Official Title: A Phase 1b/2 Study of Tafasitamab, Tafasitamab Plus Lenalidomide, Tafasitamab Plus Parsaclisib, and Tafasitamab Plus Lenalidomide in Combination With R-CHOP in Japanese Participants With Non-Hodgkin Lymphoma (J-MIND)

NCT Number: NCT04661007

Document Date: INCMOR 0208-102 Statistical Analysis Plan Am 1 19 DEC 2024

Statistical Analysis Plan

INCMOR0208-102

A Phase 1b/2 Study of Tafasitamab, Tafasitamab Plus Lenalidomide, Tafasitamab Plus Parsaclisib, and Tafasitamab Plus Lenalidomide in Combination With R-CHOP in Japanese Participants With Non-Hodgkin Lymphoma (J-MIND)

Sponsor:	**Incyte Biosciences Japan GK** **Tokyo Midtown Hibiya** **1-1-2 Yurakucho, Chiyoda-ku** **Tokyo 100-0006, Japan**
Protocol Version:	**Protocol Amendment 7 dated 16 APR 2024**
CRF Approval Date:	**22 OCT 2024**
SAP Version:	**Amendment 1**
SAP Author:	[redacted] **Biostatistics**
Date of Plan:	**19 DEC 2024**

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

TABLE OF CONTENTS

TITLE PAGE 1
TABLE OF CONTENTS 2
LIST OF ABBREVIATIONS 7
1. INTRODUCTION 9
2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS 10
2.1. Protocol and Case Report Form Version 10
2.2. Study Objectives and Endpoints 10
3. STUDY DESIGN 14
3.1. Overall Design 14
3.1.1. Part 1 – Tafasitamab Monotherapy Dose-Finding 15
3.1.2. Part 2 – Tafasitamab Combination Therapy Dose-Finding/Assessing Recommended Clinical Dose 15
3.1.3. Part 3 – Dose Expansion With the Combination of Tafasitamab and Parsaclisib 16
3.1.4. Part 4 – Phase 2 Portion With the Combination of Tafasitamab and LEN 16
3.2. Randomization 16
3.3. Control of Type I Error 16
3.4. Sample Size Considerations 17
3.4.1. Sample Size Considerations for Parts 1, 2, and 3 17
3.4.2. Sample Size Consideration for Part 4 18
3.5. Schedule of Assessments 18
4. DATA HANDLING DEFINITIONS AND CONVENTIONS 19
4.1. Scheduled Study Evaluations and Study Periods 19
4.1.1. Day 1 19
4.1.2. Study Day 19
4.1.3. Baseline Value 19
4.1.4. Handling of Missing and Incomplete Dates 19
4.1.5. Cycle Length and Duration 21
4.2. Variable Definitions 22
4.2.1. Body Mass Index 22
4.2.2. Prior and Concomitant Medication 22
4.3. Conventions 23

5. STATISTICAL METHODOLOGY 24
5.1. General Methodology 24
5.2. Treatment Groups 24
5.3. Analysis Populations 25
5.3.1. All-Screened Population 25
5.3.2. Full Analysis Set 25
5.3.3. Safety Population 25
5.3.4. Dose-Limiting Toxicity Evaluable Population 26
5.3.5. Per-Protocol Set 26
5.3.6. Pharmacokinetic-Evaluable Population 26
5.3.7. Immunogenicity Analysis Set 26
5.3.8. Evaluable for Recommended Clinical Dose Assessment Set 26
6. BASELINE, EXPOSURE, AND DISPOSITION 27
6.1. Demographics, Baseline Characteristics, and Disease History 27
6.1.1. Demographics and Baseline Characteristics 27
6.1.2. Baseline Disease Characteristics 27
6.1.3. Disease History 27
6.1.4. Prior Therapy 28
6.1.5. Medical History 28
6.2. Disposition of Participants 28
6.3. Protocol Deviations 29
6.4. Exposure 29
6.5. Study Drug Compliance 30
6.6. Dose Intensity and Relative Dose Intensity 30
6.6.1. Dose Intensity and Relative Dose Intensity of Tafasitamab 30
6.6.2. Dose Intensity and Relative Dose Intensity of Lenalidomide 31
6.6.3. Dose Intensity and Relative Dose Intensity of Parsaclisib 31
6.7. Prior and Concomitant Medication 31
7. EFFICACY 32
7.1. General Considerations 32
7.2. Efficacy Hypotheses 32
7.3. Analysis of the Primary Efficacy Parameter 32
7.3.1. Objective Response Rate 32

7.3.2. Subgroup Analyses for Primary Endpoint 32
7.3.3. Sensitivity and Supportive Analyses for Primary Endpoint 33
7.4. Analysis of the Secondary Efficacy Parameters 33
7.4.1. Objective Response Rate per Investigator Assessment 33
7.4.2. Percent Reduction in SPD Investigator Assessment (Part 2 Group 2 Only) 34
7.4.3. Complete Response Rate 34
7.4.4. Progression-Free Survival 35
7.4.5. Duration of Response 36
7.4.6. Overall Survival 36
[redacted]
8. PHARMACOKINETICS 40
8.1. Pharmacokinetic Analysis 40
9. SAFETY AND TOLERABILITY 40
9.1. General Considerations 40
9.2. Adverse Events 40
9.2.1. Adverse Event Definitions 40
9.2.2. Dose-Limiting Toxicities 40
9.2.3. Adverse Events of Special Interest by eCRF 41
9.2.4. Adverse Events of Special Interest by Predefined List 41
9.2.4.1. Tafasitamab 42
9.2.4.2. Lenalidomide 42
9.2.4.3. Parsaclisib 42
9.2.5. Adverse Event Summaries 42
9.3. Clinical Laboratory Tests 45

9.3.1. Laboratory Value Definitions 45
9.3.2. Laboratory Value Summaries 45
9.3.3. Potential Hy's Law Events 45
9.4. Vital Signs 46
9.5. Electrocardiograms 46
10. INTERIM ANALYSES 47
10.1. Overview of Interim Analyses 47
11. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN 48
11.1. Changes to Protocol-Defined Analyses 48
11.2. Changes to the Statistical Analysis Plan 48
11.2.1. Amendment 1 48
12. REFERENCES 49
APPENDIX A. PLANNED TABLES, FIGURES, AND LISTINGS 50
APPENDIX B. BOIN OPERATING CHARACTERISTICS 61

LIST OF TABLES

Table 1: Objectives and Endpoints 10
Table 2: Decision Boundaries 17
Table 3: Sample Size of Group 6 18
Table 4: Dose Levels to Be Evaluated in Dose Finding – Part 1 24
Table 5: Dose Levels to Be Evaluated in Dose-Finding – Part 2 Except for Group 2 25
Table 6: Evaluation and Censoring of Progression-Free Survival 35
Table 7: Evaluation and Censoring of Progression-Free Survival (Sensitivity Analysis, Group 6 Only) 36
Table 8: Normal Ranges for Vital Sign Values 46
Table 9: Normal Ranges for Electrocardiogram Intervals 46
Table 10: Statistical Analysis Plan Versions 48
Table 11: Naming Convention for Titles in Tables, Figures, and Listings for .x Numbering 50

LIST OF FIGURES

Figure 1: Study Design Schema 15
Figure 2: Scheme of Dosing Schedule in Each Group 22

LIST OF ABBREVIATIONS

Abbreviation	Term
ADA	antidrug antibody
ADI	actual dose intensity
AE	adverse event
AESI	adverse events of special interest
ALT	alanine aminotransferase
AST	aspartate aminotransferase
BMI	body mass index
BOIN	Bayesian optimal interval design
CI	confidence interval
C_{max}	maximum observed plasma or serum concentration
CMR	complete metabolic response
CMV	cytomegalovirus
CR	complete response
CRF	case report form
CRR	complete response rate
CT	computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
DCR	disease control rate
DLBCL	diffuse large B-cell lymphoma
DLT	dose-limiting toxicity
DOR	duration of response
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	electronic case report form
FAS	full analysis set
FDA	Food and Drug Administration
FLIPI	Follicular Lymphoma International Prognostic Index
GCB	germinal center B cell
IRC	independent review committee
IWG	International Working Group
LDH	lactate dehydrogenase
LEN	lenalidomide
MedDRA	Medical Dictionary for Regulatory Activities
MTD	maximum tolerated dose
NCCN	National Comprehensive Cancer Network
NE	not evaluable

Abbreviation	Term
NHL	non-Hodgkin lymphoma
OR	objective response
ORR	objective response rate
OS	overall survival
PD	progressive disease
PDI	planned dose intensity
PFS	progression-free survival
PJP	*Pneumocystis jirovecii* pneumonia
PK	pharmacokinetic
PMR	partial metabolic response
PPS	per-Protocol set
Pr	probability
PR	partial response
PT	preferred term
QD	once daily
QTcB	QT interval corrected using Bazett's formula
QTcF	QT interval corrected using Fridericia's formula
QW	every week
QxW	every x weeks
RDI	relative dose intensity
RP2D	recommended Phase 2 dose
R/R	relapsed/refractory
R-CHOP	combination regimen consisting of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone
SAP	Statistical Analysis Plan
SD	stable disease
SMQ	standard MedDRA queries
SOC	system organ class
SPD	sum of the products of the longest perpendicular diameters
SPM	second primary malignancy
SpO_2	saturation of peripheral oxygen
SS	sample size
TEAE	treatment-emergent adverse event
TTNT	time to next treatment
ULN	upper limit of normal
WHO	World Health Organization

1. INTRODUCTION

This is an open-label, Phase 1b/2, multicenter, clinical study designed to assess the safety and tolerability, determine RP2Ds, assess the PK, and evaluate the efficacy of tafasitamab in combination with LEN in Japanese participants with NHL. After the addition of the Phase 2 portion (Part 4/Group 6) in Protocol Amendment 4, this study will be conducted in 4 parts and 7 groups as follows (see Figure 1): Parts 1 to 3 are the Phase 1b portion, and Part 4 is the Phase 2 portion. Parts 1 and 2 will use a BOIN design for dose findings.

Protocol Amendment 7 introduced an update in Group 2, which changes tafasitamab monotherapy in Japanese participants with R/R NHL to tafasitamab Q2W/Q4W in combination with LEN in Japanese participants with R/R DLBCL as this schedule is almost established in the MINDway study.

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

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in the INCMOR 0208-102 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.

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCMOR 0208-102 Protocol Amendment 7 dated 16 APR 2024 and CRFs approved 22 OCT 2024. 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	
Part 1: To assess the safety and tolerability and to determine the RP2D of single-agent tafasitamab (Group 1) in Japanese participants with R/R NHL.	Incidence and severity of TEAEs and incidence of DLTs with single-agent tafasitamab.
Parts 2 and 3: To assess the safety, tolerability, and to determine the recommended clinical dose (Group 2)/RP2D (Groups 3, 4a, and 5) of the following: • Tafasitamab Q2W/Q4W dosing in combination with LEN (Group 2) in Japanese participants with R/R DLBCL. • Tafasitamab in combination with LEN (Group 3) in Japanese participants with R/R DLBCL. • Tafasitamab in combination with parsaclisib (Group 4a) in Japanese participants with R/R DLBCL. • Tafasitamab in combination with LEN plus R-CHOP (Group 5) in Japanese participants with previously untreated DLBCL.	• Incidence and severity of TEAEs with tafasitamab Q2W/Q4W in combination with LEN (Group 2). • Incidence and severity of TEAEs and incidence of DLTs with tafasitamab in combination with LEN, parsaclisib, or LEN plus R-CHOP (Groups 3, 4a, and 5).
Part 4: To evaluate the efficacy of tafasitamab in combination with LEN (Group 6) in Japanese participants with R/R DLBCL.	OR, defined as the best response of CR/CMR or PR/PMR as determined by an IRC according to the Lugano criteria (Cheson et al 2014), will be analyzed on the FAS using ORR as a population-level summary, in which ORR is defined as the percentage of participants experiencing OR.

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
Secondary	
Parts 1, 2, 3, and 4: To determine the PK of the following: • Single-agent tafasitamab (Group 1) in Japanese participants with R/R NHL. • Tafasitamab Q2W/Q4W in combination with LEN (Group 2) in Japanese participants with R/R DLBCL. • Tafasitamab in combination with LEN (Groups 3 and 6) or parsaclisib (Group 4a) in Japanese participants with R/R DLBCL. • Tafasitamab in combination with LEN plus R-CHOP in Japanese participants with previously untreated DLBCL (Group 5).	PK analysis of single-agent tafasitamab and tafasitamab as part of combination treatments. Descriptive statistics of trough (ie, predose) and C_{max} levels at different timepoints.
Part 2 (Group 2 only): To evaluate the efficacy of tafasitamab Q2W/Q4W in combination with LEN in Japanese participants with R/R DLBCL.	Tumor response as follows: • Response assessment as per investigator assessment of response according to the Lugano criteria (Cheson et al 2014). • Percent reduction in SPD in up to 6 target measurable nodes and extranodal sites assessed by CT as per investigator assessment of response according to the Lugano criteria (Cheson et al 2014).
Part 4: To further evaluate the efficacy of tafasitamab in combination with LEN (Group 6) in Japanese participants with R/R DLBCL based on additional efficacy outcomes.	• CR, defined as CR/CMR as determined by an IRC according to the Lugano criteria (Cheson et al 2014), will be analyzed on the FAS using CRR as a population-level summary, in which CRR is defined as the percentage of participants experiencing CR. • DOR, defined as the time from the first documented CR/CMR or PR/PMR as determined by an IRC according to the Lugano criteria (Cheson et al 2014) until the date of first documented disease progression or death due to any cause, whichever occurs first. DOR will be analyzed on the FAS using Kaplan-Meier–estimated median survival time as a population-level summary.

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
Secondary (continued)	
Part 4: To further evaluate the efficacy of tafasitamab in combination with LEN (Group 6) in Japanese participants with R/R DLBCL based on additional efficacy outcomes (continued).	• PFS, defined as the time from the date of first dose of study treatment until the first documented disease progression as determined by an IRC according to the Lugano criteria (Cheson et al 2014) or death due to any cause, whichever occurs first. PFS will be analyzed on the FAS using Kaplan-Meier–estimated median survival time as a population-level summary. • OS, defined as the time from the first dose of study treatment until death due to any cause. OS will be analyzed on the FAS using Kaplan-Meier–estimated median survival time as a population-level summary. • OR, CR/CMR, DOR, and PFS as per investigator assessment of response according to the Lugano criteria (Cheson et al 2014). OR and CR/CMR will be summarized by the ORR and CRR, defined as the percentage of participants experiencing OR and CR/CMR respectively.
Part 4: To assess the safety and tolerability of tafasitamab in combination with LEN in Japanese participants with R/R DLBCL.	Incidence and severity of TEAEs following treatment with tafasitamab in combination with LEN.
[redacted]	

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
[redacted]	

3. STUDY DESIGN

3.1. Overall Design

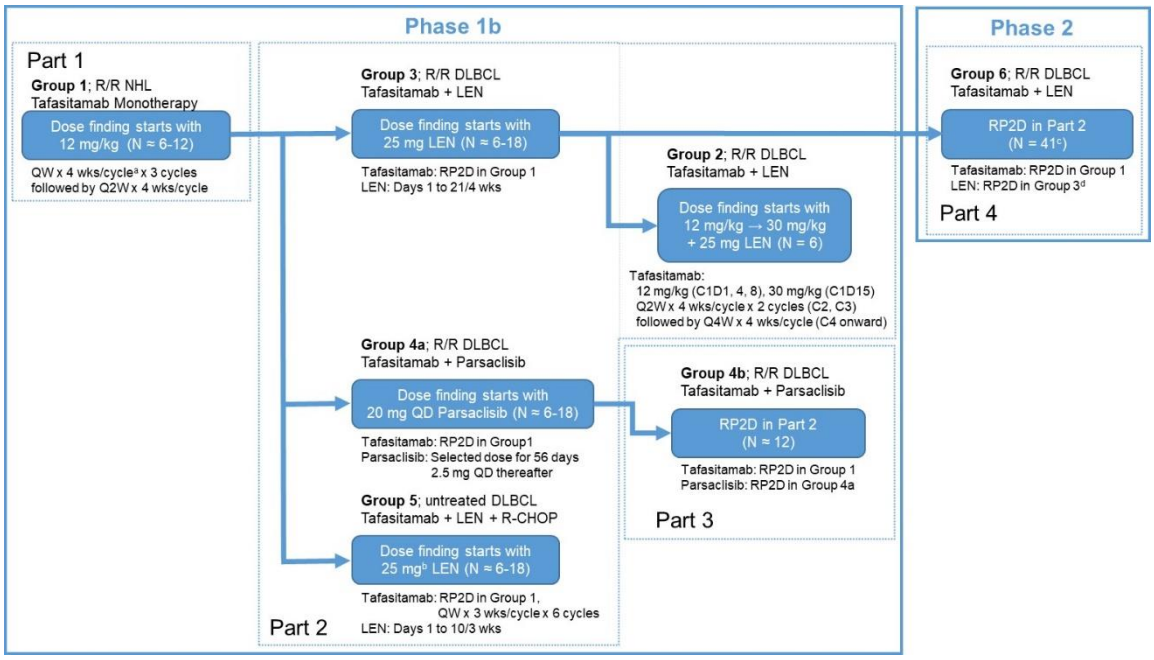
This is a Phase 1b/2, open-label, multicenter, clinical study designed to assess the safety and tolerability, determine the RP2Ds, and assess the PK and evaluate the efficacy of tafasitamab in combination with LEN in Japanese participants with NHL. After the addition of the Phase 2 portion (Part 4/Group 6) in Protocol Amendment 4 and change the objective of Group 2 in Protocol Amendment 7, this study will consist of 4 parts and 7 groups:

- Part 1 consists of tafasitamab monotherapy dose-finding to evaluate the safety and tolerability and to determine the RP2Ds of single-agent tafasitamab in Japanese participants with R/R NHL. Part 1 consists of 1 group (Group 1) to evaluate weight-based doses of tafasitamab.
- Part 2 consists of tafasitamab combination therapy dose-finding to evaluate the safety and tolerability and to determine the RP2Ds of tafasitamab when combined with LEN (Group 3) or parsaclisib (Group 4a) in participants with R/R DLBCL or LEN plus R-CHOP (Group 5) in participants with previously untreated DLBCL and to determine the recommended clinical dose of tafasitamab Q2W/Q4W when combined with LEN (Group 2) in participants with R/R DLBCL. The dose of tafasitamab will be based on the weight-based RP2D that is deemed safe and tolerable in Part 1 for Groups 3, 4a, and 5 and will be based on the weight-based RP2D that is deemed safe and tolerable in Part 1 and Part 2 Group 3 for Group 2.
- Part 3 was planned to consist of 1 dose-expansion group (Group 4b) to further evaluate the safety, tolerability, and preliminary antitumor activity of the RP2D deemed safe and tolerable in Part 2 for the combination of tafasitamab and parsaclisib. Based on the sponsor's decision, participants for Part 3 Group 4b will not be recruited. This part was removed during Protocol Amendment 5.
- Part 4 consists of 1 group (Group 6) for the Phase 2 portion of the study. Part 4 will evaluate the antitumor activity as the primary objective. The safety and tolerability of the RP2D of the combination of tafasitamab and LEN that was deemed safe and tolerable in Part 2 will also be evaluated as the secondary objectives.

For Groups 1, 3, and 4a only, participants may move to the continued access period if they still benefit from treatment after 2 years of treatment. This aim is to provide benefit for participants without any particular long-term efficacy or safety analysis.

The study design schema is presented in Figure 1.

Figure 1: Study Design Schema



Note: Part 3 was removed from the Protocol with Amendment 5.
[a] An additional loading dose of tafasitamab is to be administered on Day 4 of Cycle 1.
[b] The dose may be adjusted based on the result of First-MIND study.
[c] Evaluable for efficacy.
[d] For participants with moderate renal insufficiency (creatinine clearance ≥ 30 to < 60 mL/min), the starting dose of LEN must be reduced to 10 mg.

3.1.1. Part 1 – Tafasitamab Monotherapy Dose-Finding

Part 1 consists of 1 group:

- Group 1, tafasitamab weight-based monotherapy dosing with R/R NHL: approximately 6 to 12 evaluable participants will be enrolled.

Dose-finding for Group 1 will follow a BOIN procedure (Liu and Yuan 2015). A cohort size of 3 evaluable participants will be used. The estimated MTD for tafasitamab monotherapy in each group will be the dose at which the observed DLT rate is closest to the target DLT rate of 30%.

3.1.2. Part 2 – Tafasitamab Combination Therapy Dose-Finding/Assessing Recommended Clinical Dose

Part 2 consists of 4 groups, and the enrollment of Part 2 except for Group 2 will be initiated after the determination of weight-based RP2D for tafasitamab monotherapy in Group 1 of Part 1. Approximately 6 to 18 evaluable participants will be enrolled in each group:

- Group 3, tafasitamab in combination with LEN in participants with R/R DLBCL.
- Group 4a, tafasitamab in combination with parsaclisib in participants with R/R DLBCL.
- Group 5, tafasitamab plus LEN in combination with R-CHOP in participants with untreated DLBCL.

The enrollment of the 3 groups (Group 3, 4a and 5) in Part 2 will occur in parallel. A BOIN design (Liu and Yuan 2015) will be used to determine the MTD. A cohort size of 3 evaluable participants will be used. The estimated MTD for tafasitamab combination treatment in each group will be the dose at which the observed DLT rate is closest to the target DLT rate of 30%.

Enrollment in Group 2 will be initiated after the completion of the enrollment in Group 6. Six evaluable participants with R/R DLBCL will be enrolled in Group 2 and treated with weight-based dosing of tafasitamab Q2W/Q4W in combination with LEN. The recommended clinical dose will be assessed in Group 2.

3.1.3. Part 3 – Dose Expansion With the Combination of Tafasitamab and Parsaclisib

Part 3 was to consist of one group. The enrollment of Part 3 was to be initiated after the confirmation of RP2D for tafasitamab in combination with parsaclisib in Group 4a of Part 2.

- Group 4b, tafasitamab in combination with parsaclisib in participants with R/R DLBCL: up to approximately 12 participants will be enrolled (approximately 18 participants including Part 2 Group 4a at RP2D).

The purpose of Group 4b was to further evaluate the safety, tolerability, and preliminary antitumor activity of the selected RP2D deemed safe and tolerable for the combination of tafasitamab and parsaclisib.

An interim futility analysis was planned when the first 9 participants (Part 2 Group 4a at RP2D and Part 3 Group 4b combined) had been evaluated for response or permanently discontinued the study. Part 3 Group 4b was to be terminated for futility if ≤ 3 of the 9 participants have responded (ie, CR/CMR or PR/PMR) based on assessments provided by investigators.

As of Protocol Amendment 5, the sponsor decided not to open enrollment of Group 4b of Part 3. As a result, the planned interim analysis for Groups 4a and 4b will not be run, and the efficacy and safety analyses have been updated accordingly (See Section 10.4.1 and Section 10.4.2 of the Protocol).

3.1.4. Part 4 – Phase 2 Portion With the Combination of Tafasitamab and LEN

Part 4 Group 6 will be added after the determination of the RP2D for tafasitamab in combination with LEN in Part 2 Group 3. The purpose of Group 6 is to further evaluate the antitumor activity and safety and tolerability of the selected RP2D. Group 6 will enroll 41 participants with R/R DLBCL who are eligible for efficacy assessments.

As of Protocol Amendment 7, enrollment of participants with moderate renal insufficiency (serum creatinine clearance ≥ 30 to < 60 mL/min) is allowed.

3.2. Randomization

Not applicable.

3.3. Control of Type I Error

All statistical analyses are exploratory in nature, and no formal statistical tests will be performed.

In addition, there are no plans to stop the study early for efficacy; therefore, no adjustment for alpha-spending will be considered.

3.4. Sample Size Considerations

3.4.1. Sample Size Considerations for Parts 1, 2, and 3

The dose-finding parts of the study (Part 1 and Part 2 except for Group 2) will follow a BOIN procedure (Liu and Yuan 2015), and the sample size will depend on the frequency of DLTs and the number of cohorts before reaching the MTD. Up to 12 evaluable participants will be treated in Part 1 Group 1 and up to 18 evaluable participants will be treated in Part 2 Groups 3, 4a, and 5. The dose-finding procedure will be stopped for each group if ≥ 6 evaluable participants are treated at a dose level and the observed DLT data indicate that the dose should be retained or the maximum number of participants are reached.

The 3-point hypotheses selected for the Local BOIN design are ϕ=0.3, ϕ1=0.6*ϕ, and ϕ2=1.4*ϕ, where ϕ=0.3 is the target DLT rate, ϕ1=0.6*ϕ is the highest DLT rate that is deemed subtherapeutic, and ϕ2=1.4*ϕ is the lowest DLT rate deemed overly toxic. An equal prior probability of hypothesis being true are assigned to each of the hypotheses. The value of 0.95 is selected for the cutoff to eliminate an overly toxic dose for safety.

The estimated MTD for each group is the dose at which the observed DLT rate is closest to the target DLT rate of 30% using an isotonic method that takes the assumption of a monotonic dose-toxicity relationship into account. Table 2 will be used to guide dose escalation/ de-escalation decisions. If the number of participants with DLT(s) specified in the last column is reached, that dose level and all dose levels above it will be eliminated. If the lowest dose level is eliminated, then the dose-finding will be terminated. If the number of participants with DLT(s) is between the escalation and de-escalation boundaries specified in the second and third columns in Table 2, then the dose should be retained and another cohort of 3 evaluable participants will be enrolled in the current dose level.

Table 2: Decision Boundaries

Number of Participants Treated at Current Dose	Escalate if Number of DLTs is ≤	De-Escalate if Number of DLTs is ≥	Unacceptable Toxicity if Number of DLTs ≥
3	0	2	3
6	1	3	4
9	2	4	5
12	2	5	7
15	3	6	8
18	4	7	9

The target number of evaluable participants in Part 2 Group 2 was set at 6 as the number of participants necessary for confirmation of tolerability. With a sample size of 6 evaluable participants, there is a 31% probability to observe at least 1 occurrence of a particular AE if the natural incidence of this AE is 6%.

Part 3 Group 4b could have been expanded to approximately 18 participants (including participants who were treated at RP2D in Part 2 Group 4a). If the true ORR had been 65% for participants treated at RP2D in Group 4a and Group 4b, then with 18 total participants, there was approximately 85% probability of observing the lower bound of the 95% CI of ORR ≥ 30%.

Based on the sponsor's decision, as of Amendment 5, Part 3 Group 4b will not be opened.

3.4.2. Sample Size Consideration for Part 4

The threshold response rate in Group 6 was determined based on the ORR of 35% with rituximab monotherapy (Tobinai et al 2004). The expected response rate is set at 55%, taking into account that the ORR point estimate of the L-MIND study was 57.5% (data cutoff 30 OCT 2020; Duell et al 2021).

Assuming a threshold response rate of 35% and an expected response rate of 55%, with 41 participants evaluated for efficacy, the probability that the 90% exact binomial CI of the ORR exceeds the threshold response rate is 83% (see Table 3).

Table 3: Sample Size of Group 6

Sample Size	Probability of 90% CI Lower Bound > 0.35
39	0.736
40	0.787
41	0.831
42	0.790
43	0.833

Note: Power values were generated in base R by the "pbinom()" function, and critical values by the "qbinom()" function. The threshold rate was set at 35% and expected response rate at 55%. One-sided alpha was set to 0.05 for a 90% 2-sided CI.

3.5. Schedule of Assessments

Refer to Protocol Amendment 7 dated 16 APR 2024 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 is administered to the participant. Study drug refers to tafasitamab or any of the other drugs given in combination (if applicable; LEN, parsaclisib, or R-CHOP). The earliest date will be considered as Day 1.

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 any of the other drugs given in combination (if applicable; LEN, parsaclisib, or R-CHOP).

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.

For derivation of relapse after initial diagnosis and primary refractory variables, partial dates in prior antisystemic therapies will be handled as follows in the calculation:

- For any regimen: select the earliest complete start date and latest complete end date of the regimen component.
- Within a regimen if a component start date (mmyyyy) = the earliest complete regimen start date (mmyyyy), then the component start date will be set to the earliest complete regimen start date, otherwise use the first of the month.
- Within a regimen if component start date (yyyy) = the earliest complete regimen start date (yyyy), then the component start date will be set to the earliest complete regimen start date, otherwise use the first of January.
- Within a regimen if a component end date (mmyyyy) = the latest complete regimen stop date (mmyyyy), then the component end date will be set to the latest complete regimen stop date, otherwise use the 28th of the month.

- Within a regimen if a component end date (yyyy) = the latest complete regimen stop date (yyyy), then the component end date will be set to the latest complete regimen stop date, otherwise if the component end date (yyyy) – the earliest complete regimen start date (yyyy), then the component end date will be set to the 28th of the month of the earliest complete regimen start date, otherwise use the 28th of January.

The consistency should be checked between the start and end dates.

4.1.5. Cycle Length and Duration

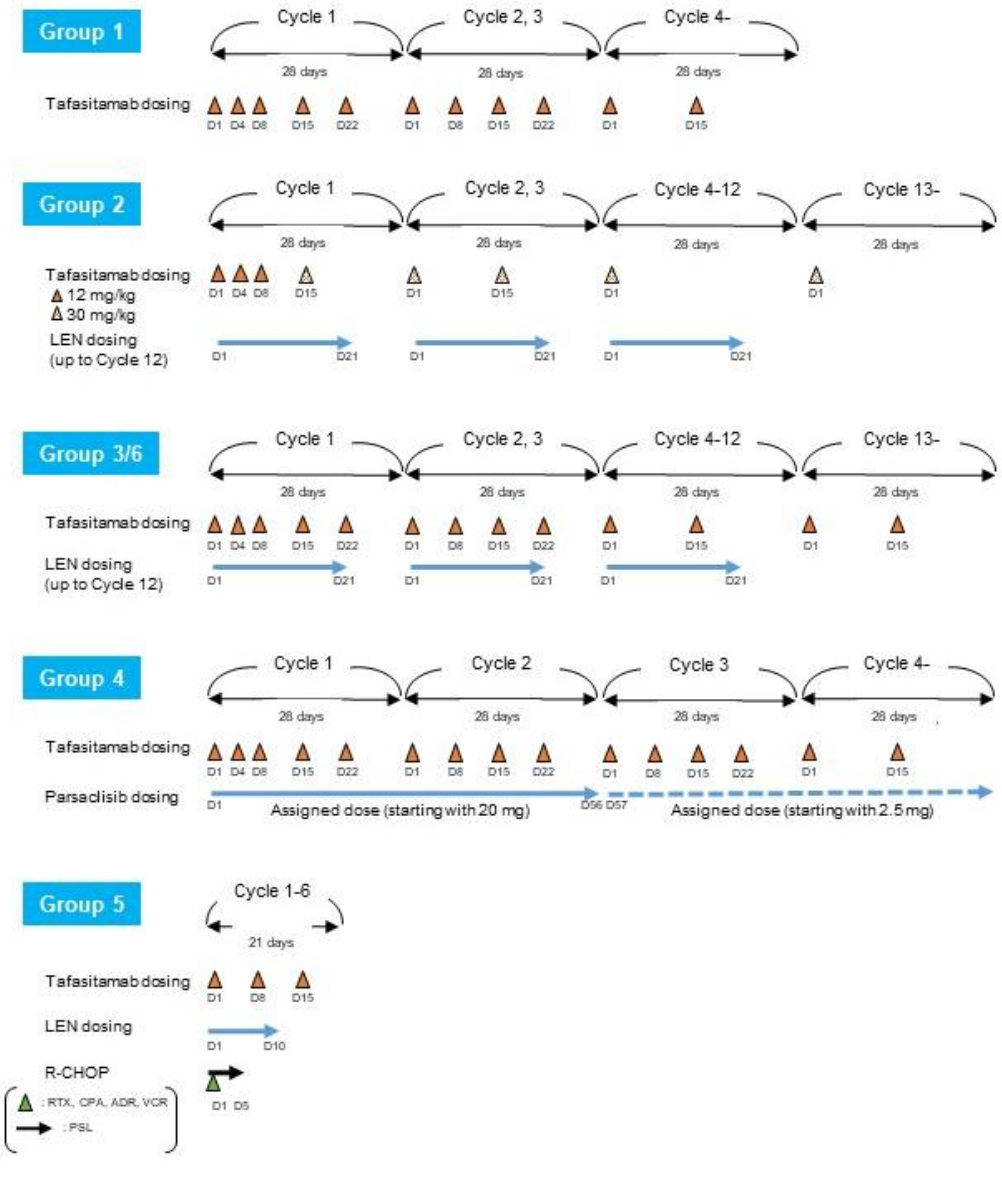
There are 2 different treatment cycles in this study.

- For Groups 1, 2, 3, 4a, and 6 the cycle length is 28 days
- For Group 5, the cycle length is 21 days.

Treatment will be given as long as the participant is receiving benefit or until the participant meets any of the discontinuation criteria (see Section 7.1.1 of the Protocol), whichever occurs earlier. Participants whose treatment period exceeds 2 years will move to the continued access period (see Section 4.1.4 of the Protocol) for Parts 1 and 2 (Groups 1, 3, and 4a).

The actual Day 1 of subsequent cycles will correspond with the first day of administration of tafasitamab, parsaclisib, LEN, or R-CHOP 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 for Groups 1, 2, 3, 4a, and 6 and different from 21 days for Group 5. The date of the Day 1 of subsequent cycles recorded on the eCRF will be used as the Day 1 of the subsequent cycles. Figure 2 shows the dosing schedule in each group, as well as length and duration of the cycles.

Figure 2: Scheme of Dosing Schedule in Each Group



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 (BMI) 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 date of first administration of tafasitamab, LEN, parsaclisib, or R-CHOP,

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

- Before the date of first administration tafasitamab, LEN, parsaclisib, or R-CHOP 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, LEN, parsaclisib or R-CHOP 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, LEN, parsaclisib, or R-CHOP. 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.

4.3. Conventions

Days to Months: Conventionally, duration in month is calculated as duration in days / 30.4375 days.

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.

Unless otherwise specified, all CIs will be 95% with the exception of Group 6, where 90% CI will be displayed primarily and 95% CI will be provided as reference.

5.2. Treatment Groups

Part 1: the dose-finding parts of the study, will follow a BOIN design (Liu and Yuan 2015).

Part 1 consists of 1 group:

- Group 1, tafasitamab weight-based monotherapy dosing with R/R NHL: approximately 6 to 12 evaluable participants will be enrolled. Up to 2 doses will be tested. Data will be summarized overall and by treatment group based on the dose regimen initially assigned (see Table 4).

Table 4: Dose Levels to Be Evaluated in Dose Finding – Part 1

Tafasitamab Weight-Based Monotherapy (Group 1)	
Dose level	**Dose**
Dose Level −1	9 mg/kg QW[a]
Dose Level 1 (starting dose)	12 mg/kg QW[a]

[a] QW for Cycles 1 through 3 (plus a loading dose at C1D4); Q2W thereafter.

Part 2 consists of tafasitamab combination therapy dose-finding to evaluate the safety and tolerability and to determine the RP2Ds for tafasitamab when combined with LEN (Group 3) or parsaclisib (Group 4a) in participants with R/R DLBCL or LEN plus R-CHOP (Group 5) in participants with previously untreated DLBCL. The dose of tafasitamab will be based on the weight-based RP2D that is deemed safe and tolerable in Part 1.

- Group 3 and 5: Up to 3 doses will be tested. Data will be summarized overall and by treatment group based on the dose (see Table 5)
- Group 4a: Up to 3 doses will be tested. Data will be summarized overall and by treatment group based on the dose (see Table 5)

Table 5: Dose Levels to Be Evaluated in Dose-Finding – Part 2 Except for Group 2

Lenalidomide (Groups 3 and 5)		Parsaclisib (Group 4a)	
Dose Level	**Dose**	**Dose Level**	**Dose**
Dose Level 1 (starting dose)	25 mg QD[a,b]	Dose Level 1 (starting dose)	20 mg QD[c]
Dose Level −1	20 mg QD[b]	Dose Level −1	10 mg QD[c]
Dose Level −2	15 mg QD[b]	Dose Level −2	5 mg QD[c]

[a] The starting dose of Group 5 may be adjusted based on the result of First-MIND study. In case a lower starting dose is selected, Dose Level −1 and Dose Level −2 will be 5 mg and 10 mg lower than the starting dose, respectively.
[b] Group 3: QD on Days 1 to 21 of each 28-day cycle; Group 5: QD on Days 1 through 10 of each 21-day cycle.
[c] QD on Days 1 through 56 followed by a 2.5 mg QD.

Six evaluable participants with R/R DLBCL will be enrolled in Group 2 and treated with weight-based dosing of tafasitamab Q2W/Q4W in combination with LEN.

Part 3 was to use an open-label dose expansion design and the dose that had been deemed safe and tolerable for the combination of tafasitamab and parsaclisib was to be further tested. Data would have been summarized by group based on the dose regimen initially assigned. In the event that several dose regimens tested were deemed substantially below the MTD, these doses may have been combined for summary purposes.

Part 4 will use an open-label design and the RP2D as determined in Part 2 Group 3. This is an open-label, single treatment group study. Participants will be summarized by total only.

5.3. Analysis Populations

5.3.1. All-Screened Population

The all-screened population will include all participants who signed the ICF.

5.3.2. Full Analysis Set

The FAS will include all participants who received at least 1 dose of study treatment (at least 1 dose of tafasitamab, LEN, parsaclisib, or R-CHOP). For Group 6, both study drugs (tafasitamab and LEN) must have been administered at least once. The FAS will be used for the summary of demographics, baseline characteristics, participant disposition, and analyses of all efficacy data. For Group 6, participants who were inadvertently enrolled although they do not meet the eligibility requirements of the study may be excluded from the FAS (see Section 5.5 of the Protocol).

5.3.3. Safety Population

The safety population will include all enrolled participants who received at least 1 dose of tafasitamab, LEN, parsaclisib, or R-CHOP. Treatment groups for this population will be determined according to the actual treatment the participant received regardless of assigned study drug treatment. All safety analyses will be conducted using the safety population.

5.3.4. Dose-Limiting Toxicity Evaluable Population

The DLT evaluable population (Groups 1, 3, 4a, and 5) will include participants who have received at least:

- 4 doses of tafasitamab in Group 1 in the first cycle (28 days)
- 17 of 21 doses of LEN and at least 4 doses of tafasitamab in Group 3 in the first cycle (28 days)
- 23 of 28 doses of parsaclisib and at least 4 doses of tafasitamab in Group 4a in the first cycle (28 days)
- 8 of 10 doses of LEN, 3 doses of tafasitamab, and at least 1 of the component of R-CHOP in Group 5 in the first cycle (21 days)

Participants who have had a DLT are considered evaluable. Participants who are NE will be replaced.

5.3.5. Per-Protocol Set

The PPS will include all participants in the FAS who have undergone at least 1 postbaseline response assessment without having a major Protocol deviation. The PPS will be used for all sensitivity analyses on Group 6.

5.3.6. Pharmacokinetic-Evaluable Population

The PK-evaluable population will include all participants who received at least 1 dose of tafasitamab, LEN, parsaclisib, or R-CHOP and provided at least 1 quantifiable tafasitamab serum concentration. All PK analyses will be conducted using the PK-evaluable population.

5.3.7. Immunogenicity Analysis Set

The immunogenicity analysis set will include all participants who received at least 1 dose of study treatment and have at least 1 evaluable anti-tafasitamab antibody assessment.

5.3.8. Evaluable for Recommended Clinical Dose Assessment Set

In Group 2, the recommended clinical dose-evaluable population will include participants who have received treatment from Cycle 1 Day 1 through Cycle 2 Day 1, completed safety assessments through Cycle 2 Day 7 (Day 35 relative to the first dose), and/or experience a prespecified AE (unequivocally unrelated to study treatment) through Day 35.

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, age groups (< 65; ≥ 65), sex, race, ethnicity, weight at baseline, height at baseline, and BMI at baseline.

6.1.2. Baseline Disease Characteristics

The following baseline disease characteristics will be summarized for the FAS:

- ECOG performance status at screening and baseline (0, 1, 2-4),
- LDH levels at baseline (≤ ULN vs > ULN),
- Bulky disease (defined as having a longest lesion diameter of ≥ 7.5 cm as assessed by investigator assessment or central radiological assessment; present vs absent),
- Time since discontinuation of last prior anti-NHL treatment (months).

6.1.3. Disease History

The following baseline disease history will be summarized for the FAS.

The time since diagnosis, initial presence of B-symptoms, and current presence of B-symptoms will be summarized and listed for all groups.

Time since diagnosis will be calculated as follows:

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

For participants with follicular lymphoma, initial grade, initial cytogenetics, initial Ann Arbor staging, initial FLIPI risk category, current grade, current cytogenetics, current Ann Arbor staging, and current FLIPI risk category will be summarized and listed.

For participants with DLBCL, stage at initial diagnosis, initial disease subtype, international prognostic index at initial stage, date of current diagnosis, current stage, current international prognostic index, current DLBCL subtype, current subtype determination reference, and current diagnosis type will be summarized and listed. Early relapse (defined as relapse ≤ 12 months after initial DLBCL diagnosis) and late relapse (defined as relapse > 12 months after initial DLBCL diagnosis) will also be summarized and listed. Primary refractory is defined as disease progression in the course of the first line regimen or showing a response of less than PR (ie, PD or SD) as best response to the first line regimen, or disease progression within ≤ 6 months from the completion of the first line regimen.

For participants with marginal zone lymphoma, initial subtype, infection-related (yes/no), *Helicobacter pylori*–induced infection-related (yes/no), initial cytogenetics, initial Ann Arbor staging, current cytogenetics, and current Ann Arbor staging will be summarized and listed.

The number of participants who had flow cytometry information available will be summarized for the FAS. Date of flow cytometry, sample type, cell marker, and other marker information will be listed.

6.1.4. Prior Therapy

This section is focusing only on antilymphoma therapies; prior medications for any other related diseases will be analyzed as described in Section 6.7.

The number of prior systemic cancer therapy regimens will be summarized for all participants in the FAS. The number of prior systemic treatment lines of antilymphoma therapies and number of participants with 1 versus 2 versus ≥ 3 prior medications, as well as the most frequent regimen names, will be summarized.

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

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

The number of participants who had prior surgery or surgical procedure for the 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 prior 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, and drug used with the transplant will be listed.

The number of participants who had tumor marker information available will be summarized for the FAS. Date of tumor marker test, tumor marker type, tumor marker test, method of test will be listed.

The number of participants who received bendamustine will be summarized for the FAS.

The number of participants who were refractory to the last rituximab-containing therapy will be summarized for the FAS.

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 a medical history event for each body system/organ class as documented on the eCRF.

6.2. Disposition of Participants

The number and percentage of participants who were treated, who were ongoing with study treatment, who completed 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 site will also be provided.

6.3. Protocol Deviations

Important Protocol deviations will be summarized and listed.

6.4. Exposure

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

- Tafasitamab:
  - **Duration of treatment with tafasitamab (days):** date of last dose of tafasitamab − date of first dose of tafasitamab + 1.
  - **Number of cycles of tafasitamab**
  - **Number of infusions of tafasitamab**
  - **Tafasitamab dose modifications:** number of participants who had tafasitamab infusion interruption.
- 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 Dosing form and Drug Accountability 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.
- Lenalidomide
  - **Duration of treatment with LEN (days):** date of last dose of LEN − date of first dose of LEN + 1.
  - **Total actual dose of LEN (mg):** Total actual dose taken will be calculated based on the information entered on the Dosing form and Drug Accountability eCRF.
  - **Average daily dose of LEN (mg/day):** total actual LEN dose taken (mg) / duration of treatment with LEN (days).
  - **Lenalidomide dose modifications:** number of participants who had LEN dose reduction or interruption.
- R-CHOP
  - **Duration of treatment with R-CHOP (days):** date of last dose of R-CHOP − date of first dose of R-CHOP + 1.
  - **Number of infusions of R-CHOP**
  - **R-CHOP dose modifications:** any modifications reported for any individual drugs of the R-CHOP regimen.

6.5. Study Drug Compliance

For participants in the safety population, overall compliance (%) for the oral study drugs parsaclisib and LEN 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. 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 if applicable.

6.6. Dose Intensity and Relative Dose Intensity

For participants in the safety population, ADI and RDI of tafasitamab, parsaclisib, and LEN will be summarized descriptively. The ADI or PDI will be calculated by summing up the visit-wise actual or planned doses.

6.6.1. Dose Intensity and Relative Dose Intensity of Tafasitamab

For participants in the safety population, dose intensity and 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) / participant 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]) / participant 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: The planned dose is 12 mg/kg per infusion except Group 2 as per Protocol. The planned dose for Group 2 is 12 mg/kg per infusion up to Cycle 1 Day 8, and 30 mg/kg per infusion from Cycle 1 Day 15 and thereafter.
- RDI (unit: %): RDI expresses the amount of drug administered compared to the planned amount of drug across all infusions.

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

6.6.2. Dose Intensity and Relative Dose Intensity of Lenalidomide

- ADI (unit: mg): the actual dose the participant was exposed to (this is captured in "Dosing - Lenalidomide" eCRF form).
- PDI (unit: mg): The planned dose of LEN is 25 mg QD on Days 1 to 21 of each 28-day cycle for Groups 2, 3, and 6 or Days 1 to 10 of each 21-day cycle for Group 5. Lenalidomide can be given for up to a total of 12 cycles in Groups 2, 3, and 6 and up to 6 cycles in Group 5. For Group 6, the participants with moderate renal insufficiency (creatinine clearance ≥ 30 to < 60 mL/min), the planned dose of LEN is 10 mg QD on Days 1 to 21.
- RDI (unit: %): RDI expresses the amount of drug administered compared to the planned amount of drug at all time.

  RDI = ADI / PDI × 100

The total actual dose taken will be calculated based on information entered on the Dosing form and 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.

6.6.3. Dose Intensity and Relative Dose Intensity of Parsaclisib

- ADI (unit: mg): the actual dose the participant was exposed.
- PDI (unit: mg): The planned dose of parsaclisib is 20 mg QD on days 1 through 56 followed by a 2.5 mg QD dose for Group 4a.
- RDI (unit: %): RDI expresses the amount of drug administered compared to the planned amount of drug at all time.

  RDI = ADI / PDI × 100

The total actual dose taken will be calculated based on information entered on the Dosing form and 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.

6.7. 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.

7.1. General Considerations

Timing of analysis

The primary analysis for Group 1, 3, 4a, and 5 will be conducted when the last participants in Group 5 performs the last follow-up visit.

The primary analysis for Group 2 will be conducted when all participants in Group 2 have been followed at least Cycle 3 Day 28 or discontinued study treatment prior to Cycle 3 Day 28.

The primary analysis for Group 6 will be conducted when all participants when all participants have reached their Cycle 6 Day 28 and follow-up analysis will be run when all participants have reached their Cycle 12 Day 28.

7.2. Efficacy Hypotheses

Not applicable.

7.3. Analysis of the Primary Efficacy Parameter

Applicable for Part 4 only.

7.3.1. Objective Response Rate

For Part 4 (Group 6), ORR is defined as the percentage of participants experiencing a CR/CMR or PR/PMR as determined by an IRC according to the Lugano criteria (Cheson et al 2014) at any time during the study before disease progression and start of a new antilymphoma treatment.

The ORR as determined by an IRC and its 90% exact binomial CI will be summarized. The 95% CI will be provided as reference. 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.

The primary population for this analysis is the FAS population.

7.3.2. Subgroup Analyses for Primary Endpoint

This is applicable for Group 6 only.

The following subgroups will be analyzed for the primary endpoint:

- Cell of origin determined by immunohistochemistry assessment: GCB phenotype versus non-GCB phenotype
- International Prognostic Index score (low risk [0 or 1] and low-intermediate risk [2] vs high-intermediate risk [3] and high risk [4 or 5])
- Number of prior treatment lines (1 vs ≥ 2)

- Prior autologous stem cell transplant (yes vs no)
- Age (≤70 years vs >70 years)
- Age (≤65 years vs >65 years)
- Age (≤60 years vs >60 years)
- LDH levels at baseline (≤ ULN vs > ULN)
- Refractoriness to last rituximab-containing therapy (yes vs no) - rituximab refractoriness is defined as having reached less than a PR (ie, SD or PD) as best overall response to any rituximab-containing treatment regimen, progression during the course of treatment, or progression within ≤ 6 months from the completion of any rituximab-containing (ie, the 'End Date' for any rituximab-containing therapy line as entered on the eCRF page 'Prior Cancer Therapies')
- Refractoriness to last prior therapy (yes vs no) - refractoriness to the last prior treatment is defined as having less than a PR (ie, SD or PD) as best overall response to the most recent therapy, progression during the course of treatment, or progression within ≤ 6 months from the completion of the most recent therapy line (ie, the 'End Date' for any prior therapy line as entered on the eCRF page 'Prior Cancer Therapies')
- Primary refractory
- Time to tafasitamab/LEN from end of last treatment (≤ 6 months vs > 6 months and ≤ 12 months vs > 12 months)
- ECOG: 0-1, ≥ 2
- Ann Arbor Disease Stage dichotomized (I and II vs III and IV)
- Prior Bendamustine (yes vs no)
- Time to tafasitamab/LEN from end of last bendamustine dose (< 9 months vs ≥ 9 months vs no bendamustine)

Some subgroups might not be run when less than 5 participants are included in one of the defined subgroup levels.

7.3.3. Sensitivity and Supportive Analyses for Primary Endpoint

The primary endpoint will be analyzed using the PPS population as a sensitivity analysis to the FAS.

7.4. Analysis of the Secondary Efficacy Parameters

Applicable for Part 2 (Group 2) and Part 4 (Group 6) only.

7.4.1. Objective Response Rate per Investigator Assessment

For Part 2 (Group 2) and Part 4 (Group 6), ORR is defined as the percentage of participants experiencing a CR/CMR or PR/PMR as determined by investigator assessment of response according to the Lugano criteria (Cheson et al 2014) at any time during the study before disease

progression and start of a new antilymphoma treatment. For Part 2 (Group 2), ORR was listed as both secondary and exploratory endpoints, it is considered as a secondary endpoint.

For Part 4 (Group 6) the ORR as determined by investigator assessment and its 90% exact binomial CI will be summarized. The 95% CI will be provided as reference. 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.

For Part 2 (Group 2) the ORR as determined by investigator assessment and its 95% exact binomial CI will be summarized. 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.

The population for this analysis is the FAS population.

7.4.2. Percent Reduction in SPD Investigator Assessment (Part 2 Group 2 Only)

The sum of the products of the longest perpendicular diameters (SPD) is calculated by sum the products of the two longest perpendicular diameters for each target lesion or any extranodal lesion.

Percent reduction in SPD from baseline in up to 6 target measurable nodes and extranodal sites assessed by CT as per investigator assessment of response according to the Lugano criteria (Cheson et al 2014) will be calculated per assessment and the highest reduction will be analyzed.

The population for this analysis is the FAS population.

7.4.3. Complete Response Rate

For Part 4 (Group 6), CRR is defined as the percentage of participants experiencing a CR/CMR as determined by an IRC according to the Lugano criteria (Cheson et al 2014) at any time during the study before disease progression and start of a new antilymphoma treatment.

The CRR as determined by an IRC and its 90% exact binomial CI will be summarized. The 95% CI will be provided as reference. 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 CRR.

CRR as determined by the investigator according to response criteria for lymphomas (Cheson et al 2014) will be summarized in the same manner.

The population for these analyses is the FAS population.

For Part 4 (Group 6), the subgroup analyses listed in Section 7.3.2 might be conducted for the CRR as determined by the IRC.

7.4.4. Progression-Free Survival

For Part 4 (Group 6), PFS is defined as the time from the date of first dose of study treatment until the first documented PD as determined by an IRC according to the Lugano criteria (Cheson et al 2014) or death due to any cause, whichever occurs first.

The population for this analysis is the FAS population. It will be analyzed using the PPS population as a sensitivity analysis to the FAS.

Censoring of PFS will follow FDA guidance (FDA 2015, FDA 2018) outlined in Table 6 and Table 7. The total number of participants who progressed or died and number of participants censored will be summarized. Kaplan-Meier estimation of median PFS as determined by an IRC and its 90% CI will be summarized. The 95% CI will be provided as reference.

PFS as determined by the investigator according to response criteria for lymphomas (Cheson et al 2014) will be summarized in the same manner.

The 90% CI will be calculated using the generalization of Brookmeyer and Crowley's method (1982) with log-log transformation (Klein and Moeschberger 1997). In addition, PFS rates at 6,12, 18, 24, 36, and 48 months (as applicable) may be provided along with the corresponding 2-sided 90% CIs.

For Part 4 (Group 6), the subgroup analyses listed in Section 7.3.2 might be conducted for the PFS as determined by the IRC.

Table 6: Evaluation and Censoring of Progression-Free Survival

Situation	Outcome	Date of Progression or Censoring
No baseline tumor assessments	Censored	Day 1
No valid postbaseline response assessments	Censored	Day 1
Progression documented between scheduled response assessments	Progressed	Date of first overall response of PD
No progression	Censored	Date of last valid radiologic assessment (not NE and not missing)
Study discontinuation for undocumented progression	Censored	Date of last valid radiologic assessment (not NE and not missing)
Treatment or study discontinuation for toxicity or other reason	Censored	Date of last valid radiologic assessment (not NE and not missing)
New anticancer treatment started	Censored	Date of last valid radiologic assessment (not NE and not missing) on/before starting a new anticancer treatment
Death before first progressive response assessment	Progressed	Date of death
Death between adequate response assessments	Progressed	Date of death
Death or progression after 2 or more missed assessments	Censored	Date of last valid radiologic assessment (not NE and not missing)

Table 7: Evaluation and Censoring of Progression-Free Survival (Sensitivity Analysis, Group 6 Only)

Situation	Outcome	Date of Progression or Censoring
No baseline tumor assessments	Censored	Day 1
No valid postbaseline response assessments	Censored	Day 1
Progression documented between scheduled response assessments	Progressed	Date of first overall response of PD
No progression	Censored	Date of last valid radiologic assessment (not NE and not missing)
Treatment or study discontinuation for undocumented progression	Censored	Date of last valid radiologic assessment (not NE and not missing)
Treatment or study discontinuation for toxicity or other reason	Censored	Date of last valid radiologic assessment (not NE and not missing)
New anticancer treatment started	Progressed	Date of last valid radiologic assessment (not NE and not missing) on/before starting a new anticancer treatment
Death before first progressive response assessment	Progressed	Date of death
Death between adequate response assessments	Progressed	Date of death
Death or progression after 2 or more missed assessments	Censored	Date of last valid radiologic assessment (not NE and not missing)

7.4.5. Duration of Response

For Part 4 (Group 6), DOR is defined as the time from first documented CR/CMR or PR/PMR until the date of first documented disease progression or death due to any cause, whichever occurs first, among participants who achieve a CR/CMR or PR/PMR as determined by an IRC according to the Lugano criteria (Cheson et al 2014).

Censoring of DOR will follow the same algorithm as the censoring of PFS (see Section 7.4.4). Total number of objective responders, number of participants who progressed or died, and number of participants censored will be summarized.

Kaplan-Meier estimation of the median DOR and its 90% CIs will be presented for participants who achieve an OR (CR/CMR or PR/PMR as per the Lugano classification [Cheson et al 2014]) per IRC assessment for the FAS population. The 95% CI will be provided as reference.

Another analysis will be run per investigator assessment for the FAS population.

DOR as determined by the investigator according to response criteria for lymphomas (Cheson et al 2014) will be summarized in the same manner.

7.4.6. Overall Survival

For Part 4 (Group 6), OS is defined as the time from first dose of study treatment (at least 1 dose of tafasitamab, LEN, parsaclisib, or R-CHOP) until death due to any cause.

The cause of death ("disease progression," "adverse event," or "other") will be summarized.

Participants who are not reported as a death at the time of the analysis cutoff will be censored at the earlier of the analysis cutoff and date of last known alive, regardless if a new antilymphoma therapy was started.

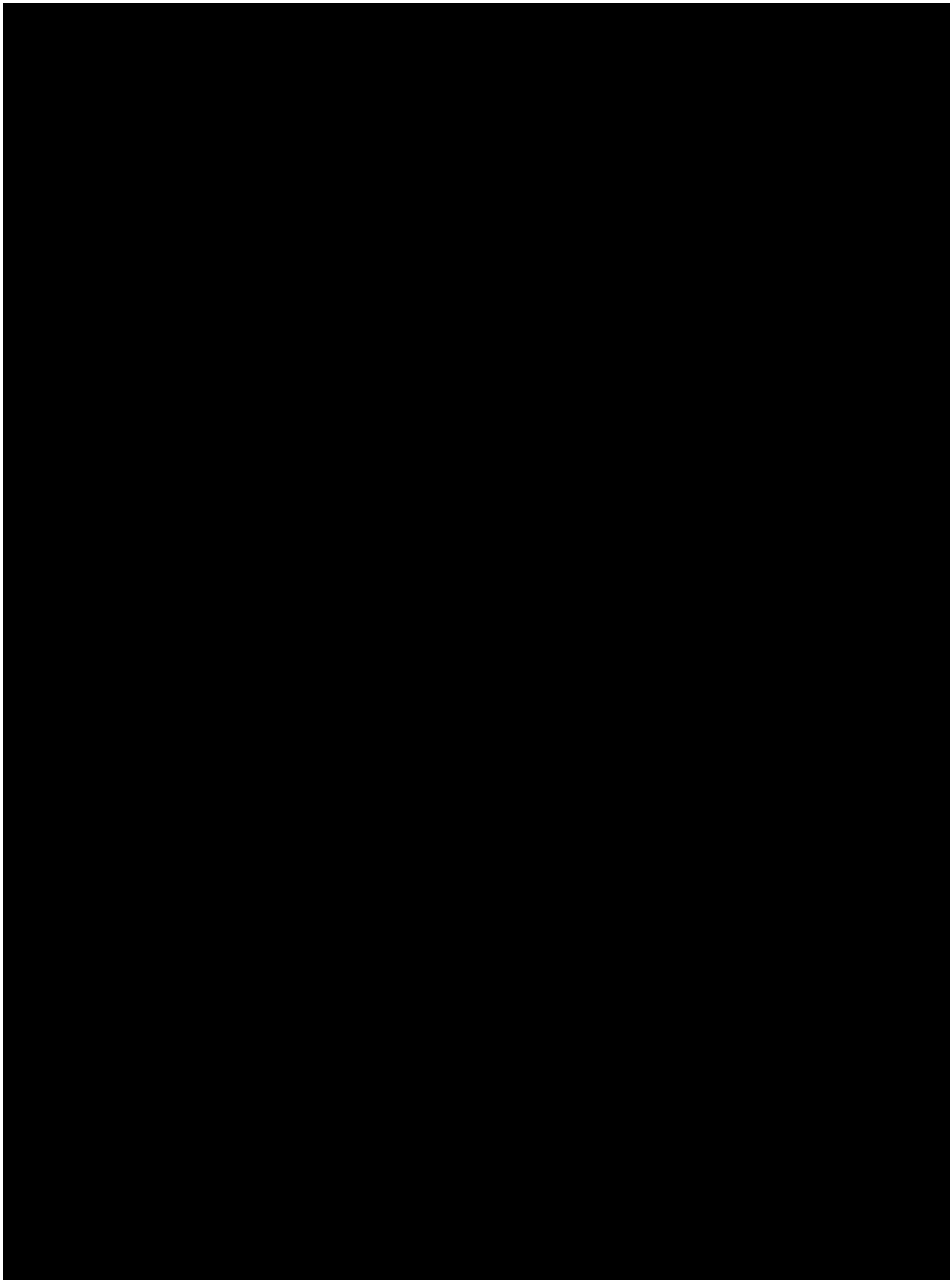
The last known alive date is defined as the later of the last study visit and the date the participant was last known alive from the "Survival Follow-Up," "End of Treatment," "End of Study," "Adverse event," and "Concomitant therapies" eCRFs.

Partial death dates will be handled using the rules described in Section 4.1.4.

Kaplan-Meier curve, median, and 90% CI will be presented on the FAS population. The 95% CI will be provided as reference.

7.5. Analysis of Exploratory Efficacy Variables







8. PHARMACOKINETICS

8.1. Pharmacokinetic Analysis

Details of the PK analysis will be described in a separate analysis plan, and results of the analysis will be described in a separate population PK report.

9. SAFETY AND TOLERABILITY

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

9.1. General Considerations

Safety analyses will be conducted for the safety population. No formal statistical testing will be performed.

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.

Quantitative safety variables and their changes from baseline (laboratory and vital signs) will be summarized with descriptive statistics. Abnormal values outside of established ranges will be flagged and tabulated based on predefined criteria.

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 until 90 days after the last dose of study drug (participants enrolled before Protocol Amendment 3 were followed only 30 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.

9.2.2. Dose-Limiting Toxicities

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

9.2.3. Adverse Events of Special Interest by eCRF

The number (%) of participants who had an AESI will be summarized.

"Whether an AE is an AESI" and "which AESI it is" should be found in the "Adverse Event" eCRF form. This information will be used to identify AESIs.

Adverse events of special interest for tafasitamab include the following:

- Tumor lysis syndrome
- Infusion-related reactions and allergic reactions to study drug ≥ Grade 3
- Cytokine release syndrome
- SPMs
- Hepatitis B reactivation
- Progressive multifocal leukoencephalopathy

Adverse events of special interest for LEN include SPMs.

Adverse events of special interest for parsaclisib include the following:

- Colitis
- Diarrhea
- Exfoliative dermatitis
- Febrile neutropenia
- Rash
- Intestinal perforation
- Pneumonitis
- Pneumonia
- PJP infection
- CMV infection
- Herpes simplex
- Varicella zoster virus infection

9.2.4. Adverse Events of Special Interest by Predefined List

A second method will also be used to identify AESI programmatically using standardised MedDRA queries, custom MedDRA queries, and/or selected PTs.

9.2.4.1. Tafasitamab

Adverse events of special interest for tafasitamab include the following:

Standardised MedDRA Queries

- Tumour lysis syndrome
- Hypersensitivity (≥ Grade 3)

Preferred terms

- Cytokine release syndrome
- Second primary malignancy
- Hepatitis B reactivation
- Progressive multifocal leukoencephalopathy

9.2.4.2. Lenalidomide

Adverse events of special interest for LEN include the following:

- Second primary malignancy

The analysis of AESI by category and PT will be carried out as described in Section 9.2.3.

9.2.4.3. Parsaclisib

Adverse events of special interest for parsaclisib include the following:

- Colitis
- Diarrhea
- Exfoliative dermatitis
- Febrile neutropenia
- Rash
- Intestinal perforation
- Pneumonitis
- Pneumonia
- PJP infection
- CMV infection
- Herpes simplex
- Varicella zoster virus infection

9.2.5. Adverse Event Summaries

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

- Number (%) of participants who had any TEAEs

- Number (%) of participants who had any DLTs
- 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 tafasitamab
- Number (%) of participants who had any TEAEs related to parsaclisib
- Number (%) of participants who had any TEAEs related to LEN
- Number (%) of participants who had any TEAEs related to R-CHOP
- Number (%) of participants who had any serious TEAEs related to tafasitamab
- Number (%) of participants who had any serious TEAEs related to parsaclisib
- Number (%) of participants who had any serious TEAEs related to LEN
- Number (%) of participants who had any serious TEAEs related to R-CHOP
- Number (%) of participants who had any Grade 3 or higher TEAEs related to tafasitamab
- Number (%) of participants who had any Grade 3 or higher TEAEs related to parsaclisib
- Number (%) of participants who had any Grade 3 or higher TEAEs related to LEN
- Number (%) of participants who had any Grade 3 or higher TEAEs related to R-CHOP
- Number (%) of participants who had any fatal 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 had LEN dose reductions because of TEAEs
- Number (%) of participants who had R-CHOP dose reductions because of TEAEs
- Number (%) of participants who had tafasitamab dose interruption because of TEAEs
- Number (%) of participants who had parsaclisib dose interruption because of TEAEs
- Number (%) of participants who had LEN dose interruption because of TEAEs
- Number (%) of participants who had R-CHOP dose interruption because of TEAEs
- Number (%) of participants who discontinued from tafasitamab because of TEAEs
- Number (%) of participants who discontinued from parsaclisib because of TEAEs
- Number (%) of participants who discontinued from LEN because of TEAEs
- Number (%) of participants who discontinued from R-CHOP because of TEAEs

The following summaries will be produced by MedDRA term:

- 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 TEAEs by MedDRA SOC, PT, and CTCAE grade category
- 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 tafasitamab 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 and PT
- Summary of LEN treatment-related TEAEs by MedDRA SOC and PT
- Summary of R-CHOP treatment-related TEAEs by MedDRA SOC and PT
- Summary of Grade 3 or higher tafasitamab treatment-related TEAEs by MedDRA SOC and PT
- Summary of tafasitamab 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 withdrawal from the study by MedDRA SOC and PT
- Summary of TEAEs leading to tafasitamab dose reduction by MedDRA SOC and PT
- Summary of TEAEs leading to parsaclisib dose reduction by MedDRA SOC and PT
- Summary of TEAEs leading to LEN dose reduction by MedDRA SOC and PT
- Summary of TEAEs leading to R-CHOP dose reduction by MedDRA SOC and PT
- Summary of TEAEs leading to tafasitamab dose interruption by MedDRA SOC and PT
- Summary of TEAEs leading to parsaclisib dose interruption by MedDRA SOC and PT
- Summary of TEAEs leading to LEN dose interruption by MedDRA SOC and PT
- Summary of TEAEs leading to R-CHOP dose interruption by MedDRA SOC and PT

- Summary of TEAEs leading to discontinuation of tafasitamab by MedDRA SOC and PT
- Summary of TEAEs leading to discontinuation of parsaclisib by MedDRA SOC and PT
- Summary of TEAEs leading to discontinuation of LEN by MedDRA SOC and PT
- Summary of TEAEs leading to discontinuation of R-CHOP by MedDRA SOC and PT
- Summary of TEAEs requiring concomitant medications by MedDRA SOC and PT
- Summary of Protocol-defined TEAEs of special interest by maximum severity

9.3. Clinical Laboratory Tests

9.3.1. 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.

9.3.2. 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, neutrophils, ALT, and AST.

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.

9.3.3. 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.

9.4. Vital Signs

Values at each scheduled visit, change, and percentage change from baseline for vital signs, including systolic blood pressure, diastolic blood pressure, pulse, temperature, SpO_2, and weight will be summarized descriptively.

Normal ranges for vital sign values are defined in Table 8. 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 8: Normal Ranges for Vital Sign Values

Parameter	High Threshold	Low Threshold
Systolic blood pressure	< 140 mmHg	≥ 90mmHg
Diastolic blood pressure	< 90 mmHg	≥ 60 mmHg
Pulse	≤ 100 bpm	≥ 55 bpm
Temperature	≤ 38°C	≥ 36.1°C
SpO_2	—	≥ 88%

9.5. Electrocardiograms

Twelve-lead ECGs, including PR, RR, QT, QRS, QTcB, and QTcF intervals, 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.

Normal ranges for ECG values are defined in Table 9. 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, QTcB, and QTcF values, defined as absolute values > 450 millisecond, > 500 millisecond, or change from baseline > 30 millisecond, will be summarized.

Table 9: Normal Ranges for Electrocardiogram Intervals

Parameter	High Threshold	Low Threshold
PR	≤ 220 ms	≥ 75 ms
RR	≤ 1330 ms	≥ 600 ms
QT	≤ 500 ms	≥ 300 ms
QRS	≤ 120 ms	≥ 50 ms
QTcB, QTcF	≤ 450 ms	≥ 295 ms

10. INTERIM ANALYSES

For participants treated with tafasitamab plus parsaclisib, an interim futility analysis was originally planned when the first 9 participants (Part 2 Group 4a at RP2D and Part 3 Group 4b combined) have been evaluated for response or have permanently discontinued study. Part 3 Group 4b was supposed to be terminated for futility if ≤ 3 of the 9 participants had responded (ie, CR/CMR or PR/PMR) based on assessments provided by investigators. If the true ORR was 65% for participants treated at RP2D in Group 4a and Group 4b, then with 18 total participants, there was approximately 85% probability of observing the lower bound of the 95% CI of ORR ≥ 30%.

Recruitment for treatment with tafasitamab plus parsaclisib was closed based on the sponsor's decision before the accrual of 9 participants, and this interim analysis will therefore not be performed.

10.1. Overview of Interim Analyses

No formal interim analysis is planned in this study.

11. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 10.

Table 10: Statistical Analysis Plan Versions

SAP Version	Date
Original	04 OCT 2023
Amendment 1	19 DEC 2024

11.1. Changes to Protocol-Defined Analyses

Part 1 Group 2 was removed from Part 1 dosing finding to Part 2 Group 2 with 6 evaluable participants as described in Section 3.4.1.

11.2. Changes to the Statistical Analysis Plan

11.2.1. Amendment 1

- Section 1, Section 3.1.2, Section 3.4.1, Figure 2, Section 5.2, Section 5.3.4, Section 6.6.1, Section 7.4, and Section 7.5.4 were updated to reflect the change in Group 2 due to Protocol Amendment 7. For Section 1, text was simplified based on detailed information provided in Section 3.1.
- Table 1, Section 3.1, Figure 1, and Section 6.6.2were updated to align with the Protocol Amendment 7.
- Section 5.3.8 was added for the recommended clinical dose-evaluable population for Group 2 to align with Protocol Amendment 7.
- For Section 7.1, timing of the primary analysis was updated for Group 6 and information of Group 2 primary analysis was added.
- For Section 7.3.2, the primary refractory subgroup analysis was added.
- For Section 7.4.1, the ORR secondary endpoint was extended to Group 2 due to Protocol Amendment 7.
- Section 7.4.2 was added for percent reduction in SPD as a Group 2 secondary efficacy endpoint to align with Protocol Amendment 7.
- For Section 7.4.4, PPS analysis was added as sensitivity analysis.
- Appendix A was updated reflect the additional endpoint for Group 2 to align with Protocol Amendment 7. Figure 4.7.x, "Swimmer Plots for Duration of Response per IRC (Lugano 2014 Criteria)" was added for Groups 2 and 6.
- Other, minor, administrative changes have been incorporated throughout the SAP.

12. REFERENCES

Brookmeyer R, Crowley J. A confidence interval for the median survival time. Biometrics 1982;38:29-41.

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.

Cheson BD, Pfistner B, Juweid ME, et al. Revised response criteria for malignant lymphoma. J Clin Oncol 2007;25:579-586.

Duell J, Maddocks KJ, González-Barca E, et al. Long-term outcomes from the phase II L-MIND study of tafasitamab (MOR208) plus lenalidomide in patients with relapsed or refractory diffuse large B-cell lymphoma. Haematologica 2021;106:2417-2426.

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: Integrated Summary of Effectiveness. 2015.

Klein JP, Moeschberger ML. Survival Analysis: Techniques for Censored and Truncated Data. Springer-Verlag; 1997.

Liu S, Yuan, Y. Bayesian optimal interval designs for phase I clinical trials. J R Stat Soc C 2015;64:507-523.

Tobinai K, Igarashi T, Itoh K, et al. Japanese multicenter phase II and pharmacokinetic study of rituximab in relapsed or refractory patients with aggressive B-cell lymphoma. Ann Oncol 2004;15:821-830.

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 v1.12.

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.

In developing numbering, the first 2 numbers follow medical writing conventions for numbering and keep standard table numbering the same.

The 3rd digit within the section represents particular analysis outputs.

The 4th digit within the section represents analysis cohorts with the following convention for the titles (see Table 11).

Table 11: Naming Convention for Titles in Tables, Figures, and Listings for .x Numbering

Value for .x	Title to be added
1	Group 1 R/R NHL: Weight-Based Dose Monotherapy
2	Group 2 R/R DLBCL: Tafasitamab Q2W/Q4W + Lenalidomide
3	Group 3 R/R DLBCL: Tafasitamab + Lenalidomide
4	Group 4 R/R DLBCL: Tafasitamab + Parsaclisib
5	Group 5 Untreated DLBCL: R-CHOP + Tafasitamab + Lenalidomide
6	Group 6 R/R DLBCL: Tafasitamab + Lenalidomide

Tables

Table No.	Title	Population	Standard
Baseline and Demographic Characteristics			
1.1.1.x (x=1-6)	Analysis Populations – Title X	Screened	X
1.1.2.x (x=1-6)	Summary of Participant Disposition – Title X	Screened	X
1.1.3.x (x=1-6)	Summary of Number of Participants Enrolled by Site – Title X	FAS	X
1.1.4.x (x=1-6)	Summary of Protocol Deviations – Title X	FAS	X
1.2.1.x (x=1-6)	Summary of Demographics and Baseline Characteristics – Title X	FAS	X
1.3.1.x (x=1-6)	Summary of Baseline Disease Characteristics – Title X	FAS	X
1.3.2.x (x=1-6)	Summary of Disease History – Title X	FAS	

Table No.	Title	Population	Standard
1.3.3.x (x=1-6)	Summary of Prior Systemic Cancer Therapy by WHO Drug Class and Preferred Term – Title X	FAS	
1.3.4.x (x=1-6)	Summary of Participant With a Transformed Lymphoma – Title X	FAS	
1.3.5.x (x=1-6)	Summary of Flow Cytometry Performed Quantitatively at Screening – Title X	FAS	
1.3.6.x (x=1-6)	Summary of Flow Cytometry Performed Qualitatively at Screening – Title X	FAS	
1.4.1.x (x=1-6)	Summary of Prior Medications – Title X	FAS	X
1.4.2.x (x=1-6)	Summary of Concomitant Medications – Title X	FAS	X
1.5.1.x (x=1-6)	Summary of General Medical History – Title X	FAS	X
Efficacy			
2.1.1.x (x=6)	Summary of Best Overall Response, Objective Response Rate, Complete Response Rate, and Disease Control Rate per IRC (Lugano 2014 Criteria) – Title X	FAS	
2.1.2.x (x=6)	Summary of Best Overall Response, Objective Response Rate, Complete Response Rate, and Disease Control Rate per IRC (Lugano 2014 Criteria) – Sensitivity Analysis – Title X	PPS	
2.2.1.x (x=6)	Summary of Duration of Response per IRC (Lugano 2014 Criteria) – Title X	FAS	
2.2.2.x.1 (x=6)	Summary of Progression-Free Survival per IRC (Lugano 2014 Criteria) – Title X	FAS	
2.2.2.x.2 (x=6)	Summary of Progression-Free Survival per IRC (Lugano 2014 Criteria) – Sensitivity Analysis – Title X	PPS	
2.2.3.x (x=6)	Summary of Overall Survival – Title X	FAS	
2.2.4.x (x=6)	Summary of Best Overall Response and Objective Response Rate per Investigator (Lugano 2014 Criteria) – Title X	FAS	
2.2.5.x (x=6)	Summary of Duration of Response per Investigator (Lugano 2014 Criteria) – Title X	FAS	
2.2.6.x (x=6)	Summary of Progression-Free Survival per Investigator (Lugano 2014 Criteria) – Title X	FAS	
2.2.7.x (x=2)	Summary of Best Percent Reduction in SPD per Investigator (Lugano 2014 Criteria) – Title X	FAS	
2.3.1.x (x=3,6)	Summary of Best Overall Response and Objective Response Rate per IRC (Cheson 2007 Criteria) – Title X	FAS	
2.3.2. x (x=3,6)	Summary of Progression-Free Survival per IRC (Cheson 2007 Criteria) – Title X	FAS	
2.3.3.x (x=3,6)	Summary of Duration of Response per IRC (Cheson 2007 Criteria) – Title X	FAS	

Table No.	Title	Population	Standard
2.3.4.x (x=1-5)	Summary of Best Overall Response and Objective Response Rate per Investigator (Lugano 2014 Criteria) – Title X	FAS	
2.3.5.x (x=1-5)	Summary of Progression-Free Survival per Investigator (Lugano 2014 Criteria) – Title X	FAS	
2.3.6.x (x=1-5)	Summary of Duration of Response per Investigator (Lugano 2014 Criteria) – Title X	FAS	
2.3.7.x (x=6)	Summary of Time to Next Treatment – Title X	FAS	
2.3.8.x (x=1-6)	Summary of Immunogenicity – Title X	FAS	
2.3.9.1.x (x=6)	Summary of Subgroup Analyses for Objective Response Rate per IRC – Title X	FAS	
2.3.9.2.x (x=6)	Summary of Subgroup Analyses for Complete Response per IRC – Title X	FAS	
2.3.9.3.x (x=6)	Summary of Subgroup Analyses for Progression-Free Survival per IRC – Title X	FAS	
2.3.10.x (x=6)	Summary of Concordance Between IRC and INV Assessment of Best Objective Response (Lugano 2014 Criteria) – Title X	FAS	
2.3.11.x (x=6)	Summary of Duration of Survival Follow-Up – Title X	FAS	
Safety			
3.1.1.1.x (x=1-6)	Summary of Exposure and Duration of Exposure to Tafasitamab – Title X	Safety	X
3.1.1.2.x (x=4)	Summary of Exposure and Duration of Exposure to Parsaclisib – Title X	Safety	X
3.1.1.3.x (x=3,5,6)	Summary of Exposure and Duration of Exposure to Lenalidomide – Title X	Safety	X
3.1.1.4.x (x=5)	Summary of Exposure and Duration of Exposure to R-CHOP – Title X	Safety	X
3.1.2.1.x (x=4)	Summary of Compliance with Parsaclisib – Title X	Safety	X
3.1.2.2.x (x=3,5,6)	Summary of Compliance with Lenalidomide – Title X	Safety	X
3.2.1.x (x=1-6)	Overall Summary of Treatment-Emergent Adverse Events – Title X	Safety	X
3.2.2.x (x=1-6)	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.3.x (x=1-6)	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency – Title X	Safety	X
3.2.4.x (x=1-6)	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity – Title X	Safety	X

Table No.	Title	Population	Standard
3.2.5.x (x=1-6)	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.6.x (x=1-6)	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency – Title X	Safety	X
3.2.7.x (x=1-6)	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.8.x (x=1-6)	Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency – Title X	Safety	X
3.2.9.x (x=1-6)	Summary of Tafasitamab Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.10.x (x=1-6)	Summary of Tafasitamab Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency – Title X	Safety	X
3.2.11.1.x (x=1-6)	Summary of Tafasitamab Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity – Title X	Safety	X
3.2.12.1.x (x=1-6)	Summary of Grade 3 or Higher Tafasitamab Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.13.1.x (x=1-6)	Summary of Tafasitamab Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.11.2.x (x=4)	Summary of Parsaclisib Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity – Title X	Safety	X
3.2.12.2.x (x=4)	Summary of Grade 3 or Higher Parsaclisib Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.13.2.x (x=4)	Summary of Parsaclisib Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.11.3.x (x=3,5,6)	Summary of Lenalidomide Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity – Title X	Safety	X
3.2.12.3.x (x=3,5,6)	Summary of Grade 3 or Higher Lenalidomide Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.13.3.x (x=3,5,6)	Summary of Lenalidomide Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.11.4.x (x=5)	Summary of R-CHOP Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity – Title X	Safety	X

Table No.	Title	Population	Standard
3.2.12.4.x (x=5)	Summary of Grade 3 or Higher R-CHOP Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.13.4.x (x=5)	Summary of R-CHOP Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.14.x (x=1-6)	Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.15.1.x (x=1-6)	Summary of Tafasitamab Treatment-Related Treatment-Emergent Adverse Events Leading to Discontinuation of Tafasitamab by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.15.2.x (x=4)	Summary of Parsaclisib Treatment-Related Treatment-Emergent Adverse Events Leading to Discontinuation of Parsaclisib by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.15.3.x (x=3,5,6)	Summary of Lenalidomide Treatment-Related Treatment-Emergent Adverse Events Leading to Discontinuation of Lenalidomide by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.15.4.x (x=5)	Summary of R-CHOP Treatment-Related Treatment-Emergent Adverse Events Leading to Discontinuation of R-CHOP by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.16.1.x (x=1-6)	Summary of Treatment-Emergent Adverse Events Leading to Tafasitamab Dose Reduction by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.16.2.x (x=4)	Summary of Treatment-Emergent Adverse Events Leading to Parsaclisib Dose Reduction by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.16.3.x (x=3,5,6)	Summary of Treatment-Emergent Adverse Events Leading to Lenalidomide Dose Reduction by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.16.4.x (x=5)	Summary of Treatment-Emergent Adverse Events Leading to R-CHOP Dose Reduction by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.17.1.x (x=1-6)	Summary of Treatment-Emergent Adverse Events Leading to Tafasitamab Dose Interruption by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.17.2.x (x=4)	Summary of Treatment-Emergent Adverse Events Leading to Parsaclisib Dose Interruption by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.17.3.x (x=3,5,6)	Summary of Treatment-Emergent Adverse Events Leading to Lenalidomide Dose Interruption by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.17.4.x (x=5)	Summary of Treatment-Emergent Adverse Events Leading to R-CHOP Dose Interruption by MedDRA System Organ Class and Preferred Term – Title X	Safety	X
3.2.18.x (x=1-6)	Summary of Treatment-Emergent Adverse Events Requiring Concomitant Medications by MedDRA System Organ Class and Preferred Term – Title X	Safety	X

Table No.	Title	Population	Standard
3.2.19.1.x (x=1-6)	Summary of Tafasitamab Treatment-Emergent Adverse Events of Special Interest by Category and Preferred Term Based on eCRF – Title X	Safety	X
3.2.19.2.x (x=4)	Summary of Parsaclisib Treatment-Emergent Adverse Events of Special Interest by Category and Preferred Term Based on eCRF – Title X	Safety	X
3.2.19.3.x (x=3,5,6)	Summary of Lenalidomide Treatment-Emergent Adverse Events of Special Interest by Category and Preferred Term Based on eCRF – Title X	Safety	X
3.2.20.1.x (x=1-6)	Summary of Tafasitamab Treatment-Emergent Adverse Events of Special Interest by Category and Preferred Term Based on Standardised MedDRA Queries – Title X	Safety	X
3.2.20.2.x (x=4)	Summary of Parsaclisib Treatment-Emergent Adverse Events of Special Interest by Category and Preferred Term Based on Standardised MedDRA Queries – Title X	Safety	
3.2.20.3.x (x=3,5,6)	Summary of Lenalidomide Treatment-Emergent Adverse Events of Special Interest by Category and Preferred Term Based on Standardised MedDRA Queries – Title X	Safety	
3.3.1.1.x (x=1-6)	Summary of Laboratory Values – Hematology – Title X	Safety	X
3.3.1.2.x (x=1-6)	Summary of Laboratory Values – Chemistry – Title X	Safety	X
3.3.1.3.x (x=1-6)	Summary of Laboratory Values – Coagulation – Title X	Safety	X
3.3.1.4.x (x=1-6)	Summary of Laboratory Values – Urinalysis – Title X	Safety	X
3.3.2.1.x (x=1-6)	Shift Summary of Hematology Laboratory Values in CTCAE Grade - to the Worst Abnormal Value – Title X	Safety	X
3.3.2.2.x (x=1-6)	Shift Summary of Chemistry Laboratory Values in CTCAE Grade - to the Worst Abnormal Value – Title X	Safety	X
3.3.2.3.x (x=1-6)	Shift Summary of Coagulation Laboratory Values in CTCAE Grade - to the Worst Abnormal Value – Title X	Safety	X
3.3.2.4.x (x=1-6)	Treatment-Emergent Worsening of Laboratory Abnormalities – Hematology – Title X	Safety	X
3.3.2.5.x (x=1-6)	Treatment-Emergent Worsening of Laboratory Abnormalities – Chemistry – Title X	Safety	X
3.3.2.6.x (x=1-6)	Treatment-Emergent Worsening of Laboratory Abnormalities – Coagulation – Title X	Safety	X
3.3.3.1.x (x=1-6)	Shift Summary of Hematology Laboratory Values in CTCAE Grade - to the Last Value – Title X	Safety	X
3.3.3.2.x (x=1-6)	Shift Summary of Chemistry Laboratory Values in CTCAE Grade - to the Last Value – Title X	Safety	X
3.3.3.3.x (x=1-6)	Shift Summary of Coagulation Laboratory Values in CTCAE Grade - to the Last Value – Title X	Safety	X

Table No.	Title	Population	Standard
3.4.1.x (x=1-6)	Summary of Systolic Blood Pressure – Title X	Safety	X
3.4.2.x (x=1-6)	Summary of Diastolic Blood Pressure – Title X	Safety	X
3.4.3.x (x=1-6)	Summary of Pulse – Title X	Safety	X
3.4.5.x (x=1-6)	Summary of Body Temperature – Title X	Safety	X
3.4.6.x (x=1-6)	Summary of Weight – Title X	Safety	X
3.4.7.x (x=1-6)	Summary of Oxygen Saturation – Title X	Safety	X
3.5.1.x (x=1-6)	Summary of PR Interval (ms) From 12-Lead ECG – Title X	Safety	X
3.5.2.x (x=1-6)	Summary of QRS Interval (ms) From 12-Lead ECG – Title X	Safety	X
3.5.3.x (x=1-6)	Summary of QT Interval (ms) From 12-Lead ECG – Title X	Safety	X
3.5.4.x (x=1-6)	Summary of QTcB Interval (ms) From 12-Lead ECG – Title X	Safety	X
3.5.5.x (x=1-6)	Summary of QTcF Interval (ms) From 12-Lead ECG – Title X	Safety	X
3.5.6.x (x=1-6)	Summary of RR Interval (ms) From 12-Lead ECG – Title X	Safety	X
3.5.7.x (x=1-6)	Summary of Outliers of QT, QTcB, and QTcF Interval Values (ms) From 12-Lead ECG – Title X	Safety	X
3.5.8.x (x=1-6)	Summary of Clinically Significant ECG Abnormality – Title X	Safety	X

Figures

Figure No.	Title
4.2.x.1 (x=6)	Kaplan-Meier Estimates of Progression-Free Survival per IRC (Lugano 2014 Criteria) – Title X
4.2.x.2 (x=6)	Kaplan-Meier Estimates of Duration of Response per IRC (Lugano 2014 Criteria) – Title X
4.2.x.3 (x=6)	Kaplan-Meier Estimates of Overall Survival (Lugano 2014 Criteria) – Title X
4.2.x.4 (x=6)	Kaplan-Meier Estimates of Duration of Response per Investigator (Lugano 2014 Criteria) – Title X
4.2.x.5 (x=6)	Kaplan-Meier Estimates of Progression-Free Survival per Investigator (Lugano 2014 Criteria) – Title X

Figure No.	Title
4.3.x.1 (x=3,6)	Kaplan-Meier Estimates of Progression-Free Survival per IRC (Cheson 2007 Criteria) – Title X
4.3.x.2 (x=3,6)	Kaplan-Meier Estimates of Duration of Response per IRC (Cheson 2007 Criteria) – Title X
4.3.x.3 (x=1,3,4,5)	Kaplan-Meier Estimates of Progression-Free Survival per Investigator (Lugano 2014 Criteria) – Title X
4.3.x.4 (x=1,3,4,5)	Kaplan-Meier Estimates of Duration of Response per Investigator (Lugano 2014 Criteria) – Title X
4.3.x (x=6)	Kaplan-Meier Estimates of Time to Next Treatment – Title X
4.6.x.1 (x=1-6)	Line Graph of Selected Laboratory Values by Study Visit: Hemoglobin – Title X
4.6.x.2 (x=1-6)	Line Graph of Selected Laboratory Values by Study Visit: Platelet Counts – Title X
4.6.x.3 (x=1-6)	Line Graph of Selected Laboratory Values by Study Visit: Circulating Lymphocyte Counts – Title X
4.6.x.4 (x=1-6)	Line Graph of Selected Laboratory Values by Study Visit: Neutrophils – Title X
4.6.x.5 (x=1-6)	Line Graph of Selected Laboratory Values by Study Visit: ALT – Title X
4.6.x.6 (x=1-6)	Line Graph of Selected Laboratory Values by Study Visit: AST – Title X
4.7.x (x=2,6)	Swimmer Plots Duration of Response per IRC (Lugano 2014 Criteria)

Listings

Listing No.	Title
2.1.1.x (x=1-6)	Participant Enrollment and Disposition Status – Title X
2.1.2.x (x=1-6)	Participant Inclusion and Exclusion Criteria Violations – Title X
2.2.x (x=1-6)	Protocol Deviations – Title X
2.3.x (x=1-6)	Analysis Population – Title X
2.4.1.x (x=1-6)	Demographic and Baseline Characteristics – Title X
2.4.2.x (x=1-6)	Initial Disease History – Title X
2.4.3.x (x=1-6)	Current Disease History – Title X

Listing No.	Title
2.4.4.x (x=1-6)	Prior Radiation Treatment – Title X
2.4.5.x (x=1-6)	Prior Systemic Therapy – Title X
2.4.6.x (x=1-6)	Prior Surgery or Surgical Procedure – Title X
2.4.7.x (x=1-6)	Prior Stem Cell Transplant – Title X
2.4.8.x (x=1-6)	Medical History – Title X
2.4.9.x (x=1-6)	Prior and Concomitant Medication – Title X
2.4.10.x (x=3,6)	Refractoriness to Prior Therapies and Early/Late Relapse After Diagnosis of DLBCL – Title X
2.4.11.x (x=1-6)	Tafasitamab Premedication – Title X
2.5.1.1.x (x=1-6)	Study Drug Compliance – Tafasitamab – Title X
2.5.1.2.x (x=1-6)	Study Drug Administration – Tafasitamab – Title X
2.5.1.3.x (x=1-6)	Average Dosing and Relative Dosing Intensity– Tafasitamab – Title X
2.5.2.1.x (x=4)	Study Drug Compliance – Parsaclisib – Title X
2.5.2.2.x (x=4)	Study Drug Administration – Parsaclisib – Title X
2.5.2.3.x (x=4)	Average Dosing and Relative Dosing Intensity– Parsaclisib – Title X
2.5.3.1.x (x=3,5,6)	Study Drug Compliance – Lenalidomide – Title X
2.5.3.2.x (x=3,5,6)	Study Drug Administration – Lenalidomide – Title X
2.5.3.3.x (x=3,5,6)	Average Dosing and Relative Dosing Intensity– Lenalidomide – Title X
2.5.4.2.x (x=5)	Study Drug Administration – R-CHOP – Title X
2.6.1.x (x=1-6)	Deaths – Title X
2.6.2.1.x (x=1-6)	Best Overall Response, Duration of Response, and Progression-Free Survival per Investigator (Lugano 2014 Criteria) – Title X
2.6.2.2.x (x=1-6)	Overall Response Assessment by Visit per Investigator (Lugano 2014 Criteria) – Title X

Listing No.	Title
2.6.3.1.x (x=6)	Best Overall Response, Duration of Response, and Progression-Free Survival per IRC (Lugano 2014 Criteria) – Title X
2.6.3.2.x (x=6)	Overall Response Assessment by Visit per IRC (Lugano 2014 Criteria) – Title X
2.6.4.1.x (x=3,6)	Best Overall Response, Duration of Response, and Progression-Free Survival per IRC (Cheson 2007 Criteria) – Title X
2.6.4.2.x (x=3,6)	Overall Response Assessment by Visit per IRC (Cheson 2007 Criteria) – Title X
2.6.5.x (x=1-6)	Response Assessment: Target Lesions – Title X
2.6.6.x (x=1-6)	Response Assessment: Nontarget Lesions – Title X
2.6.7.x (x=1-6)	Response Assessment: New Lesions – Title X
2.6.8.x (x=1-6)	ECOG Status – Title X
2.6.9.x (x=1-6)	Immunogenicity Data – Title X
2.7.1.x (x=1-6)	Adverse Events – Title X
2.7.2.x (x=1-6)	Dose-Limiting Toxicities – Title X
2.7.3.x (x=1-6)	Serious Adverse Events – Title X
2.7.4.x (x=1-6)	Grade 3 and Higher Adverse Events – Title X
2.7.5.x (x=1-6)	Fatal Adverse Events – Title X
2.7.6.x (x=1-6)	Treatment-Related Adverse Events – Title X
2.7.7.1.x (x=1-6)	Adverse Events Leading to Interruption, Reduction, or Discontinuation of Tafasitamab – Title X
2.7.7.2.x (x=1-6)	Adverse Events Leading to Interruption, Reduction, or Discontinuation of Lenalidomide – Title X
2.7.7.3.x (x=1-6)	Adverse Events Leading to Interruption, Reduction, or Discontinuation of Parsaclisib – Title X
2.7.7.4.x (x=1-6)	Adverse Events Leading to Interruption, Reduction, or Discontinuation of R-CHOP – Title X
2.7.8.1.x (x=1-6)	Adverse Events of Special Interest of Tafasitamab (eCRF and search terms) – Title X
2.7.8.2.x (x=1-6)	Adverse Events of Special Interest of Lenalidomide (eCRF and search terms) – Title X

Listing No.	Title
2.7.8.3.x (x=1-6)	Adverse Events of Special Interest of Parsaclisib (eCRF and search terms) – Title X
2.7.8.5.x (x=1-6)	Adverse Events of Special Interest: MedDRA Preferred Terms and Standardised MedDRA Queries per Study Drug – Title X
2.8.1.x (x=1-6)	Clinical Laboratory Values – Hematology – Title X
2.8.2.x (x=1-6)	Clinical Laboratory Values – Chemistry – Title X
2.8.3.x (x=1-6)	Abnormal Clinical Laboratory Values – Title X
2.8.4.x (x=1-6)	Potential Hy's Law Events – Title X
2.8.5.x (x=1-6)	PK Blood Sampling Times – Title X
2.8.6.x (x=1-6)	PK Urine Sampling Times – Title X
2.8.7.x (x=1-6)	Central Laboratory Collection Times – Title X
2.9.1.x (x=1-6)	Vital Signs – Title X
2.9.2.x (x=1-6)	Abnormal Vital Sign Values – Title X
2.9.3.x (x=1-6)	Alert Vital Sign Values – Title X
2.10.1.x (x=1-6)	12-Lead ECG Values – Title X
2.10.2.x (x=1-6)	Abnormal 12-Lead ECG Values – Title X
2.10.3.x (x=1-6)	Alert 12-Lead ECG Values – Title X
2.11.1.x (x=1-6)	Physical Examinations – Title X
2.11.2.x (x=1-6)	Body Weight – Title X

APPENDIX B. BOIN OPERATING CHARACTERISTICS

Using the BOIN package (CRAN v2.7.2) in R (v3.6.1), the following are the operating characteristic estimates regarding expected SS, probability of dose selection, and expected number of participants and DLTs per study assuming a cohort size of 3.

In each scenario, the probability of dose selection is highest for the dose that is closest to the target DLT rate of 30% without going over.

Under Scenario 1, the probability of dose selection is highest for dose level 1, with an expected SS of 5.8 and 1.7 expected DLTs.

Under Scenario 2, the probability of dose selection is highest for dose level 2, with an expected SS of 5.2 and 1.5 expected DLTs.

Under Scenario 3, the probability of dose selection is highest for dose level 5, with an expected SS of 5.0232 and 1.2608 expected DLTs.

Table B1: Operating Characteristics in Scenario 1

	Dose Level			
	-1	**1**	**2**	**3**
Pr(DLT)	10%	30%	45%	60%
Pr(Selection)	19.9%	58.0%	18.9%	2.8%
Expected SS	5.1	5.8	2.6	0.4
Expected DLTs	0.5	1.7	1.2	0.3

Pr(DLT) is the probability of a DLT.
Pr(Selection) is the probability of dose selection.
Expected SS is the expected sample size.
Expected DLTs is the expected number of DLTs.

Table B2: Operating Characteristics in Scenario 2

	Dose Level			
	-1	**1**	**2**	**3**
Pr(DLT)	5%	10%	30%	50%
Pr(Selection)	1.9%	23.9%	55.0%	19.2%
Expected SS	3.5	4.8	5.2	2.1
Expected DLTs	0.2	0.5	1.5	1.0

Pr(DLT) is the probability of a DLT.
Pr(Selection) is the probability of dose selection.
Expected SS is the expected sample size.
Expected DLTs is the expected number of DLTs.

Table B3: Operating Characteristics in Scenario 3

	Dose Level			
	-1	**1**	**2**	**3**
Pr(DLT)	5%	10%	20%	30%
Pr(Selection)	2.3%	13.9%	34.9%	48.9%
Expected SS	3.5	4.2	4.5	3.4
Expected DLTs	0.2	0.4	0.9	1.0

Pr(DLT) is the probability of a DLT.
Pr(Selection) is the probability of dose selection.
Expected SS is the expected sample size.
Expected DLTs is the expected number of DLTs.