**Official Title:** A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of Tafasitamab Plus Lenalidomide in Addition to Rituximab Versus Lenalidomide in Addition to Rituximab in Patients with Relapsed/Refractory (R/R) Follicular Lymphoma Grade 1 to 3a or R/R Marginal Zone Lymphoma

**NCT Number:** NCT04680052

**Document Date:** Statistical Analysis Plan (Amendment 3): 25 JUN 2024

# Statistical Analysis Plan

## INCMOR 0208-301

## A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of Tafasitamab Plus Lenalidomide in Addition to Rituximab Versus Lenalidomide in Addition to Rituximab in Patients With Relapsed/Refractory (R/R) Follicular Lymphoma Grade 1 to 3a or R/R Marginal Zone Lymphoma

| | |
|---|---|
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| **Protocol Version:** | **Protocol Amendment 7 dated 18 APR 2023** |
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| **SAP Author:** | [redacted]<br>**Biostatistics** |
| **Date of Plan:** | **25 JUN 2024** |

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

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# LIST OF ABBREVIATIONS

| Abbreviation | Term |
|---|---|
| 2D-ECHO | 2-dimensional echocardiogram |
| ADI | actual dose intensity |
| AE | adverse event |
| AESI | adverse event of special interest |
| ALT | alanine aminotransferase |
| AST | aspartate aminotransferase |
| [redacted] | [redacted] |
| CI | confidence interval |
| [redacted] | [redacted] |
| CMH | Cochran Mantel-Haenszel |
| [redacted] | [redacted] |
| CMQ | customized MedDRA query |
| CNS | central nervous system |
| COVID-19 | coronavirus disease 2019 |
| CR | complete response |
| CRF | case report form |
| CRS | cytokine release syndrome |
| CTCAE | Common Terminology Criteria for Adverse Events |
| DLBCL | diffuse large B-cell lymphoma |
| [redacted] | [redacted] |
| DOR | duration of response |
| ECG | electrocardiogram |
| ECOG | Eastern Cooperative Oncology Group |
| eCRF | electronic case report form |
| EMA | European Medicines Agency |
| EORTC QLQ | European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire |
| EOT | end of treatment |
| EQ-5D-5L | EuroQol 5-dimension 5-level |
| EWB | emotional well-being |
| FACT-G | Functional Assessment of Cancer Treatment – General |
| FACT-Lym | Functional Assessment of Cancer Treatment – Lymphoma |
| FAS | full analysis set |
| FDA | Food and Drug Administration |
| FDG | fluorodeoxyglucose |

| Abbreviation | Term |
|---|---|
| FL | follicular lymphoma |
| FLIPI | follicular lymphoma international prognostic index |
| FPFV | first participant first visit |
| FWB | functional well-being |
| GELF | Groupe d'Etude des Lymphomes Folliculaires |
| HLT | high level term |
| HR | hazard ratio |
| ICF | informed consent form |
| IDMC | Independent Data Monitoring Committee |
| INV | investigator |
| IRC | independent review committee |
| IRR | infusion-related reaction |
| IRT | interactive response technology |
| LPLV | last participant last visit |
| LVEF | left-ventricular ejection fraction |
| LymS | lymphoma subscale |
| mAb | monoclonal antibody |
| MedDRA | Medical Dictionary for Regulatory Activities |
| MOA | mechanism of action |
| MRD | minimal residual disease |
| MUGA | multigated acquisition |
| MZL | marginal zone lymphoma |
| NCI | National Cancer Institute |
| NE | not evaluable |
| NEC | not elsewhere classified |
| [redacted] | [redacted] |
| [redacted] | [redacted] |
| ORR | overall response rate |
| OS | overall survival |
| PD | progressive disease |
| PDI | planned dose intensity |
| PET | positron-emission tomography |
| PFS | progression-free survival |
| [redacted] | [redacted] |
| [redacted] | [redacted] |
| PML | progressive multifocal leukoencephalopathy |

| Abbreviation | Term |
|---|---|
| PO | *per os,* oral(ly) |
| POD24 | progression of disease within 24 months after initial diagnosis |
| PPS | per protocol set |
| PR | partial response |
| PT | preferred term |
| PWB | physically well-being |
| QD | *qua die*, once daily |
| QoL | quality of life |
| QTc | corrected QT interval |
| RDI | relative dose intensity |
| [redacted] | [redacted] |
| RMST | restricted mean survival time |
| R/R | relapsed/refractory |
| SAF | safety analysis set |
| SAP | Statistical Analysis Plan |
| SD | stable disease |
| SmPC | summary of product characteristics |
| SMQ | standard MedDRA query |
| SNP | single-nucleotide polymorphism |
| SOC | system organ class |
| SWB | social/family well-being |
| TEAE | treatment-emergent adverse event |
| TGA | Treatment Group A |
| TGB | Treatment Group B |
| TLS | tumor lysis syndrome |
| [redacted] | [redacted] |
| ULN | upper limit of normal |
| USPI | United States prescribing information |
| WHO | World Health Organization |

# 1. INTRODUCTION

Study INCMOR 0208-301 is a Phase 3, randomized, double-blind, placebo-controlled, multicenter study designed to investigate whether tafasitamab and lenalidomide as an add-on to rituximab provides improved clinical benefit compared with placebo and lenalidomide as an add-on to rituximab in participants with an INV-assessed diagnosis of R/R FL Grade 1 to 3a or R/R MZL who have been previously treated with at least 1 anti-CD20 antibody containing therapy (eg, rituximab, obinutuzumab). The primary endpoint is PFS by INV assessment in the FL population. The 3 key secondary endpoints are PFS by INV assessment in the overall population (FL and MZL populations), PET-CR rate at EOT by INV assessment in the FL population, and OS in the FL population.

The study consists of the screening period (≤ 28 days), treatment period (up to twelve 28-day cycles, with rituximab administered up to 5 cycles), and a 5-year follow-up period.

Approximately 528 participants with R/R FL and 60 to 90 participants with R/R MZL will be randomized at a 1:1 ratio to 1 of the 2 treatment groups. Stratified randomization will be performed separately for FL and MZL.

An interim analysis for futility will be performed at approximately 20% information rate (35 PFS events approximately) in the FL population (an HR of ≥ 1.05 will be considered as a nonbinding futility boundary).

An IDMC will be established to monitor data, to ensure the safety of the participants enrolled in this study, and to evaluate the efficacy of the treatment during planned interim analysis. Details of the IDMC review are defined in a separate IDMC charter.

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in the INCMOR 0208-301 Protocol.

[redacted]

# 2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

## 2.1. Protocol and Case Report Form Version

This SAP is based on INCMOR 0208-301 Protocol Amendment 7 dated 18 APR 2023 and CRFs approved 19 SEP 2023. 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** | |
| To compare the efficacy of tafasitamab and lenalidomide in addition to rituximab to the efficacy of placebo and lenalidomide in addition to rituximab in terms of PFS in participants with R/R FL. | PFS by INV assessment in the FL population, using the Lugano 2014 criteria (Cheson et al 2014). PFS is defined as the time from randomization to first documented disease progression, or death from any cause, whichever occurs first. |
| **Secondary** | |
| **Key Secondary Endpoints** | |
| To compare the efficacy of tafasitamab and lenalidomide in addition to rituximab versus placebo and lenalidomide in addition to rituximab in terms of PFS in the overall population (FL and MZL). | PFS by INV assessment in the overall population (FL and MZL populations). |
| To compare the efficacy of tafasitamab and lenalidomide in addition to rituximab versus placebo and lenalidomide in addition to rituximab in terms of PET-CR rate in FDG-avid FL participants and OS in the FL population. | • PET-CR rate by INV in the FDG-avid FL population, defined as a complete metabolic response at any time after start of treatment.<br>• OS in the FL population. |
| **Other Secondary Endpoints** | |
| To compare the efficacy of tafasitamab and lenalidomide in addition to rituximab versus placebo and lenalidomide in addition to rituximab. | • PET-CR rate by INV in the FDG-avid overall population.<br>• MRD-negativity rate (at thresholds of $10^{-4}$ and $10^{-5}$) at EOT in the FL and the overall population.<br>• ORR by INV in the FL and overall populations.<br>• DOR by INV in the FL and overall populations.<br>• OS in the overall population. |
| To compare the efficacy between treatment groups based on IRC assessment. | • PFS by IRC in the FL and overall populations.<br>• ORR by IRC in the FL and overall populations.<br>• DOR by IRC in the FL and overall populations. |

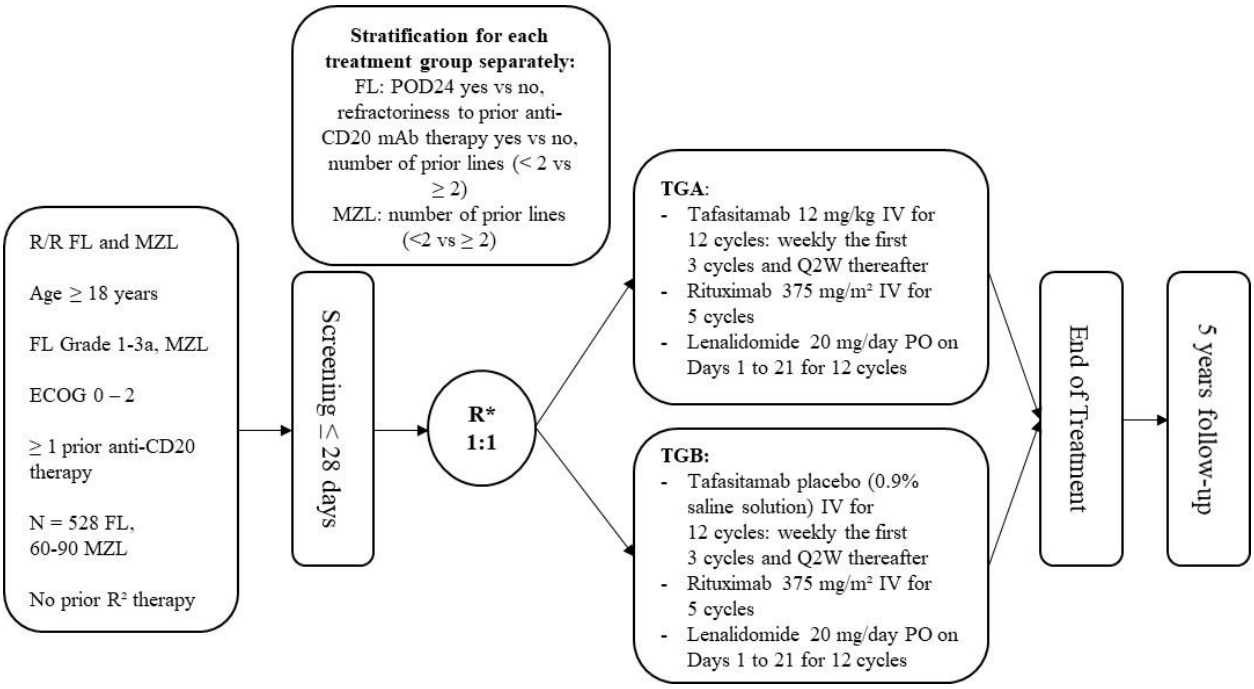
## Table 1: Objectives and Endpoints (Continued)

| Objectives | Endpoints |
|---|---|
| **Other Secondary Endpoints (continued)** | |
| To evaluate QoL of tafasitamab and lenalidomide in addition to rituximab versus placebo and lenalidomide in addition to rituximab in the FL and overall population. | QoL as measured by the EORTC QLQ-C30, the EQ-5D-5L, and FACT-Lym tools in the FL and overall populations. |
| To compare the safety of tafasitamab and lenalidomide in addition to rituximab versus placebo and lenalidomide in addition to rituximab in the FL and overall population. | Safety based on the incidence and severity of TEAEs in the FL and overall population. |
| [redacted] | |

# 3. STUDY DESIGN

This study is a 1:1 randomized, double-blind, placebo-controlled, parallel group, multicenter, Phase 3 clinical study to compare the efficacy and safety of tafasitamab and lenalidomide in addition to rituximab versus placebo and lenalidomide in addition to rituximab in participants with R/R FL and R/R MZL. The overall study design is shown in Figure 1.

**Figure 1: Study Design Schema**




*Randomization will apply separately for FL versus MZL populations.

## 3.1. Randomization

Participants will be randomized (separately for FL and MZL) with a 1:1 ratio to 1 of the following 2 treatment groups:

- TGA: tafasitamab + lenalidomide + rituximab
- TGB: placebo + lenalidomide + rituximab

It is planned to randomize approximately 528 participants with FL and 60 to 90 participants with MZL. The overall recruitment is completed if the required 528 participants with FL for the primary analysis and at least 60 participants with MZL are randomized. The recruitment of participants with MZL is limited to a maximum of 90 participants.

Stratified randomization will be performed separately for participants with FL and MZL and will be done through IRT.

Participants with FL will be stratified at the time of randomization for the following factors:

- POD24: yes versus no
- Refractoriness to prior anti-CD20 mAb therapy: yes versus no

(Note: Refractory to anti-CD20 mAb is defined as not achieving a response of CR or PR to a prior regimen containing anti-CD20 mAb, or disease progression occurring during treatment with, or relapse within 6 months after last dose of anti-CD20 mAb.)

- The number of prior lines of therapy: < 2 versus ≥ 2

Participants with MZL will be stratified at the time of randomization for the following factor:

- The number of prior lines of therapy: < 2 versus ≥ 2

## 3.2. Control of Type I Error

The primary endpoint (PFS in FL population) and the 3 key secondary endpoints (PFS in overall population, PET-CR rate in FL population, and OS in FL population) will be tested with inferential statistics.

Hypothesis testing for other secondary and exploratory endpoints may be performed for exploratory purposes. Estimates and p-values will be reported for illustrative and exploratory purpose for those endpoints.

Statistical tests will use a 0.05 significance level and will be 2-sided unless otherwise noted. Confidence intervals, both individual and simultaneous, will be at 95% confidence level unless stated otherwise.

In order to control the study-wise Type I error due to the multiple testing of the primary and key secondary endpoints, a hierarchical order of testing will be implemented.

The primary endpoint analysis of PFS by INV in the FL population will serve as a gatekeeper.

If the null hypothesis is rejected, the key secondary endpoints can be tested in the following fixed order:

1. PFS by INV in overall population (FL and MZL)
2. PET-CR rate by INV in FL population
3. OS in FL population

If the null hypothesis is not rejected, the formal sequential testing will be stopped, and the p-values for the remaining key secondary endpoints will be reported for exploratory and illustrative purposes.

The primary analysis will be performed after approximately 174 PFS events based on INV assessment are observed in the FL population in the FAS. The primary analysis is independent of the number of enrolled MZL participants. Recruitment will be stopped when the required 528 participants with FL for the primary analysis and at least 60 MZL participants have been randomized. The maximum number of randomized participants with MZL is 90.

An interim analysis for futility will be performed for OS at the time of the PFS primary analysis using a nonbinding rule, HR will be estimated.

The final analysis will be performed at the end of the study. The end of study will occur after the last participant has completed a minimum of 5 years of post-treatment follow-up. This is expected to occur approximately 8 years after the first participant is enrolled.

At the time of final analysis, the last key secondary endpoint, OS, will be tested using a 2-sided, 5% significance level if the primary endpoint and other key secondary endpoints achieve statistical significance.

Other secondary and exploratory endpoints will be tested using a 2-sided, 5% significance level without multiplicity adjustment. Estimates and nominal p-values will be reported for exploratory purposes. Additional follow-up analyses for safety or efficacy endpoints may be performed if needed or requested by regulatory authorities.

## 3.3. Sample Size Considerations

The primary objective of the study is to detect a statistically significant difference in PFS (INV) for the tafasitamab-lenalidomide combination in addition to rituximab relative to placebo-lenalidomide in addition to rituximab for participants with FL.

Based on the assumptions in Table 2, a total number of 174 PFS events in the FL population are required to detect an HR of 0.65 with 80% power at the primary analysis, using a 2-sided, log-rank test at an alpha level of 5% and a 1:1 randomization ratio between the 2 treatment groups. Assuming a median PFS of 27.8 months for placebo-lenalidomide in addition to rituximab (TGB), 21 months of enrollment, 12 months of follow-up for PFS, and 15% of dropouts, 528 evaluable FL participants need to be randomized.

**Table 2: Sample Size Assumptions**

| | |
|---|---|
| **Primary Endpoint** | PFS (INV-assessed) for the FL population |
| **Median PFS in TGA** | 42.8 months |
| **Median PFS in TGB** | 27.8 months |
| **Randomization Ratio** | 1:1 |
| **Assumed HR** | 0.65 |
| **Alpha (2-Sided)** | 5% |
| **Power** | 80% |
| **Enrollment Duration** | 21 months |
| **Follow-Up for PFS (Starting From Last Participant Randomized)** | 12 months |
| **Accrual Rate** | 0.1 participant/site/month |
| **PFS Events Required at Primary Analysis** | 174 |
| **Total Participants (Without Dropout)** | 448 |
| **Assumed Dropout Rate** | 15% |
| **Total Randomized Participants** | 528 |

A minimum of 60 and up to 90 additional participants with MZL will be randomized at a 1:1 ratio to 1 of the 2 treatment groups. The number of participants with MZL is based on the expected enrollment proportion of participants with FL and MZL.

A 2-stage design with 1 interim analysis for a potential futility stop will be applied (see Section 9.1.1).

## 3.4. Schedule of Assessments

Refer to the protocol for a full description of all study procedures and assessment schedules for this study.

# 4. DATA HANDLING DEFINITIONS AND CONVENTIONS

## 4.1. Scheduled Study Evaluations and Study Periods

### 4.1.1. Day 1

Day 1 is the date that the first dose of study drug (tafasitamab/placebo, lenalidomide, or rituximab) is administered to the participants.

For randomized participants not treated with any study drug, Day 1 is defined as the date of randomization.

### 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/placebo, lenalidomide, or rituximab, unless otherwise defined.

For randomized participants not treated with any study drug, baseline is defined as the last nonmissing assessment before randomization for all parameters.

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 FL or MZL, a partial 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 calculating the time between last prior therapy and randomization, a partial last prior therapy date will be handled as described above for diagnosis date.

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.

When calculating time to onset or duration of a TEAE, a partial or missing AE onset/end date will be handled in the calculation as follows:

- If only the day is missing, then the first day of the month or Day 1, whichever is later, will be used as the onset date; the earlier date of the last day of the month or the date that the participant withdrew from the study or died will be used as the end date.
- If both the month and day are missing, then 01 JAN or Day 1, whichever is later, will be used as the onset date; the earlier date of 31 DEC or the date that the participant withdrew from the study or died will be used as the end date.
- Otherwise, Day 1 will be used as the onset date, and the missing end date will not be handled.

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

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

### 4.1.5. Cycle Length and Duration

The scheduled cycle length is 28 days.

Cycle 1 Day 1 is the day that the first dose of study drug (tafasitamab/placebo, lenalidomide, or rituximab) is administered. The actual Day 1 of subsequent cycles will correspond with the first day of administration of tafasitamab/placebo, lenalidomide, or rituximab in that cycle. The date of the Day 1 of subsequent cycles recorded on the eCRF will be used as the Day 1 of the subsequent cycles.

The study consists of the screening period (≤ 28 days), treatment period (up to twelve 28-day cycles for tafasitamab/placebo and lenalidomide, and up to five 28-day cycles for rituximab), and a 5-year follow-up period. The safety follow-up visit (EOT visit) after treatment discontinuation is defined as 90 days after last treatment. The total duration is up to approximately 6 years per participant. The total study duration from FPFV to LPLV is expected to be approximately 8 years.

## 4.2. Variable Definitions

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

### 4.2.1. Body Surface Area

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

Body surface area ($m^2$) = $\{[\text{weight (kg)} \times \text{height (cm)}] / 3600\}^{1/2}$.

### 4.2.2. Prior and Concomitant Medication

Prior medication is defined as any nonstudy medication started before the first dose of tafasitamab/placebo, lenalidomide, or rituximab.

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

- Before the date of first administration of tafasitamab/placebo, lenalidomide, or rituximab 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/placebo, lenalidomide, or rituximab and is ongoing or ends during the course of study.
- If the day of start of administration date is missing, and the first day of the month is on or after the first dose date.
- If the month of start of administration date is missing, and the first day of the year is on or after the first dose date.

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

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

# 5. STATISTICAL METHODOLOGY

## 5.1. General Methodology

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

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

## 5.2. Treatment Groups

This is a randomized, double-blind, parallel treatment group design. Participants will be summarized by treatment group (see Table 3) for the FL and MZL populations separately and for the overall population.

**Table 3: Treatment Groups, Dose Paradigm, and Cycle Length**

| TGA | TGB |
|---|---|
| Tafasitamab:<br>12 mg/kg IV on Days 1, 8, 15, and 22 of Cycles 1 to 3 and on Days 1 and 15 (every second week) of Cycles 4 to 12. Cycle length is 28 days. | Matching placebo (0.9% saline solution):<br>IV on Days 1, 8, 15, and 22 of Cycles 1 to 3 and on Days 1 and 15 (every second week) of Cycles 4 to 12. Cycle length is 28 days. |
| Rituximab (including biosimilars):<br>375 mg/m$^2$ IV every week in Cycle 1 on Days 1, 8, 15, and 22 and on Day 1 of every 28-day cycle from Cycles 2 to 5.<br>Note: rituximab should be administered approximately 30 minutes after the tafasitamab/placebo infusion is completed. For logistical reasons, rituximab may be administered on the day after the tafasitamab infusion, or administration may be split over 2 consecutive days, according to local practice and the institution's standard of care. | |
| Lenalidomide (including generics):<br>20 mg PO QD on Days 1 to 21 of every 28-day cycle for 12 cycles.<br>Note: a participant with moderate renal insufficiency (creatinine clearance ≥ 30 mL/minute to < 60 mL/minute) will receive a starting dose of 10 mg daily on the same schedule. After 2 cycles, if no lenalidomide-related toxicities of Grade 3/4 occur, the dose may be increased to 15 mg QD on Days 1 to 21 of each cycle. | |

## 5.3. Analysis Populations

A full description of the populations for analysis is presented in Table 4.

**Table 4: Analysis Populations**

| Population | Description |
|---|---|
| All screened | All participants who sign the ICF. |
| FAS | All randomized participants. Treatment groups for this population will be determined according to the treatment they were assigned at the time of randomization.<br>The FAS will be used for the summary of demographics, baseline characteristics, participant disposition, and analyses of all efficacy data. |
| PPS | The subset of the participants in the FAS who are compliant with the requirements of the clinical study Protocol with no important Protocol deviations. All important protocol deviations or conditions leading to exclusion from the PPS will be detailed in the Protocol Deviation Specifications and identified prior to database lock for the primary analysis.<br>Sensitivity analyses of the primary endpoint may be performed using the PPS. |
| MRD blood-evaluable set | All participants in the FAS who received at least 1 dose of tafasitamab/placebo, lenalidomide, or rituximab with identifiable clonality in blood sample at Cycle 1 Day1. |
| MRD bone marrow-evaluable set | All participants in the FAS who received at least 1 dose of tafasitamab/placebo, lenalidomide, or rituximab with either identifiable clonality in bone marrow at screening or identifiable clonality in blood sample at Cycle 1 Day 1. |
| SAF | All randomized participants who received at least 1 dose of tafasitamab/placebo, lenalidomide, or rituximab. Treatment groups for this population will be determined according to the actual treatment the participant received regardless of assigned treatment at the time of randomization.<br>All safety analyses will be conducted using the SAF. |
| FDG-avid population | All randomized participants with a PET scan at baseline with a resulting Deauville score of 4 or 5. |

# 6. BASELINE, EXPOSURE, AND DISPOSITION

Appendix A provides a list of data displays including the population selected for each analysis (FL, MZL, overall, Japanese FL, Japanese overall). 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 group (< 65 years, ≥ 65 years), sex (with reproductive status for females and menstrual status for women of childbearing potential), race, ethnicity, geographic region, weight at screening, height at screening, ECOG performance status, and COVID-19 vaccination status at screening.

### 6.1.2. Baseline Disease Characteristics and Disease History

The following baseline disease characteristics will be summarized for the FAS when applicable to FL or MZL:

- B-symptoms (fever, night sweats, weight loss) at initial diagnosis and at study entry
- Time since initial diagnosis of FL or MZL
- Lymphoma type
- FL grade at initial diagnosis and at study entry
- MZL subtype (splenic, nodal, extranodal)
- [redacted]
- Ann Arbor Staging at initial diagnosis and at study entry
- CNS involvement
- FLIPI
- GELF criteria

Bone marrow involvement of disease at baseline and R/R status to the most recent prior therapy will be summarized. Concordance between local and central pathology for FL/MZL diagnosis will also be summarized.

Time since diagnosis will be calculated as follows:

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

The following stratification factors per the eCRF will also be summarized: POD24 (yes versus no; FL only), refractoriness to prior anti-CD20 mAb therapy (yes versus no; FL only), and the number of prior lines of therapy (< 2 versus ≥ 2).

### 6.1.3. Prior Therapy

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

The number of prior systemic anti-CD20 immunotherapy and the number of participants who received each regimen will be summarized for all participants in the FAS. The regimen name, purpose of the regimen, best response, reason for discontinuation, date of relapse/progression, medication, start and stop dates, and route will be listed.

The number of participants who received prior radiotherapy will be summarized for the FAS. The anatomical site, start and stop dates, best response, regimen number under the Prior Therapy for Disease CRF (if this oncology radiotherapy is a part of any regimen recorded on the Prior Therapy for Disease under study CRF), number of fractions received, and total dose will be listed.

The number of participants who had prior surgery or a 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 a prior autologous stem cell transplantation might be summarized for the FAS population.

### 6.1.4. Medical History

For participants in the FAS, medical history will be summarized by assigned treatment group. This summary will include the number and percentage of participants with medical and surgical history event for each body system/organ class as documented on the eCRF. Medical condition/surgery, start date, if it is ongoing at screening, end date, if treated with medication, and worst grade known if ongoing will be listed.

## 6.2. Disposition of Participant

The number and percentage of participants who were screened, screening disposition and reasons will be summarized for the all screened population. The number and percentage of participants who were randomized, 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 randomized by country and site will also be provided by treatment group.

## 6.3. Protocol Deviations

Protocol deviations will be summarized and listed. Important protocol deviations leading to exclusion from the PPS will be identified prior to database lock for the primary analysis and summarized by categories.

## 6.4. Exposure

For participants in the safety population, exposure to tafasitamab, lenalidomide, and rituximab will be summarized descriptively as follows. Lenalidomide exposure will also be displayed by creatinine clearance group (≥ 30 and < 60 mL/minute vs ≥ 60 mL/minute).

### 6.4.1. Exposure to Tafasitamab

- **Duration of exposure to tafasitamab (days):** date of last dose of tafasitamab – date of first dose of tafasitamab + 1.
- **Duration category of tafasitamab exposure:** the number and percentage of participants in each duration category (ie, < 1 month, 1 to < 3 months, 3 to < 6 months, 6 to < 9 months, 9 to ≤ 12 months, > 12 months) will be summarized. Duration of exposure in month categories will be calculated based on the conversion that each month has 30.4375 days.
- **Number of infusions:** number of infusions with a nonzero dose.
- **Number of cycles:** number of cycles with at least 1 nonzero dose infusion.

### 6.4.2. Exposure to Rituximab

- **Duration of exposure to rituximab (days):** date of last dose of rituximab – date of first dose of rituximab + 1.
- **Duration category of rituximab exposure:** the number and percentage of participants in each duration category (ie, < 1 month, 1 to < 3 months, 3 to ≤ 6 months) will be summarized. Duration of exposure in month categories will be calculated based on the conversion that each month has 30.4375 days.
- **Number of infusions:** number of infusions with a nonzero dose.
- **Number of cycles:** number of cycles with at least 1 nonzero dose infusion.

### 6.4.3. Exposure to Lenalidomide

- **Duration of treatment with lenalidomide (days)**: date of last dose of lenalidomide – date of first dose of lenalidomide + 1.
- **Duration category of lenalidomide exposure:** the number and percentage of participants in each duration category (ie, < 1 month, 1 to < 3 months, 3 to < 6 months, 6 to < 9 months, 9 to ≤ 12 months, > 12 months) will be summarized. Duration of exposure in month categories will be calculated based on the conversion that each month has 30.4375 days.
- **Total dose received (mg):** the sum of the cumulative actual dose of lenalidomide that has been taken by the participant.

## 6.5. Dose Intensity, Relative Dose Intensity

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

### 6.5.1. Dose Intensity and Relative Dose Intensity of Tafasitamab

**Actual dose intensity (mg/kg):** the actual dose the participant was exposed to. The ADI per infusion will be derived as follows:

- If the question "was the entire infusion administered" on the "Tafasitamab/Placebo Infusion" eCRF page was answered with
  - Yes

    ADI at the visit = 12 mg/kg
  - No

    ADI at the visit = 12 mg/kg (actual volume administered / prepared volume)
- 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.

**Planned dose intensity (mg/kg):** The planned dose is 12 mg/kg per infusion as per Protocol.

**Relative dose intensity (%):** The RDI expresses the amount of drug administered compared with the planned amount of drug across all infusions.

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

### 6.5.2. Dose Intensity and Relative Dose Intensity of Rituximab

**Actual dose intensity ($mg/m^2$):** the actual dose to which the participant was exposed. The ADI per infusion will be derived as follows:

- If the question regarding whether the participant was given the protocol standard 375 $mg/m^2$ dose was answered with
  - **Yes**

    Actual rituximab dose level ($mg/m^2$) = 375 $mg/m^2$
  - No

    Actual rituximab dose level ($mg/m^2$) = total prepared dose (mg) / participant BSA ($m^2$) on Day 1 of the cycle
- If the question "was the entire infusion administered" on the "Rituximab Infusion" eCRF page answered with
  - Yes

    ADI at the visit = actual rituximab dose level ($mg/m^2$)

– N**o**

ADI at the visit = actual rituximab dose level (mg/m$^2$) × (actual volume administered / planned volume)

- 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.

**Planned dose intensity (mg/m$^2$):** The planned dose is 375 mg/m$^2$ as per Protocol.

**Relative dose intensity (%):** The RDI expresses the amount of drug administered compared with the planned amount of drug across all infusions.

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

### 6.5.3. Dose Intensity and Relative Dose Intensity of Lenalidomide

**Actual dose intensity (mg):** the actual dose the participant was exposed to (this is captured in "Study Drug Administration - Lenalidomide" eCRF form).

**Planned dose intensity (mg):** The planned dose is 20 mg QD on Days 1 to 21 of each cycle. A participant with moderate renal insufficiency will receive a starting dose of 10 mg daily on the same schedule. After 2 cycles, if no lenalidomide-related toxicities of Grade 3/4 occur, the planned dose may be increased to 15 mg QD on Days 1 to 21 of each cycle.

**Relative dose intensity (%):** The RDI expresses the amount of drug administered compared with the planned amount of drug at all time.

RDI = ADI / PDI × 100

## 6.6. Lenalidomide Compliance

For participants in the safety population, overall compliance (%) for lenalidomide 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 INV accounting for dose modifications.

The total actual dose taken will be calculated based on drug dispensing information and/or administration information entered on the "Study Drug Administration - Lenalidomide" eCRF form.

If the drug accountability data are not appropriately collected, relative dose intensity is considered as an approximation of lenalidomide compliance and will be used as surrogate.

## 6.7. Dose Modifications

Dose reductions of tafasitamab or placebo are not permitted. Delaying the tafasitamab or placebo dose is permitted for no more than 2 days. Alternatively, a tafasitamab or placebo infusion may be skipped completely, and the next scheduled dose will be administered. Tafasitamab/placebo administration can also be interrupted during infusion. The number and percentage of participants with a dose interruption, dose delay, or skipped dose of tafasitamab/placebo will be

summarized by treatment group. The reason for dose interruption/delay/skipped will be summarized as captured on the "Tafasitamab/Placebo Infusion" eCRF page.

The lenalidomide dose can be either interrupted or reduced per the dose levels in Table 5. The number and percentage of participants with lenalidomide dose interruptions/reductions and the lowest dose level achieved per participant will be summarized by treatment group. Reasons for dose interruptions/reductions for lenalidomide will be summarized as captured on the "Study Drug Changes - Lenalidomide" eCRF page.

**Table 5: Dose Reduction Steps for Lenalidomide**

| | |
|---|---|
| **Starting dose** | 20 mg QD on Days 1-21, every 28 days |
| **Dose level −1** | 15 mg QD on Days 1-21, every 28 days |
| **Dose level −2** | 10 mg QD on Days 1-21, every 28 days |
| **Dose level −3** | 5 mg QD on Days 1-21, every 28 days |

Dose modifications of rituximab are not mandated unless clinically indicated as per the SmPC, the USPI, and applicable institutional guidelines (MabThera 2020, Rituxan 2020). The number and percentage of participants with a dose interruption, dose delay, or skipped dose of rituximab will be summarized by treatment group. The reason for dose interruption/delay/skipped will be summarized as captured on the "Rituximab Infusion" eCRF page.

## 6.8. 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.

Premedication given prior to tafasitamab/placebo administration to mitigate potential infusion-related reactions will be listed.

# 7. EFFICACY

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

## 7.1. General Considerations

All efficacy analyses will be based on the FAS. Unless otherwise stated, all stratified efficacy analyses will use the same stratification factors as for randomization, which are specified in Section 3.1 and based on the data obtained from IRT.

## 7.2. Efficacy Hypotheses

The primary hypothesis is that tafasitamab in combination with lenalidomide and rituximab will improve PFS compared with lenalidomide and rituximab alone in participants with R/R FL. Assume $S_1(t)$ is the survival function of tafasitamab in combination with lenalidomide and rituximab, and $S_2(t)$ is the survival function of lenalidomide and rituximab alone. The hypotheses of the study are as follows:

- $H_0$ (null hypothesis): $S_1(t) = S_2(t)$
- $H_A$ (alternative hypothesis): $S_1(t) \neq S_2(t)$

## 7.3. Analysis of the Primary and Key Secondary Efficacy Endpoints

### 7.3.1. Primary Efficacy Analysis for Progression-Free Survival in Follicular Lymphoma

Progression-free survival by INV assessment is defined as the time from the date of randomization to the date of first documented disease progression, as determined by disease assessment per the Lugano classification (Cheson et al 2014) or death due to any cause, whichever occurs earlier. For the primary analysis, PFS will be censored if no PFS event is observed before the cutoff date or the date that a new antilymphoma therapy is started. Censoring for PFS will follow the algorithm outlined in Table 6, which is based on the FDA Guidance (FDA 2015, FDA 2018).

**Table 6: Evaluation and Censoring of Progression-Free Survival**

| Situation | Date of Progression or Censoring | Outcome | Censoring Reason |
|---|---|---|---|
| No baseline tumor assessments | Date of randomization | Censored | No baseline assessment |
| No valid postbaseline response assessments | Date of randomization | Censored | No postbaseline assessment |
| Progression documented between scheduled response assessments | Date of first overall response of PD | Progressed | Not applicable |
| No progression | Date of last adequate tumor assessment (not NE and not missing) prior to cutoff date | Censored | Ongoing |
| Study discontinuation without documented progression | Date of last adequate tumor assessment (not NE and not missing) prior to cutoff date | Censored | Study discontinuation |
| New antilymphoma treatment started | Date of last adequate tumor assessment with no documented progression (not NE and not missing) on/before starting a new antilymphoma treatment | Censored | Start of new antilymphoma treatment |
| Death before first progressive response assessment | Date of death | Progressed | Not applicable |
| Death between adequate response assessments | Date of death | Progressed | Not applicable |
| Death or progression after 2 or more missed assessments | Date of last progression assessment with documented nonprogression | Censored | Death or PD after 2 or more missed assessments |

The date of last adequate tumor assessment is the date of the last tumor assessment with an overall lesion response of CR, PR, or SD. In this case, the last tumor evaluation date at that assessment is used. If a PFS event is observed after a single missing or nonadequate tumor assessment, the actual date of event will be used, as per the Lugano classification (Cheson et al 2014).

The distribution of PFS by INV assessment will be compared between the 2 treatment groups using a stratified log-rank test at 2-sided 5% level of significance. The strata information will be based on the data obtained from IRT that was used for randomization.

A stratified Cox proportional hazard model will be used to estimate the HR between TGA (tafasitamab + lenalidomide + rituximab) versus TGB (placebo + lenalidomide + rituximab), along with 2-sided 95% CI.

The distribution of PFS will be estimated using the Kaplan-Meier method. The number of events, censoring, and censoring reasons will be summarized. The median along with 2-sided 95% CIs will be presented by treatment group. The 95% 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 may be provided along with the corresponding 2-sided 95% CIs.

All analyses mentioned above will be performed for participants with FL in the FAS.

If the null hypothesis is rejected at a 2-sided significance level of 5%, the primary endpoint is met. Alpha of 5% will be passed down to test the key secondary endpoints per the hierarchical testing order specified in Section 7.3.2. The p-value obtained from the stratified log-rank test for PFS in the FL population of the FAS will be used for hierarchical testing.

If a participant was randomized into the MZL cohort but after randomization was confirmed by the site to have a diagnosis of FL, the eCRF-derived information for medical history will be used to derive the 2 missing stratification factors for the FL cohort: POD24 status (yes versus no) and refractoriness to prior anti-CD20 mAb therapy (please refer to the definition in Section 3.1). If a participant was randomized into the FL cohort but after randomization was confirmed by the site to have a diagnosis of MZL, the IRT-derived stratification factor needed for this cohort (number of prior lines of therapy: $< 2$ versus $\geq 2$) will be used.

[redacted]

### 7.3.2. Analyses of Key Secondary Efficacy Endpoints

As specified in Section 3.2, a hierarchical testing procedure will be implemented for the key secondary endpoints, with the primary endpoint PFS serving as a gatekeeper. This hierarchical testing procedure will maintain the study-wise Type I error rate at 2-sided 5%. If the primary null hypothesis is rejected, the key secondary endpoints can be tested in the following fixed order:

1. PFS by INV in the overall population (FL and MZL)
2. PET-CR rate by INV in the FDG-avid FL population
3. OS in the FL population

#### 7.3.2.1. Progression-Free Survival in the Overall Population

Progression-free survival by INV assessment in the overall population (FL and MZL) will be compared and analyzed in the same manner as described in Section 7.3 for the PFS in the FL population. The strata information for the stratified log-rank test will be based on the randomization factor used for both cohorts, FL and MZL: number of prior lines of therapy ($< 2$ versus $\geq 2$).

The p-value obtained from the stratified log-rank test for PFS in the overall population, using the strata information based on IRT that was used for randomization, as well as stratification by FL versus MZL, will be used for hierarchical testing.

As mentioned in Section 7.3, participants with different initial diagnosis by INV and in the IRT will be considered as mentioned in the eCRF.

[redacted]

#### 7.3.2.2. Positron-Emission Tomography-Complete Response Rate in the FDG-Avid Follicular Lymphoma Population

The PET-CR rate is defined as the proportion of FDG-avid participants who achieved a CR as per Lugano classification (Cheson et al 2014) with a PET-negative result defined as a complete metabolic response at any time after start of treatment over the FDG-avid FL population at baseline. FDG-avid FL participants with no postbaseline assessment by PET or those who did not achieve a PET-CR will be classified as "non–CR-responder."

The CR rate will be compared between the 2 treatments groups using a stratified CMH test. The odds ratio and its 95% CIs calculated from the stratified CMH test will also be presented. The number of participants classified as PET-CR responders and the respective rates as well as 95% CIs (using Clopper-Pearson) will be presented.

Analysis of the key secondary endpoint of PET-CR will be performed for participants with FDG-avid FL in the FAS. If the null hypothesis is rejected at a 2-sided significance level of 5%, this key secondary endpoint is met. The p-value obtained from the CMH test for PET-CR rate by INV assessment in the FDG-avid FL population, using the strata information based on IRT that was used for randomization, will be used for hierarchical testing.

[redacted]

#### 7.3.2.3. Overall Survival in the Follicular Lymphoma Population

Overall survival is defined as the time from randomization until death from any cause. All participants should be followed until death or until the end of study, whichever comes first, as specified in the Protocol.

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. 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," and "End of Study" eCRFs. Partial death dates will be handled using the rules described in Section 4.1.4.

Overall survival will be compared and analyzed using stratified tests as described in Section 7.3 for PFS with FL in the FAS at the time of interim, primary, and final analysis. Participants will be censored at the last date they were known to be alive, regardless if a new antilymphoma therapy was started.

[redacted]

Post-treatment systemic antilymphoma therapies will be summarized and listed.

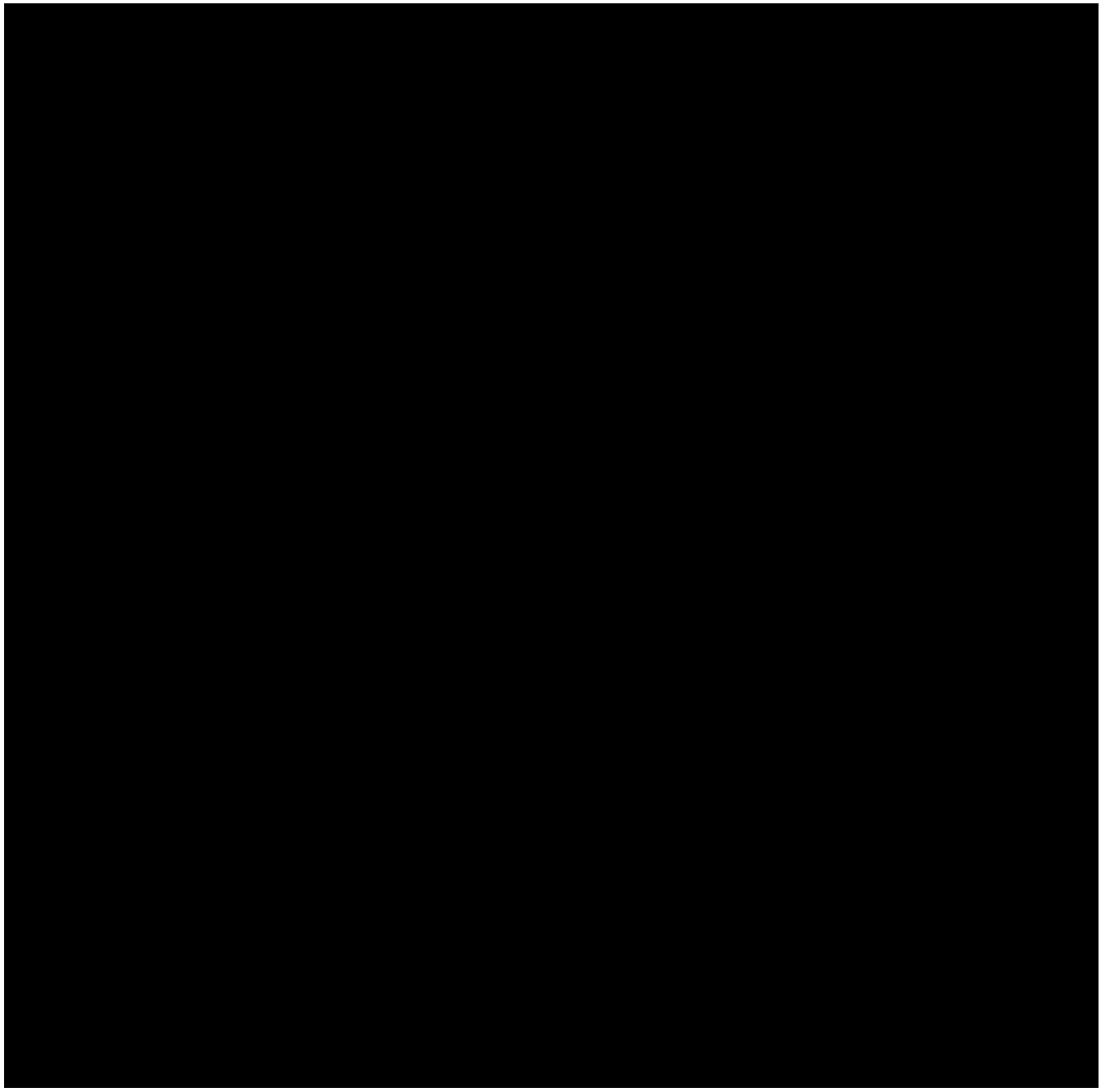
### 7.3.3. Currentness of Progression-Free Survival and Overall Survival Data

To assess the currentness of PFS data, the time from the last tumor assessment to the data cutoff date in months will be summarized by treatment group and overall for the FL population and the overall FAS. Participants who have a PFS event will be considered as current for this analysis.

Currentness of OS data will be summarized by treatment group and overall for the FL population and the overall FAS in months from the last known alive date to the data cutoff date. Participants who have a death event will be considered as current for this analysis.

### 7.3.4. Progression-Free Survival/Overall Survival Follow-Up Time

Follow-up time for PFS/OS will be defined from the date of randomization and will use the inverse of the censoring rules for PFS/OS. The median PFS/OS follow-up time and 95% CI will be estimated by reversed Kaplan-Meier method by treatment group and overall for the FL population and the overall FAS.



## 7.4. Analysis of Other Secondary Efficacy Parameters

### 7.4.1. Positron-Emission Tomography-Complete Response Rate in the FDG-Avid Overall Population

The PET-CR rate in the FDG-avid overall population (FL and MZL) will be compared and analyzed in the same manner as described in Section 7.3.2.2 for the PET-CR rate in the FDG-avid FL population.

### 7.4.2. Minimal Residual Disease-Negativity Rate at End of Treatment in the MRD-Evaluable Follicular Lymphoma Population and MRD-Evaluable Overall Population

The MRD-negativity rate is defined as the proportion of participants who achieved a negative MRD result in peripheral blood at the EOT. The threshold used for the analysis is $10^{-5}$ cells. Participants with no postbaseline assessment, or who did not achieve a negative MRD result will be classified as "non–MRD-negative." Analysis of the MRD-negativity rate at EOT will be performed for participants in the MRD-blood evaluable FL population and the MRD-blood evaluable overall population (FL and MZL).

The MRD-negativity in the 2 treatment groups will be compared and analyzed in the same manner as described in Section 7.3.2.2 for the PET-CR rate.

The MRD analysis will be performed using samples with a time interval of ≤ 5 days between sample collection and receipt by the laboratory to ensure sample integrity.

Reasons for missing MRD assessments will be summarized, for example, missed assessment, unevaluable assessment.

Sensitivity analysis will be performed on:

- Using peripheral blood sample at both C4 and C8 (in the MRD-blood evaluable population)
- Using bone marrow sample at EOT (in the MRD-bone marrow evaluable population)
- Using bone marrow sample at CR (in the MRD-bone marrow evaluable population)

Estimates of the MRD-negativity rate along with its exact 95% CIs using the Clopper-Pearson method will be calculated for each treatment group. No statistical comparison will be performed for this analysis.

[redacted].

### 7.4.3. Overall Response Rate in Follicular Lymphoma and Overall Populations

Overall response rate is defined as the proportion of participants who achieved a best overall response of CR or PR as determined per the Lugano classification (Cheson et al 2014) at any time during the study but before the first PD and before/at the start of a new antilymphoma treatment.

Overall response rate will be compared and analyzed in the same manner as described in Section 7.3.2.2 for PET-CR rate in the FDG-avid FL population.

Overall response rate will be analyzed for the FL population and the overall population. Overall response rate will also be analyzed in the MZL population.

### 7.4.4. Duration of Response in the Follicular Lymphoma and Overall Populations

Duration of response is defined as the time from first tumor response (CR or PR as per the Lugano classification [Cheson et al 2014]) until the time of first documented disease progression, or death from any cause, whichever is earlier, among participants who achieve an objective response (CR or PR as per the Lugano classification [Cheson et al 2014]). Censoring of DOR will follow the same algorithm as the censoring of PFS (see Section 7.3.1).

Kaplan-Meier estimation of the median DOR and its 95% CIs will be presented by treatment group for participants who achieve an objective response (CR or PR as per the Lugano classification [Cheson et al 2014]). No statistical comparison will be performed for this analysis.

Duration of response will be analyzed for the FL population and the overall population. Duration of response will also be analyzed for the MZL population.

### 7.4.5. Overall Survival in Overall Population

Overall survival in the overall population (FL and MZL) will be compared and analyzed in the same manner as described in Section 7.3.2.3 for the OS in the FL population. The only difference will be that the strata information for the stratified log-rank test will be based on the randomization factor used for both cohorts, FL and MZL: number of prior lines of therapy ($< 2$ versus $\geq 2$).

### 7.4.6. Analysis of Efficacy Endpoints by Independent Review Committee

The endpoints PFS, ORR, and DOR, as determined by IRC assessment using International Working Group 2014 response criteria (Cheson et al 2014) will be analyzed in the FL, MZL, and overall populations. The above mentioned outcomes will be analyzed the same way as described for the respective efficacy endpoints by INV (Section 7.3.1, Section 7.4.3, and Section 7.4.4).

The response assessment concordance rate between INV assessment and IRC assessment will be evaluated in term of:

- Best overall response

The concordance rate is the number of concordant participants over the total number of assessed participants and will be calculated.

### 7.4.7. Quality of Life Questionnaires in Follicular Lymphoma and Overall Populations

Quality of life will be assessed using three questionnaires: the EORTC QLQ-C30, the EQ-5D-5L, and FACT-Lym tools.

#### 7.4.7.1. EORTC QLQ-C30

The EORTC QLQ-C30 v3 is a 30-item scale (Aaronson et al 1993). The EORTC QLQ-C30 is composed of both multi-item scales and single-item measures. These include 5 functional scales, 3 symptom scales, a global health status scale, and 6 single items (see Table 7).

All of the scales and single-item measures range in score from 0 to 100. A high scale score represents a higher response level. Therefore, a high score for a functional scale represents a high/healthy level of functioning and a high score for the global health status/QoL represents a high QoL. A high score for a symptom scale/item represents a high level of symptomatology/problems.

Scores will be calculated using the EORTC QLQ-C30 scoring manual (third edition) as well as handling of missing data (Fayers et al 2001).

Descriptive statistics for each of the scores will be tabulated. The EORTC QLQ-C30 will be analyzed using change from baseline and percentage of change from baseline for each visit and treatment group in both FL and overall population, according to the functional scores and the recommendations in the EORTC scoring manual.

Statistical tests might be performed in an exploratory manner. Mann-Whitney tests for simple comparison and longitudinal data modeling techniques might be conducted to analyze the scores.

**Table 7: EORTC QLQ-C30 Scales**

| Functional Scales (15 Questions) | Symptom Scales (7 Questions) | Single Items (6 Questions) | Global Quality of Life (2 Questions) |
|---|---|---|---|
| Physical (Items 1 to 5) | Fatigue (Items 10, 12, 18) | Constipation (Item 16) | Global QoL (Items 29, 30) |
| Role (Items 6, 7) | Pain (Items 9, 19) | Diarrhea (Item 17) | – |
| Cognitive (Items 20, 25) | Nausea/Vomiting (Items 14, 15) | Sleep (Item 11) | – |
| Emotional (Items 21 to 24) | – | Dyspnea (Item 8) | – |
| Social (Items 26, 27) | – | Appetite (Item 13) | – |
| – | – | Financial (Item 28) | – |

#### 7.4.7.2. EQ-5D-5L

The EQ-5D-5L is a 5-items questionnaire and a visual analogue scale ranging from 0 (worst imaginable health state) to 100 (best imaginable health state).

The 5 questions cover mobility, self-care, usual activities, pain/discomfort, and anxiety/depression and have 5 response levels: no problems, slight problems, moderate problems, severe problems, and unable to/extreme problems.

As described in the EQ-5D-5L manual (EuroQol 2019) descriptive statistics will be reported for the visual analogue scale. Change from baseline and percentage of change from baseline for each visit and treatment group in both FL and overall population will be analyzed as mentioned in Section 7.4.7.1.

The results from the 5 questions will analyzed as follows: the numbers and percentages in each of the 5 levels will be reported by treatment and visit as well as the presence of any severe to extreme problems (levels 4-5).

#### 7.4.7.3. FACT-Lym

The FACT-Lymphoma (v4) is composed of 42 items with a 5-point Likert-type scale (Hlubocky et al 2013).

The questionnaire is composed of 5 subscales:

- Physical well-being sub-scale includes 7 items measured on 0- to 4-point scale: total score ranges from 0-28.
- Social/Family well-being sub-scale includes 7 items measured on 0-to 4-point scale: total score ranges from 0-28.
- Emotional well-being sub-scale includes 6 items measured on 0- to 4-point scale: total score ranges from 0-24.
- Functional well-being sub-scale includes 7 items measured on 0- to 4-point scale: total score ranges from 0-28.
- Lymphoma sub-scale includes 15 items, and scores range from 0 to 60.

The scoring will be performed following the official guideline (FACT-Lym Scoring 2005) as follows:

For each subscale:

- Reversals should be performed as indicated and individual items should be summed to obtain a score.
- The sum of the item scores should be multiplied by the number of items in the subscale, then divided by the number of items answered. This produces the subscale score.

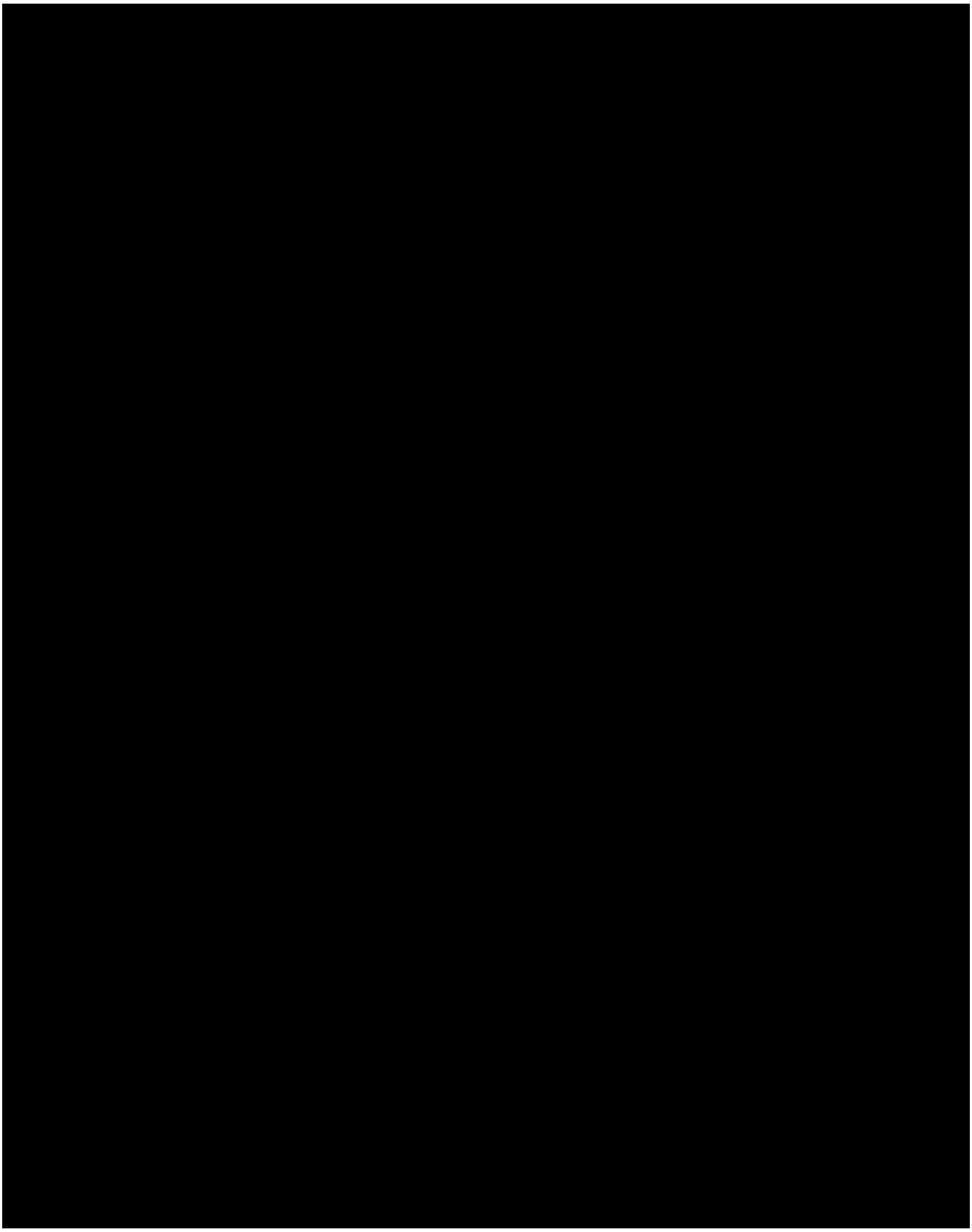
Three total scores can be derived by adding the subscales as follows:

- FACT-Lymphoma Trial Outcome Index (TOI): (PWB score) + (FWB score) + (LymS score); total score ranges from 0-116.
- FACT-G total score: (PWB score) + (SWB score) + (EWB score) + (FWB score); total score ranges from 0-108.
- FACT-Lymphoma total score: (PWB score) + (SWB score) + (EWB score) + (FWB score) + (LymS score); total score ranges from 0-168.

The higher the score, the better the QoL.

Descriptive statistics will be reported for each of the subscales and the 3 total scores. Change from baseline and percentage of change from baseline for each visit and treatment group in both FL and overall population will be analyzed as mentioned in Section 7.4.7.1.

[redacted]



[redacted]

## 7.6. Sensitivity and Supportive Analyses for Efficacy Endpoints

The following sensitivity analysis may be performed:

- [redacted]
- For time-to-event endpoints, the assumption of proportional hazard may be tested using a goodness-of-fit test based on Schoenfeld residuals (Kleinbaum and Klein 2012), and Schoenfeld residuals may be displayed graphically. In case the test reveals a significant deviation from the assumption of proportional hazards, weighted log-rank test (Zucker and Lakatos 1990), or RMST (Royston and Parmar 2013) may be performed.
- For time-to-event endpoints, an unstratified log-rank test may be performed and an unadjusted HR may be obtained using the unstratified Cox Proportional Hazard model.
- Stratification factors per IRT will be summarized: POD24 (yes versus no; FL only), refractoriness to prior anti-CD20 mAb therapy (yes versus no; FL only), the number of prior lines of therapy ($< 2$ versus $\geq 2$). The number of participants with disagreement for each stratification factor between IRT and the eCRF will be summarized if any. Stratified analyses may be performed using stratification factors from the eCRF if at least 1 stratification factor per IRT and eCRF disagrees for at least 5% of the total randomized participants.
- For binary endpoints such as PET-CR rate and ORR, Fisher's exact test may be performed.
- For the primary and key secondary endpoint of PFS in the FL population and the overall population, the analysis may be performed considering participants having an event after 2 or more missed visits as having a PFS event. The censoring rule is the same as described in Section 7.3 for PFS, except for death or progression after 2 or more missed assessments, the outcome is progression, and date of death or progression will be used. The change in censoring rules is presented in Table 8.

**Table 8: Change in Censoring Rules in Sensitivity Analysis Versus Primary Analysis of PFS When PD/Death After 2 or More Missed Assessments is Treated as PFS Event**

| Situation | Outcome as per Primary Analysis | Censoring Date as per Primary Analysis | Outcome as per Sensitivity Analysis | Date of Event as per Sensitivity Analysis |
|---|---|---|---|---|
| Death or progression after 2 or more missed assessments | Censored | Date of last adequate tumor assessment | Event | Date of progression/death |

- For the primary and key secondary endpoint of PFS in the FL population and the overall population, the analysis will correct for potential bias in the follow-up schedules for disease assessment by assigning the dates for censoring and events only at scheduled visit dates. It is the same as the primary analysis described in Section 7.3 except that the date of progression is approximated as the date of the Protocol-scheduled visit immediately after the radiologic assessment of PD. The change in censoring rules is presented in Table 9.

**Table 9: Change in Censoring Rules in Sensitivity Analysis Versus Primary Analysis of PFS When Protocol-Scheduled Visit is Used as the Date of Progression**

| Situation | Outcome as per Primary Analysis | Censoring Date as per Primary Analysis | Outcome as per Sensitivity Analysis | Date of Event as per Sensitivity Analysis |
|---|---|---|---|---|
| Progression documented between scheduled response assessments | Progressed | Date of first overall response of PD | Progressed | Date of next scheduled visit |

- For the primary and secondary efficacy endpoints, sensitivity analyses may be performed to evaluate the impact of subsequent antilymphoma therapy. For the PFS and DOR endpoints, sensitivity analyses may be performed per EMA guidelines to consider new antilymphoma treatment as an event or consider all disease progressions and deaths as events regardless of whether they occur after initiating new antilymphoma treatment. Participants without an event observed should be censored at the last time known to be alive. The change in censoring rules is presented in Table 10 and Table 11.

**Table 10: Change in Censoring Rules in Sensitivity Analysis Versus the Primary Analysis of PFS When New Antilymphoma Treatment is Treated as an Event**

| Situation | Outcome as per Primary Analysis | Censoring Date as per Primary Analysis | Outcome as per Sensitivity Analysis | Date of Event as per Sensitivity Analysis |
|---|---|---|---|---|
| New antilymphoma treatment started | Censored | Date of last adequate tumor assessment with no documented progression (not NE and not missing) on/before starting a new antilymphoma treatment | Progressed | Date of new antilymphoma treatment |

**Table 11: Change in Censoring Rules in Sensitivity Analysis Versus the Primary Analysis of PFS When PD/Death is Treated as an Event Regardless of Initiation of New Antilymphoma Treatment**

| Situation | Outcome as per primary analysis | Censoring date as per primary analysis | Outcome as per sensitivity analysis | Date of event as per sensitivity analysis |
|---|---|---|---|---|
| New antilymphoma treatment started | Censored | Date of last adequate tumor assessment with no documented progression (not NE and not missing) on/before starting a new antilymphoma treatment | Not applicable | Not applicable |

- As supportive analysis, treatment switch-adjusted OS might be performed to correct for the start of new antilymphoma treatment.

Additional sensitivity analysis may be conducted as needed.

# 8. SAFETY AND TOLERABILITY

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

## 8.1. General Considerations

Safety analyses will be conducted for the SAF. 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.

All TEAEs, clinical laboratory measurements, and vital sign measurements will be summarized by treatment group for the FL, MZL, and overall populations. 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.

## 8.2. Adverse Events

### 8.2.1. Adverse Event Definitions

A TEAE is any AE either reported for the first time or worsening of a pre-existing event on or after the first dose of study treatment until 90 days after the last dose of study treatment. Analysis of AEs (as discussed below) will be limited to TEAEs, but data listings will include all AEs regardless of their timing in relation to study treatment administration. For the 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 NCI CTCAE v5. The CTCAE reporting guidelines and grading details are available on the Cancer Therapy Evaluation Program website.

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

### 8.2.2. Adverse Events of Special Interest by eCRF

The number (%) of participants who had an AESI, the time to onset of each AESI, and the longest duration of each AESI will be summarized by treatment group.

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

Adverse events of special interest for tafasitamab/placebo include TLS, IRRs and allergic reactions to study drug ≥ Grade 3, CRS, SPMs, hepatitis B reactivation, and PML.

Adverse events of special interest for lenalidomide include SPMs.

The longest duration of an AESI is defined as the longest interval between the date of occurrence of an AESI and the date of resolution. If participants have a missing or partial onset/end date of an AESI, the partial or missing dates will be handled using the rules explained in Section 4.1.4. Participants who have a missing end date of an AESI at the time of analysis will be right-censored using the following algorithm:

- If the AESI is serious, then the participant will be censored at the earlier date of data cutoff, study discontinuation, or death.
- If the AESI is not serious,
  - If the participant is ongoing with study treatment, then the participant will be censored at the data cutoff date.
  - If the participant discontinued treatment, then the participant will be censored at date of safety follow-up visit, or 90 days after the EOT visit (or after the last dose if the EOT visit was not performed), whichever is later; the censored date will be truncated by the earlier date of data cutoff, study discontinuation, or death if beyond.

The Kaplan-Meier estimate of median time to resolution/improvement and its 95% CIs will be provided, with the CIs calculated using the generalization of Brookmeyer and Crowley's method (1982) with log-log transformation (Klein and Moeschberger 1997). Resolution/improvement rates at selected timepoints will also be provided with 95% CIs calculated using Greenwood's formula to estimate the standard error. Such analysis for an AESI will not be conducted if 10 or fewer participants had the AESI.

### 8.2.3. Adverse Events of Special Interest by Category and Preferred Term

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

Adverse events of special interest for tafasitamab/placebo include:

- Standard MedDRA Queries
  - Tumour lysis syndrome
  - Hypersensitivity (≥ Grade 3)
- Preferred terms
  - Cytokine release syndrome
  - Second primary malignancy
  - Hepatitis B reactivation

Progressive multifocal leukoencephalopathy

Adverse events of special interest for lenalidomide include:

- Preferred term
- Second primary malignancy

The analysis of the AESI by category and PT will be carried out as described in Section 8.2.2.

A listing will display the complete selected category and PTs from custom MedDRA queries and/or the selected PTs, defined by the sponsor. This will be used as reference listing.

### 8.2.4. Adverse Event Summaries

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

- Number (%) of participants who had any TEAEs
- Number (%) of participants who had any serious TEAEs
- Number (%) of participants who had any Grade 3 or 4 TEAEs
- Number (%) of participants who had any fatal TEAEs
- Number (%) of participants who had any TEAEs related to tafasitamab/placebo
- Number (%) of participants who had any serious TEAEs related to tafasitamab/placebo
- Number (%) of participants who had any Grade 3 or 4 TEAEs related to tafasitamab/placebo
- Number (%) of participants who had any fatal TEAEs related to tafasitamab/placebo
- Number (%) of participants who had any TEAEs related to lenalidomide
- Number (%) of participants who had any serious TEAEs related to lenalidomide
- Number (%) of participants who had any Grade 3 or 4 TEAEs related to lenalidomide
- Number (%) of participants who had any fatal TEAEs related to lenalidomide
- Number (%) of participants who had any TEAEs related to rituximab

- Number (%) of participants who had any serious TEAEs related to rituximab
- Number (%) of participants who had any Grade 3 or 4 TEAEs related to rituximab
- Number (%) of participants who had any fatal TEAEs related to rituximab
- Number (%) of participants who had any TEAE leading to interruption of tafasitamab/placebo
- Number (%) of participants who had any TEAE leading to interruption of lenalidomide
- Number (%) of participants who had any TEAE leading to interruption of rituximab
- Number (%) of participants who had any TEAE leading to dose delay of tafasitamab/placebo
- Number (%) of participants who had any TEAE leading to dose delay of rituximab
- Number (%) of participants who had any TEAE leading to permanent discontinuation of tafasitamab/placebo
- Number (%) of participants who had any TEAE leading to permanent discontinuation of lenalidomide
- Number (%) of participants who had any TEAE leading to permanent discontinuation of rituximab
- Number (%) of participants who had any TEAE leading to dose reduction of lenalidomide

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

- Summary of TEAEs by MedDRA SOC and PT
- Summary of TEAEs by MedDRA PT in decreasing order of frequency
- Summary of TEAEs by MedDRA SOC, PT, and maximum severity
- Summary of Grade 3 or 4 TEAEs by MedDRA SOC and PT
- Summary of Grade 3 or 4 TEAEs by MedDRA PT in decreasing order of frequency
- Summary of TEAEs with a fatal outcome by MedDRA SOC and PT
- Summary of serious TEAEs by MedDRA SOC and PT
- Summary of serious TEAEs by MedDRA PT in decreasing order of frequency
- Summary of tafasitamab/placebo treatment-related TEAEs by MedDRA SOC and PT
- Summary of lenalidomide treatment-related TEAEs by MedDRA SOC and PT
- Summary of rituximab treatment-related TEAEs by MedDRA SOC and PT
- Summary of tafasitamab/placebo treatment-related TEAEs by MedDRA PT in decreasing order of frequency

- Summary of lenalidomide treatment-related TEAEs by MedDRA PT in decreasing order of frequency
- Summary of rituximab treatment-related TEAEs by MedDRA PT in decreasing order of frequency
- Summary of Grade 3 or 4 tafasitamab/placebo treatment-related TEAEs by MedDRA SOC and PT
- Summary of fatal tafasitamab/placebo treatment-related TEAEs by MedDRA SOC and PT
- Summary of Grade 3 or 4 lenalidomide treatment-related TEAEs by MedDRA SOC and PT
- Summary of fatal lenalidomide treatment-related TEAEs by MedDRA SOC and PT
- Summary of Grade 3 or 4 rituximab treatment-related TEAEs by MedDRA SOC and PT
- Summary of fatal rituximab treatment-related TEAEs by MedDRA SOC and PT
- Summary of tafasitamab/placebo treatment-related serious TEAEs by MedDRA SOC and PT
- Summary of lenalidomide treatment-related serious TEAEs by MedDRA SOC and PT
- Summary of rituximab treatment-related serious TEAEs by MedDRA SOC and PT
- Summary of TEAEs leading to lenalidomide dose reduction by MedDRA SOC and PT
- Summary of TEAEs leading to tafasitamab/placebo dose interruption by MedDRA SOC and PT
- Summary of TEAEs leading to lenalidomide dose interruption by MedDRA SOC and PT
- Summary of TEAEs leading to rituximab dose interruption by MedDRA SOC and PT
- Summary of TEAEs leading to tafasitamab/placebo dose delay by MedDRA SOC and PT
- Summary of TEAEs leading to rituximab dose delay by MedDRA SOC and PT
- Summary of TEAEs leading to discontinuation of tafasitamab/placebo by MedDRA SOC and PT
- Summary of TEAEs leading to discontinuation of lenalidomide by MedDRA SOC and PT
- Summary of TEAEs leading to discontinuation of rituximab by MedDRA SOC and PT

- Summary of AESIs for tafasitamab/placebo and lenalidomide (eCRF) by grouped term and PT
- Summary of AESIs for tafasitamab/placebo and lenalidomide by grouped term and PT

The following groups will be displayed for the FL, MZL, and overall populations:

- Age group (< 65 vs ≥ 65 years , < 75 vs ≥ 75 years), sex, race and MZL subtype (for MZL population only) will be displayed for the following tables:
  - Overall Summary of TEAEs
  - Summary of TEAEs by MedDRA SOC and PT
  - Summary of Serious TEAEs by MedDRA SOC and PT
  - Summary of Grade 3 or 4 TEAEs by MedDRA SOC and PT
  - Summary of TEAEs with a fatal outcome by MedDRA SOC and PT
- Creatinine Clearance (≥ 30 and < 60 ml/min vs ≥ 60) will be displayed for the following tables:
  - Overall Summary of TEAEs
  - Summary of TEAEs by MedDRA SOC and PT
  - Summary of Serious TEAEs by MedDRA SOC and PT
  - Summary of Grade 3 or 4 TEAEs by MedDRA SOC and PT
  - Summary of TEAEs with a fatal outcome by MedDRA SOC and PT
  - Summary of lenalidomide treatment related TEAEs by MedDRA SOC and PT
  - Summary of TEAEs leading to lenalidomide dose reduction by MedDRA SOC and PT
  - Summary of TEAEs leading to discontinuation of lenalidomide by MedDRA SOC and PT

In addition, the following summaries will be produced:

Selected hematological TEAEs (neutropenia, febrile neutropenia, anemia, thrombocytopenia) of Grade 3 or 4 and fatal by SOC, PT, and grade.

- PTs used to identify neutropenia: "neutropenia," "neutrophil count decreased"
- PTs used to identify anemia: "anemia," "red blood cell count decreased"
- PTs used to identify thrombocytopenia: "platelet count decreased," "thrombocytopenia"
- PTs used to identify febrile neutropenia: "febrile neutropenia"

- Duration of TEAEs of the selected PTs and customized MedDRA queries:
  - Neutropenia ≥ Grade 3 (PTs "neutropenia," "neutrophil count decreased")
  - Thrombocytopenia ≥ Grade 3 (PTs "thrombocytopenia," "platelet count decreased")
  - Infections and infestations ≥ Grade 3 (SOC "infections and infestations")
  - Infective pneumonia ≥ Grade 3 (SMQ code 20000231, narrow scope)
  - Urinary tract infection ≥ Grade 3 (HLT "bladder infections and inflammations," HLT "Genitourinary infections and inflammations NEC," HLT "Glomerulonephritis and nephrotic syndrome")
  - Sepsis ≥ Grade 3 (SMQ "sepsis" and SMQ "agranulocytosis")
  - Febrile neutropenia, all grades (PT "febrile neutropenia")
  - Thromboembolic event, all grades (SMQ code 2000081)
  - Thromboembolic event ≥ Grade 3 (SMQ code 2000081)
  - Opportunistic infections ≥ Grade 3 (SMQ "opportunistic infections")

Selected AEs included in the previous summaries will be listed as a reference.

### 8.2.5. Adverse Event Summaries for the Japanese Population

A subset of the above-mentioned summary will be generated for the Japanese overall population. The complete list is available in Appendix A.

## 8.3. Clinical Laboratory Tests

### 8.3.1. Laboratory Value Definitions

The measurement of all laboratory parameters (except pregnancy testing) as indicated in the Protocol will be performed centrally. 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.

### 8.3.2. Laboratory Value Summaries

All test results and associated normal ranges from central laboratories will be reported in or converted to SI units.

When there are multiple nonmissing laboratory values for a participant's particular test within a visit window, the convention described in Table 12 will be used to determine the record used for by-visit tabulations and summaries.

**Table 12: Identification of Records for Postbaseline By-Visit Summaries**

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

Shift tables based on the worst postbaseline value recorded will use all postbaseline values occurring within 90 days of stopping study treatment.

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, and neutrophils.

For test results that will be summarized with available normal ranges, the number and percentage of participants with laboratory values being low (but never high), normal, high (but never low), and both low and high will be calculated for each test. This shift summary will be produced for each test for the safety population. The denominator for the percentage calculation will use the number of participants in the baseline category (ie, low, high, normal, missing) as the denominator for the percentage in each of the categories during the study.

The number of participants who experienced worsening of laboratory abnormalities will be summarized by maximum severity.

In cases where differentials of hematology parameters are obtained without corresponding absolute count data, efforts will be made to investigate if the conversion to an absolute value will lead to additional abnormalities. This will be discussed with the clinical team regarding appropriate documentation and action.

### 8.3.3. Potential Drug-Induced Liver Injuries

Participants with elevated ALT or AST $\geq 3 \times$ ULN range and alkaline phosphatase $< 2 \times$ ULN range accompanied by total bilirubin $\geq 2 \times$ ULN range within $\pm$ 7 days will be listed by treatment group.

## 8.4. Vital Signs

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

Normal ranges for vital sign values are defined in Table 13. 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 or weight. The abnormal values for participants exhibiting alert vital sign abnormalities will be listed.

**Table 13: Normal Ranges for Vital Sign Values**

| Parameter | High Threshold | Low Threshold |
|---|---|---|
| Systolic blood pressure | ≤ 155 mmHg | ≥ 85 mmHg |
| Diastolic blood pressure | ≤ 100 mmHg | ≥ 40 mmHg |
| Pulse | ≤ 100 bpm | ≥ 45 bpm |
| Temperature | ≤ 38°C | ≥ 35.5°C |
| Respiratory rate | ≤ 24 breaths/min | ≥ 8 breaths/min |

## 8.5. Electrocardiograms

The INV will evaluate the clinical significance of each ECG value outside the reference ranges (including QTc assessment), according to the nature and degree of the observed abnormality. Any new abnormal values or those deteriorating from baseline considered to be clinically significant should be reported as AEs. The INV-evaluated ECG abnormalities are captured on the "12-Lead ECG" eCRF form. Incidences of such abnormalities and a description of the clinically significant abnormality will be listed with study visit and assigned treatment group.

A 2D-ECHO or cardiac MUGA scan will be obtained at screening to evaluate cardiac function, including assessment of LVEF. This information will be listed.

# 9. INTERIM ANALYSES

## 9.1. Overview of Progression-Free Survival Interim Analyses

An IDMC will be involved in reviewing the PFS interim analysis results and will provide their recommendation for a potential nonbinding futility stop based on comparative efficacy and safety data. The IDMC will consist of clinicians and an IDMC statistician. The sponsor will remain blinded, and IDMC decisions will be communicated through sponsor management as dictated in the IDMC charter.

### 9.1.1. Progression-Free Survival Interim Efficacy Analysis

A PFS interim analysis for futility will be performed after 20% (approximately 35) of the required INV-assessed PFS events have been observed in participants with FL in the FAS. This is expected to occur approximately 15 months after the first participant is randomized and approximately 338 (out of 528 total) participants with FL have been randomized in the study.

The PFS HR will be calculated, and the IDMC may recommend to stop the study if the observed HR of tafasitamab plus lenalidomide in addition to rituximab (TGA) over placebo plus lenalidomide in addition to rituximab (TGB) is ≥ 1.05 for participants with FL in the FAS (nonbinding futility boundary; see Table 14). Early stop for efficacy is not planned.

The false negative rate for a futility stop with a futility boundary of HR = 1.05 is approximately 8% if the true HR is 0.65 and approximately 15% if the true HR is 0.74.

The false positive rate for continuation of the study with a futility boundary of HR = 1.05 is approximately 62% if the true HR is 0.95.

**Table 14: Guidelines for Decisions - Progression-Free Survival**

| | **Interim Analysis** | |
|---|---|---|
| Projected timing | 15 months | |
| Projected randomized participants | 338 participants | |
| Number of PFS events | 35 events | |
| Decision outcome | **Futility Boundary** | **Continue** |
| Estimated HR | ≥ 1.05 | < 1.05 |

At the PFS interim analysis for futility, the IDMC will review both efficacy and safety data. The IDMC recommendation to stop the study for futility will be based on totality of evidence including evaluation of the primary endpoint, PFS, as well as other efficacy endpoints including ORR, DOR, PET-CR rate, and OS. Additional operational details of the interim analysis, including tables, figures, and listings provided to the IDMC will be provided in the IDMC charter.

### 9.1.2. Interim Safety Review

After the first 60 randomized participants (approximately 30 in each treatment group) complete at least the first 2 study treatment cycles (8 weeks), the IDMC will review the safety data to monitor and evaluate the safety of the combination treatment and provide recommendation on whether the combination treatments are safe. Thereafter, the IDMC will review the safety data approximately every 6 months.

Additional operational details of the interim analyses, including tables, figures, and listings provided to the IDMC will be provided in the IDMC charter.

Additional safety analyses may be performed at the discretion of the IDMC chair.

## 9.2. Overview of Overall Survival Interim Analyses

At the time of the PFS primary analysis, an interim futility analysis of OS will be conducted.

### 9.2.1. Overall Survival Interim Analysis

To estimate the number of deaths at the time of the PFS primary analysis the same hypothesis as specified in the sample size section will be used (see Section 3.3). A median OS of 10 years in the control group, a PFS HR of 0.65, a 21 months accrual rate, a 12 months follow up, and a 15% drop out rate would result in approximately 47 deaths at the time of the PFS primary analysis estimated 33.5 months after the first participant is randomized.

The final analysis for the study will still be expected to occur approximately 96 months after the first participant is randomized.

The OS interim futility analysis will be implemented using an O'Brien and Fleming beta spending function with the characteristics as presented in Table 15.

**Table 15: Guideline for Decision - Overall Survival**

| | | |
|---|---|---|
| Assumed true HR | 0.65 | |
| Median OS in control arm | 120 months | |
| Alpha level | One-sided 2.5% | |
| Power | 80% | |
| Futility rule | Stop for Futility if observed HR > 1.24 (non-binding) | |
| Futility boundary (z-value scale) | −0.744 | |
| Futility Rule Operating Characteristic | True HR | Probability of reaching futility boundary |
| | True HR = 0.65 | 1.40% |
| | True HR = 1 | 22.85% |
| | True HR = 1.25[a] | 52.25% |
| | True HR = 1.5[a] | 74.98% |

[a] Obtained running 10000 simulations using the get simulation survival function from Rpact with a seed = 1234.

## 9.3. Data Cutoff for Interim Analysis

### 9.3.1. Progression-Free Survival Interim Efficacy Analysis for Futility

For analysis of the primary endpoint, a cutoff for clinical data used in the interim futility analysis will be based on the date of the 35th PFS event (disease progression or death) and will include all participant visits occurring on or before this date.

### 9.3.2. Overall Survival Interim Analysis

The cutoff used in the OS interim analysis will be at the time of the PFS primary analysis. It will be based on the date of the occurrence of the 174th PFS event (disease progression or death) and will include all participant visits occurring on or before this date.

# 10. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 16.

**Table 16: Statistical Analysis Plan Versions**

| SAP Version | Date |
|---|---|
| Original | 01 DEC 2021 |
| Amendment 1 | 26 OCT 2022 |
| Amendment 2 | 19 JAN 2024 |
| Amendment 3 | 25 JUN 2024 |

## 10.1. Changes to Protocol-Defined Analyses

The MRD-evaluable set analysis population was added in the SAP to support the sensitivity analysis for the summary of MRD-negativity rate.

The following analyses were added in the SAP to provide additional study information:

- Summary of currentness of PFS and OS data (see Section 7.3.3)
- Summary of PFS and OS follow-up time (see Section 7.3.4)
- Summary of time to objective response (see Section 7.5.4)
- Overall survival for PFS with FL for interim analysis (see Section 7.3.2.3 and Section 9.1.1)

As of SAP Amendment 2, the MRD-negativity rate threshold used other secondary efficacy analysis will be $10^{-5}$ and the threshold of $10^{-4}$ will be used for sensitivity (see Section 7.4.2).

## 10.2. Changes to the Statistical Analysis Plan

### 10.2.1. Amendment 1

The following clarifications have been added in the SAP:

- Table 1 was updated to align with Protocol Amendment 6.
- Section 7.3 was updated to clarify how to handle participants with confirmed diagnosis different to the one used for randomization.
- Section 7.3.2.1 and Section 7.4.5 were updated to clarify the stratification factors to be included in the analysis.
- Section 7.3.2.3 and Section 7.6 were updated to clarify the censoring rules for overall survival.
- Section 8.2.3 was added.
- Section 8.2.4 was updated to clarify the AE summaries.
- Appendix A was updated to reflect the additional tables/listings from Section 8.2.3 and the modification listed in Section 8.2.4.

In addition, other minor, administrative changes have been incorporated throughout the SAP and are noted in the redline version of the amendment.

### 10.2.2. Amendment 2

The following clarifications and modification have been added in the SAP:

- Table 1, Section 3.2, Section 7.3, and Section 7.4 were updated to align with Protocol Amendment 7.
- Section 3.2 was updated and Section 9.2 was added to describe an OS futility interim analysis to be performed at the time of the PFS primary analysis.
- Section 4.1.4 was updated to clarify how to handle a partial last prior therapy date.
- Section 4.2.2 was updated to clarify the definition of prior and concomitant medication in case of partial drug administration dates.
- Section 5.3 was updated to change the MRD evaluable set (to include the sample origin) and the FDG-avid population.
- Section 6.1.1 was updated to add COVID-19 vaccination status at screening to the analyzed baseline characteristics.

[redacted]

- Section 6.4 was updated to add the lenalidomide exposure table by creatinine clearance groups. Duration category for tafasitamab and lenalidomide were updated.
- Section 6.5.1 was updated to clarify the calculation.

[redacted]

- Section 7.4.2 was modified to clarify the origin of the MRD samples, the definition of sample stability, the threshold to be used to define negativity, and the denominator to calculate the MRD negativity rates.
- Section 7.4.6 was added to describe the IRC-related analysis.
- Section 7.4.7 was updated to clarify the analysis of the three quality of life questionnaire included in the study.

[redacted]

- Section 7.6 was updated to remove the option of running Renyi test as additional sensitivity analysis. This test was considered redundant with the other options proposed.
- Section 8.2.4 was updated to add the list of tables to be generated by sub-groups (age, gender, race, and creatinine clearance).

- Section 8.3.2 was updated to clarify that only line graph will be used for laboratory values graphical representations.
- Section 9.1 was updated specify the interim analysis described in the section will be for PFS.
- Section 9.3 was updated to discuss PFS and OS interim analysis separately.
- Appendix A was updated to reflect the additional tables/listings from Section 6, Section 7, Section 8.2.4, and Section 8.2.5 and to include sensitivity analysis, [redacted] and QoL listings. Numbering and title of the listings were modified to adhere to the company standard shells. The population to be used in each listing was added as well.

In addition, other minor, administrative changes have been incorporated throughout the SAP and are noted in the redline version of the amendment.

### 10.2.3. Amendment 3

The following clarifications and modification have been added in the SAP:

- Section 3.2 was updated to correct a typographical error: "An interim analysis for futility will be performed for OS at the time of the PFS interim analysis using a nonbinding rule, HR will be estimated" is now "An interim analysis for futility will be performed for OS at the time of the PFS **primary** analysis using a nonbinding rule, HR will be estimated."
- Section 6.1.3 was updated to include addition to optionally report the number of participants with prior autologous stem cell transplantation.
- Section 6.6 was updated with clarification about the relative dose intensity to be a surrogate for compliance if the accountability is not properly recorded.
- Section 7.3.1, Table 6, the last row in the "Date of Progression or Censoring" column was changed from "Date of last adequate tumor assessment with overall lesion response of CR, PR, or SD prior to PD or death" to "Date of last progression assessment with documented nonprogression" as mentioned in the guidance for industry Clinical Trial Endpoints for the Approval of Non-Small Cell Lung Cancer Drugs and Biologics, Appendix C (FDA 2015).

[redacted]

- Section 7.4.2 was updated to remove the sensitivity analysis using peripheral blood sample at EOT with a $10^{-4}$ as threshold to define negativity (in the MRD-blood evaluable population) as it will not be performed.
- Section 7.4.6 was updated to include concordance between investigator and IRC analysis for the MZL population and to restrict concordance analyses to best overall response.

- Section 8.2.3 was updated to include a reference listing for the category and PT terms selected.

[redacted]

In addition, other minor, administrative changes have been incorporated throughout the SAP and are noted in the redline version of the amendment.

# 11. REFERENCES

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# APPENDIX A. PLANNED TABLES, FIGURES, AND LISTINGS

This appendix provides a list of the planned tables, figures, and listings for the Clinical Study Report.

Shells are provided in a separate document for tables that are not in the Standard Safety Tables v1.11.

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

## Tables

In the Table number the .x will specify the subset of participant included:

- .1: FL
- .2: MZL
- .3: Overall
- .4: Japanese FL
- .5 Overall Japanese

| Table No. | Title | Pop | FL | MZL | Overall | Jap FL | Jap Overall | Standard |
|---|---|---|---|---|---|---|---|---|
| **Baseline and Demographic Characteristics** | | | | | | | | |
| 1.1.1 | Analysis Populations | All screened | | | | | | X |
| 1.1.2 | Summary of Screen Disposition | All screened | | | | | | X |
| 1.1.3.x | Summary of Participant Disposition | FAS | X | X | X | X | X | X |
| 1.1.4.x | Summary of Number of Participants Enrolled by Country and Site | FAS | X | X | X | | | X |
| 1.1.5.x | Summary of Important Protocol Deviations | FAS | X | X | X | X | X | X |
| 1.2.1.x | Summary of Demographics and Baseline Characteristics | FAS | X | X | X | X | X | X |
| 1.3.1.x | Summary of Baseline Disease Characteristics and Disease History | FAS | X | X | X | X | X | X |
| 1.3.2.x | Summary of Prior Therapy | FAS | X | X | X | X | X | |
| 1.4.1.x | Summary of Prior Medications | FAS | X | X | X | X | X | X |
| 1.4.2.x | Summary of Concomitant Medications | FAS | X | X | X | X | X | X |
| 1.5.1.x | Summary of General Medical History | FAS | X | X | X | X | X | X |
| 1.6.1.x | Summary of Stratification Factors and Concordance between IRT and eCRF | FAS | X | X | X | X | X | |
| **Efficacy** | | | | | | | | |
| 2.1.1.x | Summary of Progression-Free Survival by Investigator Assessment | FAS | X | X | X | X | X | |
| 2.1.2.x | Summary of Progression-Free Survival by IRC | FAS | X | X | X | X | X | |
| 2.1.3.x | Sensitivity Analysis for Summary of Progression-Free Survival by Investigator Assessment | FAS | X | | X | X | X | |
| 2.1.4.x | Sensitivity Analysis for Summary of Progression-Free Survival by Investigator Assessment – Change in Censoring | FAS | X | | X | X | X | |

| Table No. | Title | Pop | FL | MZL | Overall | Jap FL | Jap Overall | Standard |
|---|---|---|---|---|---|---|---|---|
| 2.2.1.x | Summary of Positron-Emission Tomography-Complete Response Rate by Investigator Assessment | FDG-avid FAS | X | X | X | X | X | |
| 2.2.2.x | Sensitivity Analysis for Summary of Positron-Emission Tomography-Complete Response Rate by Investigator | FDG-avid FAS | X | | X | X | X | |
| 2.2.3.x | Summary of Overall Survival | FAS | X | X | X | X | X | |
| 2.2.4.x | Sensitivity Analysis for Summary of Overall Survival | FAS | X | | X | X | X | |
| 2.2.5.x | Summary of Minimal Residual Disease-Negativity Rate in Peripheral Blood at End of Treatment | MRD-blood evaluable | X | X | X | X | X | |
| 2.2.6.x | Sensitivity Analysis for Summary of Minimal Residual Disease Negativity Rate in Peripheral Blood | MRD-blood evaluable | X | | X | X | X | |
| 2.2.7.x | Sensitivity Analysis for Summary of Minimal Residual Disease Negativity Rate in Bone Marrow | MRD-bone marrow evaluable | X | | X | X | X | |
| 2.2.8.x | Summary of Overall Response Rate by Investigator Assessment | FAS | X | X | X | X | X | |
| 2.2.9.x | Summary of Overall Response Rate by IRC | FAS | X | X | X | X | X | |
| 2.2.10.x | Sensitivity Analysis for Summary of Overall Response Rate by Investigator Assessment | FAS | X | | X | X | X | |
| 2.2.11.x | Summary of Duration of Response by Investigator Assessment | FAS | X | X | X | X | X | |
| 2.2.12.x | Summary of Duration of Response by IRC | FAS | X | X | X | X | X | |
| 2.2.13.x | Sensitivity Analysis for Summary of Duration of Response by Investigator Assessment | FAS | X | | X | X | X | |
| 2.2.14.x | Summary of Concordance Rates Between Investigator Assessment and IRC Review | FAS | X | X | X | X | X | |
| 2.2.15.x | Summary of Currentness of Progression-Free Survival and Overall Survival | FAS | X | | X | X | X | |
| 2.2.16.x | Summary of Progression-Free Survival and Overall Survival Follow-Up Time | FAS | X | | X | X | X | |
| 2.2.17.x | Summary of Quality of Life Assessments - EORTC QLQ-C30 | FAS | X | | X | X | X | |
| 2.2.18.x | Summary of Quality of Life Assessments - EQ-5D-5L | FAS | X | | X | X | X | |
| 2.2.19.x | Summary of Quality of Life Assessments - FACT-Lym | FAS | X | | X | X | X | |
| [redacted] | | | | | | | | |
| 2.3.3.x | Summary of Post-Treatment Systemic Antilymphoma Therapies | FAS | X | | X | X | X | |
| [redacted] | | | | | | | | |

| Table No. | Title | Pop | FL | MZL | Overall | Jap FL | Jap Overall | Standard |
|---|---|---|---|---|---|---|---|---|
| [redacted] | | | | | | | | |
| 2.90.4.x | Summary of Progression-Free Survival by Investigator Assessment in PPS | PPS | X | X | X | X | X | |
| [redacted] | | | | | | | | |
| 2.90.8.x | Summary of Overall Survival in PPS | PPS | X | X | X | X | X | |
| [redacted] | | | | | | | | |
| **Safety** | | | | | | | | |
| 3.1.1.x | Summary of Exposure to Tafasitamab/Placebo | SAF | X | X | X | | X | X |
| 3.1.2.x | Summary of Exposure to Rituximab | SAF | X | X | X | | X | X |
| 3.1.3.x | Summary of Exposure to Lenalidomide | SAF | X | X | X | | X | X |
| 3.1.4.x | Summary of Exposure to Lenalidomide by Creatinine Clearance | SAF | X | X | X | | X | X |
| 3.2.1.x | Overall Summary of Treatment-Emergent Adverse Events | SAF | X | X | X | | X | X |
| 3.2.2.x | Summary of Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.3.x | Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency | SAF | X | X | X | | X | X |
| 3.2.4.x | Summary of Treatment-Emergent Adverse Events by MedDRA SOC, Preferred Term, and Maximum Severity | SAF | X | X | X | | X | X |
| 3.2.5.x | Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.6.x | Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency | SAF | X | X | X | | X | X |
| 3.2.7.x | Summary of Serious Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.8.x | Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency | SAF | X | X | X | | X | X |

| Table No. | Title | Pop | FL | MZL | Overall | Jap FL | Jap Overall | Standard |
|---|---|---|---|---|---|---|---|---|
| 3.2.9.x | Summary of Tafasitamab/Placebo Treatment-Related Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.10.x | Summary of Lenalidomide Treatment-Related Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.11.x | Summary of Rituximab Treatment-Related Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.12.x | Summary of Tafasitamab/Placebo Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency | SAF | X | X | X | | X | X |
| 3.2.13.x | Summary of Lenalidomide Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency | SAF | X | X | X | | X | X |
| 3.2.14.x | Summary of Rituximab Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency | SAF | X | X | X | | X | X |
| 3.2.15.x | Summary of Grade 3 or 4 Tafasitamab/Placebo Treatment-Related Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.16.x | Summary of Fatal Tafasitamab/Placebo Treatment-Related Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.17.x | Summary of Grade 3 or 4 Lenalidomide Treatment-Related Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.18.x | Summary of Fatal Lenalidomide Treatment-Related Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.19.x | Summary of Grade 3 or 4 Rituximab Treatment-Related Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.20.x | Summary of Fatal Rituximab Treatment-Related Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.21.x | Summary of Tafasitamab/Placebo Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.22.x | Summary of Lenalidomide Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |

| Table No. | Title | Pop | FL | MZL | Overall | Jap FL | Jap Overall | Standard |
|---|---|---|---|---|---|---|---|---|
| 3.2.23.x | Summary of Rituximab Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.24.x | Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.25.x | Summary of Treatment-Emergent Adverse Events Leading to Lenalidomide Dose Modification by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.26.x | Summary of Treatment-Emergent Adverse Events Leading to Tafasitamab/Placebo Dose Modification by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.27.x | Summary of Treatment-Emergent Adverse Events Leading to Rituximab Dose Modification by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.28.x | Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Tafasitamab/Placebo by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.29.x | Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Lenalidomide by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.30.x | Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Rituximab by MedDRA SOC and Preferred Term | SAF | X | X | X | | X | X |
| 3.2.31.x | Summary of Treatment-Emergent Adverse Events of Special Interest (eCRF) by Category, Preferred Term, and Maximum Severity | SAF | X | X | X | | X | X |
| 3.2.32.x | Summary of Time to Onset and Longest Duration of Treatment-Emergent Adverse Events of Special Interest (eCRF) | SAF | X | X | X | | X | |
| 3.2.33.x | Summary of Treatment-Emergent Adverse Events of Special Interest by AESI Category, Preferred Term, and Maximum Severity | SAF | X | X | X | | X | X |
| 3.2.34.x | Summary of Time to Onset and Longest Duration of Treatment-Emergent Adverse Events of Special Interest | SAF | X | X | X | | X | |
| 3.2.35.x | Summary of Grade 3 or 4 Selected Hematological Treatment-Emergent Adverse Events | SAF | X | X | X | | X | X |
| 3.2.36.x | Summary of Fatal Selected Hematological Treatment-Emergent Adverse Events | SAF | X | X | X | | X | X |
| 3.2.37.x | Summary of Duration of Treatment-Emergent Adverse Events of the Selected Preferred Terms and Customized MedDRA Queries | SAF | X | X | X | | X | |

| Table No. | Title | Pop | FL | MZL | Overall | Jap FL | Jap Overall | Standard |
|---|---|---|---|---|---|---|---|---|
| 3.2.38.x | Summary of Death | SAF | X | X | X | | X | |
| 3.2.39.x | Overall Summary of Treatment-Emergent Adverse Events by Age Group | SAF | X | X | X | | | |
| 3.2.40.x | Overall Summary of Treatment-Emergent Adverse Events by Sex | SAF | X | X | X | | | |
| 3.2.41.x | Overall Summary of Treatment-Emergent Adverse Events by Race | SAF | X | X | X | | | |
| 3.2.42.x | Overall Summary of Treatment-Emergent Adverse Events by Creatinine Clearance | SAF | X | X | X | | | |
| 3.2.43.x | Summary of Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term by Age Group | SAF | X | | X | | | |
| 3.2.44.x | Summary of Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term by Sex | SAF | X | | X | | | |
| 3.2.45.x | Summary of Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term by Race | SAF | X | | X | | | |
| 3.2.46.x | Summary of Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term by Creatinine Clearance | SAF | X | | X | | | |
| 3.2.47.x | Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term by Age Group | SAF | X | | X | | | |
| 3.2.48.x | Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term by Sex | SAF | X | | X | | | |
| 3.2.49.x | Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term by Race | SAF | X | | X | | | |
| 3.2.50.x | Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term by Creatinine Clearance | SAF | X | | X | | | |
| 3.2.51.x | Summary of Serious Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term by Age Group | SAF | X | | X | | | |
| 3.2.52.x | Summary of Serious Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term by Sex | SAF | X | | X | | | |
| 3.2.53.x | Summary of Serious Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term by Race | SAF | X | | X | | | |
| 3.2.54.x | Summary of Serious Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term by Creatinine Clearance | SAF | X | | X | | | |
| 3.2.55.x | Summary of Treatment-Emergent Adverse Events with a Fatal Outcome by MedDRA SOC and Preferred Term by Age Group | SAF | X | | X | | | |

| Table No. | Title | Pop | FL | MZL | Overall | Jap FL | Jap Overall | Standard |
|---|---|---|---|---|---|---|---|---|
| 3.2.56.x | Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA SOC and Preferred Term by Sex | SAF | X | | X | | | |
| 3.2.57.x | Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA SOC and Preferred Term by Race | SAF | X | | X | | | |
| 3.2.58.x | Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA SOC and Preferred Term by Creatinine Clearance | SAF | X | | X | | | |
| 3.2.59.x | Summary of Lenalidomide Treatment-Related Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term by Creatinine Clearance | SAF | X | | X | | | |
| 3.2.60.x | Summary of Treatment-Emergent Adverse Events leading to Lenalidomide Dose Modification by MedDRA SOC and Preferred Term by Creatinine Clearance | SAF | X | | X | | | |
| 3.2.61.x | Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Lenalidomide by MedDRA SOC and Preferred Term by Creatinine Clearance | SAF | X | | X | | | |
| 3.2.62.x | Summary of Treatment-Emergent Adverse Events of Special Interest (eCRF) by Category, Preferred Term, and Maximum Severity by Creatinine Clearance | SAF | X | | X | | | |
| 3.2.63.x | Summary of Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term - Differences Between Japanese and Non-Japanese Participants | SAF | | | X | | | |
| 3.2.64.x | Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency Difference Between Japanese and Non-Japanese Participants | SAF | | | X | | | |
| 3.2.65.x | Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency Difference Between Japanese and Non-Japanese Participants | SAF | | | X | | | |
| 3.2.66.x | Summary of Treatment-Emergent Adverse Events with a Fatal Outcome by MedDRA Preferred Term in Decreasing Order of Frequency Difference Between Japanese and Non-Japanese Participants | SAF | | | X | | | |
| 3.2.67.x | Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency Difference Between Japanese and Non-Japanese Participants | SAF | | | X | | | |

| Table No. | Title | Pop | FL | MZL | Overall | Jap FL | Jap Overall | Standard |
|---|---|---|---|---|---|---|---|---|
| 3.2.68.x | Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by MedDRA Preferred Term in Decreasing Order of Frequency Difference Between Japanese and Non-Japanese Participants | SAF | | | X | | | |
| 3.2.69.x | Summary of Treatment-Emergent Adverse Events Leading to Dose Modification of Tafasitamab/Placebo by MedDRA Preferred Term in Decreasing Order of Frequency Difference Between Japanese and Non-Japanese Participants | SAF | | | X | | | |
| 3.2.70.x | Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA SOC, Preferred Term (Differences Between Japanese and Non-Japanese Participants) | SAF | | | X | | | |
| 3.2.71.x | Summary of Grade 5 Treatment-Emergent Adverse Events by MedDRA SOC, Preferred Term (Differences Between Japanese and Non-Japanese Participants) | SAF | | | X | | | |
| 3.2.72.x | Overall Summary of Treatment-Emergent Adverse Events by Age Group (< 75 vs >= 75) | SAF | X | X | X | | | |
| 3.2.73.x | Summary of Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term by Age Group (< 75 vs >= 75) | SAF | X | X | X | | | |
| 3.2.74.x | Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term by Age Group (< 75 vs >= 75) | SAF | X | X | X | | | |
| 3.2.75.x | Summary of Serious Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term by Age Group (< 75 vs >= 75) | SAF | X | X | X | | | |
| 3.2.76.x | Summary of Treatment Emergent Adverse Events with a Fatal Outcome by MedDRA SOC and Preferred Term by Age Group (< 75 vs >= 75) | SAF | X | X | X | | | |
| 3.2.77.x | Overall Summary of Treatment-Emergent Adverse Events by MZL Subtype | SAF | | X | | | | |
| 3.2.78.x | Summary of Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term by MZL subtype | SAF | | X | | | | |
| 3.2.79.x | Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term by MZL Subtype | SAF | | X | | | | |
| 3.2.80.x | Summary of Serious Treatment-Emergent Adverse Events by MedDRA SOC and Preferred Term by MZL Subtype | SAF | | X | | | | |

| Table No. | Title | Pop | FL | MZL | Overall | Jap FL | Jap Overall | Standard |
|---|---|---|---|---|---|---|---|---|
| 3.2.81.x | Summary of Treatment Emergent Adverse Events with a Fatal Outcome by MedDRA SOC and Preferred Term by MZL subtype | SAF | | X | | | | |
| 3.3.1.1.x | Summary of Laboratory Values - Hematology | SAF | X | X | X | | | X |
| 3.3.1.2.x | Summary of Laboratory Values - Chemistry | SAF | X | X | X | | | X |
| 3.3.1.3.x | Summary of Laboratory Values - Coagulation | SAF | X | X | X | | | X |
| 3.3.1.4.x | Summary of Laboratory Values - Urinalysis | SAF | X | X | X | | | X |
| 3.3.2.1.x | Shift Summary of Hematology Values - to the Worst Abnormal Value | SAF | X | X | X | | | X |
| 3.3.2.2.x | Shift Summary of Chemistry Values - to the Worst Abnormal Value | SAF | X | X | X | | | X |
| 3.3.2.3.x | Shift Summary of Coagulation Values - to the Worst Abnormal Value | SAF | X | X | X | | | X |
| 3.3.3.1.x | Shift Summary of Hematology Laboratory Values in CTCAE Grade - to the Worst Abnormal Value | SAF | X | X | X | | | X |
| 3.3.3.2.x | Shift Summary of Chemistry Laboratory Values in CTCAE Grade - to the Worst Abnormal Value | SAF | X | X | X | | | X |
| 3.3.3.3.x | Shift Summary of Coagulation Laboratory Values in CTCAE Grade - to the Worst Abnormal Value | SAF | X | X | X | | | X |
| 3.3.3.4.x | Treatment-Emergent Worsening of Laboratory Abnormalities - Hematology | SAF | X | X | X | | | X |
| 3.3.3.5.x | Treatment-Emergent Worsening of Laboratory Abnormalities - Chemistry | SAF | X | X | X | | | X |
| 3.3.3.6.x | Treatment-Emergent Worsening of Laboratory Abnormalities - Coagulation | SAF | X | X | X | | | X |
| 3.4.1.x | Summary of Systolic Blood Pressure | SAF | X | X | X | | | X |
| 3.4.2.x | Summary of Diastolic Blood Pressure | SAF | X | X | X | | | X |
| 3.4.3.x | Summary of Pulse | SAF | X | X | X | | | X |
| 3.4.4.x | Summary of Respiratory Rate | SAF | X | X | X | | | X |
| 3.4.5.x | Summary of Body Temperature | SAF | X | X | X | | | X |
| 3.4.6.x | Summary of Weight | SAF | X | X | X | | | X |

## Figures

In the figure number the .x will specify the subset of participant included:

- .1: FL
- .2: MZL
- .3: Overall
- .4: Overall Japanese Population

| Figure No. | Title | Pop | FL | MZL | Overall | Jap Overall |
|---|---|---|---|---|---|---|
| 4.1.x | Kaplan-Meier Estimates of Progression-Free Survival | FAS | X | X | X | X |
| 4.2.x | Kaplan-Meier Estimates of Overall Survival | FAS | X | X | X | X |
| 4.3.x | Kaplan-Meier Estimates of Duration of Response | FAS | X | X | X | X |
| [redacted] | | | | | | |
| 4.7.x | Kaplan-Meier Estimates of Progression-Free Survival on Next Treatment | FAS | X | X | X | X |
| [redacted] | | | | | | |
| 4.8.2.x | Kaplan-Meier Estimates of Progression-Free Survival by Number of Prior Lines | FAS | X | X | X | X |
| [redacted] | | | | | | |
| 4.8.4.x | Kaplan-Meier Estimates of Progression-Free Survival by Refractoriness to Anti-CD20 | FAS | X | | X | X |
| 4.8.5.x | Kaplan-Meier Estimates of Progression-Free Survival by CR at End of Treatment | FAS | X | | X | X |
| 4.8.6.x | Kaplan-Meier Estimates of Progression-Free Survival by MRD Status at End of Treatment | FAS | X | | X | X |
| 4.9.1.x | Line Graph of B-cell Counts Across Visits | FAS | X | X | X | X |
| 4.9.2.x | Line Graph of Neutrophils Cell Counts Across Visits | FAS | X | X | X | X |
| 4.9.3.x | Line Graph of Platelets Cell Counts Across Visits | FAS | X | X | X | X |
| [redacted] | | | | | | |
| 4.9.5.x | Line Graph of IgG Across Visits | FAS | X | X | X | X |
| 4.9.6.x | Line Graph of IgA Across Visits | FAS | X | X | X | X |
| 4.9.7.x | Line Graph of IgM Across Visits | FAS | X | X | X | X |

## Listings

In the listing number the .x will specify the subset of participant included:

- 1: Overall Population
- 2: Overall Japanese Population

| Listing No. | Title | Population | Overall | Japanese Overall |
|---|---|---|---|---|
| 2.1.1.x | Participant Enrollment and Disposition Status | FAS | X | X |
| 2.1.2.x | Participant Inclusion and Exclusion Criteria Violations | Screen Failed | X | X |
| 2.2.1.x | Protocol Deviations | FAS | X | X |
| 2.3.1.x | Analysis Population | FAS | X | X |
| 2.4.1.x | Demographic and Baseline Characteristics | FAS | X | X |
| 2.4.2.x | Baseline Disease Characteristics and Disease History | FAS | X | X |
| 2.4.3.x | Prior Radiation Treatment | FAS | X | X |
| 2.4.4.x | Prior Therapy | FAS | X | X |
| 2.4.5.x | Prior Surgery or Surgical Procedure | FAS | X | X |
| 2.4.6.x | Medical History | FAS | X | X |
| 2.4.7.x | Prior and Concomitant Medication | FAS | X | X |
| 2.4.8.x | Premedication Given Prior to Tafasitamab/Placebo Administration to Mitigate Potential Infusion-Related Reactions | FAS | X | X |
| 2.4.9.x | Stratification Factors IRT versus eCRF | FAS | X | X |
| 2.5.1.x | Study Drug Information - Tafasitamab | SAF | X | X |
| 2.5.2.x | Study Drug Administration - Tafasitamab | SAF | X | X |
| 2.5.3.x | Study Drug Information - Rituximab | SAF | X | X |
| 2.5.4.x | Study Drug Administration - Rituximab | SAF | X | X |
| 2.5.5.x | Study Drug Information - Lenalidomide | SAF | X | X |
| 2.5.6.x | Study Drug Administration - Lenalidomide | SAF | X | X |
| 2.6.1.x | Deaths | FAS | X | X |
| 2.6.2.x | Best Overall Response, Duration of Response, and Progression-Free Survival per Investigator and IRC | FAS | X | X |
| 2.6.3.x | Overall Response Assessment by Visit per Investigator and IRC | FAS | X | X |
| 2.6.4.x | Response Assessment: Target Lesions per Investigator | FAS | X | X |
| 2.6.5.x | Response Assessment: Nontarget Lesions per Investigator | FAS | X | X |
| 2.6.6.x | Response Assessment: New Lesions per Investigator | FAS | X | X |
| 2.6.7.x | Spleen Size | FAS | X | X |
| 2.6.8.x | ECOG Status | FAS | X | X |
| 2.6.9.x | Post-Treatment Systemic Antilymphoma Therapies | FAS | X | X |
| 2.6.10.x | Summary of Quality of Life Assessments - EORTC QLQ-C30 | FAS | X | X |
| 2.6.11.x | Summary of Quality of Life Assessments - EQ-5D-5L | FAS | X | X |
| 2.6.12.x | Summary of Quality of Life Assessments - FACT-Lym | FAS | X | X |
| 2.6.13.x | Progression-Free Survival - Change in Censoring | FAS | X | X |
| [redacted] | | | | |
| 2.6.16.x | Summary of Minimal Residual Disease-Negativity Rate | FAS | X | X |

| Listing No. | Title | Population | Overall | Japanese Overall |
|---|---|---|---|---|
| 2.7.1.x | Adverse Events | SAF | X | X |
| 2.7.2.x | Serious Adverse Events | SAF | X | X |
| 2.7.3.x | Grade 3 and 4 Adverse Events | SAF | X | X |
| 2.7.4.x | Fatal Adverse Events | SAF | X | X |
| 2.7.5.x | Tafasitamab/Placebo Treatment-Related Adverse Events | SAF | X | X |
| 2.7.6.x | Lenalidomide Treatment-Related Adverse Events | SAF | X | X |
| 2.7.7.x | Rituximab Treatment-Related Adverse Events | SAF | X | X |
| 2.7.8.x | Adverse Events Leading to Dose Modification of Tafasitamab/Placebo | SAF | X | X |
| 2.7.9.x | Adverse Events Leading to Dose Modification of Lenalidomide, | SAF | X | X |
| 2.7.10.x | Adverse Events Leading to Dose Modification of Rituximab | SAF | X | X |
| 2.7.11.x | Adverse Events of Special Interest Terms by eCRF and Preferred Terms | SAF | X | X |
| 2.7.12.x | Adverse Events That Occurred in Japanese Overall population But Not Occurred in Non-Japanese Overall population | SAF | X | |
| 2.7.13 | Adverse Events of Special Interest Terms | | | |
| 2.7.14 | Selected Hematological and Infection Adverse Events | | | |
| 2.8.1.x | Clinical Laboratory Values – Hematology | SAF | X | X |
| 2.8.2.x | Clinical Laboratory Values – Chemistry | SAF | X | X |
| 2.8.3.x | Clinical Laboratory Values – Coagulation | SAF | X | X |
| 2.8.4.x | Clinical Laboratory Values – Urinalysis | SAF | X | X |
| 2.8.5.x | Abnormal Clinical Laboratory Values | SAF | X | X |
| 2.8.6.x | Potential Drug-Induced Liver Injuries | SAF | X | X |
| 2.9.1.x | Vital Signs | SAF | X | X |
| 2.9.2.x | Abnormal Vital Sign Values | SAF | X | X |
| 2.9.3.x | Alert Vital Sign Values | SAF | X | X |
| 2.10.1.x | Clinically Significant ECG Abnormality | SAF | X | X |
| 2.10.2.x | 2D-ECHO and MUGA at Screening | SAF | X | X |