drug Administration
FL	follicular lymphoma
iDSMB	internal Data Safety Monitoring Board
IPI	International Prognostic Index
IRR	infusion-related reaction
iwCLL	International Working Group for Chronic Lymphocytic Leukemia
MCL	mantle cell lymphoma

Abbreviation	Term
MedDRA	Medical Dictionary for Regulatory Activities
MIPI	Mantle Cell Lymphoma International Prognostic Index
MRD	minimal residual disease
MZL	marginal zone lymphoma
NCCN	National Comprehensive Cancer Network
NE	not evaluable
NGS	next generation sequencing
NHL	non-Hodgkin lymphoma
ORR	objective response rate
OS	overall survival
PD	progressive disease
PDI	planned dose intensity
PFS	progression-free survival
PI3K	phosphoinositide 3-kinase
PJP	*Pneumocystis jirovecii* pneumonia
PK	pharmacokinetic
PMR	partial metabolic response
PR	partial response
PT	preferred term
QD	once daily
QTcF	QT interval corrected using Fridericia's formula
R/R	relapsed/refractory
RDI	relative dose intensity
RNA	ribonucleic acid
RP2D	recommended Phase 2 dose
SAP	Statistical Analysis Plan
SD	stable disease
SLL	small lymphocytic lymphoma
SOC	system organ class
TEAE	treatment-emergent adverse event
t_{max}	time to maximum observed concentration
ULN	upper limit of normal
WHO	World Health Organization

1. INTRODUCTION

Study INCMOR0208-101 is an open-label, single-arm, multicenter, Phase 1b/2a study designed to evaluate whether the anti-CD19 monoclonal antibody tafasitamab and the PI3Kδ inhibitor parsaclisib can be safely combined at the RP2D and dosing regimen that was established for each of the 2 compounds as a treatment option for adult participants with R/R B-cell malignancies. Part 1 is a dose confirmation period, during which the safety, tolerability, PK, and preliminary efficacy of combination therapy with tafasitamab and parsaclisib will be assessed. Part 2 is a dose expansion period, during which the preliminary efficacy of combination therapy with tafasitamab plus parsaclisib will be assessed.

Section 2 of the Protocol provides a detailed description of the investigational products, target patient population, rationale for doses to be examined, and potential risks and benefits of treatment with tafasitamab and parsaclisib.

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in the INCMOR 0208-101 Protocol. Population PK analysis will be conducted by the Incyte pharmacokineticist, and the details of the analysis methodology and results will appear in a separate report. The exploratory analyses of biomarkers and pharmacodynamics are not described in this SAP and will appear in a separate report.

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCMOR 0208-101 Protocol Amendment 1 dated 08 OCT 2021 and CRFs approved 12 MAY 2021. Unless superseded by an amendment, this SAP will be effective for all subsequent Protocol amendments and eCRF versions.

2.2. Study Objectives and Endpoints

Table 1 presents the objectives and endpoints.

Table 1: Objectives and Endpoints

Objectives	Endpoints
Primary	
Dose confirmation period (Phase 1b): To determine the safety, tolerability, and DLTs of combination therapy with tafasitamab + parsaclisib in participants with R/R NHL or CLL who have been previously treated with at least 2 prior lines of systemic antilymphoma therapy.	Incidence and severity of TEAEs and incidence of DLTs.
Dose expansion period (Phase 2a): To assess the preliminary efficacy of combination therapy with tafasitamab + parsaclisib in participants with R/R NHL or CLL who have been previously treated with at least 2 prior lines of systemic antilymphoma therapy.	ORR, defined as the percentage of participants having best response of CR/CMR or PR/PMR per investigator assessment.
Secondary	
To estimate the PK of tafasitamab when given as combination therapy with parsaclisib.	PK parameters of tafasitamab when given in combination with parsaclisib. C_{trough} (ie, predose), C_{max}, t_{max}, C_{min}, and AUC_t will be summarized by descriptive statistics.

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
Exploratory	
[redacted]	

3. STUDY DESIGN

The overall objective of this single-arm, open-label, Phase 1b/2a, multicenter basket study is to evaluate whether the anti-CD19 monoclonal antibody tafasitamab and the PI3Kδ inhibitor parsaclisib can be safely combined at the RP2D and dosing regimen that was established for each of the 2 compounds as a treatment option for adult participants with R/R B-cell malignancies.

The safety, tolerability, PK, and preliminary efficacy of combination therapy with tafasitamab and parsaclisib will be assessed in a dose confirmation period followed by a dose expansion period. Participants will be assigned to 1 of 5 disease-specific cohorts based on the histology of their underlying disease:

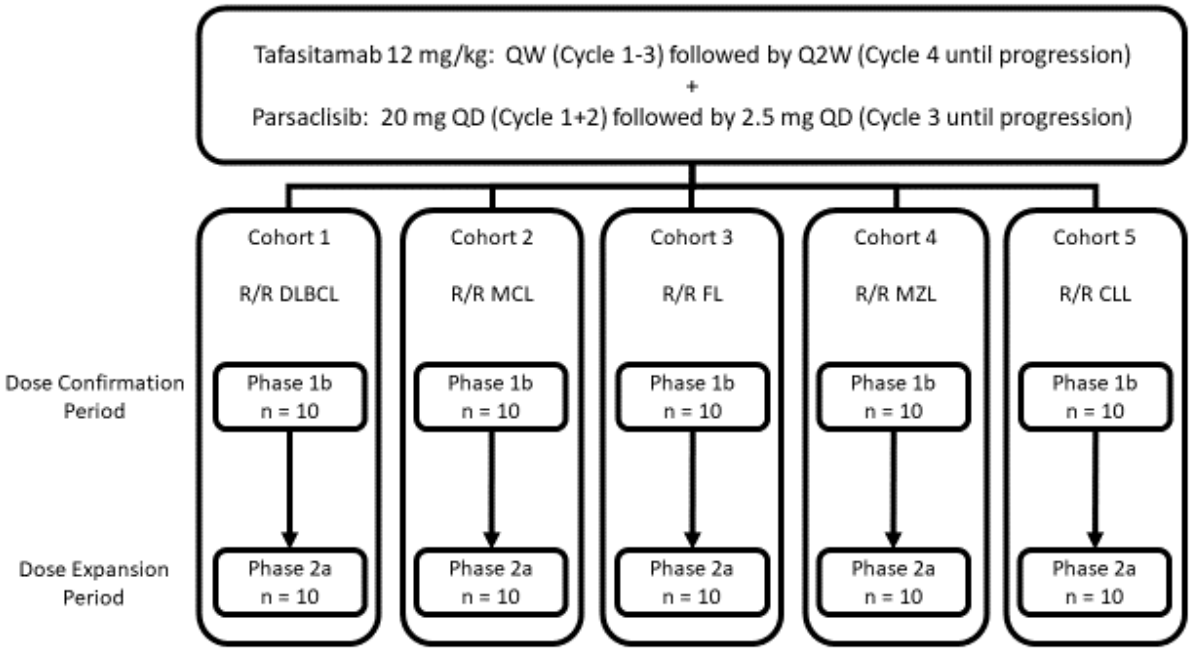
- Cohort 1: R/R DLBCL
- Cohort 2: R/R MCL
- Cohort 3: R/R FL
- Cohort 4: R/R MZL
- Cohort 5: R/R CLL/SLL

During the dose confirmation period, participants will be enrolled in 1 of the 5 cohorts in a parallel fashion. Each cohort will enroll 10 evaluable participants, and each participant will be observed for a DLT evaluation period of 1 cycle (28 days). Participants must have received at least 3 of 4 doses of tafasitamab and 21 days of treatment with parsaclisib 20 mg QD during the first cycle (28 days) or have experienced a DLT to be considered evaluable for the dose confirmation period. Participants who are considered not evaluable for DLT will be replaced.

An iDSMB will review data once the 10th DLT-evaluable participant from any cohort completes the DLT evaluation period (Cycle 1 Day 28) or experiences a DLT. Reviews will be repeated approximately every 4 months thereafter. The occurrence of 2 DLTs within the first 10 DLT-evaluable participants will also trigger iDSMB review of overall safety data and specifics from the case.

The decision to continue enrollment into each of the malignancy subtype cohorts will be based on the frequency of DLTs observed in the first 10 evaluable participants and review of ongoing safety data. After the safety review is completed and the dose confirmation decision is made, the dose expansion period for that cohort will begin, and up to 10 additional participants will be enrolled (up to a total of 20 evaluable participants in each cohort across both study periods; see Figure 1).

Figure 1: Study Design Schema



3.1. Randomization

Not applicable.

3.2. Control of Type I Error

No adjustment for alpha spending is considered as there are no plans to stop the study early for efficacy. All statistical analyses are exploratory in nature. Unless otherwise specified, all CIs provided will be at the 95% confidence level.

3.3. Sample Size Considerations

Up to 10 evaluable participants will be treated in each of the 5 disease-specific cohorts during the dose confirmation period. Enrollment into a cohort will be paused if the dose is not considered tolerable or once 10 evaluable participants have been treated for 28 days.

If the dose confirmation period for a disease-specific cohort confirms the dose is tolerable, that particular cohort will be opened for enrollment into the dose expansion period. Up to 10 additional participants will be enrolled up to a total of 20 evaluable participants in each of the 5 disease-specific cohorts (up to 100 evaluable participants in the whole study).

With 10 participants in each disease-specific cohort during the dose confirmation period, there is approximately 89.3% probability of observing at least 1 DLT if the underlying DLT rate is 20% and 97.2% probability of observing at least 1 DLT if the underlying DLT rate is 30%. If ≤ 1 of 10 participants in each disease-specific cohort during the dose confirmation period experience a DLT, the upper limit of the 95% 1-sided CI for the underlying DLT rate will not be > 39.5%. If none of 10 participants experience a DLT in each disease-specific cohort during the dose

confirmation period, the upper limit of the 95% 1-sided CI for the underlying DLT rate will not be > 25.9%.

With 10 participants in each disease-specific cohort, there is approximately 97.2% probability of observing at least 1 objective response during the dose confirmation period if the underlying response rate is 30%. For a reference of the precision of the ORR estimate with 10 or 20 participants in each disease-specific cohort, the 2-sided 95% CIs for different observed ORRs ranging from 10% to 100% are provided in Table 2.

Table 2: Two-Sided 95% Confidence Interval for Different ORR Estimates

Sample Size	Observed ORR	95% CI
n = 10	10%	(0.3%, 44.5%)
	20%	(2.5%, 55.6%)
	30%	(6.7%, 65.3%)
	40%	(12.2%, 73.8%)
	50%	(18.7%, 81.3%)
	60%	(26.2%, 87.8%)
	70%	(34.8%, 93.3%)
	80%	(44.4%, 97.5%)
	90%	(55.5%, 99.8%)
	100%	(69.2%, 100.0%)
n = 20	10%	(1.2%, 31.7%)
	20%	(5.7%, 43.7%)
	30%	(11.9%, 54.3%)
	40%	(19.1%, 63.9%)
	50%	(27.2%, 72.8%)
	60%	(36.1%, 80.9%)
	70%	(45.7%, 88.1%)
	80%	(56.3%, 94.3%)
	90%	(68.3%, 98.8%)
	100%	(83.2%, 100.0%)

3.4. Schedule of Assessments

Refer to INCMOR 0208-101 Protocol Amendment 1 dated 08 OCT 2021 for a full description of all study procedures and assessment schedules for this study.

4. DATA HANDLING DEFINITIONS AND CONVENTIONS

4.1. Scheduled Study Evaluations and Study Periods

4.1.1. Day 1

Day 1 is the date that the first dose of study drug (tafasitamab or parsaclisib) is administered to the participants.

4.1.2. Study Day

If a visit/reporting date is on or after Day 1, then the study day at the visit/reporting date will be calculated as

Day # = (visit/reporting date – Day 1 date + 1).

If the visit/reporting date is before Day 1, then the study day at the visit/reporting date will be calculated as

Day # = (visit/reporting date – Day 1 date).

A study day of –1 indicates 1 day before Day 1.

4.1.3. Baseline Value

Baseline is the last nonmissing measurement obtained before the first administration of tafasitamab or parsaclisib, unless otherwise defined.

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

- If both a scheduled and an unscheduled 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 Dates

In general, values for missing dates will not be handled unless methods for handling missing dates are specified in this section or relevant sections. The original reported dates collected on the eCRF should be used in all relevant listings. The following rules will be used for handling partial dates for analyses requiring dates.

When calculating the time since diagnosis of disease, a partial disease diagnosis date will be handled as follows in the calculation:

- If only the day is missing, then the first day of the month will be used.
- If both the month and day are missing, then 01 JAN of the year will be used.
- If the diagnosis date is completely missing, then the time since diagnosis will not be calculated.

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

- If only the day is missing, then the earlier date of the last day of the month or the date that the participant discontinued treatment will be used.
- If both the month and day are missing, then the earlier date of 31 DEC of the year or the date that the participant discontinued treatment will be used.
- Otherwise, the date that the participant discontinued treatment will be used as the date of the last dose.

For relevant efficacy endpoints, a partial date of the death date will be handled as follows in the calculation:

- If mmyyyy for the last known alive date = mmyyyy for the death date, then the death date will be set to the day after the last known alive date.
- If mmyyyy for the last known alive date < mmyyyy for the death date, then the death date will be set to the first day of the death month.
- Otherwise, the partial death date will not be imputed.

4.1.5. Cycle Length and Duration

Cycle 1 Day 1 is the day that the first dose of tafasitamab or parsaclisib is administered. The scheduled cycle length is 28 days. The actual Day 1 of subsequent cycles will correspond with the first day of administration of tafasitamab or parsaclisib in that cycle; thus, treatment cycles may become out of sync with the originally planned schedule, and the cycle length may be different from 28 days. 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

The following variables will only be calculated if not reported on the eCRF.

4.2.1. Body Mass Index

Body mass index will be calculated as follows:

Body mass index (kg/m^2) = [weight (kg)] / [height (m)]^2.

4.2.2. Prior and Concomitant Medication

Prior medication is defined as any nonstudy medication started before the first dose of tafasitamab or parsaclisib.

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

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

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

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

5. STATISTICAL METHODOLOGY

5.1. General Methodology

Unless otherwise noted, SAS® software (SAS Institute Inc, Cary, NC; v9 or later) will be used for the generation of all tables, graphs, and statistical analyses. Descriptive summaries for continuous variables will include but not be limited to the number of observations, mean, standard deviation, median, minimum, and maximum. Descriptive summaries for categorical variables will include the number and percentage of participants in each category.

5.2. Treatment Groups

This is an open-label, single treatment group study. Participants will be summarized overall by total only for each disease-specific cohort.

5.3. Analysis Populations

5.3.1. All-Screened Population

The all-screened population will include all participants who signed the informed consent form.

5.3.2. Full Analysis Set

The FAS will include all participants who received at least 1 dose of tafasitamab or parsaclisib. The FAS will be used for the summary of demographics, baseline characteristics, participant disposition, and analyses of all safety and efficacy data.

5.3.3. Efficacy Evaluable Set

The efficacy evaluable population will include all participants enrolled in the study who have received at least 1 dose of tafasitamab or parsaclisib and completed a baseline scan and meet at least one of the following criteria:

- $\geq$ 1 postbaseline scan.
- Participation in the study for a minimum of 42 days.
- Discontinued from treatment or died prior to the first scheduled postbaseline scan.

5.3.4. Dose-Limiting Toxicity Evaluable Population

The DLT evaluable population will include participants who have received at least 3 of 4 doses of tafasitamab and 21 days of treatment with parsaclisib 20 mg QD during the first cycle (28 days) or have experienced a DLT. Participants who are considered not evaluable will be replaced.

5.3.5. Pharmacokinetic Evaluable Population

The PK evaluable population will include all participants who received at least 1 dose of tafasitamab or parsaclisib and provided at least 1 postdose PK plasma sample.

5.3.6. Immunogenicity Analysis Set

The immunogenicity analysis set will include all participants who received at least 1 dose of tafasitamab or parsaclisib and have at least 1 evaluable antitafasitamab antibody (ADA) assessment.

6. BASELINE, EXPOSURE, AND DISPOSITION

Appendix A provides a list of data displays. Sample data displays are included in a separate document.

6.1. Demographics, Baseline Characteristics, and Disease History

6.1.1. Demographics and Baseline Characteristics

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

6.1.2. Baseline Disease Characteristics

The following baseline disease characteristics will be summarized for the FAS: ECOG performance status.

6.1.3. Disease History

The date of initial diagnosis, time since diagnosis, and initial presence of B symptoms will be summarized and listed for all cohorts.

Time since diagnosis will be calculated as follows:

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

For Cohort 1 (R/R DLBCL), initial DLBCL type, initial stage, current stage, NCCN-IPI at initial diagnosis, and NCCN-IPI at current diagnosis will be summarized and listed.

For Cohort 2 (R/R MCL), initial cytogenetics, current cytogenetics, initial Ann Arbor stage, current Ann Arbor stage, initial vitamin D information, current vitamin D information, initial blastoid variant, current blastoid variant, initial MIPI risk category, current MIPI risk category, initial beta-2 globulin, current beta-2 globulin, initial Ki-67 proliferation index, current Ki-67 proliferation index, initial CD5 surface expression, current CD5 surface expression, initial CD23 surface expression, current CD23 surface expression, initial CCND1, current CCND1, initial tp3, current tp3, initial SOX11, and current SOX11 will be summarized and listed.

For Cohort 3 (R/R FL), initial grade, current grade, initial cytogenetics, current cytogenetics, initial Ann Arbor stage, and current Ann Arbor stage will be summarized and listed.

For Cohort 4 (R/R MZL), disease subtype, current grade, initial cytogenetics, current cytogenetics, initial Ann Arbor stage, and current Ann Arbor stage will be summarized and listed.

For Cohort 5 (R/R CLL/SLL), initial Rai staging, current Rai staging, initial Rai clinical feature supporting staging, current Rai clinical feature supporting staging, initial Binet staging, current Binet staging, initial involved areas supporting Binet staging, current involved areas supporting Binet staging, initial cytogenetics, current cytogenetics, initial Ann Arbor staging, current Ann Arbor staging, and initial presence of constitutional symptoms will be summarized and listed.

If there are limited participants in 1 or more disease subtypes (eg, fewer than 5 participants in a disease-specific cohort), summaries may not be tabulated.

6.1.4. Prior Therapy

The number of prior systemic cancer therapy regimens will be summarized for all participants in the FAS. The component drugs of prior systemic therapy regimens will be coded using the WHO Drug Dictionary. The number and percentage of participants who received each drug will be summarized by WHO drug class and WHO drug PT. The regimen name, component drugs, start and stop dates, best response, reason for regimen, and date of relapse/progression will be listed.

The number of participants who received prior radiation will be summarized for the FAS. The radiotherapy type, anatomic location of the administration, start and stop dates, total dose, and best response will be listed.

The number of participants who had prior surgery or surgical procedure for malignancies under study will be summarized for the FAS. The date and description of the surgery/procedure will be listed.

The number of participants who had hematopoietic stem cell transplant will be summarized for the FAS. Date of transplant, type of transplant, source of cells, line of therapy, best response, date of relapse/progression, regimen name, and drug used with the transplant will be listed.

6.1.5. Medical History

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

6.2. Disposition of Participant

The number and percentage of participants who were treated, who were ongoing with study treatment, who discontinued study treatment with a primary reason for discontinuation, who were still in the study, who completed the study, and who withdrew from the study with a primary reason for withdrawal will be summarized for the FAS. The number of participants enrolled by country and/or site will also be provided for the FAS.

6.3. Protocol Deviations

Protocol deviations recorded on the eCRF will be summarized and listed.

6.4. Exposure

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

- Tafasitamab:

  Duration of tafasitamab (days): Date of last dose of tafasitamab − date of first dose of tafasitamab + 1.

  - **Number of cycles of tafasitamab:** number of cycles of tafasitamab.
  - **Number of infusions of tafasitamab:** number of infusions of tafasitamab.
  - **Tafasitamab dose modifications:** number of participants who had tafasitamab infusion interruption and infusion delay.

- Parsaclisib:

  Duration of treatment with parsaclisib (days): Date of last dose of parsaclisib – date of first dose of parsaclisib + 1.

  - **Total actual dose of parsaclisib (mg):** Total actual dose taken will be calculated based on the information entered on the Dose eCRF.
  - **Average daily dose of parsaclisib (mg/day):** total actual parsaclisib dose taken (mg) / duration of treatment with parsaclisib (days).
  - **Parsaclisib dose modifications:** number of participants who had parsaclisib dose reduction or interruption.

6.5. Dose Intensity, Relative Dose Intensity, and Study Drug Compliance

For participants in the FAS population, actual dose intensity and relative dose intensity of tafasitamab and parsaclisib will be summarized descriptively. The actual or planned dose intensity will be calculated by summing the visit-wise actual or planned doses.

6.5.1. Dose Intensity and Relative Dose Intensity of Tafasitamab

For participants in the FAS, the RDI of tafasitamab will be calculated for all participants as follows:

- ADI (unit: mg/kg): the actual dose the participant was exposed to. ADI per infusion will be derived as follows:
  - If the question "was the entire infusion administered" on the "Tafasitamab Infusion" eCRF page was answered with "yes":

    ADI at the visit = tafasitamab visit dose (mg) / patient weight at the visit
  - If the question "was the entire infusion administered" on the "Tafasitamab Infusion" eCRF page was answered with "no":

    ADI at the visit = (tafasitamab visit dose [mg] × [estimated volume delivered/prepared volume]) / patient weight at the visit

  - Skipped doses will result in an ADI of 0 for the particular visit.
- The ADI will be calculated by summing up all infusion-wise actual doses.
- PDI (mg/kg): 12 mg/kg per infusion as per Protocol.
- **Relative dose intensity (%):** The RDI expresses the amount of drug administered compared with the planned amount of drug across all infusions.

  RDI = ADI / (PDI × the number of infusions) × 100

6.5.2. Study Drug Compliance of Parsaclisib

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

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 for compliance 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. The number and percentage of participants in the FAS for each prior and concomitant medication will be summarized by WHO drug class and WHO drug PT.

7. EFFICACY

Appendix A provides a list of data displays. Sample data displays are included in a separate document. The FAS will be used for the analyses of efficacy data.

7.1. Efficacy Hypotheses

Not applicable.

7.2. Analysis of the Primary Efficacy Parameter

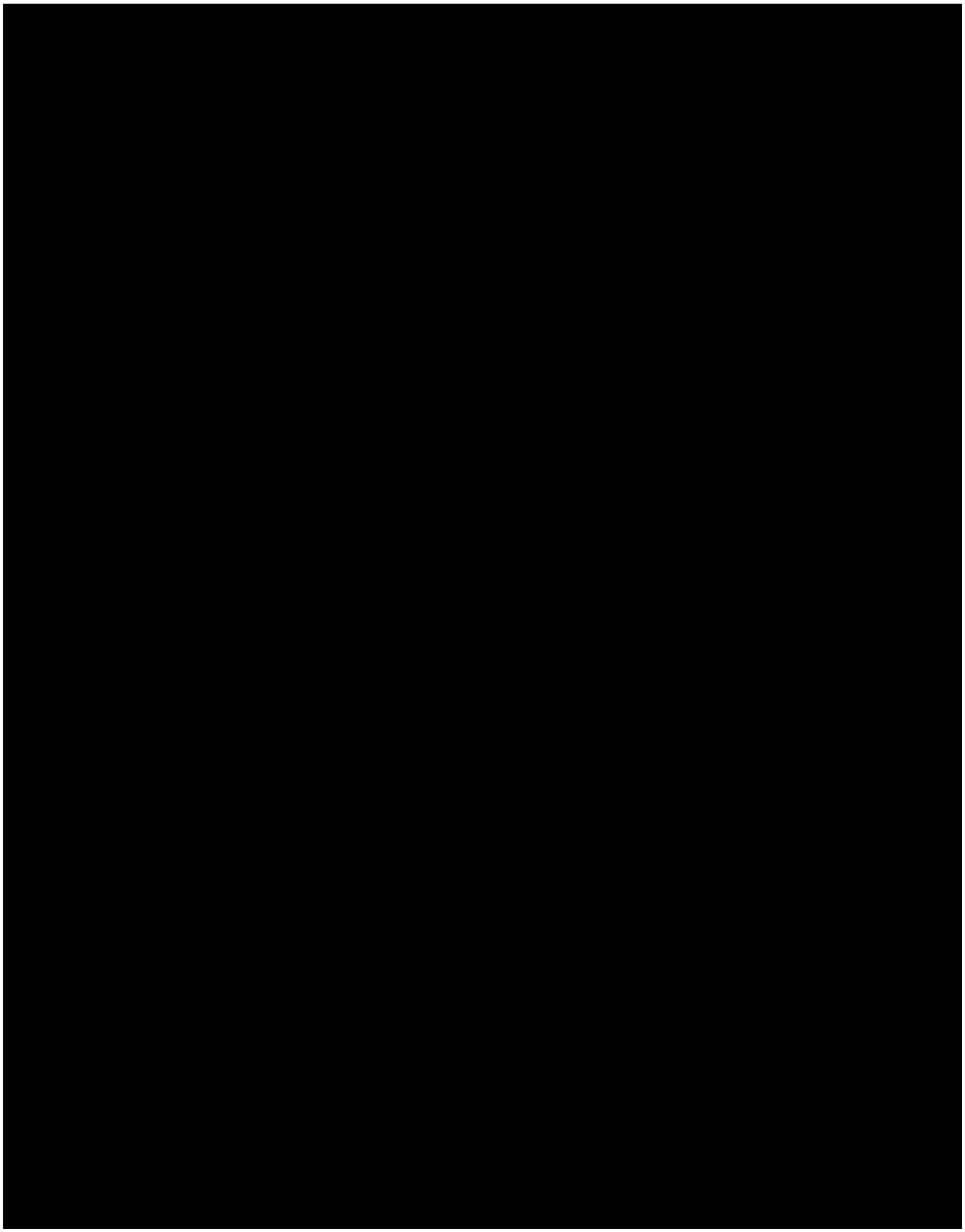
7.2.1. Objective Response Rate

Objective response rate is defined as the percentage of participants experiencing a best overall response of CR/CMR or PR/PMR according to the Lugano criteria (Cheson et al 2014) for NHL and the iwCLL criteria (Hallek et al 2018) for CLL [redacted]

The ORR and its 95% exact binomial CIs will be summarized by cohort. Participants whose baseline disease assessment or on-study response assessments cannot be adequately assessed for response will be considered as nonresponders. These participants will be included in the denominators in the calculations of ORR.

7.3. Analysis of Exploratory Efficacy Variables

[redacted]



8. SAFETY AND TOLERABILITY

Appendix A provides a list of data displays. Sample data displays are included in a separate document. The FAS will be used for the summary and analyses of all safety data.

8.1. General Considerations

Summary tables may be replaced with listings when appropriate. For instance, an AE frequency table may be replaced with a listing if it only contains a few unique PTs reported on relatively few participants. Unless otherwise stated, table summaries will be limited to TEAEs.

8.2. Adverse Events

8.2.1. Adverse Event Definitions

A TEAE is any AE either reported for the first time or worsening of a pre-existing event after the first dose of study drug until 90 days after the last dose of study drug. Analysis of AEs (as discussed below) will be limited to TEAEs, but data listings will include all AEs regardless of their timing in relation to study drug administration. For purposes of analysis, all AEs will be considered TEAEs unless the AE can unequivocally be defined as not treatment-emergent.

Adverse events will be tabulated by MedDRA PT and SOC. Severity of AEs will be graded using the National Cancer Institute CTCAE v5.0. The CTCAE reporting guidelines and grading details are available on the Cancer Therapy Evaluation Program website.

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.

8.2.2. Dose-Limiting Toxicities

The participants with DLTs and the type of DLT will be listed by dose level.

8.2.3. Events of Clinical Interest

An ECI is an AE (serious or nonserious) that Incyte wishes to document in an organized manner for monitoring or understanding. An ECI does not require rapid communication by an investigator to Incyte unless it meets criteria for rapid communication as an SAE.

The following laboratory abnormalities and/or clinical AEs are considered ECIs:

- Tafasitamab:
  - Tumor lysis syndrome
  - IRRs
  - Allergic reactions to study drug ≥ Grade 3
  - CRS
  - Secondary primary malignancy

  - Hepatitis B reactivation
  - Progressive multifocal leukoencephalopathy
- Parsaclisib
  - ALT ≥ 5 × ULN
  - AST ≥ 5 × ULN
  - Colitis
  - Diarrhea ≥ Grade 3
  - Intestinal perforation
  - Rash ≥ Grade 3
  - Exfoliative dermatitis
  - Pneumonitis
  - PJP infection
  - CMV infection
  - Herpes simplex virus infection
  - Varicella zoster virus infection

The number of participants who experienced the events of interest listed above will be summarized by maximum severity.

8.2.4. Adverse Event Summaries

An overall summary of AEs by cohort 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 fatal TEAEs
- Number (%) of participants who had a DLT
- Number (%) of participants who had any TEAEs related to tafasitamab
- Number (%) of participants who had any TEAEs related to parsaclisib
- Number (%) of participants who interrupted tafasitamab because of TEAEs
- Number (%) of participants who interrupted parsaclisib because of TEAEs
- Number (%) of participants who permanently discontinued tafasitamab because of TEAEs
- Number (%) of participants who permanently discontinued parsaclisib because of TEAEs

- Number (%) of participants who had tafasitamab dose reductions because of TEAEs
- Number (%) of participants who had parsaclisib dose reductions because of TEAEs
- Number (%) of participants who withdrew from the study because of TEAEs

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

- Summary of TEAEs by MedDRA SOC and PT
- Summary of TEAEs by MedDRA PT in decreasing order of frequency
- Summary of TEAEs by MedDRA SOC, PT, and maximum severity
- Summary of Grade 3 or higher TEAEs by MedDRA SOC and PT
- Summary of Grade 3 or higher TEAEs by MedDRA PT in decreasing order of frequency
- Summary of serious TEAEs by MedDRA SOC and PT
- Summary of serious TEAEs by MedDRA PT in decreasing order of frequency
- Summary of tafasitamab treatment-related TEAEs by MedDRA SOC and PT
- Summary of parsaclisib treatment-related TEAEs by MedDRA SOC and PT
- Summary of tafasitamab treatment-related TEAEs by MedDRA PT in decreasing order of frequency
- Summary of parsaclisib treatment-related TEAEs by MedDRA PT in decreasing order of frequency
- Summary of tafasitamab treatment-related TEAEs by MedDRA SOC, PT, and maximum severity
- Summary of parsaclisib treatment-related TEAEs by MedDRA SOC, PT, and maximum severity
- Summary of Grade 3 or higher tafasitamab treatment-related TEAEs by MedDRA SOC and PT
- Summary of Grade 3 or higher parsaclisib treatment-related TEAEs by MedDRA SOC and PT
- Summary of tafasitamab treatment-related serious TEAEs by MedDRA SOC and PT
- Summary of parsaclisib treatment-related serious TEAEs by MedDRA SOC and PT
- Summary of TEAEs with a fatal outcome by MedDRA SOC and PT
- Summary of TEAEs leading to dose reduction by MedDRA SOC and PT
- Summary of TEAEs leading to dose interruption by MedDRA SOC and PT
- Summary of TEAEs leading to discontinuation of study drugs by MedDRA SOC and PT

- Summary of TEAEs of tafasitamab ECI by ECI class, PT, and maximum severity
- Summary of TEAEs of parsaclisib ECI by ECI class, PT, and maximum severity
- Summary of Dose-Limiting Toxicities

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 v5.0.

8.3.2. Laboratory Value Summaries

All laboratory test results and associated normal ranges from local laboratories will be reported in SI units. Any laboratory test results and associated normal ranges from local laboratories will be converted to SI units. When there are multiple nonmissing laboratory values for a participant'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, circulating lymphocyte counts, and neutrophils.

Severity grades will be assigned to laboratory test values based on the numerical component of CTCAE v5.0. Shift tables will be presented showing change in CTCAE grade from baseline to worst grade postbaseline. Separate summaries for abnormally high and abnormally low laboratory values will be provided when the laboratory parameter has both high and low grading criteria. The denominator for the percentage calculation will be the number of participants in the baseline category. The number of participants who experienced worsening of laboratory abnormalities will be summarized by maximum severity.

8.3.3. Potential Hy's Law Events

Participants with elevated ALT or AST > 3 × ULN range and alkaline phosphatase < 2 × ULN range accompanied by total bilirubin > 2 × ULN range at the same visit will be listed by treatment group.

8.4. Vital Signs

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

Normal ranges for vital sign values are defined in Table 4. For participants exhibiting vital sign abnormalities, the abnormal values 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 and weight. The abnormal values for participants exhibiting alert vital sign abnormalities will be listed.

Table 4: 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, QTc intervals, and heart rate will be obtained for each participant during the study. Values at each scheduled visit, 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 tafasitamab or parsaclisib.

Normal ranges for ECG values are defined in Table 5. ECG values will also be considered abnormal if the absolute percentage change from baseline is more than 25% (30% for QRS interval). Participants exhibiting ECG abnormalities will be listed with study visit and assigned treatment group. Abnormal values for participants with alert ECG values, defined as both the absolute value and the percentage change from baseline being outside normal ranges, will be identified and listed. Outliers of QT, and QTcF values, defined as absolute values > 450 millisecond, > 500 millisecond, or change from baseline > 30 millisecond, will be summarized.

Table 5: 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	≤ 450 ms	≥ 295 ms

9. INTERIM ANALYSES

Not applicable.

10. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 6.

Table 6: Statistical Analysis Plan Versions

SAP Version	Date
Original	31 MAR 2022

10.1. Changes to Protocol-Defined Analyses

A DLT evaluable population was added for analyzing results from the dose confirmation part of the study.

10.2. Changes to the Statistical Analysis Plan

Not applicable.

11. REFERENCES

Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. J Clin Oncol 2014;32:3059-3068.

Food and Drug Administration. Guidance for Industry: Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics. 2018.

Food and Drug Administration. Guidance for Industry: Clinical Trial Endpoints for the Approval of Non-Small Cell Lung Cancer Drugs and Biologics. 2015.

Hallek M, Cheson BD, Catovsky D, et al. iwCLL guidelines for diagnosis, indications for treatment, response assessment, and supportive management of CLL. Blood 2018;131:2745-2760.

APPENDIX A. PLANNED TABLES, FIGURES, AND LISTINGS

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

The lists of tables, figures, and listings are to be used as guidelines. Modifications of the lists that do not otherwise affect the nature of the analysis will not warrant an amendment to the SAP.

Tables

Table No.	Title	Population	Standard
Baseline and Demographic Characteristics			
1.1 Disposition			
1.1.1	Analysis Populations	FAS	X
1.1.2	Summary of Participant Disposition	FAS	X
1.1.3	Summary of Number of Participants Enrolled by Country and Site	FAS	X
1.1.4	[redacted]	FAS	X
1.2 Demography and Baseline Characteristics			
1.2.1	Summary of Demographics and Baseline Characteristics	FAS	X
1.3 Baseline Disease Characteristics			
1.3.1	Summary of Baseline Disease Characteristics	FAS	X
1.3.4	Summary of Prior Cancer Therapy	FAS	
1.4 Prior Medication and Concomitant Medications			
1.4.1	Summary of Prior Medications	FAS	X
1.4.2	Summary of Concomitant Medications	FAS	X
1.5+ Others			
1.5.1	Summary of General Medical History	FAS	X
Efficacy			
2.1 Primary Efficacy			
2.1.1	Summary of Best Overall Response and Objective/Complete Response Rate	FAS	
2.1.2	Summary of Best Response	FAS	
2.3 Exploratory Endpoint			
2.3.1	[redacted]	FAS	
2.3.2		FAS	
2.3.3		FAS	
Safety			
3.1 Dose Exposure			
3.1.1.1	Summary of Exposure and Duration of Exposure to Parsaclisib	FAS	X
3.1.1.1.2	Summary of Exposure and Duration of Exposure During Initial QD Dosing Period to Parsaclisib	FAS	X
3.1.1.1.3	Summary of Exposure and Duration of Exposure During Maintenance Dosing Period to Parsaclisib	FAS	X
3.1.1.2	Summary of Exposure and Duration of Exposure to Tafasitamab	FAS	X

Table No.	Title	Population	Standard
3.2 Adverse Events			
3.2.1	Overall Summary of Treatment-Emergent Adverse Events	FAS	X
3.2.2	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	FAS	X
3.2.3	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	FAS	X
3.2.4	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	FAS	X
3.2.6	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	FAS	X
3.2.7	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	FAS	X
3.2.8	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	FAS	X
3.2.9	Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	FAS	X
3.2.10.1	Summary of Tafasitamab Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	FAS	X
3.2.10.2	Summary of Parsaclisib Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	FAS	X
3.2.11.1	Summary of Tafasitamab Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	FAS	X
3.2.11.2	Summary of Parsaclisib Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	FAS	X
3.2.12.1	Summary of Tafasitamab Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	FAS	X
3.2.12.2	Summary of Parsaclisib Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	FAS	X
3.2.14.1	Summary of Grade 3 or Higher Tafasitamab Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	FAS	X
3.2.14.2	Summary of Grade 3 or Higher Parsaclisib Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	FAS	X
3.2.15.1	Summary of Tafasitamab Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	FAS	X
3.2.15.2	Summary of Parsaclisib Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	FAS	X
3.2.16	Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term	FAS	X
3.2.18	Summary of Treatment-Emergent Adverse Events Leading to Dose Reduction by MedDRA System Organ Class and Preferred Term	FAS	X

Table No.	Title	Population	Standard
3.2.19	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption by MedDRA System Organ Class and Preferred Term	FAS	X
3.2.20	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drugs by MedDRA System Organ Class and Preferred Term	FAS	X
3.2.21.1	Summary of Treatment-Emergent Adverse Events of Tafasitamab Events of Clinical Interest by Events of Clinical Interest Class, Preferred Term, and Maximum Severity	FAS	X
3.2.21.2	Summary of Treatment-Emergent Adverse Events of Parsaclisib Events of Clinical Interest by Events of Clinical Interest Class, Preferred Term, and Maximum Severity	FAS	X
3.2.22	Summary of Dose-Limiting Toxicities	FAS	X
3.3 Laboratory			
3.3.1.1	Summary of Laboratory Values – Hematology	FAS	X
3.3.1.2	Summary of Laboratory Values – Chemistry	FAS	X
3.3.1.3	Summary of Laboratory Values – Coagulation	FAS	X
3.3.1.4	Summary of Laboratory Values – Urinalysis	FAS	X
3.3.3.1	Shift Summary of Hematology Laboratory Values in CTCAE Grade – to the Worst Abnormal Value	FAS	X
3.3.3.2	Shift Summary of Chemistry Laboratory Values in CTCAE Grade – to the Worst Abnormal Value	FAS	X
3.3.3.3	Shift Summary of Coagulation Laboratory Values in CTCAE Grade – to the Worst Abnormal Value	FAS	X
3.3.3.4	Treatment-Emergent Worsening of Laboratory Abnormalities – Hematology	FAS	X
3.3.3.5	Treatment-Emergent Worsening of Laboratory Abnormalities – Chemistry	FAS	X
3.3.3.6	Treatment-Emergent Worsening of Laboratory Abnormalities – Coagulation	FAS	X
3.4 Vital Signs			
3.4.1	Summary of Systolic Blood Pressure	FAS	X
3.4.2	Summary of Diastolic Blood Pressure	FAS	X
3.4.3	Summary of Pulse	FAS	X
3.4.4	Summary of Respiratory Rate	FAS	X
3.4.5	Summary of Body Temperature	FAS	X
3.4.6	Summary of Weight	FAS	X
3.5 ECG			
3.5.1	Summary of PR Interval (ms) From 12-Lead ECG	FAS	X
3.5.2	Summary of QRS Interval (ms) From 12-Lead ECG	FAS	X
3.5.3	Summary of QT Interval (ms) From 12-Lead ECG	FAS	X
3.5.4	Summary of QTcB Interval (ms) From 12-Lead ECG	FAS	X
3.5.5	Summary of QTcF Interval (ms) From 12-Lead ECG	FAS	X
3.5.7	Summary of Heart Rate (bpm) From 12-Lead ECG	FAS	X
3.5.8	Summary of Outliers of QT, QTcB, and QTcF Interval Values (milliseconds) From 12-Lead ECG	FAS	X
3.5.9	Summary of Clinically Significant ECG Abnormality	FAS	X

Figures

Figure No.	Title
4.3 Exploratory Efficacy	
4.3.2	Kaplan-Meier Estimates of Progression-Free Survival
4.3.3	Kaplan-Meier Estimates of Duration of Response
4.3.4	Kaplan-Meier Estimates of Overall Survival
4.6 Laboratory Data	
4.6.1	Line Graph of Selected Laboratory Values by Study Visit

Listings

Listing No.	Title
2.1 Discontinued Participants (Participant Disposition)	
2.1.1	Participant Enrollment and Disposition Status
2.2 Protocol Deviations	
2.2.1	Protocol Deviations
2.3 Data Excluded From PK, Efficacy, and/or Safety Analyses	
2.3.1	Analysis Population
2.4 Demographic and Baseline Characteristics (Including Prior and Concomitant Medications)	
2.4.1	Demographic and Baseline Characteristics
2.4.2	Disease History
2.4.3	Prior Radiation Treatment
2.4.4	Prior Systemic Therapy
2.4.5	Prior Surgery or Surgical Procedure
2.4.6	Prior Hematopoietic Cell Transplant
2.4.7	Medical History
2.4.8	Prior and Concomitant Medication
2.5 Drug Compliance	
2.5.1	Study Drug Administration of Tafasitamab
2.5.2	Study Drug Administration of Parsaclisib
2.5.3	Study Drug Compliance of Parsaclisib
2.6 Efficacy (and/or PK Data)	
2.6.1	Deaths
2.6.2	Best Overall Response, Duration of Response, and Progression-Free Survival
2.6.3	Overall Response Assessment by Visit
2.7 Adverse Events	
2.7.1	Adverse Events
2.7.2	Grade 3 and Higher Adverse Events
2.7.3	Serious Adverse Events
2.7.4	Fatal Adverse Events
2.7.5	Adverse Events Leading to Interruption, Reduction, or Discontinuation of Study Drugs
2.7.6	Dose-Limiting Toxicities
2.7.7	Tafasitamab Events of Clinical Interest
2.7.8	Parsaclisib Events of Clinical Interest
2.7.9	Treatment-Related Adverse Events

Listing No.	Title
2.8 Laboratory Data	
2.8.1.1	Clinical Laboratory Values – Hematology
2.8.1.2	Clinical Laboratory Values – Chemistry
2.8.1.3	Clinical Laboratory Values – Urinalysis
2.8.1.1.1	Abnormal Laboratory Values – Hematology
2.8.1.2.1	Abnormal Laboratory Values – Chemistry
2.8.1.3.1	Abnormal Laboratory Values – Urinalysis
2.8.4	Potential Hy's Law Events
2.9 Vital Signs	
2.9.1	Vital Signs
2.9.2	Abnormal Vital Sign Values
2.9.3	Alert Vital Sign Values
2.10 ECG	
2.10.1	12-Lead ECG Values
2.10.2	Abnormal 12-Lead ECG Values
2.10.3	Alert 12-Lead ECG Values