STATISTICAL ANALYSIS PLAN

Version 4.0

MorphoSys AG

Semmelweisstr. 7
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GERMANY

A Phase Ib, open-label, randomized study to assess safety and preliminary efficacy of Tafasitamab in addition to R-CHOP or Tafasitamab plus Lenalidomide in addition to R-CHOP in patients with newly diagnosed Diffuse Large B-Cell Lymphoma (DLBCL) – First-MIND

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SIGNATURE PAGE

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1. DOCUMENT HISTORY

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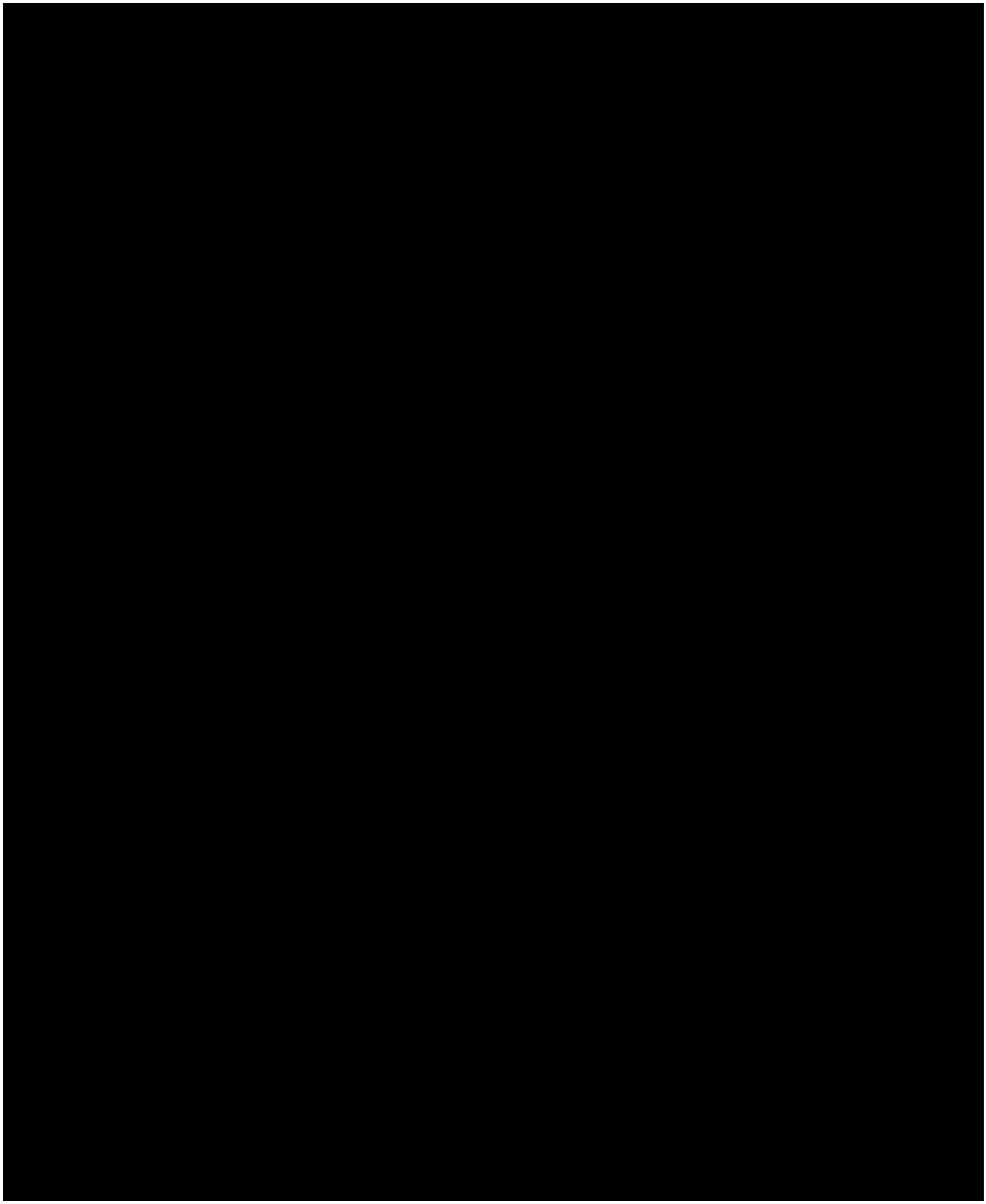
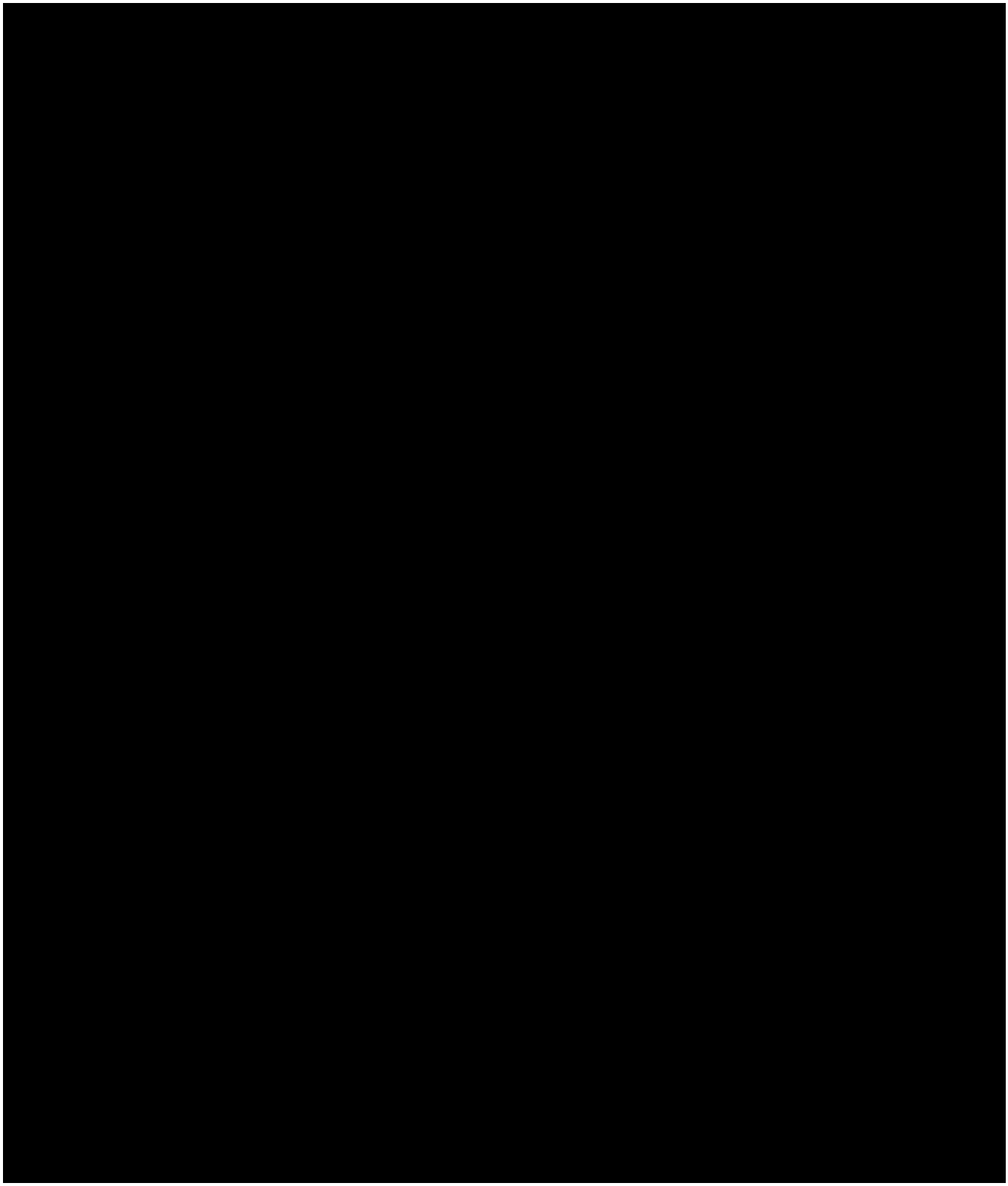
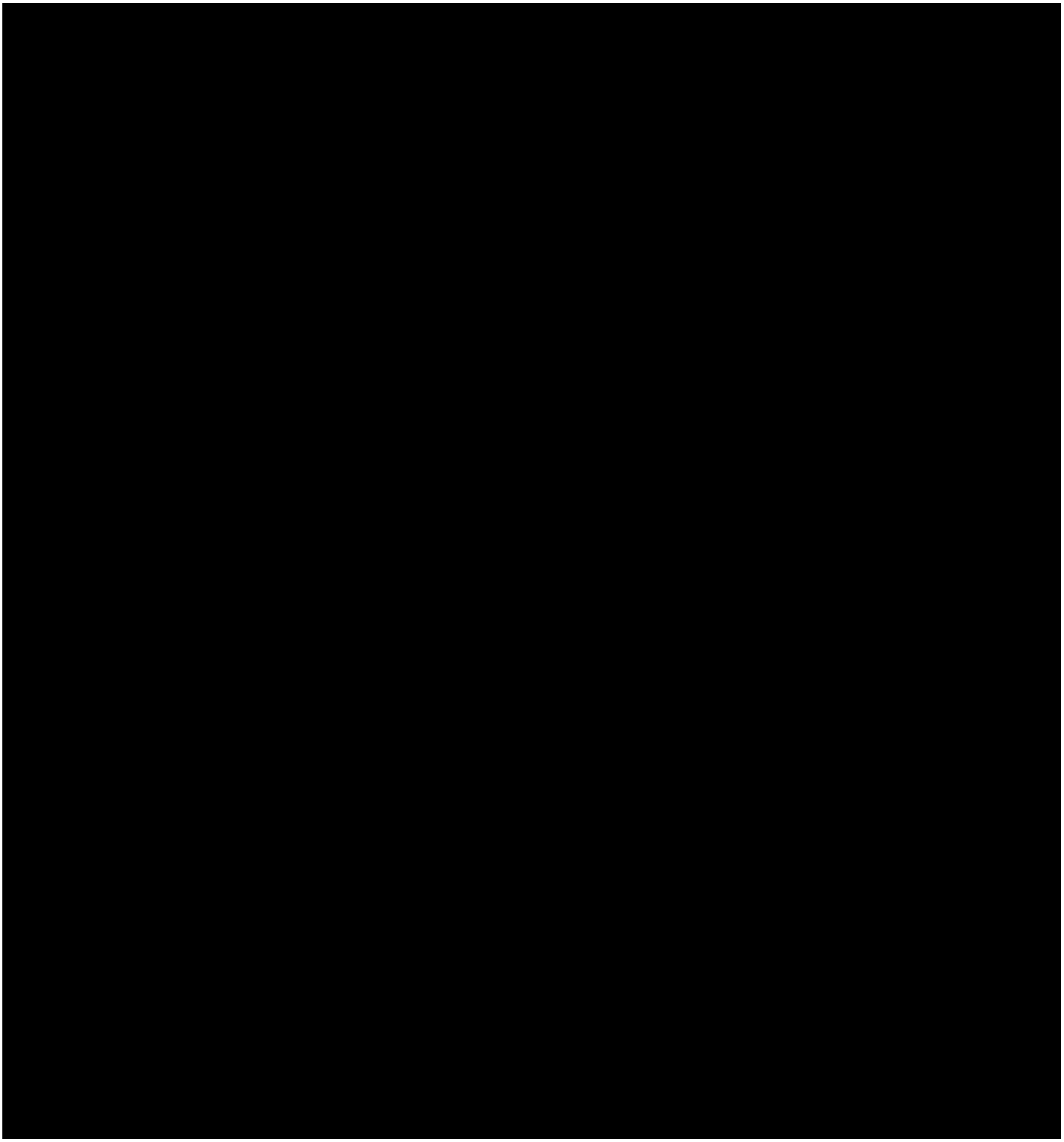




2. CHANGE FROM PROTOCOL



3. LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

AE	Adverse event
AESI	Adverse Event of Special Interest
ALP	Alkaline phosphatase
ALT	Alanine amino Transferase
ANC	Absolute Neutrophil Count
aPTT	Activated Partial Thromboplastin Time
AST	Aspartate amino Transferase
ATC	Anatomical Therapeutic Chemical
BLQ	Below the Limit of Quantification
CHOP	Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone
CI	Confidence Interval
Cmax	Concentration max.
CNS	Central Nervous System
COO	Cell of Origin
CR	Complete Response
CRO	Contract Research Organization
CT	Computerised Tomography
CTCAE	Common Terminology Criteria for Adverse Events
ctDNA	Circulating Tumor DNA
Ctrough	Concentration trough
CSR	Clinical Study Report
DLBCL	Diffuse Large B-cell Lymphoma
DNA	Deoxyribonucleic Acid
DOR	Duration of Response
DoCR	Duration of Complete Response
ECG	Electrocardiogram
ECHO	Echocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic Case Report Form
EFS	Event Free Survival
EMA	European Medicines Agency
EOT	End of Treatment
FAS	Full Analysis Set
FCBP	Females of childbearing potential
FDA	Food and Drugs Administration
FDG	Fluorodeoxyglucose
FU	Follow-up
GCP	Good Clinical Practice
GI	Gastrointenstinal
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
Anti-HBc	Hepatitis B Core Antibody
Anti-HBs	Hepatitis B Surface Antibody
Anti-HCV	Hepatitis C Virus Antibody
IAS	Immunogenicity Analysis Set
ICF	Informed Consent Form

ICH	International Council for Harmonisation
IHC	Immunohistochemistry
IgA	Immunoglobulin A
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IMP	Investigational Medicinal Product
IPI	International Prognostic Index
IRR	Infusion-related reaction
IV	Intravenous
LDH	Lactate Dehydrogenase
LEN	Lenalidomide
LVEF	Left Ventricular Systolic Function
mAb	Monoclonal Antibody
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
mL	Millilitre
MRD	Minimal Residual Disease
MUGA	Multigated Acquisition
NCI	National Cancer Institute
ng	Nanogram
NK	Natural Killer
NKCC	Natural Killer Cell Count
ORR	Objective Response Rate
OS	Overall Survival
PCR	Polymerase Chain Reaction
PD	Progressive Disease
PE	Physical Examination
PET	Positron Emission Tomography
PFS	Progression Free Survival
PK	Pharmacokinetics
PKAS	Pharmacokinetic Analysis Set
PML	Progressive Multifocal Leukoencephalopathy
PPS	Per Protocol Set
PR	Partial Response
PT	Preferred Term
PTT	Partial Thromboplastin Time
RBC	Red Blood Cell
R-CHOP	Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone
RNA	Ribonucleic Acid
R/R	Relapsed/Refractory
SAP	Statistical Analysis Plan
SAE	Serious adverse event
SAF	Safety Set
StD	Standard Deviation
SoC	System Organ Class
SOP	Standard Operating Procedure
TEAE	Treatment Emergent Adverse Event
TLS	Tumor Lysis Syndrome

TTNT	Time to Next Anti-lymphoma Treatment
TTP	Time to Progression
ULN	Upper Limit of Normal
WBC	White Blood Cell
WHO	World Health Organisation

4. INTRODUCTION

This Statistical Analysis Plan (SAP) describes the planned analysis and reporting of data collected from MorphoSys protocol MOR208C107, Version 6.0, dated 05-Feb-2020. Any amendments to the protocol which do not affect the statistical aspects of the trial will not necessitate an SAP update.

This study is an open-label, randomized, phase Ib study to assess safety and preliminary efficacy of Tafasitamab in addition to R-CHOP or Tafasitamab plus Lenalidomide in addition to R-CHOP in patients with newly diagnosed diffuse large B-cell lymphoma. The structure and content of this SAP provides sufficient detail to meet the requirements identified by the Food and Drug Administration (FDA), European Medicines Agency (EMA), and International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use: Guidance on Statistical Principles in Clinical Trials. All work planned and reported from this SAP will follow internationally accepted guidelines, published by the American Statistical Association and the Royal Statistical Society, for statistical practice.

The planned analyses identified in this SAP may be included in clinical study report (CSRs) and/or in relevant summary report documents (e.g. regulatory submissions, or future manuscripts). Also, *post-hoc* exploratory analyses not necessarily identified in this SAP may be performed to further examine study data and will not require updating the final SAP. Any post-hoc, or unplanned, exploratory analysis performed will be clearly identified as such and described in the final CSR.

The following documents were reviewed in preparation of this SAP:

- Clinical Trial Protocol MOR208C107, Version 6.0, dated 05-Feb-2020
- Annotated electronic Case report forms (eCRFs), Version final 5.0, dated 03-Feb-2022
- ICH Guidance on Statistical Principles for Clinical Trials (E9)

The reader of this SAP is encouraged to also read the clinical trial protocol, and other identified documents, for details on the design and planned conduct of this study. Operational aspects related to collection and timing of planned clinical assessments are not repeated in this SAP unless relevant to the planned analysis.

5. STUDY OBJECTIVES AND ENDPOINTS

An overview of the study objectives and endpoints is depicted in Table 1.

Table 1: Study objectives and endpoints

	Objective	Endpoint	SAP section
Primary	To assess safety and tolerability of tafasitamab in addition to R-CHOP and tafasitamab plus lenalidomide in addition to R-CHOP	Incidence and severity of treatment emergent adverse events (TEAEs)	Section 11.1
Key Secondary	To assess efficacy (based on Lugano 2014 criteria) of tafasitamab in addition to R-CHOP and tafasitamab plus lenalidomide in addition to R-CHOP	Objective Response Rate (ORR) at the end of treatment	Section 10.1.2
		Metabolic, positron emission tomography (PET)-negative complete response (CR) rate at the end of treatment	Section 10.1.3
Secondary	To assess long-term safety and tolerability of tafasitamab in addition to R-CHOP and tafasitamab plus lenalidomide in addition to R-CHOP	Incidence and severity of adverse events (AEs) in the follow-up period	Section 11.1
	To assess long term efficacy (based on Lugano 2014 criteria) of tafasitamab in addition to R-CHOP and tafasitamab plus lenalidomide in addition to R-CHOP	Best Objective Response Rate (ORR) until the end of study	Section 10.1.2
		Metabolic, PET-negative complete response (CR) rate until the end of study	Section 10.1.3
		Progression-free survival (PFS) at 12 and 24 months	Secion 10.1.5
		Event-free survival (EFS) at 12 and 24 months	Section 10.1.6
		Overall survival (OS) at 12 and 24 months	Section 10.1.77
		Time to next anti-lymphoma treatment (TTNT)	Section 10.1.88
	To assess the pharmacokinetic (PK) profile of tafasitamab in each treatment arm	Tafasitamab serum concentrations, i.e., Concentration trough (Ctrough) levels and Concentration max (Cmax) levels on Day 1 of each cycle	Section 10.2
	To assess the potential immunogenicity of tafasitamab in each treatment arm	Number and percentage of patients developing anti-tafasitamab antibodies, and	Section 10.3

	Objective	Endpoint	SAP section
		semi-quantitative titer assessments.	
Exploratory*	To evaluate residual disease burden by serial circulating tumor DNA (ctDNA) assessment	Descriptive statistics of ctDNA by visit	Section 10.4
	To assess the relationship between potential molecular or cellular markers and efficacy of tafasitamab in addition to R-CHOP or tafasitamab and lenalidomide in addition to R-CHOP	The relationship of the following endpoints will be assessed for the following markers: Endpoints: i. ORR ii. PFS Biomarkers: i. Cell of origin ii. Quantitative and semi-quantitative CD19 expression on tumor cells (in diagnostic biopsies and at progression/relapse if available) iii. Quantitative and semi-quantitative CD20 expression on tumor cells (in diagnostic biopsies and at progression/relapse if available)	Section 10.4

*A limited number of biomarkers (listed above) will be considered and will be presented in CSR.

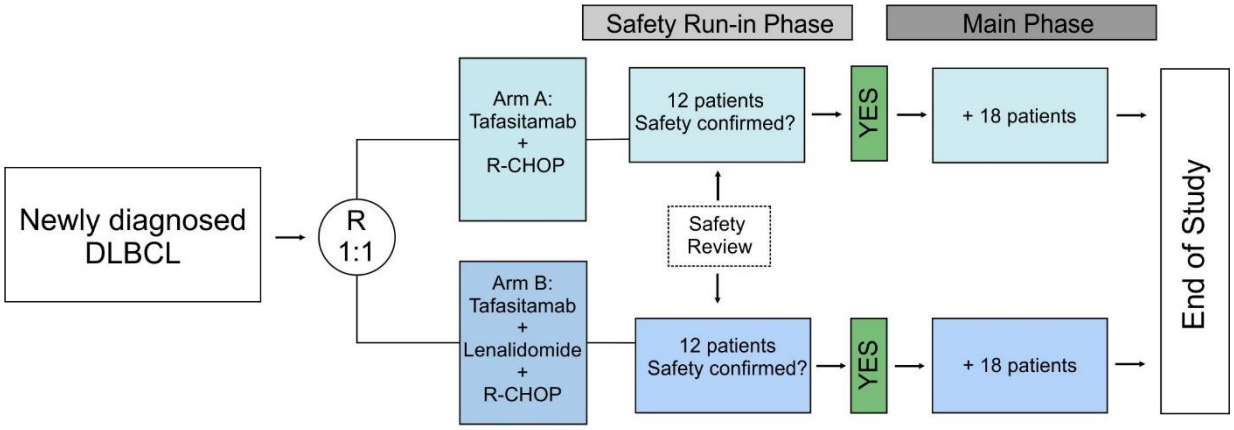
6. STUDY DESIGN

6.1 General study design

This is a multicenter, open-label, randomized, Phase Ib trial to assess safety and preliminary efficacy of tafasitamab in addition to R-CHOP or tafasitamab plus lenalidomide in addition to R-CHOP in adult patients with newly diagnosed diffuse large B-cell lymphoma (DLBCL). Approximately 60 patients (approximately 30 in each arm) will be randomized in this study. If a patient discontinues the trial for any reason other than treatment related toxicity, progression/relapse of disease or death, this patient may be replaced.

The trial consists of two phases, see Figure 1.

Figure 1: Trial design



All patients are expected to receive 6 cycles of treatment (each cycle consisting of 21 days) and to be followed up for 24 months (or 731 days) from the date of randomization.

6.2 Schedule of assessments

For a detailed schedule of assessments, please refer to the protocol section 10.

6.3 Determination of sample size

As this is a Phase Ib study primarily conducted to explore safety endpoints, no formal statistical hypothesis has been established for the sample size calculation of this trial.

With a sample size of 12 patients in each arm, there is a 60% probability to observe 4 or more patients with unacceptable toxicity if the underlying incidence rate of these toxicities is 33%.

With a sample size of 30 patients in each arm, there is a 55% probability to observe 10 or more patients with unacceptable toxicity if the underlying incidence rate of these toxicities is 33%.

6.4 Timing of analyses

6.4.1 Safety run-in analyses

A safety run-in phase with 24 patients , 12 patients in each arm, will be performed. In order to evaluate the safety in accordance with the stopping rules, enrolment may be paused when12 patients in each arm have been recruited and have been followed for 21 days after cycle 1 day 1 (C1D1). Details of stopping rules can be referred to in protocol section 6.3. Sponsor safety review meetings will be performed on an ongoing basis by representatives of the sponsor with medical and pharmacovigilance expertise and the medical monitors of the contract research organization. A Safety Committee (SC) consisting of sponsor representatives with at least two representatives of the participating investigators of this clinical trial. This committee will meet regularly until all patients have completed treatment. During the safety run-in the SC committee meets approximately on a monthly basis. In addition, an independent Data and Safety Monitoring Board (iDSMB) consisting of independent haematologists will be established. The iDSMB will provide a recommendation at the end of safety run-in phase when all patients in both arms have finished their first treatment cycle. Details of the SC and the iDSMB are outlined in the respective Charters and corresponding SAPs as available.

6.4.2 Primary completion analysis

The primary completion analysis will be performed based on a data cut-off 30 days after all patients have performed their End of Treatment (EoT) Visit or discontinued study treatment.

Primary and key secondary objectives will be analyzed at the time of primary completion analysis. All results of the primary completion analysis will be made available to Morphosys AG prior to finalization of the primary completion analysis/CSR.

6.4.3 Final analysis

After the last patient completed the last visit, a final analysis will be performed.

At the time of final completion analysis, analyses performed during primary completion analysis will be repeated using updated data in addition to the performance of secondary and exploratory objectives.

Additional safety and follow-up analyses may be performed by the sponsor as and when deemed necessary.

7. DEFINITIONS AND GENERAL METHODOLOGY

7.1 Enrolment date

Enrolment date is defined to be the date that patients signed the informed consent form.

7.2 Treatment arm

There are two treatment arms in this study, which are denoted as treatment arm A and treatment arm B respectively. Treatment arm A refers to the group of patients receiving tafasitamab in addition to R-CHOP as planned, whereas treatment arm B refers to the groups of patients receiving tafasitamab plus lenalidomide in addition to R-CHOP.

7.3 Study drug and study treatment

For the purpose of the SAP and data presentation/analysis, **study drug** refers to tafasitamab or lenalidomide or any component of R-CHOP.

Study treatment refers to tafasitamab plus R-CHOP for treatment arm A and tafasitamab plus lenalidomide in addition to R-CHOP for treatment arm B.

Study treatment completion refers to that the record of 'Subject completed treatment per protocol' is filled for **all components of study treatment** in the 'End of Treatment/Early Study Treatment Discontinuation' eCRF page for the patients. If a patient reduces lenalidomide or any component of R-CHOP, or interrupts tafasitamab/lenalidomide/any component of R-CHOP per investigators' instruction, he/she is still counted as completing study treatment, as long as he/she finishes the End of Treatment visit without any permanent discontinuation record. Patients with permanent discontinuation of **any component of the study treatment** fail the concept of study treatment completion.

Completion of Tafasitamab: Completion of Tafasitamab implies that the primary reason for stopping treatment is filled as 'Subject Completed Treatment Per Protocol' for the treatment "Tafasitamab" in the 'End of Treatment/Early Study Treatment Discontinuation' eCRF page.

Premature discontinuation of Tafasitamab: If the primary reason for stopping treatment is filled as anything other than 'Subject Completed Treatment Per Protocol' for the treatment "Tafasitamab" in the 'End of Treatment/Early Study Treatment Discontinuation' eCRF page, then the patient is said to discontinue Tafasitamab prematurely.

Completion of Lenalidomide: Completion of Lenalidomide implies that the primary reason for stopping treatment is filled as 'Subject Completed Treatment Per Protocol' for the treatment "Lenalidomide" in the 'End of Treatment/Early Study Treatment Discontinuation' eCRF page.

Premature discontinuation of Lenalidomide: If the primary reason for stopping treatment is filled as anything other than 'Subject Completed Treatment Per Protocol' for the treatment "Lenalidomide" in the 'End of Treatment/Early Study Treatment Discontinuation' eCRF page, then the patient is said to discontinue Lenalidomide prematurely.

Completion of Rituximab: Completion of Rituximab implies that the primary reason for stopping treatment is filled as 'Subject Completed Treatment Per Protocol' for the treatment "Rituximab" in the 'End of Treatment/Early Study Treatment Discontinuation' eCRF page.

Premature discontinuation of Rituximab: If the primary reason for stopping treatment is filled as anything other than 'Subject Completed Treatment Per Protocol' for the treatment "Rituxamab" in the 'End of Treatment/Early Study Treatment Discontinuation' eCRF page, then the patient is said to discontinue Rituximab prematurely.

Completion of Cyclophosphamide: Completion of Cyclophosphamide implies that the primary reason for stopping treatment is filled as 'Subject Completed Treatment Per Protocol' for the treatment "Cyclophosphamide" in the 'End of Treatment/Early Study Treatment Discontinuation' eCRF page.

Premature discontinuation of Cyclophosphamide: If the primary reason for stopping treatment is filled as anything other than 'Subject Completed Treatment Per Protocol' for the treatment "Cyclophosphamide" in the 'End of Treatment/Early Study Treatment Discontinuation' eCRF page, then the patient is said to discontinue Cyclophosphamide prematurely.

Completion of Doxorubicin: Completion of Doxorubicin implies that the primary reason for stopping treatment is filled as 'Subject Completed Treatment Per Protocol' for the treatment "Doxorubicin" in the 'End of Treatment/Early Study Treatment Discontinuation' eCRF page.

Premature discontinuation of Doxorubicin: If the primary reason for stopping treatment is filled as anything other than 'Subject Completed Treatment Per Protocol' for the treatment "Doxorubicin" in the 'End of Treatment/Early Study Treatment Discontinuation' eCRF page, then the patient is said to discontinue Doxorubicin prematurely.

Completion of Vincristine: Completion of Vincristine implies that the primary reason for stopping treatment is filled as 'Subject Completed Treatment Per Protocol' for the treatment "Vincristine" in the 'End of Treatment/Early Study Treatment Discontinuation' eCRF page.

Premature discontinuation of Vincristine: If the primary reason for stopping treatment is filled as anything other than 'Subject Completed Treatment Per Protocol' for the treatment "Vincristine" in the 'End of Treatment/Early Study Treatment Discontinuation' eCRF page, then the patient is said to discontinue Vincristine prematurely.

Completion of Prednisone: Completion of Prednisone implies that the primary reason for stopping treatment is filled as 'Subject Completed Treatment Per Protocol' for the treatment "Prednisone" in the 'End of Treatment/Early Study Treatment Discontinuation' eCRF page.

Premature discontinuation of Prednisone: If the primary reason for stopping treatment is filled as anything other than 'Subject Completed Treatment Per Protocol' for the treatment "Prednisone" in the 'End of Treatment/Early Study Treatment Discontinuation' eCRF page, then the patient is said to discontinue Prednisone prematurely.

Completion of R-CHOP: Completion of R-CHOP implies that the primary reason for stopping treatment is filled as 'Subject Completed Treatment Per Protocol' for all the components of R-CHOP in the 'End of Treatment/Early Study Treatment Discontinuation' eCRF page.

Premature discontinuation of R-CHOP: If the primary reason for stopping treatment is filled as anything other than 'Subject Completed Treatment Per Protocol' for any of the components of R-CHOP in the 'End of Treatment/Early Study Treatment Discontinuation' eCRF page, then the patient is said to discontinue R-CHOP prematurely.

Premature study treatment discontinuation refers to all components of study treatment have been prematurely discontinued. In other words, permanent study treatment discontinuation means that no components of treatment have 'Subject completed treatment per protocol' on the 'End of Treatment/Early Study Treatment Discontinuation' eCRF page.

7.4 Treatment cycle and treatment phase

A complete treatment cycle is defined as 21 calendar days during which tafasitamab in addition to R-CHOP (treatment arm A) or tafasitamab and lenalidomide in addition to R-CHOP (treatment arm B) will be administered. Details of doses and dosing days of each component of study treatment administration is depicted in protocol section 8.1.

In this study, **treatment phase** refers to the 6 cycles of study treatment.

7.5 Dates of study drug/study treatment administration

7.5.1 Date of first administration of study drug

Date of first administration of study drug, which is also named as 'Start date of study drug', refers to the date of first non-zero dose of administration of each study drug.

7.5.2 Date of last administration of study drug

Date of last administration of study drug, which is also named as 'End date of study drug', refers to the date of last non-zero dose of administration in each study drug.

7.5.3 Date of first administration of study treatment

Date of first administration of study treatment refers to the date of first non-zero dose of administration of any study treatment component in each treatment arm.

7.5.4 Date of last administration of study treatment

Date of last administration of study treatment refers to latest of the last date of non-zero dose administration of any study treatment component in each treatment arm. For example, the date of administration of tafasitamab on cycle 6 day 15 ideally will be the date of last administration of study treatment for both arms, if none of the study drugs was discontinued early.

7.6 Reference start date, reference end date and study day

For this randomized study the **reference start date for all safety assessments** (e.g. adverse event onset, laboratory/ vital sign measurement, study drug administration, prior and concomitant medication (CM), medical history (MH) etc.), demographic and baseline assessment, pharmacokinetics analysis and biomarker analysis will be the date of first administration of study treatment. The reference start date **for efficacy assessments** (e.g. tumor assessment, death, ECOG performance status) and duration of overall survival follow-up period will be the randomization date.

The reference start date is designated as Study Day 1. Study Day –1 is the day that precedes Study Day 1. Study Day 0 is not defined.

In this study, the **reference end date** is designated to be the date of end of treatment. As per protocol, end of treatment is defined as the day 21 of the last treatment cycle the patient started. Ideally, the date of end of treatment is cycle 6 day 21, if patient does not discontinue the treatment phase early. If a patient discontinues the treatment prematurely and stays in the study, the date end of treatment will be day 21 of the last treatment cycle the patient started. If the patient died or discontinued both the treatment and study, date of death or date of discontinuation of treatment will be taken as date end of treatment. The reference end date is identical with date of end of treatment, and it will be used only for defining treatment emergent adverse event and permissible visit window for capturing disease response at end of treatment visit/early study treatment discontinuation visit, but not be applied to the calculation of exposure of study treatment.

The **study day** describes the day of the event or assessment date, relative to the reference start date.

The study day will be calculated as:

- If the event/assessment is on or after the reference start date, study day = [Date of the event/assessment - reference start date + 1]
- If the event/assessment precedes the reference start date, study day = [Date of the event/assessment - reference start date]

The study day will be displayed in the data listings.

7.7 Date of last contact

The date of last contact is derived as the latest date among the following:

- Actual assessment dates considering all assessments, including scheduled and unscheduled visits (Laboratory sample collection dates, vital signs, ECOG performance status, B-symptoms, ECG measurement, tumor imaging).
- New anti-lymphoma treatment date administered after study drug discontinuation.
- Adverse events end date. If the adverse event is still ongoing, then the adverse event start date will be used.
- Date of last interaction with patient collected on the "End of study/Early Follow-up Discontinuation" eCRF page for the lost to follow-up patients.
- Date of death from the from the "End of study/Early Follow-up Discontinuation" eCRF page.
- Date of study completion or discontinuation from the "End of study/Early Follow-up Discontinuation" eCRF page.
- Date of study treatment completion or discontinuation from the "End of Treatment/Early Study Treatment Discontinuation" eCRF page.

7.8 Screening failure

Patients who signed the informed consent form, but failed to fulfill the Inclusion/Exclusion criteria, are considered as screening failures. Information of screening failures will be presented in the listings of patient disposition, inclusion/exclusion criteria, death and protocol deviation.

7.9 Time unit

Unless specifically mentioned, month will be used as the time unit for analysis. A month-length is 30.4375 days (365.25/12). If duration is to be reported in months, duration in days is divided by 30.4375. If duration is to be reported in years, duration in days will be divided by 365.25.

7.10 Baseline

Baseline is the result of an investigation describing the "true" uninfluenced state of the patient, defined as the period from the date of signing any informed consent document to the start date of study treatment or the date of randomization. Assessments, specified to be collected post-dose on the first date of treatment (e.g. vital signs assessments during the tafasitamab infusion) are not considered as baseline values.

For efficacy evaluations, the last non-missing assessment, including unscheduled assessments on or before the date of randomization is taken as "baseline" value or "baseline" assessment.

For safety evaluations, unless otherwise stated, the last non-missing assessment, including unscheduled assessments on or before the date of start of study treatment is taken as "baseline" value or "baseline" assessment.

If patients have no value as defined above, the baseline result will be missing.

Change from baseline calculation

Absolute change from baseline will be calculated as

[visit value – baseline value]

and percentage change from baseline will be calculated as

$$[\frac{\text{visit value}-\text{baseline value}}{\text{baseline value}} \times 100\ ].$$

7.11 On-treatment event and post-treatment event

On-treatment and post-treatment event will be flagged.

An **on-treatment event** is defined as any event happening after the start date of study treatment, i.e. events happening in the following time interval (including the lower and upper limits): [Reference start date; Reference end date + 30 days].

A **post-treatment event** is defined as events happening in the following time interval (including the lower and upper limits): [Reference end date + 30 days + 1; date of End of study or Date of Study Discontinuation].

7.12 Analysis visit windows and eCRF visit windows

Unless otherwise specified, for parameters that will be summarized by visit, the nominal visit as collected in the eCRF page will be used. For hematology and biochemistry data, analysis visit window will be applied in addition to nominal visit.

7.12.1 eCRF visit and anchoring date

In the eCRF, visits are derived based on the CxD1, where x refers to the cycle number. Day 1 of each cycle is defined as the day on which tafasitamab is first administered in the cycle. In case tafasitamab is skipped due to any reason, day 1 of the cycle will be the day when the first component of R-CHOP is administered. In treatment arm B, in case both tafasitamab and R-CHOP is skipped, day 1 of the cycle is the day when first dose of lenalidomide is taken. If none of the component of study treatment is administered, day 1 of the cycle is the day when the first procedure for this visit is conducted (denoted as 'first assessment' in the following content). This CxD1 will be referred as anchoring CxD1. Anchoring date will be applied in defining analysis visit window (in section 7.12.2).

The concept of anchoring date is added to differentiate the actual date of study drug administration and the collected eCRF visit. For example, if the C1D1 is anchored on 2019-02-01, an allowed administration visit window of tafasitamab for C1D8, as per protocol, is between 2019-02-06 and 2019-02-10. If tafasitamab is infused on 2019-02-06, the anchoring date of C1D8 visit is 2019-02-06, even though it is presented in the eCRF as C1D8 visit. Likewise, if tafasitamab is interrupted for this visit, the administration of R-CHOP/lenalidomide or the first assessment of this visit will be applied as anchoring date. The following table elaborate the scheme of applying anchoring date in each visit.

Table 2. Anchoring date of treatment arm A:

Planned visit*	Tafasitamab administration	R-CHOP administration	First assessment	Anchoring date
CxD1	Yes	Yes	Yes	Date of tafasitamab administration
	No	Yes	Yes	Date of administration of first component of R-CHOP
	No	No	Yes	Date of the first assessment
CxD8 / CxD15	Yes	Not applicable	Yes	Date of tafasitamab administration
	Interrupted	Not applicable	Yes	Date of the first assessment

*Cx refers to cycle 1 to cycle 6.

Table 3. Anchoring date of treatment arm B:

Planned visit*	Tafasitamab administration	RCHOP administration	Lenalidomide administration	First assessment	Anchoring date
CxD1	Yes	Yes	Yes	Yes	Date of tafasitamab administration
	No	Yes	Yes	Yes	Date of administration of first component of R-CHOP
	No	No	Yes	Yes	Date of lenalidomide administration
	No	No	No	Yes	Date of the first assessment
CxD8	Yes	Not applicable	Yes	Yes	Date of tafasitamab administration
	No	Not applicable	Yes	Yes	Date of lenalidomide administration
	No	Not applicable	No	Yes	Date of the first assessment
CxD15	Yes	Not applicable	Not applicable	Yes	Date of tafasitamab administration
	No	Not applicable	Not applicable	Yes	Date of first assessment

*Cx refers to cycle 1 to cycle 6.

7.12.2 Analysis visit windows

Analysis visit windows is based on anchoring date and it would be applied to **hematology and biochemistry measurements only**. The detailed strategy for analysis visit and analysis visit window is depicted in the table below. Any assessment that falls outside of the analysis visit window will be presented as unscheduled visit.

Table 4. Analysis visit

Start date*	End date**	Analysis visit
Date of signing ICF	Anchoring C1D1 minus 2 days	Screening visit
Anchoring C1D1 minus 1 day	Anchoring C1D1	C1D1
Anchoring C1D1 plus 3 days	Anchoring C1D8	C1D8

Anchoring C1D8 plus 3 days	Anchoring C1D15	C1D15
Anchoring CxD1 minus 3 days	Anchoring CxD1	CxD1
Anchoring CxD1 plus 3 days	Anchoring CxD8	CxD8
Anchoring CxD8 plus 3 days	Anchoring CxD15	CxD15

*Cx refers to cycle 2 to cycle 6 and Dy refers to day (1, 8, 15).

** Per protocol, local laboratory and central biomarker data should be collected at pre-dose timepoint. As a consequence, if the anchoring date is on basis of study treatment administration, post-dose assessments will be excluded from the corresponding analysis visit.

7.13 Selection of data in the event of multiple records in a window

Unless otherwise noted throughout the rest of this document, when a single value is needed, the following rules apply:

- If more than one assessment occurs during the same nominal visit time window of the planned visit, select the record closest to the nominal day for that particular visit day/timepoint.
- If there are two assessments that are equidistant from the nominal planned visit day, the data of the assessment after the scheduled study day will be used.
- If more than one assessment is collected on the same day, the latest assessment on that day will be used.

7.14 Unscheduled visits

In this study, unscheduled visits, following defined as unscheduled eCRF visits, are time points not planned in the protocol. In addition, the unscheduled analysis visits is defined as section 7.12.

In listings, unscheduled eCRF visits will be listed. In addition, unscheduled analysis visits will also be presented in hematology and biochemistry data listings. All visits will be ordered chronologically including the dates of unscheduled eCRF visits.

Unscheduled visit will be incorporated in the baseline calculation and overall post-baseline summary. If the date is incomplete, but it can be determined whether values were measured in the treatment phase, they will be incorporated in overall post-baseline summaries. Unscheduled visits will be excluded from the per timepoint/visit presentation.

7.15 Analysis sets

7.15.1 Screened patients population

The screened patients population consists of all patients who signed the ICF and completed the informed consent eCRF page.

7.15.2 Full analysis set (FAS)

All patients who are randomized to either treatment arm will be included in FAS. Patients will be analyzed according to the study treatment they are randomized to. The FAS will be the primary population for the analysis of efficacy and baseline characteristics.

7.15.3 Safety Set (SAF)

All patients who received at least one dose of any component of study treatment are included into safety set. Safety analyses will be performed on SAF, presented on the basis of the following actual treatment arm:

Table 5. Actual treatment arm of SAF set

Did patient receive at least one dose of tafasitamab	Did patient receive at least one dose of lenalidomide	Did patient receive at least one dose of R-CHOP	Treatment arm in SAF set
Yes	Yes	Yes	Treatment arm B
Yes	No	Yes	Treatment arm A
Yes	Yes	No	Tafasitamab + Lenalidomide
Yes	No	No	Tafasitamab only
No	Yes	Yes	Lenalidomide + R-CHOP
No	Yes	No	Lenalidomide only
No	No	Yes	R-CHOP only
No	No	No	Excluded from SAF set

If for a given actual treatment arm (except treatment arm A and treatment arm B) less than 5 patients are included, Safety analysis for these patients will only be listed.

7.15.4 Per protocol set (PPS)

Patients included in FAS with at least one non-zero dose of any component of study treatment and one valid post-baseline response assessment, and without any important protocol deviation that would confound efficacy analysis are included into per protocol set.

All protocol deviations or conditions leading to exclusion from the PPS will be detailed in protocol deviation specification and summarized in the disposition table. Sensitivity analyses apply to some secondary endpoints are performed using PPS (see section 7.15.8).

7.15.5 PK analysis set (PKAS)

The PKAS will include all patients who received at least one non-zero dose of tafasitamab and have at least one quantifiable serum tafasitamab concentration.

7.15.6 Immunogenicity analysis set (IAS)

The IAS will include all patients who received at least one non-zero dose of tafasitamab and have at least one valid anti-tafasitamab antibody assessment.

7.15.7 Reason of exclusion from analysis sets

Patients may be excluded from the analysis sets for the following reasons. Note that if a patient has more than one reason for not being included in any analysis set, then only the reason which is higher in the order of the reason numbering will be considered. That is for PPS, if a patient is excluded because of "Not randomized" and "No dose of any component of study treatment", then only "Not randomized" will be counted while summarizing the reasons for excludion from PPS.

Table 6. Reasons of exclusion from analysis sets

Analysis set	Reason of exclusion from analysis set
Screened patients	Not applicable
FAS	1. Not randomized
SAF	1. No dose of any component of study treatment
PPS	1. Not randomized 2. Not centrally confirmed DLBCL NOS. 3. No dose of any component of study treatment 4. No post-baseline response assessment 5. Major protocol deviations that influence efficacy
PKAS	1. No dose of tafasitamab 2. No quantifiable serum tafasitamab concentration
IAS	1. No dose of tafasitamab 2. No valid anti-tafasitamab antibody assessment

7.15.8 Planned analyses for the different populations

The number of patients in each analysis set will be summarized. Table 7 and Table 8 give an overview of the assessments performed on the different analysis sets.

Table 7: Overview of the analyses performed on the different analysis sets for summary analyses

Analysis	All patients screened	FAS	PPS	SAF	PKAS	IAS
Patient disposition	x	x		x		
Protocol deviation	x					
Summary of Study Duration		x				
Summary of baseline and demographic characteristics		x	x	x		
Summary of incidence and severity of adverse event (except for pre-treatment AEs)				x		
Summary of adverse events (except for pre-treatment AEs) of other aspects				x		
Summary of Pre-treatment AEs	x					
Summary of death	x			x		
Metabolic, PET-negative complete response rate (CR) at end of treatmen visit and metabolic, PET-negative CR until end of study		x				
PFS , OS, ORR, DoR		x	x			
All other Efficacy Endpoints		x				
Descriptive biomarker analyses		x				
ORR and PFS stratified by biomarkers		x				
Eastern Cooperative Oncology Group (ECOG) performance status and B-symptoms		x				
Summary of study treatment and study drug administration				x		
Summary of pre-medication, prior/concomitant medication, non-medication procedures and new anti-lymphoma treatment		x		x		
Summary of medical history and current medical condition		x		x		
Summary of vital signs, electrocardiogram (ECG), local and central laboratory safety evaluations and physical examination				x		
Pharmacokinetic analyses					x	

Analysis	All patients screened	FAS	PPS	SAF	PKAS	IAS
Immunogenicity analyses						x

Table 8: Overview of the analyses performed on the different analysis sets for listing

Analysis	Analysis set to be used	Affiliated analysis set to be flagged in additional column
Patient disposition	All patients screened	FAS/SAF/PPS
Protocol deviation	All patients screened	FAS/SAF/PPS
Survival follow-up period, patient status, demographics and baseline charateristics	FAS	FAS/SAF/PPS
Medical history and concomitant medication	FAS	FAS/SAF/PPS
Study drug/treatment administration	SAF	FAS/SAF/PPS
All efficacy endpoints, including tumor response, B symptoms and ECOG	FAS	FAS/SAF/PPS
Descriptive biomarker analyses	FAS	FAS/SAF/PPS
All safety endpoints (except for pre-treatment AEs)	SAF	NA
Pre-treatment AEs	All subects screened	FAS/SAF/PPS
Listing of deaths	All patients screened	FAS/SAF/PPS
Pharmacokinetic analyses	PKAS	NA
Immunogenicity analyses	IMAS	NA

7.15.9 Withdrawal of informed consent

Any data collected in the clinical database after a patient withdraws informed consent from any further participation in the trial, will not be included in the analysis data sets. The date on which a patient withdraws full consent is recorded in the 'End of Study/Early Follow-up Discontinuation' eCRF page. Note: Patients who withdraw consent from study treatment but consent to study follow-up are considered as having only withdrawn consent of study treatment and this date captured in the eCRF is not to be considered as the date of withdrawal of full consent. Such post-treatment assessments will be included in the analysis data sets.

Any data that is entered in the clinical database without the consent of the patient will be excluded from the analysis sets. Only exceptions are the information entered to identify date of withdrawal of consent e.g. End of Treatment, End of Study.

Third party data, e.g. PK, biomarker etc., collected in the clinical database without having obtained consent for collection or if consent was withdrawn, will be excluded in the analysis data sets.

7.16 Medical coding

Coding for adverse event, medical history and non-drug treatments and procedurewill be performed using the Medical Dictionary for Regulatory Activities (MedDRA) version 24.0.

Prior, concomitant and pre-medications will be recorded and coded using the current WHO Drug Dictionary Enhanced (WHO-DDE) and grouped by Anatomical Therapeutic Chemical (ATC) Level 2 class and preferred name.

Toxicity grade of adverse event and medical history and are captured directly from eCRF. Toxicity grade of local laboratory data will be coded according to National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) V5.0 (exception for 'Tumor Flare Reaction' which will be coded using CTCAE V6.0).

8. STATISTICAL METHODOLOGY

8.1 General principles of statistical programming and handling analysis dataset

The statistical analysis will be performed on the analysis study database with appropriate software, SAS® Software version 9.4 or above (SAS Institute, Cary, N.C.).

For submission purpose all the source data from eCRF is implemented to agree with Study Data Tabulation Model (SDTM) v1.4 dataset and SDTM implementation guide v3.2 , and all analysis data for TLF creation is based on CDISC Analysis Data Model (ADaM) v2.1 dataset and ADaM implementation guide v1.1. Accordingly the complete metadata specification and data reviewers guide for both SDTM and ADaM will be provided.

8.2 Variable types and descriptive statistics

Descriptive statistics will be calculated according to the data type as follows:

Continuous variables (e.g. laboratory, vital signs, etc.): number of non-missing observations, number of missing observations, arithmetic mean, standard deviation (StD), minimum and maximum values and quartiles (median, Q1 and Q3) will be presented in the descriptive summary tables. For tafasitamab pharmacokinetics concentrations, coefficient of variation CV (%), geometric mean and geometric CV (%) will also be presented in the descriptive statistics.

CV% = coefficient of variation (%) = StD/mean*100%
Geometric CV% = sqrt (exp (variance for log transformed data)-1)*100%

If not otherwise specified, the following rules are applied:

- Percentages are presented to 1 decimal points.
- Percentage equal to 0 or 100 are presented as such without a decimal point.
- Ratios/Event rate are reported to 3 decimal points.
- The minimum and maximum will be reported to the same number of decimal places as the raw data recorded in the database. The mean, median, lower quartile and upper quartile will be reported to one more decimal place than the raw data recorded in the database, while the StD will be reported to two more decimal places. In general, the maximum number of decimal places reported shall be four for any summary statistic.
- If there are less than 5 observations, only the number of non-missing observations, arithmetic mean, median, minimum and maximum will be presented.

Categorical variables (e.g. Abnormality of laboratory evaluation): Number and percentage of patients/events will be tabulated. Unless otherwise specified, the percentage denominator will be the number of patients in the concerned analysis set who are still in the trial (including missing values) at the respective time point in the analysed population. Categories with frequency of 0 will not be presented if not differently specified.

In case of subcategories, the relative frequencies will be calculated on the basis of the patients in the respective category, in this case a footnote will be added explaining the different denominators.

Time variables (duration of DLBCL since diagnosis etc.)**:** This will be summarized using arithmetic mean, StD, minimum and maximum values, median and quartiles (Q1, Q3) and will be presented in months (unless differently specified).

Time to event variables (PFS, EFS, OS, etc.): Unless differently specified, Kaplan Meier estimates of Q1, Median, and Q3 along with their 95% Confidence Intervals will be presented.

Incidence reporting (AE, CM, MH and non-medication procedures): Unless differently specified, number and percentage of patients, along with the event counts will be reported in the summary tables of adverse event, concomitant medication and medical history. Patient will be counted only once if he/she comes across more than one time of the same AE/CM/MH event capturing the highest intensity/toxicity/worst outcome ect. The AE, MH and non-medication procedures summary tables will be sorted in terms of decreasing frequency for system organ class (SOC) and the preferred term (PT) within SOC. The CM summary tables will be ordered in terms of decreasing frequency of ATC level and the preferred name within the ATC level.

8.3 Handling of incomplete or missing date/time information

The dates that are missing or incomplete are derived as follows:

- Dates are split in 3 parts: year, month and day. Year is the top-level, month is medium level and day is low level. If a part expected to contain a number is numeric but the value is outside a valid range, the complete date is handled as missing. For example, if date = 44Nov2000 the whole date is considered to be missing.
- If a part is missing, all other parts of a lower level are considered to be missing. This means that a ddmmyy date '21--99' is considered as '----99'.

Missing parts for specific dates/times are changed into acceptable non-missing values as described in the table below.

In the following, 'lower limit' and 'upper limit' refer to the minimum or maximum, respectively, of a possible date.

For example, if the day is missing, the lowest limit is the first day of the given month and the upper limit is the last day of the given month.

If the day and month are missing, the lower limit refers to the first day of the given year and the upper limit to the last day of the given year.

For a partial date, the range of possible dates is defined as the period from lower to upper limit (both included).

The earliest and the latest dates refer to the first or last date, respectively, when ordered in sequence.

Other sources should be considered for possible dates including death date, cut-off date and date of withdrawal from study when determining possible dates.

Table 9 Convention for Missing Data

Type of date/time	Date/time is incomplete	Date/time is missing
Study drug/treatment start date	- Day is missing: Replaced by the lower limit. - Day and month are missing: no replacement In case the resulting date is before randomization date, randomization date will be used.	No imputation
Study drug/treatment end date	Use the earliest date among: upper limit, date of death, date of last contact.	Use the earliest date among: date of death, date of last contact.
Actual assessment dates (Labs, vital signs, performance status, tumor imaging,) including disease assessment date. Baseline Tumor Assessment	The lower limit In case the lower limit is before reference start date, than ICF signature date will be used The lower limit	No imputation, the assessment cannot be used No approximation, the assessment cannot be used
New Anti-Lymphoma Treatment (NALT)/Prior and Con Meds	The lower limit In case the lower limit is before Reference Start Date date, than Reference Start Date will be used	No imputation, the therapy information cannot be used
"Date of last contact"	The lower limit In case the lower limit is before Reference Start Date, than Reference Start Datewill be used	No imputation

Date of Death	The Lower limit unless other qualifying study data support survival until a later date during the same month.	No imputation

The following imputation rules pertain to adverse event, concomitant medication and will be implemented in ADaM datasets only:

For adverse event and concomitant medication: no imputation will be performed for missing dates. Hence the worst case will be applied when defining TEAE and prior/concomitant medication.

- If the start time of an AE is missing but the start date is on the same date with study treatment, an AE will be counted as TEAE unless the AE end date/time is before date of first treatment.
- If start time and day are missing but the start month is complete, an AE will only be excluded from TEAE for the following scenarios: 1) start month is before month of first treatment; 2) start month is after end month of treatment-emergent period and this AE has no causality with any component of study treatment; 3) AE end date/time is before start of first treatment.
- If start day and month are missing but the start year is complete, an AE will only be excluded from TEAE if it meets one of the following scenarios: 1) start year is before year of first treatment; 2) start year is after end year of treatment-emergent period and it has no causality with any component of study treatment; 3) AE end date/time is before start of first treatment.
- If start date is completely missing, an AE will not be excluded from TEAE unless the AE end date/time is before start of first treatment.
- If start day of a medication is missing, and the month appears to be the same month with study treatment, medication will be counted as both prior and concomitant medication, unless the end date is before treatment start, then this case will be counted as prior medication only.
- If start day and month are missing but year of a medication appears to be the same year with study treatment, medication will counted as both prior and concomitant medication, unless the end date is before treatment start, then this case will be counted as prior medication only.

The above will be applicable for assigning AEs to treatment cycles.

8.4 Data included in the analysis and cut-off date

For primary completion analysis, cut-off date is defined as 30 days after all patients have performed their End of Treatment Visit or Early Study Treatment Discontinuation Visit. Analyses of patient disposition, demographics and baseline characteristics, medical history, prior and concomitant medications, study drug/treatment exposures, primary and key secondary endpoints and other safety analysis will be performed using data within cut-off date for the primary completion analysis.

Any data assessed after the cut-off will be excluded from primary completion analysis, except for the data with an assessment date or event start date (e.g. vital sign assessment date or start date of an adverse event) prior to or on the cut-off date. For example, if the cut-off date is 2020-11-15 then an AE starting on 2020-Nov-15 will be reported, whereas an AE with start date on 2020-Nov-17 will not be reported.

For adverse event and concomitant medication, events with an event start date either before or on the cut-off date and an event end date after the cut-off date will be reported as "Ongoing" and the outcome of the adverse event will be reported as 'Unknown'. The same rule will be applied to events starting either before or on the cut-off date and not having a documented end date. A footnote will be added in the corresponding tables and listings to indicate these events are ongoing based on cut-off date. For serious adverse events with admitted date of hospitalization after cut-off date, seriousness and admitted date of hospitalization will be reported as collected in the source data, no conversion will be performed.

8.5 Pooling of investigative sites

In this study, data from all participating sites will be combined for the analyses. No site effect or treatment-by-site interaction will be assessed.

9. PATIENT DISPOSITION, BACKGROUND AND BASELINE CHARACTERISTICS

9.1 Patient disposition

Patient disposition will be performed for all screened patients, tabulated by treatment arm and overall. The detailed analysis are listed out as below:

9.1.1 Enrollment status

1. Number and percentage of patients screened.
2. Number and percentage of patients randomized/not randomized. Reasons of being not randomized (Reasons are obtained from "Randomisation" eCRF page) will be listed.
3. Number and percentage of patients enrolled in each Analysis set by Treatment Arm.
4. Summary of all enrolled subjects will be presented for each country.

For all the above cases, the percentage will be based on the total number of patients screened.

9.1.2 Completion and premature discontinuation of study treatment and study drugs

1. Number and percentage of patients who completed all 6 Cycles of treatment as per protocol.
2. Number and percentage of patients who completed the first 3 Cycles of treatment.
3. Number and percentage of patients who completed more than 3 Cycles of treatment.
4. Number and percentage of patients who have a "premature study treatment discontinuation" (definition: section 7.3), including the reason for treatment discontinuation (in case of sequential discontinuation of the components, the reason that led to discontinuation of the drug that was discontinued latest will be presented).
    a. Number and percentage of patients who entered follow-up period after end of treatment.
    b. Number and percentage of patients who discontinued study after end of treatment, incl. the reasons for study discontinuation.
5. Number and percentage of patients who completed study treatment (definition: section 7.3)
    a. Number and percentage of patients who entered follow-up period after end of treatment.
    b. Number and percentage of patients who discontinued study after end of treatment, incl. the reasons for study discontinuation.
6. Number of patients who prematurely discontinued at least one but not all the components of study treatment, incl. the reasons for treatment discontinuation (in case of discontinuation of multiple

drugs, all reasons will be considered in the tabulation; that is, the numbers of discontinuation reasons may be larger than the number of patients who discontinued at least one but not all components of the study treatment).
    a. Number and percentage of patients who entered follow-up period after end of treatment.
    b. Number and percentage of patients who discontinued study after end of treatment, incl. the reasons for study discontinuation.
7. Number and percentage of patients who completed whole study including study treatment, follow-up and their scheduled last-visit. This information is obtained from "Did the subject complete the study?" in the "End of Study/Early Follow-up Discontinuation" eCRF page.
8. Number and percentage of patients who completed each study drug as per study Clinical Trial Protocol (CTP). For definition see section 7.3.
9. Number and percentage of patients who discontinued prematurely each study drug as per study CTP. For definition see section 7.3. Reason for premature discontiuantion will be presented for each study drug.
10. Number and percentage of patients who completed all cycles of R-CHOP as per study CTP. For definition see section 7.3.
11. Number and percentage of patients who discontinued study treatment within the first 21 days of the study.

In all the above cases, percentages will be based on the respective analysis set.

9.1.3 Patient status in each treatment cycle

1. Number and percentage of patients who completed each component of study treatment as per study protocol in each treatment cycle. If a patient takes all the planned doses of a treatment component for a cycle, that patient is counted as one who completes that cycle as per protocol.
2. Number and percentage of patients who have proceeded to next treatment cycle. A patient who discontinues a treatment component at a particular cycle will not be considered under this category for that treatment component.
3. Number and percentage of patients who discontinue any component of study treatment will be presented per cycle along with reasons for discontinuation.
4. Number and percentage of patients who have treatment cycle delay in each treatment cycle. This applies to cycle 2 to cycle 6, along with reasons of the delay of each treatment cycle.
5. Summary of days of delay in each treatment cycle. This applies to cycle 2 to cycle 6.

9.1.4 Patient status in follow-up period

The following will be summarized based on the FAS population:

1. Number and percentage of patients who entered the follow-up period.
2. Among patients who entered follow-up:
    a. Number and percentage of patients who completed the whole study (including study treatment, follow-up and their scheduled last-visit).
    b. Number and percentage of patients who discontinued study, along with reasons of discontinuation.

Patient disposition listing will be provided for FAS to present patient identifier, age/sex/race, treatment arm, ICF signed date, date of randomization, date of first administration of study treatment, date of last

administration of study treatment, reference end date, reason for treatment discontinuation, date of death, cause of death, date of disease progression, date of last contact.

A summary table will be presented showing number of patients enrolled into the study by country based on the FAS.

In addition, patient status listing will be provided using FAS population to present patient identifier, treatment arm, visit, delay of treatment cycle (yes or no), number of days of delay, reason of delay. A patient visit listing will present date of each visit, using FAS population. For patients who fail the inclusion/exclusion criteria, a listing will be created to display the details. For FAS population, a listing will be created to present the randomized allocation to treatment.

Summary information regarding the follow-up of patients is displayed in order to describe the maturity of data and quality of follow-up.

Duration of Follow-up for PFS, EFS, OS and time to next anti-lymphoma treatment will be presented by means of reverse Kaplan Meier analysis, where the status indicator is reversed, meaning the event of interest (PFS or OS) will be considered as censored at that time point, and censor becomes event. The summary statistics as described for Time to event endpoints will be presented. For details please see the respective sections. (Sections 10.1.5, 10.1.6, 10.1.7, 10.1.8)

The following will also be presented:

- Summary statistic of Randomization (recruitment) period = (Date of last patient randomized - Date of first patient randomized + 1)/30.4375 (months),
- Date of 1st patient randomized.
- Date of last patient randomized
- Cut-off date

Listings will also be provided.

9.2 Protocol deviations

Protocol deviations will be identified based on reviews of the data prior to database lock. All important protocol deviations will be listed to describe the patient information, treatment arm, category, exact item and date of protocol deviation. In addition, a listing of patients excluded from the efficacy analysis will be provided. The protocol deviation consists of the following categories:

- Entry criteria not satisfied
- Developed withdrawal criteria but not withdrawn
- Failure to collect data for primary/key secondary endpoint
- Wrong treatment or incorrect dose
- Prohibited concomitant treatment
- GCP deviation
- Study Procedures
- Other

The number and percentage of patients in the FAS, with at least one of important protocol deviations, will be summarized by treatment arm and overall according to the above mentioned categories.

9.3 Analysis sets

Number and percentage of patients included/excluded in each analysis set will be summarized by treatment arm and overall, along with reasons of exlusion from analysis sets (defined in section 7.15.7). The percentages will be calculated based on all screened patients.

9.4 Baseline and demographic characteristics

Descriptive statistics will be tabulated for continuous variables. The number and percentage of patients in each category will be presented for categorical variables. All summaries will be presented for the FAS and the PPS, by treatment arm and overall. For categorical variables, the number and percentage of patients with missing data will be provided. Listings for demographic data will be produced.

The following continuous variables will summarized:

- Age at time of Informed Consent [years]
- Weight at Baseline [kg]

The following categorical variables will be summarized:

- Age group at screening:
  - ≤ 60 vs. > 60 years
  - < 65 vs ≥ 65 years
  - 18-64 vs. 65 – 84 vs. ≥ 85 years
  - ≤70 vs. >70 years.
- Sex (Male or Female)
- Race. If more than one races have been chosen, it will be presented as ‘Other’ with concatenated items.
- Childbearing potential for female patients (Yes or No), along with reasons of no childbearing potential.
- Pre-planned radiotherapy at screening (Yes or No)
- Pre-planned intrathecal chemotherapy (Yes or No)
- Pre-planned central nervous system (CNS) Prophylaxis with Intravenous (IV) Methotrexate at screening (Yes or No)

All demographic data, along with childbearing potential, pregnancy and risk counseling, plan and result of pre-planned radiotherapy and pre-planned CNS prophylaxis will be listed.

9.5 Medical history and concomitant medical conditions

9.5.1 Definition

Generally, medical history is defined as medical records which start and end prior to study treatment, whereas current medical conditions are defined as medical records that start prior to study treatment and are ongoing when study treatment starts. Specifically for this study, the diagnosis of DLBCL is the prerequisite for the patients' recruitment.

9.5.2 Data presentation

For the non-DLBCL medical history, number and percentages of patients and number of events will be tabulated per SOC and PT for each treatment arm and overall, using FAS population.

Based on the eCRF page 'Diagnosis of DLBCL' the following will be summarised using FAS population:

- Time between Diagnosis and Start of Treatment (days)
- Time between diagnostic biopsy was taken and Date of Diagnosis of DLBCL (days)
- Biopsy taken from (Nodal vs Extra-nodal) and the nodal or extra-nodal site respectively
- COO assessed locally (yes vs No).
- Method of COO Used (IHC-Hans algorithm vs. Gene Expression Profiling vs Other)
- Result of COO (GCB vs Non-GCB vs Unclassified vs ABC)

Based on the eCRF page 'DLBCL staging and disease risk assessment' the following will be summarised using FAS population:

- Ann Arbor Disease Staging Assessment performed (Yes or No)
- Ann Arbor Disease Staging (Stage I, Stage II, Stage III or Stage IV)
- Ann Arbor Disease Staging grouped by categories: Stage I/II vs Stage III/IV
- International Prognostic Index (IPI) assessment performed (Yes or No)
- Patients with age older than 60 (Yes or No)
- Patients with lactate dehydrogenase level higher than normal (Yes or No)
- Patients with ECOG performance status score of 2 or greater (Yes or No)
- Patients with Stage III or IV disease (Yes or No)
- More than one involved extranodal disease site (Yes or No)
- IPI score (0 to 5)
- IPI score grouped as Low: 0 or 1, Low-Intermediate: 2, High-Intermediate: 3, and High: 4 or 5
- Age-adjusted IPI for patients <= 60 years (based on the risk factors: Ann Arbor Stage III or IV, Elevated LDH, and ECOG performance status >= 2) will be grouped and presented as Low: 0, Low-intermediate: 1, High-intermediate: 2, and High: 3
- Patients for whom screening for CNS lymphoma involvement has been performed (Yes or No)
- Patients for whom diagnostic lumbar puncture with cerebrospinal fluid (CSF) evaluation (cytology, flow cytometry) was performed to exclude CNS infiltration (Yes or No)
    - Patients for whom lymphoma cells detected in the CSF (Yes or No)
- Patients for whom head CT and/or head MRI performed to exclude CNS infiltration (Yes or No)
    - Signs of Lymphoma involvement (Yes or No)
- Presence of bulky disease (Yes or No)
- Based on the eCRF page 'ECOG Performance Status' the following will be summarised using FAS and SAF population

- ECOG at screening (0 to 4)

Based on the eCRF page 'Assessment of B-symptoms', the following will be summarised using FAS population:

- Patients for whom the assessment was performed (Yes or No)
- Reasons for not performing the assessment will be listed.
- Time between B-symptom assessment and start of treatment (days)
- Unintentional weight loss of more than 10% of body weight within the previous 6 months (Present, Absent, or Unknown)
- Fever for at least 3 consecutive days without evidence of infection (Present, Absent, or Unknown)
- Drenching night sweats without evidence of infection (Present, Absent, or Unknown)

Based on the eCRF page 'Pre-planned Radiotherapy, or Pre-planned CNS Prophylaxis', the following will be summarised using FAS population:

- Patients for whom local radiotherapy pre-planned to be administered to initial sites of bulky or extranodal disease after the last treatment cycle and after the end of treatment tumor assessment by PET/CT or PET/MRI (Yes or No)
- Location of irradiation (Nodal vs Extranodal)

Based on the eCRF page 'Bone Marrow Aspiration and Biopsy', the following will be summarised using FAS population:

- Patients for whom bone marrow assessment was performed (Yes or No)
- Reasons for not doing the assessment will be listed.
- Type of bone marrow assessment (Aspiration, Biopsy, or Aspiration and Biopsy)
- Bone marrow ivolvement by DLBCL (Yes, No, or Not Applicable)
- Percentage of bone marrow infiltration by DLBCL
- Bone marrow involvement by different histological type of lymphoma (Yes, No, or Not Applicable)
- Percentage of bone marrow infiltration by lymphoma subtype

Based on the eCRF page 'Pathology Central Diagnosis', the following will be summarised using FAS and SAF population:

- Cell of Origin by Hans Classifier: GC-type, Non GC-type, or Not applicable

FISH Status (MYC rearrangement: Negative, Positive, or Not Done; BCL-2 rearrangement: Negative, Positive, or Not Done; BCL-6 rearrangement: Negative, Positive, or Not Done)

For IPI score derivation, please refer to Section 16, Appendix D of the Clinical Trial Protocol (CTP).

Listings will be created to present both general medical history, DLBCL-specific medical history, bone marrow aspiration, performance of tumor biopsy and fresh tumor tissue, biopsy and pathology central diagnosis, on the basis of FAS population.

9.6 Prior and concomitant medications and non-drug treatments/procedures

9.6.1 Definitions

- **Pre-medication**: Medication given prior to tafasitamab administration to mitigate potential infusion-related reactions. Pre-medication encompasses oral acetaminophen, antihistamine and glucocorticosteroids. For details please refer to protocol section 8.7.1.1. All pre-medications are captured in eCRF page 'Pre-infusion Medications for tafasitamab'.
- **Prior medication/non-drug treatment:** If both the start and stop dates of the treatment are before the start date of study treatment, the medication will be classified as prior medication.
- **Concomitant medication/non-drug treatment:** If the start date of medication is on or after the start date of study treatment, the medication will be considered as concomitant medication.
- **Prior and concomitant medication/non-drug treatment and procedures:** Medications with start date before start date of study treatment but ongoing or with stop date after the start of study treatment will be considered both as prior and as concomitant medications. Therefore such case will be reported in both prior and concomitant medication summaries.
- **Prior corticosteroid Treatment:** According to the protocol, patients are allowed to take one week prednisone or equivalent treatment prior to randomization.

For any medication with missing start date, strategies depicted in section 8.3 will be applied to handle such cases.

9.6.2 Data presentation

Summary tables will be performed on each treatment arm and overall patients. Prior/Concomintant medication will be presented by ATC class and preferred name, while the non-treatment procedures will be presented by SOC and PT name.The following topics will be tabulated:

- Pre-medication.
- Prior medications.
- Concomitant medications.
- Prior non-drug treatments and procedures.
- Concomitant non-drug treatments and procedures.
- Patients taking corticosteroid treatment prior to randomisation.
- Prior and concomitant COVID-19 vaccinations by ATC class and preferred name (from eCRF form "Prior and Concomitant Medications")
- Concomitant medications due to COVID-19 by ATC class and preferred name (from eCRF form "Prior and Concomitant Medications").

All summaries will be conducted on FAS population. Listings will be shown for pre-medication, prior medication, and concomitant medication, prior and concomitant non-drug treatments/procedures. In particular, a listing of prior medication of steroids will be presented, using data collected in 'Prior Medications - Steroids' eCRF page. In addition, a supplementary list of WHO preferred name of steroids

may be utilized to identify steroids medication from 'Prior and concomitant medication' eCRF page. The above listings will cover patient number, ATC class and standard drug name, start/end date, start/end study day, dose and unit, route, frequency and indication.

9.6.3 DLBCL-specific prior therapies

This section does not apply for this study.

9.6.4 New anti-lymphoma treatments

9.6.4.1 Definition

New anti-lymphoma treatments (NALT) applies to patients who have disease progression/relapse or if an end of treatment tumor assessment indicates residual (partial metabolic response, i.e. PR) or no metabolic response. In the eCRF page 'New anti-lymphoma treatments', the patients who have answered the question "Any new anti-lymphoma treatment administered?" as "Yes" will be considered as patients with NALT.

9.6.4.2 Data presentation

The following tabulation will be done for evaluating the new anti-lymphoma treatments ATC Level 2 class and preferred name on FAS and SAF population per treatment arm and overall patients:

- Number and percentage of patients who receieves NALT.
- Number and percentage of patients who receives NALT before the completing 6 cycles of study treatment as mentioned in the CTP.
- Number and percentage of patients who receieves NALT after completing 6 cycles of study treatment as mentioned in the CTP.
- Number and percentage of patients who receieves NALT after documented disease progression.
- Number and percentage of patients who receieves NALT prior to documented disease progression.
- Best documented response after receiving NALT

Data collected from eCRF page 'New anti-lymphoma treatment' will be reported in listings, presenting patient number, medication/procedure name, start/end date (or ongoing), start/end study day, intention of ASCT proceeding.

9.7 Study treatment and study drug administration

All the analysis realated to study drug administration and study treatment will be done based on the SAF.

9.7.1 Definitions

9.7.1.1 Duration of exposure to study drug/study treatment

Study Drug	Definition
Tafasitamab	Duration of exposure of Tafasitamab [days] = [last date of administration of the tafasitamab + (length of time interval – 1)]. Length of time interval is defined to be 7 days. In case a patient has the last contact date before the defined last date of exposure, the last date of exposure will be set as the last contact date.

Lenalidomide	Duration of exposure of Lenalidomide [days] = [last date of exposure to Lenalidomide – date of first administration of Lenalidomide + 1].
Rituximab	Duration of exposure of Rituximab [days] = [last date of exposure to Rituximab + (length of time interval – 1)]. Length of time interval is defined to be 21 days. In case a patient has the last contact date before the defined last date of exposure, the last date of exposure will be set as the last contact date.
Cyclophosphamide	Duration of exposure of Cyclophosphamide [days] = [last date of exposure to Cyclophosphamide + (length of time interval – 1)]. Length of time interval is defined to be 21 days. In case a patient has the last contact date before the defined last date of exposure, the last date of exposure will be set as the last contact date.
Vincristine	Duration of exposure of Vincristine [days] = [last date of exposure to Vincristine + (length of time interval – 1)]. Length of time interval is defined to be 21 days. In case a patient has the last contact date before the defined last date of exposure, the last date of exposure will be set as the last contact date.
Doxorubicin	Duration of exposure of Doxorubicin [days] = [last date of exposure to Doxorubicin + (length of time interval – 1)]. Length of time interval is defined to be 21 days. In case a patient has the last contact date before the defined last date of exposure, the last date of exposure will be set as the last contact date.
Prednisone	Duration of exposure of Prednisone [days] = [last date of exposure to Prednisone – date of first administration of Prednisone + 1].

9.7.1.2 Cumulative Expsoure

Cumulative dose of tafasitamab [mg]:

Dosage of tafasitamab in each infusion is calculated as: [40mg/ml * ml of tafasitamab added to the infusion bag * (Calculated volume of infusion/250ml)]

The overall culmulative dose of tafasitamab of study treatment is calculated as the sum of all individual tafasitamab doses.

Cumulative dose of lenalidomide [mg]:

The cumulative dose of lenalidomide is defined as the total dose taken (in mg) by a patient across all the cycles of the study. Days where no lenalidomide pill is taken are counted as days with a dose of 0 mg. The difference in number of capsules dispensed and returned will not be considered.

Exemplified calculation:

Cycle	Dosing start day	Dosing end day	Days of lenalidomide taken	Dose strengh [mg]	Total dose
1	1	10	10	25	25 x 10 = 250
2	1	10	10	25	25 x 10 = 250
3*	1	5	5	25	25 x 5 = 125
3*	8	10	3	20	20 x 3 = 60
4*	1	7	7	20	20 x 7 = 140
Cumulative dose = 250 + 250 +125 + 60 +140 = 825 [mg]					

*In this example the patient experienced dose interruption and dose reduction in cycle 3 and discontinued lenalidomide in cycle 4.

9.7.1.3 Dose Intensity, Planned Dose Intensity and Relative Dose Intensity

Dose Intensity of Rituximab, Cyclophosphamide, Vincristine and Doxorubicin

1. (Actual) Dose Intensity (ADI)

- Definition: ADI is an index of an actual dose per cycle.
- Unit: mg/m2 per cycle
- Formula: [actual dose per cycle (mg/m2)] / cycle]

2. Planned Dose Intensity (PDI)

- Definition: PDI is an index of a scheduled dose per cycle.
- Unit: mg/m2 per cycle
- Formula: [planned dose per cycle (mg/m2)] / cycle]

3. Relative Dose Intensity (RDI)

- Definition: RDI expresses the amount of drug administered per unit of time compared to the planned amount of drug at the scheduled time.
- Unit: %
- Formula: [ADI/PDI] * 100

Dose Intensity of Prednisone

For Prednisone, the above will be defined in a similar fashion, only, instead of actual dose per cycle in mg/m2, total dose administered per cycle in mg would be considered.

Average Relative Dose Intensity of R-CHOP (ARDI)

- Definition: The intensity of the entire R-CHOP regimen is better defined by the ARDI, which is calculated as the mean of RDIs of all the components of R-CHOP for a particular cycle.
- Unit: %

Dose Intensity of Lenalidomide

For Lenalidomide, the above will be defined in a similar fashion to Prednisone.

9.7.1.4 Dose Interruption

Tafasitamab:

There are two scenarios of tafasitamab interruption. Firstly, a patient can skip a visit and thus the administration of tafasitamab of that visit. This is defined as 'Skipping of tafasitamab administration'. Secondly, tafasitamab administration can be interrupted during the infusion, this will be defined as 'Interruption of tafasitamab during infusion'. Furthermore, a patient interrupting Tafasitamab infusion can have the following scenarios: either the patient takes the full dosage after the infusion interruption or the patient does not take the full dose after the infusion interruption.

Lenalidomide:

If a patient does not take a particular dose of Lenalidomide, that is, skips a Lenalidomide dose, then it is considered as an interruption.

Rituximab:

There are two scenarios of Rituximab interruption. Firstly, a patient can skip a visit and thus the administration of Rituximab of that visit. This is defined as 'Skipping of Rituximab administration'. Secondly, Rituximab administration can be interrupted during the infusion, this will be defined as 'Interruption of Rituximab during infusion'. Furthermore, a patient interrupting Rituximab infusion can have the following scenarios: either the patient takes the full dosage after the infusion interruption or the patient does not take the full dose after the infusion interruption.

Cyclophosphamide:

If a patient does not take a particular dose of Cyclophosphamide, that is, skips a Cyclophosphamide dose, then it is considered as an interruption.

Vincristine:

If a patient does not take a particular dose of Vincristine, that is, skips a Vincristine dose, then it is considered as an interruption.

Doxorubicin:

If a patient does not take a particular dose of Doxorubicin, that is, skips a Doxorubicin dose, then it is considered as an interruption.

Prednisione:

If a patient does not take a particular dose of Prednisione, that is, skips a Prednisione dose, then it is considered as an interruption.

9.7.1.5 Dose Delay

R-CHOP:

If "Dose Delay" is ticked as 'Yes' for a patient for any of the components of R-CHOP in the R-CHOP Dosage Administration eCRF page, then it is considered as a delay for the corresponding R-CHOP component.

9.7.1.6 Dose Reduction

Lenalidomide and R-CHOP:

A dose reduction is defined as a decrease in dose from the protocol planned starting dose (e.g. for '25 mg daily' to '20 mg daily'). Information of dose reductions is captured in the dosing eCRF page for lenalidomide and R-CHOP.

9.7.2 Data Presentation

All study treatment and study drug administration and exposure related summaries would consider the SAF analysis population.

For all the dose intensity parameters (relative dose intensity, average relative dose intensity of R-CHOP), descriptive statistics, viz. mean, standard deviation, median, Q1, Q3, minimum, and maximum will be presented per cycle and overall.

Descriptive statistics, viz. mean, standard deviation, median, Q1, Q3, minimum, and maximum will be presented for duration of exposure and cumulative duration of exposure.

For Tafasitamab and Rituximab interruptions/skipping, the following will be presented by cycle and overall:

- Number and percentage of patients without any 'Skipping of tafasitamab administration'.
- Number and percentage of patients without any 'Skipping of Rituximab administration'.
- Number and percentage of patients with at least one 'Skipping of tafasitamab administration'. Reasons of skipping will be listed.
- Number and percentage of patients with at least one 'Skipping of Rituximab administration'. The reasons of skipping will be listed.
- Number and percentage of patients without any 'Interruption of tafasitamab during infusion'.
- Number and percentage of patients without any 'Interruption of rituximab during infusion'.
- Number and percentage of patients with at least one 'Interruption of tafasitamab administration during infusion', along with reasons of interruption.
- Number and percentage of patients with at least one 'Interruption of Rituximab administration during infusion'. Reasons of interruption will be listed.
- Number and percentage of patients having Tafasitamab infusion interruption but completing the full dose.
- Number and percentage of patients having Rituximab infusion interruption but completing the full dose.
- Number and percentage of patients having Tafasitamab infusion interruption and not completing the full dose.
- Number and percentage of patients having Rituximab infusion interruption but not completing the full dose.

For Lenalidomide, Cyclophosphamide, Vincristine, Doxorubicin, and Prednisone interruptions, the following will be presented:

- Number and percentage of patients without any doses skipped.
- Number and percentage of patients with at least one dose skipped. Reasons of skipping will be listed.
- Number and percentage of patients with different numbers of skipped doses, i.e. number and percentage of patients with 1 dose skipped/2 doses skipped/3 doses skipped, etc.

For dose delay, the number and percentage of patients with at least one delay of any R-CHOP component, along with reasons of delay will be presented.

For lenalidomide dose reduction, the following will be presented:

- Number and percentage of patients without any dose reduction
- Number and percentage of patients with at least one dose reduction, along with reasons of dose reduction.
- Number and percentage of patients with a reduction to the level of 20 mg (but not lower)
- Number and percentage of patients with a reduction to the lowest level of 15 mg, namely, if a patient modifies his lenalidomide from 25 mg to 20 mg and 15 mg, this patient will be counted in the level group of 15 mg.
- Number and percentage of patients with a reduction to the lowest level of 10 mg, namely, if a patient modifies his lenalidomide from 25 mg to 20 mg, 15 mg and 10 mg, this patient will be counted in the level group of 10 mg.

For dose reduction of R-CHOP, the following will be summarized for each treatment arm and overall:

- Number and percentage of patients without any dose reduction of all components of R-CHOP
- Number and percentage of patients with at least one dose reduction of any component of R-CHOP

In addition, dose reduction of each component of R-CHOP, namely rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone, will be summarized for the following points on each component:

- Number and percentage of patients without any dose reduction
- Number and percentage of patients with at least one dose reduction, along with reasons of dose reduction

Additionally, the number and percentage of patients who skipped at least one dose of Lenalidomide and Tafasitamab will be presented for each cycle and overall.

Number and percentage of patients who skipped Lenalidomide and Tafasitamab doses on individual treatment days will be presented for each cycle.

Number and percentage of patients who skipped Lenalidomide and Tafasitamab doses will be presented for each cycle and overall by the number of doses skipped.

Percentage of protocol based dose will be presented for each cycle and overall. This will be calculated as:

[(Number of Lenalidomide doses administered to patients in a particular cycle)/(Expected number of Lenalidomide doses administered in that cycle)] * 100 %.

The above defined summaries will also be presented for Tafasitamab.

According to the protocol, a patient in Arm B will be taking ten doses of Lenalidomide per cycle and patients in both arms will be taking three doses of Tafasitamab per cycle.

9.7.3 Listing presentation of exposure

Listings will be created to present the study treatment for tafasitamab, lenalidomide and R-CHOP respectively, the following items should be included: patient identifier, treatment arm, visit, occurrence of administration, administered start date/time and end date/time, dosage and unit, reason if not done. For tafasitamab, the occurance of infusion interruption and the corresponding reason should be displayed in the listing. For lenalidomide and R-CHOP, the following two items should also be listed: Occurance of dose reduction and reason of dose reduction. For lenalidomide, a listing will be created to present number of capsules dispensed, number of capsules taken by patients, number of capsules returned, dose strength and reason for drug non-compliance.

10. EFFICACY EVALUATION

10.1 Analysis of Response and progression evaluation

10.1.1 General definition

10.1.1.1 Response criteria

Efficacy assessments will be made according to the revised response criteria for malignant lymphoma based on the guidelines of the Lugano Classification (as reported by Cheson, 2014) and will be based on investigator assessment (See protocol appendix E). In this study, the response assessment is captured in eCRF page 'Radiographic Imaging Assessment' and 'Disease Response Assessment'.

10.1.1.2 Tumor assessment and assessment date

Tumor response assessment is performed per schedule in protocol. The result, date and modality of tumor response assessment are documented in the eCRF page 'Disease Response Assessment'.

For efficacy summaries (e.g., ORR tables, PFS Kaplan-Meier analyses etc.), only response assessments as per Cheson 2014 criteria will be considered. That is, response assessments based on physical examination only (i.e., in absence of radiological evaluation or decisive biopsy/aspirate data) will not be considered. The following eCRF records will be taken into account:

(1) Response assessments based on radiological evaluation (based on radiological evaluation only or radiological evaluation plus other assessments, e.g., physical examination). The tumor assessment date is the scan date of the radiological evaluation.

(2) Response assesssments with outcome "Progressive Disease" based on biopsy (i.e., selected as 'other evaluation' and specified as 'biopsy' in Disease Response Assessment eCRF page). For response outcomes of PD based on biopsy, the date of tumor biopsy as recorded in Tumor Biopsy eCRF page is taken into consideration when deriving the tumor response date. E.g., if disease response is based on radiological evaluation and biopsy, then tumor response date would be the scan date of radiological evaluation or the date of tumor biopsy recorded in Tumor Biopsy eCRF page whichever is earlier.

10.1.1.3 Determination of missing adequate tumor assessments

The term "missing adequate tumor assessment" is defined as a tumor assessment (TA) not done or tumor assessment with overall lesion response of not evaluable or "UNK". A "missing adequate tumor assessment" will be referred to as "missing assessment".

The censoring and event date options for PFS, EFS, DoR, TTNT depend on the presence and the number of missing assessments. For example:

- In the analysis for PFS, an event occurring after two or more missing assessments or non-adequate tumor assessments will be censored on the date of last adequate tumor assessment.

For the purpose of this study, if no tumor assessments have happened in 394 days or longer (as in the follow-up phase, a CT/MRI tumor assessment is expected to happen every 6 months + 2 weeks),

then the patient will be considered as having two or more missed assessments. The handling of two or more missed assessments in discussed in each of the endpoint section.

10.1.2 Objective response rate (ORR) at EOT and Best ORR

Post-baseline response assessments will be evaluated at C3D18, end of treatment visit/early study treatment discontinuation visit, follow-up visit 2, follow-up visit 4 and end of study/early discontinuation of follow-up visit.

The "ORR at EOT" is defined as the proportion of patients with CR or PR based on the response achieved at the end of treatment visit/early treatment discontinuation visit.

In addition, "Best objective response rate" is calculated as the proportion of patients with CR or PR as the best objective response at any time on the study. This will be denoted as "Best ORR".

"Best response in the study" is defined as the best achieved response at any time on the study. The order of responses are: CR>PR>SD>PD>Not Evaluable. The "Not evaluable" category includes patients who have all response assessments after NALT, who do not have a single evaluable post-baseline response assessment as per Investigtor, or who have no post-baseline response assessment available (e.g., due to prior death or ICF withdrawal).

The denominator of "ORR at EOT" and ORR is the total number of patients in the analysis set.

CR or PR after start of NALT (as defined in section **ERROR! REFERENCE SOURCE NOT FOUND.**) will not be considered as responder for either "ORR at EOT" or "Best ORR". CR or PR after a disease progression, will also not be considered. These assessments will be denoted as "Other" and will be considered in the denominator for calculating the response rates.

The analysis of "ORR at EOT" and ORR will be performed on FAS and PPS by treatment arm and overall as below:

- Number and percentage of patients with CR/PR/SD/PD/Not evaluable/Other/Missing by visit.
- Number and percentage of patients classified as having "ORR at EOT" with associated 95% confidence limits (using the Clopper-Pearson exact method) will be presented, along with number and percentage of patients with CR/PR/SD/PD/Not evaluable at EOT. The reasons for being not evaluable will be tabulated:
    - Not evaluable (as per investigator assessment)
    - Response assessment after start of new anti-lymphoma treatment
    - Assessment not performed
    - Missing (patient discontinued prior to EOT visit)
- Number and percentage of patients classified as having Best ORR until end of study with associated 95% confidence limits (using the Clopper-Pearson exact method) will be presented.
- Number and percentage of patients with "Best Response in the study" as CR/PR/SD/PD/ Not evaluable as ORR until end of study. The "Not evaluable" category includes patients who have all response assessments after NALT, who do not have a single evaluable post-baseline response assessment as per Investigtor, or who have no post-baseline response assessment available (e.g., due to prior death or ICF withdrawal).

10.1.3 The metabolic, PET-negative complete response rate

The above analysis described in Section 10.1.2 will be perfomed by considering the following modalities only: PET/CT and PET/MRI as enetered in "Radiographic Imaging Assessment". For patients with disease

response assessment of modalities other than 'PET/CT' or 'PET/MRI', the results will be excluded, with associated reason of 'PET/CT scan or PET/MRI scan'.

This analysis will be performed on FAS.

10.1.4 Duration of Response and Duration of Complete Response

Duration of Response

For Duration of response (DoR), "Responders" are defined as any patient with a documented CR or PR prior to start of NALT or disease progression or cut-off which ever is earlier.

All other patients will be considered as "Non-responders".

DoR is defined as the elapsed time between the date of first documented CR or PR evaluation and the date of event defined as first radiologically or histologically/cytologically documented disease progression or death (from any cause).

DoR [months] = [(date of disease progression or death or date of censoring – date of assessment of first documented response of (CR or PR) + 1)/30.4375].

Non-responders will not be considered in this analysis.

The following table present the different censoring situations and rules for Responders. The DoR for these patients is:

Situation	Outcome	Date of Censoring	Censoring reason
Patient is ongoing with No event	Censored	Date of last tumor assessment with CR or PR	Ongoing without progression
Lost to follow-up (based on EOT or EOS eCRF page) with No event	Censored	Date of last tumor assessment with CR or PR	Lost to follow-up
Patient received NALT prior to documented disease progression or death	Censored	Date of last tumor assessment with CR or PR before the earlier of the cut-off date or start of new anti-lymphoma treatment	NALT started prior to event
Death or progression with no assessments in the preceding 394 days	Censored	Date of last tumor assessment with CR or PR	PD/Death documented after two or more missing tumor assessments
PD with missing assessment date	Cesnored	Date of last tumor assessment with CR or PR	Adequate assessment not available

Discontinued study with No event (Discontinued for any reason other than "Lost to follow-up")	Censored	Date of last tumor assessment with CR or PR	Discontinued study without event
Completed study with no event	Censored	Date of last tumor assessment with CR or PR	Completed as per protocol without any event

The following analysis will be performed on FAS and PPS by treatment arm:

- Number and percentage of patients who were responders/non-responders
- Number and percentage of patients with first documented response as CR
- Number and percentage of patients with first documented response as PR
- Number and percentage of patients who achieved CR as best response
- Number and percentage of patients who achieved PR as best response
- Number and percentage of Responders who are censored with the censoring reason.
- The distribution (median, Q1 and Q3 together with their 95% CI (Brookmeyer and Crowley 1982)) of DoR will be presented
- The probabilities of DoR specific time points (1 month, 3 months, 6 months, 12 months, 18 months, 24 months), and the associated 95% CIs (Greenwood formula) will be summarized.
- A plot of the Kaplan-Meier curve for DoR
- No formal hypothesis testing will be conducted.

In addition, the above analysis of DoR will be repeated for the patients who achieved CR as best response through the course of study.

Duration of Complete Response

For Duration of Complete Response (DoCR), "Responders" are defined as any patient with a documented CR prior to start of NALT or disease progression or cut-off which ever is earlier.

All other patients will be considered as "Non-responders".

DoCR is defined as the elapsed time between the date of first documented CR evaluation and the date of event defined as first radiologically or histologically/cytologically documented disease progression or death (from any cause).

DoCR [months] = [(date of disease progression or death or date of censoring censored – date of assessment of first documented response of CR + 1)/30.4375].

Non-responders will not be considered in this analysis.

The following table present the different censoring situations and rules for Responders.

Situation	Outcome	Date of Censoring	Censoring reason
Patient is ongoing with with No event	Censored	Date of last assessment with CR	Ongoing without progression
Lost to follow-up (based on EOT or EOS eCRF page) with No event	Censored	Date of last assessment with CR	Lost to follow-up
Patient received NALT prior to documented disease progression or death	Censored	Date of last tumor assessment with CR before the earlier of the cut-off date or start of NALT	NALT started prior to event
Death or progression with no assessments in the preceding 394 days	Censored	Date of last tumor assessment with CR	PD/Death documented after two or more missing tumor assessments
PD with missing assessment date	Cesnored	Date of last tumor assessment with CR	Adequate assessment not available
Discontinued study with No event (Discontinued for any reason other than "Lost to follow-up")	Censored	Date of last tumor assessment with CR	Discontinued study without event
Completed study with no event	Censored	Date of last tumor assessment with CR	Completed as per protocol without any event

The following analysis will be performed on FAS by treatment arm:

- Number and percentage of patients who were responders/non-responders
- Number and percentage of Responders who are censored with the censoring reason.
- The distribution (median, Q1 and Q3 together with their 95% CI (Brookmeyer and Crowley 1982)) of DoCR will be presented.
- The probabilities of DoCR specific time points (1 month, 3 months, 6 months, 12 months, 18 months, 24 months), and the associated 95% CIs (Greenwood formula) will be summarized.
- A plot of the Kaplan-Meier curve for DoCR
- No formal hypothesis testing will be conducted.

10.1.5 Progression-free survival

PFS is defined as the time from the date of randomization to the date of the first radiologically or histologically/cytologically documented disease progression (as per Lugano 2014) or death due to any cause. If a patient has not progressed or died at the analysis cut-off date, PFS will be censored as discussed sebelow.

Situation	Outcome	Date of Censoring	Censoring reason
Ongoing and No event until data cut-off	Censored	Date of last adequate tumor assessment	Ongoing without event
No baseline tumor assessment	Censored	Reference start date	No baseline tumor assessment
Lost to follow-up (based on EOT or EOS eCRF page) without documented progression or death	Censored	Date of last adequate tumor assessment or reference start date in case of study discontinuation before any post-baseline assessment	Lost to follow-up
Patient received NALT prior to documented disease progression or death	Censored	Date of last adequate tumor assessment before the earlier of the cut-off date or start of new anti-lymphoma treatment	NALT started prior to event
Death or progression with no assessments in the preceding 394 days	Censored	Date of last adequate tumor assessment prior to the event	Event documented after two or more missing tumor assessments
PD with missing assessment date	Cesnored	Date of last adequate tumor response assessment	Adequate assessment not available
Discontinued study without documented progressive disease or death (for any reason other than “Lost to follow-up”)	Censored	Date of last adequate tumor assessment or reference start date in case of study discontinuation without progression before any post-baseline assessment	Discontinued study without event

Completed study with no event	Censored	Date of last adequate tumor response assessment	Completed as per protocol without any event

Note: Event = Any one of the following: Documented disease progression or Death

Date of event: The first of the two (Documented disease progression or Death)

Analysis of PFS is performed per treatment arm and overall, using FAS and PPS population sets. Detailed analysis is present as below:

- Number and percentage of patients with PFS events/censoring will be described according to the type of event or censored (death, disease progression or censored).
- The reason for censoring will be tabulated
- The distribution of PFS will be estimated using the Kaplan-Meier (K-M) method. The median PFS time, 25% and 75% percentiles, with associated 95% confidence intervals will be presented (Brookmeyer and Crowley 1982).
- The PFS probabilities at specific time points (3 months, 6 months, 12 months, 18 months, 24 months), and the associated 95% CIs (Greenwood formula) will be summarized.
- The median follow-up time for PFS including a 95% confidence interval (Brookmeyer and Crowley 1982) will be calculated using the reverse Kaplan-Meier method. This method utilizes the reversed status indicator from Kaplan-Meier method. All censored cases from Kaplan-Meier method will be reversed as event in the reverse Kaplan-meier method and vice versa.
- A plot of the Kaplan-Meier curve for PFS will be provided to estimate the distribution of PFS.
- No formal hypothesis testing will be conducted.

10.1.6 Event-free survival

Event-free survival (EFS) is defined as the time from the date of randomization to the date of the first radiologically or histologically/cytologically documented disease progression or death due to any cause or start of NALT. If a patient has not progressed or died or started a new anti-lymphoma treatment by the analysis cut-off date, EFS will be censored on the Date of last adequate tumor assessment. More details about EFS censoring is presented below:.

Situation	**Outcome**	**Date of Censoring**	**Censoring reason**
Ongoing and No event until data cut-off	Censored	Date of last adequate tumor assessment	Ongoing without event
No baseline tumor assessment	Censored	Reference start date	No baseline tumor assessment
Lost to follow-up (based on EOT or EOS eCRF page) without documented progression or death or start of NALT	Censored	Date of last adequate tumor assessment or reference start date in case of study discontinuation before any post-baseline assessment	Lost to follow-up
Death or progression with no assessments in the preceding 394 days	Censored	Date of last adequate tumor assessment prior to the event	Event documented after two or more missing tumor assessments

Start of NALT or PD with missing assessment date	Cesnored	Date of last adequate tumor response assessment	Adequate assessment not available
Discontinued study without documented progressive disease or start of NALT or death (for any reason other than "Lost to follow-up")	Censored	Date of last adequate tumor assessment or reference start date in case of study discontinuation without progression before any post-baseline assessment	Discontinued study without event
Completed study with no event	Censored	Date of last adeuate tumor response assessment	Completed as per protocol without any event

Note: Event = Any one of the following- Documented disease progression or Death due to any cause or start of NALT

Date of event: The first of the three (Documented disease progression or Death or start of NALT)

Analysis of EFS is performed per treatment arm and overall in final analysis using FAS population set. Detailed analysis is present as below:

- Number and percentage of patients with EFS events/censoring will be described according to the type of event or censored (death, documented tumor progression, start of new anti-lymphoma treatment or censored).
- The reason for censoring will be tabulated.
- The distribution of EFS will be estimated using the Kaplan-Meier (K-M) method. The median EFS time, 25% and 75% percentiles, along with 95% confidence intervals will be presented (Brookmeyer and Crowley 1982).
- The EFS probabilities at specific time points (3 months, 6 months, 12 months, 18 months, 24 months), and the associated 95% CIs (Greenwood formula) will be summarized.
- The median follow-up time for EFS including a 95% confidence interval (Brookmeyer and Crowley 1982) will be calculated using the reverse Kaplan-Meier method. This method utilizes the reversed status indicator from Kaplan-Meier method. All censored cases from Kaplan-Meier method will be reversed as event in the reverse Kaplan-meier method and vice versa.
- A plot of the Kaplan-Meier curve for EFS will be provided to estimate the distribution of EFS.
- No formal hypothesis testing will be conducted.

10.1.7 Overall survival

Overall survival (OS) is defined as the time from randomization date until death from any cause and documented by the date of death. The censoring rules are presented in details below:

Situation	**Outcome**	**Date of Censoring**	**Censoring reason**
Ongoing and No event until data cut-off	Censored	Date of Last Contact	Ongoing without event
Lost to follow-up (based on EOT or EOS eCRF page) without documented death	Censored	Date of Last Contact	Lost to follow-up

Discontinued study without documented death (for any reason other than "Lost to follow-up")	Censored	Date of Last Contact	Discontinued study without event
Completed study with no event	Censored	Date of Last Contact	Completed as per protocol without any event

Note: Event = Death

Analysis of overall survival is performed per treatment arm and ovreall, using FAS and PPS population sets. Detailed analysis is present as below:

- Number and percentage of patients with OS events/censoring will be described (death or censored).
- The reasons for censoring will be tabulated
- The distribution of OS will be estimated using the Kaplan-Meier (K-M) method. The median OS time, 25% and 75% percentiles, along with 95% confidence intervals will be presented (Brookmeyer and Crowley 1982).
- The OS probabilities at specific time points (6 months, 12 months, 18 months, 24 months), and the associated 95% CIs (Greenwood formula) will be summarized.
- The median follow-up time for OS including a 95% confidence interval (Brookmeyer and Crowley 1982) will be calculated using the reverse Kaplan-Meier method. This method utilizes the reversed status indicator from Kaplan-Meier method. All censored cases from Kaplan-Meier method will be reversed as event in the reverse Kaplan-meier method and vice versa.
- A plot of the Kaplan-Meier curve for OS will be provided to estimate the distribution of OS.
- No formal hypothesis testing will be conducted.
- Sensitivity Analysis will be performed considering deaths related to COVID-19 as censored events, with the date of death as censoring date. This analysis will be performed only if COVID-19 related deaths is >5.

10.1.8 Time to next anti-lymphoma treatment

The time to next anti-lymphoma treatment (TTNT) is defined as the time from the date of randomization to the start of next anti-lymphoma therapy (therapies include- medication, surgery or radiotherapy for any reason including disease progression, treatment toxicity and patient preference) or death due to any cause, whatever comes first.

Patients without documented start of a new anti-neoplastic therapy will be censored at the date of last contact.

Situation	**Outcome**	**Date of Censoring**	**Censoring reason**
Ongoing and No event until data cut-off	Censored	Date of Last Contact	Ongoing without event
Lost to follow-up (based on EOT or EOS eCRF	Censored	Date of Last Contact	Lost to follow-up

page) without death or start of NALT			
Discontinued study without start of NALT or death (for any reason other than "Lost to follow-up")	Censored	Date of Last Contact	Discontinued study without event
Completed study with no event	Censored	Date of Last Contact	Completed as per protocol without any event

Note: Event = Any one of the following- start of NALT or death due to any cause

Date of event: The first of the two (start of NALT or death due to any cause)

Analysis of TTNT is performed per treatment arm and overall, using FAS.. Detailed analysis is present as below:

- Number and percentage of patients with TTNT events/censoring will be described (start of new anti-lymphoma treatment or censored).
- The reasons for censoring will be tabulated.
- The distribution of TTNT will be estimated using the Kaplan-Meier (K-M) method. The median TTNT, 25% and 75% percentiles, along with 95% confidence intervals will be presented (Brookmeyer and Crowley 1982).
- The TTNT probabilities at specific time points (6 months, 12 months, 18 months, 24 months), and the associated 95% CIs (Greenwood formula) will be summarized.
- The median follow-up time for TTNT including a 95% confidence interval (Brookmeyer and Crowley 1982) will be calculated using the reverse Kaplan-Meier method. This method utilizes the reversed status indicator from Kaplan-Meier method. All censored cases from Kaplan-Meier method will be reversed as event in the reverse Kaplan-Meier method and vice versa.
- A plot of the Kaplan-Meier curves for TTNT will be provided.
- No formal hypothesis testing will be conducted.

10.1.9 Primary Refractoriness at EOT

Primary refractoriness at EOT is defined for those patients who did not have any CR or PR during treatment, or patients who progressed or died due to DLBCL within 6 months after EOT or patients who had PD at EOT. The number and percentage of patients with primary refractoriness will be presented at EOT.

10.1.10 Listing of response assessment

Response assessment along with radiographic imaging assessment will be listed out in the patient data listing.

10.2 Analysis of Pharmacokinetic data

Serum samples for the tafasitamab pharmacokinetic (PK) analysis will be collected prior and 1 hour (+/-15 mins) after the tafasitamab infusion during the course of the treatment phase, end of treatment visit and the first two follow-up visits.

The following elapsed time will be calculated for each record:

- Elapsed time from the first administration of tafasitamab [days]: Date/time of assessment – date/time of the first administration of tafasitamab

For samples collected 1h after the end of the tafasitamab infusion, results will be excluded from summary statistics if the deviation of the actual collection time is beyond ± 15 min from the scheduled collection time. Such values will be flagged accordingly in the listing of PK data.

Results of tafasitamab concentrations below the limit of quantification (BLQ) will be presented in the listing. In the summary statistics and contentration-time profile graph the value of BLQ is set to be 0 for the cycle 1 day 1 pre-dose assessment, and treated as missing data in the assessments of other timepoints.

The tafasitamab serum concentration data [ng/mL] will be summarized and visualized for each treatment arm and overall using the PKAS population set. Detailed analyses are presented as below:

- Descriptive statistics of tafasitamab concentrations will be tabulated by visit and timepoint, including n, n-missing, arithmetic mean, geometric mean, StD, coefficient of variation CV (%) and geometric CV (%), median, minimum and maximum.
- Serum concentration-time profile with mean +/- StD will be visualized across visit and timepoint. This will be performed on both original serum concentration value and log(serum concentration value).
- Listings of PK data will be generated to display the patient identifier, treatment arm, visit, date/time of assessment, assessment timepoint, result, elapsed time, flag of collection time deviation, reason for undone assessment. The concentration data will be presented with maximum three decimals.

10.3 Analysis of Immunogenicity data

Serum samples for the assessment of anti-tafasitamab antibodies are collected in cycles 1, 3, 5, end of treatment visit and the first two follow-up visits. In order to determine the patient's anti-tafasitamab antibody status, as a first step, a screening assay is performed. Then all screened positive samples are tested again in a confirmatory assay. For all confirmed positive samples, a titer assay and a specificity assay will be performed.

Anti-tafasitamab antibody samples are defined as "negative" if they are screened or confirmed negative. Anti-tafasitamab antibody samples are defined as "positive" if they are reported positive in both the screening and the confirmatory assay. For all positive samples, an anti-tafasitamab antibody titer will be determined.

The immunogenicity data will be summarized for each treatment arm and overall, using the IAS population set. Detailed analyses are presented as below:

- Number and percentage of patients with anti-tafasitamab antibody response (Positive or Negative or Missing) by visit.

- Descriptive analysis of anti-tafasitamab antibody titers determinations by visit.
- A summary table of anti-tafasitamab antibody status will be created to present the following categories:
    - Number and percentage of patients with pre-existing anti-tafasitamab antibodies, which is defined as the patients with positive anti-tafasitamab antibody response on C1D1.
    - Number and percentage of patients with negative response during treatment, which is denoted as the patients with negative anti-tafasitamab antibody response on all occasions after C1D1, irrespective of the result on C1D1.
    - Number and percentage of patients with positive response during treatment, which is defined as the patients who had positive anti-tafasitamab antibody response on any occasion after C1D1, irrespective of the result on C1D1.
    - Number and percentage of patients with treatment-induced anti-tafasitamab antibodies, which is defined as the patients with negative anti-tafasitamab antibody response on C1D1 and developed positive response on any other occasion after C1D1.
    - Number and percentage of patients with treatment-boosted anti-tafasitamab antibodies, which is defined as the patients with positive anti-tafasitamab antibody response on C1D1 and developed a higher titer on any other occasion after C1D1.
- Listings of the immunogenicity data will be generated to display the patient identifier, treatment arm, visit, date/time of assessment, assessment timepoint, type of assay, result, and reason for undone assessment.

10.4 Analysis of Biomarker data

10.4.1 General definition and analysis

A limited number of biomarkers are considered for exploratory analyses those will be presented in this CSR. All others will be presented in a future biomarker report. Biomarker assessments including B-cell, T-cell, NK-cell, and ctDNA will be quantified in peripheral blood per schedule visits in the protocol (protocol section 10).

In addition, the biomarkers of CD19 and CD20, will be measured in the tumor tissue, which is collected in the screening visit.

The data of above mentioned biomarkers is collected in eCRF page ‘Pathology central diagnosis’, ‘Biomarker analysis by IHC’ and external dataset.

The following biomarker analysis per treatment arm and overall, using FAS population set:

BTNK

- Descriptive statistics, including number of non-missing observations, number of missing observations, arithmetic mean, StD, minimum and maximum values, quartiles (median, Q1 and Q3) and 95% CIs, will be tabulated for absolute values and percent change from baseline, of the B-, T-, and NK cell quantitative variables by eCRF visit.

ctDNA

- Descriptive statistics, including number of non-missing observations, number of missing observations, arithmetic mean, StD, minimum and maximum values, quartiles (median, Q1 and Q3) and 95% CIs, will be tabulated for ctDNA quantitative variables by eCRF visit.
- BLQ results of ctDNA will be treated in two separate ways:
  - as missing in descriptive analysis
  - Imputed as the Lowest Limit of Detection (LOD) to provide a number, which represents the maximum amount of ctDNA that could be present in each individual sample
- The rate with 95% CI, in percent, of MRD-negative patients among patients with evaluable MRD results (sum of MRD-negative and MRD-positive) by eCRF visit.

- Notes on BLQ value of ctDNA:
  ctDNA measurements (fraction of ctDNA among cfDNA) (ANLOC = BLOOD & SPCT=cfDNA) result can be categorized in three tiers (MRDSTAT):

  - NEGATIVE (below limit of detection and below limit of quantification)
  - POSITIVE BQN (above limit of detection and below limit of quantification)
  - POSITIVE (above limit of detection and above limit of quantification)

  If a measurement is above the Limit Of Detection (LOD) the measurement is considered positive, indicated in MRDSTAT as POSITIVE or POSITIVE BQN. However, only for POSITIVE results (above limit of detection and above limit of quantification) the TESTCD MRDRSLT containing the numeric ctDNA result is provided. Any measurement that is indicated as NEGATIVE in MRDSTAT is below the LOD and hence, these are also below limit of quantification (BLQ) – LOD is already per definition smaller than the limit of quantification. Several measurements using markers (SUBTARG) can exist for each subject visit.

  (1) The numeric ctDNA result of a subject visit is the maximum of all available ctDNA results (MRDRSLT) of a subject visit.
  (2) For subgroup analysis, only the subjects who have MRDRSLT value at baseline are included (i.e., subjects who have MRDSTAT='POSITIVE' record at C01D01). Subjects who have no MRDRSLT (either no assessment performed or no positive MRDSTAT at baseline) will be excluded. Therefore, subjects who have assessed the ctDNA but with no POSITIVE MRDSTAT at C01D01 will not be identified as BLQ, and such subjects will not be further imputed as LOD/ or counted as '<= Median'.
  (3) For baseline and post-baseline by-visit summary of ctDNA numeric values (MRDRSLT), subjects who have assessed the ctDNA but with no positive MRDSTAT will be identified as BLQ and treated in 2 ways:
      a. treated as missing (applied to ASH 2022 abstract and final analysis)
      b. imputed as the Lowest Limit of Detection (LOD) (applied to final analysis only)
  (4) For the baseline and post-baseline by-visit summary of MRD status (MRDSTAT) in final analysis, the following algorithm will be applied:
      - The subject visit is considered as POSITIVE if at least one of the measurements of subject visit is indicated as MRD-positive (i.e., MRDSTAT='POSITIVE') .
      - The subject visit is considered as POSITIVE BLQ if at least one of the measurements of subject visit is indicated as positive BQN ((i.e., MRDSTAT='POSITIVE BQN').
      - The subject visit is considered as NEGATIVE if all of the measurements of subject visit are indicated as MRD-negative (i.e., MRDSTAT='NEGATIVE').

CD19 and CD20 expression by IHC

- Descriptive statistics of CD19 and CD20, , including number of non-missing observations, number of missing observations, arithmetic mean, StD, minimum and maximum values, quartiles (median, Q1 and Q3) and 95% CIs, will be presented.
- CD19 and CD20 expression will be dichotomised into subgroups, if median = maximum then the subgroups will be < median and >= median. If median = minimum then the subgroups will be <= median and > median.

Biomarker Subgroups

- Summary of number and percentage of patients by subgroups of cell of origin based on central assessment of IHC (Hans algorithm) and gene expression profiling, ctDNA (<= Median and > Median), CD19 (<= Median and > Median), and CD20 (<= Median and > Median).

A listing will be created to present the result of biomarkers from pathology central diagnosis and external dataset.

Additional exploratory biomarker analyses may be conducted and will not be part of this CSR.

10.4.2 Relationship between survival endpoints and biomarkers

The relationship between ORR/PFS with the following biomarkers serves as exploratory endpoints:

- Cell of origin (based on central assessment of IHC-Hans algorithm [Non-GCB vs. GCB] and gene expression profiling [GCB vs. ABC]) at screening
- ctDNA at screening
- Quantitative and semi-quantitative CD19 expression on tumor cells at screening
- Quantitative and semi-quantitative CD20 expression on tumor cells at screening

The analysis of "ORR at EOT" and ORR until end of study, will be performed using FAS population per subgroups of each biomarker for each treatment arm as below:

- Number and percentage of patients classified as having "ORR at EOT" with associated 95% confidence limits (using the Clopper-Pearson exact method) will be presented. Number and percentage of patients with CR/PR/SD/PD/Not evaluable/Other/Missing at EOT will also be presented.
- Number and percentage of patients classified as having ORR until end of study with associated 95% confidence limits (using the Clopper-Pearson exact method) will be presented. Number and percentage of patients with CR/PR/SD/PD/Death/Not evaluable /Missing as best objective response until end of study will also be presented. This apply to final completion analysis only.
- ORR at EOT, ORR until end of study with it's associated 95% CI will be presented in forest plots for the different subgroups of all abovementioned biomarkers.

The analysis of PFS, will be performed using FAS population per subgroups of each biomarker for each treatment arm and overall as below:

- The distribution of PFS will be estimated for the stratified biomarker groups using the Kaplan-Meier method. The median PFS time, 25th and 75th percentiles, along with 95% confidence intervals will be presented (Brookmeyer and Crowley 1982).
- A plot of the Kaplan-Meier curve for PFS will be provided to estimate the distribution of PFS.
- The median PFS time along with its 95% CI will be presented in a forest plot for the different subgroups of all above mentioned biomarkers.
- No hypothesis testing will be performed.

To note, analysis of PFS will not be performed if less than 5 events occur in all of the subgroups per treatment arm.

10.4.3 Optional analysis of biomarkers on tumor biopsy samples

A quantitative and semi-quantitative assessment of CD19 and CD20 on malignant B-cells may be applied in a selected subset of sites, the data from the above assessment will be listed in the patient listing.

10.5 Analysis of B symptoms and ECOG status

B symptoms and ECOG status on patients are evaluated in each visit throughout the whole study. If any of the systemic symptoms, i.e. weight loss, fever or night sweat, is present, then B symptoms are defined as present. Otherwise B symptoms are absent. For ECOG status, data are categorized from 0 to 5.

Absolute and relative frequencies are tabulated for B symptoms and ECOG status per visit for each treatment arm and overall using FAS population. Detailed information of B symptoms and ECOG collected from the eCRF will be presented in patient data listings.

11. SAFETY EVALUATION

11.1 Adverse events

11.1.1 Definitions of AEs

Adverse Event (AE):

An AE is defined as any untoward medical occurrence in a patient after his/her provision of informed consent until the end of the study and it will be recorded in the eCRF , irrespective of causal relationship to this treatment. Therefore an AE can be any unfavorable and unintended sign (including an abnormal laboratory finding) or symptom, whether or not it is considered related to study treatment.

The detailed categorization of AE with regards to seriousness, intensity, toxicity, study drug relationship, outcome and action taken is depicted in protocol section 11.2.3.

As per protocol, an abnormal safety assessment that qualify as AEs, e.g. laboratory abnormalities, ECG abnormalities, might be documented in the eCRF as an AE. From programming aspect, no additional derivation of AE entries will be applied for such case.

Adverse Event prior to study treatment (Pre-treatment AE):

Any adverse event start prior to date of first administration of study treatment and without any increase of severity after study treatment will be classified as Pre-AE.

Treatment-emergent Adverse Event (TEAE):

TEAE is defined as any adverse event reported in the following time interval (including the lower and upper limits): [Reference start date of treatment administration; Reference end date of treatment administration + 30 days]. An adverse event present prior to study drug administration but increased in severity after treatment start, will also be included as TEAE.

Events with missing onset dates will be included as TEAE if the end date is not before the reference start date.

If the start date and time of an AE are partially or completely missing, the AE will be assumed to be a TEAE if it cannot be definitely shown that the AE did not occur or worsen during the treatment-emergent period (worst case approach). Missing dates and times will not be replaced. The methods for handling the missing dates for defining an TEAE is depicted in section 8.3.

AEs in the follow-up period:

If an AE occurs 30 days after the End of treatment (boundary not included), it is defined as an AE in the follow-up period.

AEs of special interest (AESIs):

Information of AESI is provided directly from the eCRF. AESIs for tafasitamab are:

- Tumor lysis syndrome (TLS),
- Second primary malignancy (SPM)
- Infusion-related reactions (IRRs) ≥ grade 3
- Allergic reactions to study drug ≥ grade 3
- Cytokine release syndrome
- Hepatitis B reactivation
- Progressive multifocal leukoencephalopathy (PML)

AESIs for lenalidomide:

- Second primary malignancy (SPM).

Death

Information of death is captured in eCRF page 'End of Study' and 'End of Treatment' page. All deaths will be flagged as 'On treatment' or 'Post-treatment' and listed. The following summary tables will be generated for both primary completion and final analysis on all screened patients and SAF population:

- A overall summary table of reasons of deaths.
- A summary table of reasons of deaths before end of treatment.
- A summary table of reasons of death after end of treatment.

11.1.2 Analysis of AEs

The following analysis of AEs will be tabulated per arm and overall patients, using SAF population set. The exception is the analysis of pre-treatment AEs, which will be based on all screened patients.

TEAEs will be classified into the following categories: seriousness, causality, toxicity (determined according to the NCI-CTCAE version 5.0), intensity, outcome and action taken.

Specifically, all summaries of study treatment related TEAEs (causality) will be divided into 5 sections: related to any component of study treatment, related to tafasitamab only, related to lenalidomide only, related to both tafasitamab and lenalidomide, and related to R-CHOP only.

All summaries of TEAEs leading to permanent study treatment discontinuation will be divided into the following sections: permanent discontinuation of tafasitamab, permanent discontinuation of lenalidomide, permanent discontinuation of both tafasiatamab and lenalidomide, permanent discontinuation of R-CHOP, permanent discontinuation of rituximab, permanent discontinuation of vincristine, permanent discontinuation of doxorubicin, permanent discontinuation of cyclophosphamide, permanent discontinuation of prednisone and permanent discontinued study treatment (if such AE leads to permanent discontinuation of tafasitamab and R-CHOP, it is categorized as 'discontinued study treatment' for Arm A, and if such AE leads to permanent discontinuation of tafasitamab, lenalidomide and R-CHOP, it is categorized as 'discontinued study treatment' for Arm B).

All summaries of TEAEs leading to study treatment interruption will be divided into following sections: interruption of tafasitamab, interruption of lenalidomide, interruption of both tafasitamab and lenalidomide, interruption of R-CHOP, interruption of rituximab, interruption of vincristine, interruption of doxorubicin, interruption of cyclophosphamide, interruption of prednisone and interruption of study treatment (if such AE leads to interruption of tafasitamab and R-CHOP, it is categorized as 'interrupted study treatment' for Arm A, and if such AE leads to interruption of tafasitamab, lenalidomide and R-CHOP, it is categorized as 'interrupted study treatment' for Arm B). Note that, from the eCRF, for a particular patient, if all the R-CHOP components are interrupted simultaneously for an AE, only then the action taken should be considered as interruption of R-CHOP for this AE.

All summaries of TEAEs leading to R-CHOP reduction will be divided into following sections: dose reduction of R-CHOP, dose reduction of rituximab, dose reduction of vincristine, dose reduction of doxorubicin, dose reduction of cyclophosphamide and dose reduction of prednisone. Note that, from the eCRF, for a particular patient, if all the R-CHOP components are reduced simultaneously for an AE, only then the action taken should be considered as R-CHOP reduced for this AE.

The incidence of TEAEs will be summarized in incidence tables. If a patient experiences more than one occurrence of the same AE, the occurrence with the greatest intensity/toxicity, worst outcome and the closest association with the study treatment will be counted in the summary tables.

All AEs will be listed by patient, along with information of treatment arm, start date/time and end date/time, duration, seriousness, causality of tafasitamab/lenalidomide/R-CHOP assessment, toxicity grade, action taken with tafasitamab/lenalidomide/R-CHOP, other actions taken, outcome, AESI flag and seriousness criteria.

11.1.2.1 Overall Summary of Adverse Event

An overall summary table of AEs will be provided with the number and percentage of patients (incidence) with at least one event, along with the total number of events presented for the following categories:

- Pre-treatment AEs
- All TEAEs
- Study treatment related TEAEs
- Serious TEAEs
- Study treatment related, serious TEAEs
- Grade 3 or higher TEAEs
- Study treatment related, grade 3 or higher TEAEs
- TEAEs leading to permanent study treatment discontinuation
- TEAEs leading to study treatment interruption
- TEAEs leading to lenalidomide/R-CHOP reduction
- TEAEs of special interest (AESIs)
- TEAEs of special interest of grade 3 or higher
- SAEs leading to death
- AEs in the follow-up period

11.1.2.2 AE summaries by SOC and PT

Number and percentage of patients experiencing the following AEs and total number of events for the following will be summarized by SOC and PT:

- Pre-treatment AEs
- All TEAEs
- TEAEs by intensity
- TEAEs by toxicity grade, along with summary of grade 3 or higher TEAEs
- TEAEs by causality
- TEAEs by seriousness
- Study treatment related, serious TEAEs
- Study treatment related, grade 3 or higher TEAEs by toxicity grade
- TEAEs leading to study treatment discontinuation
- TEAEs leading to study treatment interruption
- TEAEs leading to lenalidomide/R-CHOP reduction
- TEAEs of special interest
- TEAEs of special interest of grade 3 or higher by toxicity grade
- SAEs leading to death

- AEs in the follow-up period
- AEs in the follow-up period by intensity
- AEs in the follow-up period by toxicity grade, along with summary of grade 3 or higher AEs
- AEs in the follow-up period by causality
- AEs in the follow-up period by seriousness
- AESIs in follow-up period
- SAEs in the follow-up period
- Deaths in the follow-up period
- Non-serious TEAE regardless of study drug relationship by grade

11.1.2.3 AE summaries by cycle

Number and percentage of patients experiencing any AEs and total number of events will be summarized by SOC and PT for each cycle.

Bar plots representing the SOCs and PTs per arm will be presented for the same data by cycle.

11.1.2.4 Specific AE listings

Special AE listings displaying details of the event(s) captured on the eCRF will be provided for:

- Pre-treatment AEs
- All SAEs
- All TEAEs
- Serious TEAEs
- TEAEs related to study treatment
- TEAEs with toxicity grade higher than 3
- TEAEs of special interest
- TEAEs of special interest with toxicity grade higher than 3
- TEAEs leading to discontinuation of study treatment
- TEAEs leading to death
- AEs in the follow-up period
- Non-serious TEAE regardless of study drug relationship

11.2 Definition of abnormality, significant worsening, outlying and extreme result in safety analysis

All results demonstrating new abnormal values, showing a significant worsening signs, and results of outlying or extreme values will be noted in laboratory/vital signs data and presented in the respective listings. Definitions and calculation rules of ‘new abnormal values’, ‘significant worsening’, ‘outlying result’ and ‘extreme value’ are described as follows:

- A new abnormality will be any abnormal post baseline result for patients whose baseline was within normal limits.

- A significant worsening will be any numeric clinical laboratory result or vital sign result that represents a change from baseline by ≥25% of the baseline value, in the direction away from normal (i.e., in the direction that is clinically significant). The value with ≥25% change from baseline but still remain within the normal reference change is not counted as significant worsening.
- An outlying result for any numeric laboratory result or vital sign result will be any post-administration change from baseline that meets either of the following criteria:

  <25th Percentile - 1.5 * (interquartile range) OR >75th Percentile + 1.5 * (interquartile range)
- An extreme value for any numeric laboratory result or vital sign result will be any post-administration change from baseline that meets either of the following criteria:

  <25th Percentile - 3 * (interquartile range) OR >75th Percentile + 3 * (interquartile range)

11.3 Laboratory data

11.3.1 Laboratory variables

Laboratory blood assessment is analysed in local lab and it is classified into the following categories:

Table 10. Laboratory parameters

Hematology	Biochemistry	Coagulation	Serology and PCR diagnostic	Immunoglobulins
White blood cells (WBC)	Albumin	Activated Partial Thromboplastin Time (aPTT)	HBsAg	Immunoglobulin G
Red blood cells (RBC)	Alkaline phosphatase	Prothrombin Intl. Normalized Ration (INR)	Hepatitis B surface antibody(Anti-HBs)	Immunoglobulin A
Haemoglobin (HGB)	Alanine aminotransferase (ALT)	Prothrombin Time	Hepatitis B core antibody (Anti-HBc)	Immunoglobulin M
Haematocrit (HCT)	Aspartate aminotransferase (AST)	Partial Thromboplastin Time	Hepatitis B virus - DNA(HBV-DNA)	
Platelet count	Calcium		Hepatitis C virus antibody (Anti-HCV)	
Absolute lymphocytes	Chloride		Hepatitis C virus (HCV) RNA	
Lymphocytes %	Calculated creatinine clearance			

Absolute eosinophils	Creatinine			
Eosinophils %	Glucose			
Absolute basophils	C reactive protein			
Basophils %	Direct bilirubin			
Absolute monocytes	Phosphate			
Monocytes %	Potassium			
Absolute neutrophils	Sodium			
Neutrophils %	Total bilirubin			
	Total protein			
	LDH			
	Uric acid			
	TSH			

11.3.2 Grading of laboratory data

Laboratory data grades of severity will be derived according to the Common Terminology Criteria for Adverse Events (CTCAE) v5.0. CTCAE grade is applied to the converted measurement in SI units. A severity grade of 0 will be assigned when the value is within normal limits. In the case when a local laboratory normal range overlaps into the higher (i.e. non-zero) CTCAE grade, the CTCAE grade will be taken. Grade 5 will not be used. Laboratory values having hyper and hypo shifts will be treated as separate CTCAE lab parameters and classified into absolute CTCAE grades.

For laboratory tests for which grades of severity are not defined by CTCAE, results will be graded by the low/normal/high classifications based on laboratory normal ranges.

For duplicate laboratory measurements taken at the last assessment date on or before the start date of study treatment, the value of lower CTCAE grade will be considered as the baseline value.

In some cases when several records taken at the last assessment date have the same absolute grade, but in different directions, 2 baselines should be created for presenting shift tables, the record with hypo shift should be the baseline of the 'Hypo' parameter, and the other record should be the baseline for the 'Hyper' parameters.

For non-gradable labs with duplicate laboratory measurements taken at the last assessment date on or before the start date of study treatment:

- If both within normal range: take average value.
- If one within normal range and the other outside: take the one within normal range.
- If both outside normal range: take the one closest to the normal range.

Laboratory values with missing units or normal range may not be able to be graded or included in laboratory tables.

11.3.3 Analysis of Laboratory

All laboratory results, including hematology, biochemistry, coagulation, immunoglobulin and serology, collected in the course of study will be listed by patient, laboratory category and parameter, along with information of treatment arm, eCRF visit, sample collected date, result, reference range, within/out of reference range, clinical significance, flag of new abnormality/significant worsening/outlying result/extreme value, reason of undone assessment. The clinical significant abnormalities of each category will be additionally listed. In particular to hematology and biochemistry data, analysis visit will be added in the listing, given analysis visit deviate from eCRF visit. Besides urine and serum pregnancy test will be listed in laboratory section.

Unless otherwise stated, the following analysis will be tabulated for each treatment arm and overall, using SAF population set. In particular, hematology and biochemistry data will be presented by both eCRF visit and analysis visit, only when analysis visit deviate from eCRF visit. Other laboratory parameters will be presented by eCRF visit only.

- Descriptive statistics of each continuous parameter will be summarized, including absolute values and change from baseline by parameter and by visit.
- For continuous laboratory parameters, a summary of number and percentage of patients of clinical assessment will be tabulated by parameter and visit. Clinical assessment is classified into 'Normal', 'Abnormal, no clinical relevance' and 'Abnormal, clinical relevance'.
- A summary of number and percentage of patients with worst post-baseline CTCAE grade will be presented by parameter and visit, for the applicable laboratory parameters. The result with highest toxicity grade will be taken as worst value for overall post-baseline assessment.
- For categorical laboratory parameters, namely serology and PCR diagnostic laboratory assessments, number and percentage of patients with laboratory result will be listed by parameter and visit.
- Shift tables to compare baseline to the worst post-baseline value will be produced using:
  - CTCAE grades for continuous laboratory parameters where CTCAE grades are defined.
  - The classifications relative to the laboratory reference ranges (low/normal/high) for continuous laboratory parameters where CTCAE grades are not defined. Specifically, if a patient experience both 'low' and 'high' assessments in the course of the study, two worst values will be derived as the overall post-baseline assessments.

Spaghetti plots will be presented for the laboratory parameters absolute neutrophil count, platelets and haemoglobin for all patients across all the visits for each cycle. Box plots will also be presented for the above representation.

11.4 Vital signs

11.4.1 Vital signs variables

The Vital Signs captured in the eCRF for each patient at each visit are the following:

- Weight
- Systolic Blood Pressure
- Diastolic Blood Pressure
- Heart Rate

- Temperature

As per protocol, systolic blood pressure, diastolic blood pressure, heart rate, temperatue are to be measured pre-tafasitamab infusion, and then at least 3 times during infusion. The sequence of timepoint for the measurements during the infusion will be sorted and flagged according to the actual assessment time, to be 'First assessment during infusion', 'Second assessment during infusion', 'Third assessment during infusion' and so on.

11.4.2 Analysis of Vital signs

All vital sign results collected in the course of study will be listed by patient and vital sign parameter, along with information of treatment arm, visit, assessment date, result, clinical significance, flag of new abnormality/significant worsening/outlying result/extreme value, reason of undone assessment. The clinical significant abnormalities of each parameter will be additionally listed.

The following summaries will be performed for weight, Systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate and temperature for each treatment arm and overall, using SAF population:

- Descriptive statistics of each vital signs parameters will be summarized, including absolute values and change from baseline by visit and timepoint.
- A summary of number and percentage of patients of clinical assessment will be tabulated by visit and timepoint.

11.5 Physical examination

Full physical examination is performed at screening and end of treatment visit, while limited physical examination is performed per individual status. All physical examination results collected in the course of study will be listed by patient and body system. Listings of physical examination is based on SAF population.

11.6 Electrocardiogram (ECG)

11.6.1 ECG variables

A general interpretation of local ECG result is captured in eCRF as "Normal", "Abnormal, not clinically significant", "Abnormal, clinically significant and "Not Done".

Data listing of local ECG will be produced to present the patient identifier, treatment arm, visit, assessment time, result, abnormality and the reasons for "not done" records on the basis of SAF population.

11.6.2 Analysis of ECG

The following analysis will be performed for each treatment arm and overall, using SAF population:

- A summary of number and percentage of patients of ECG clinical assessmentby visit.

11.7 Echocardiogram (ECHO) or cardio multigated acquisition (MUGA)

11.7.1 ECHO or MUGA variables

Echocardiogram or cardiac MUGA scan will be obtained at screening and at End of Treatment Visit/ Early Study Treatment Discontinuation Visit to evaluate cardiac function, including assessment of left ventricular systolic function (LVEF). Listing will be generated on the basis of SAF population.

11.7.2 Analysis of ECHO or MUGA

The following analysis will be performed for each treatment arm and overall, using SAF population:

- Descriptive statistics of LVEF will be summarized, including absolute values and change from baseline by visit.
- Number and percentage of patients with different method of ECHO or MUGA assessment.
- A shift table to compare LVEF of baseline to EOT visit. The LVEF reference range is 50% to 70% (boundary included). The classifications relative to the reference ranges (low/normal/high) is applied.

12. ANALYSES SPECIFIC TO COVID-19 PANDEMIC

The following applies for both the primary and final analyses. Analyses that were included with the amendment of SAP v2.1 were included after the time of the primary analysis and are only included in the final analysis.

- Number and percentage of patients with positive test of COVID-19
- Number and percentage of patients with at least one and at least two missed tumor assessments because of COVD-19
- Number and percentage of patients with Study Treatment interruption/delay/discontinuation because of COVID-19
- Number and percentage of patients whose primary cause of death is COVID-19
- Number and percentage of patients who were hospitalized because of COVID-19
- Number and percentage of patients who received treatment because of COVID-19, and the treatments by ATC Level 2 class. The details can be obtained from the AE page and the Conomitant Medication eCRF Page. Number and percentage of patients experiencing any AEs and total number of events due to COVID-19 will be summarized by SOC and PT by arm and overall. This will also be listed.
- Number and percentage of patients experiencing any SAEs and total number of events due to COVID-19 will be summarized by SOC and PT by arm and overall. This will also be listed.
- Number and percentage of patients experiencing any TEAEs and total number of events due to COVID-19 will be summarized by SOC and PT by arm and overall. This will also be listed.
- Number and percentage of patients with non-AE COVID-19 impact.

In terms of efficacy, the following sensitivity analyses will be performed:

- For PFS and EFS, the descriptive reporting and treatment comparison for main analysis will be performed by changing the censoring strategy: deaths due to COVID-19 will be censored at the last adequate tumor assessment date.

- For OS, the descriptive reporting and treatment comparison for main analysis will be performed by changing the censoring strategy: deaths due to COVID-19 will be censored at the date of last contact before death.

All protocol deviations in relation to COVID-19 will be identified based on reviews of the data prior to database lock. All important protocol deviations related to COVID-19 will be listed to describe the patient information, treatment arm, category, exact item and date of protocol deviation.

The number and percentage of patients in the FAS patients, with at least one of important protocol deviations in relationship to COVID-19, will be summarized by treatment arm and overall according to the earlier described PD categories.

13. GENERAL GUIDANCE ON REPORTING

13.1 Document headers, footers and layout

The following table specifies general information of headers, footers and layout.

Orientation	Landscape
Paper Size	A4
Margins	Top: 2 cm Bottom: 2 cm Left: 2 cm Right: 2 cm Header: 1.27 cm Footer: 1.27cm
Font	Courier New 8pt
Headers	Protocol number – Type of Analysis (Cut-off date) (Left); Page X of Y (Right) TLF Number and Title
Footers	SAS program name Source Data Extract date Date,/Time of TLF generation

The font size may be reduced as necessary to allow additional columns to be presented, but not at the expense of clarity. Also the orientation may be changed to portrait if appropriate.

In the headers, the text *Type of Analysis* should be substituted to be either PA (initial of Primary Analysis) or FA (initial of Final Analysis). For example: MOR208C107 – PA (Cut-off date: 15NOV2019).

All other table-unique footers should be presented above the aforementioned footers, as the following display:

- footnote 1
- footnote 2
- footnote 3

SAS program name -- source data -- extract date -- date/time of TLF generation

In the applicable outputs, the MedDRA version and WHO-DDE version used for reporting the study will be specified as a footnote.

- MedDRA Version <xx.x> has been used for the reporting

- WHO-DDE Version <xx.x> has been used for the reporting

The latest available version of dictionaries at the time of reporting will be used.

13.2 Presentation of output numbering and titles within this document

In practice, the numbering and title for all tables, figures and listings in sections 14 and 16 defined in this document will be formatted as follows, respectively:

Table 14.x.x.x

Title Title Title Title Title Title

Population

Listing 16.x.x.x

Title Title Title Title Title Title

Population

13.3 General rules for presenting tables and listings

Unless differently specified, a summary table will be produced by different study arm and the overall number added up from by all possible arms.

All other data as documented in the eCRF will be listed and/or tabulated using descriptive statistics or counts/percentages depending on the nature of data. All the data collected and derived in the trial will be presented in patient data listings.

The following general rules for presenting listings should be applied by default for all listings.

Unless differently mentioned, all listings should contain the following information in the first three columns: "Patient identifier", "Treatment arm" and "Age/Sex/Race". For data collected on visit level, the visit should be placed in the fourth column. The default sorting order is by patient number and event/assessment date unless otherwise stated.

Where a listing or table has been planned, but no data meet the criteria, then a single line stating 'No data meeting the criteria is present' will be provided in the output.

Specifically for this study, if analysis visit does not deviate from eCRF visit for all patients, a single line stating 'This table is identical with the table of eCRF visit, as no deviation occurred between eCRF visit and analysis visit'.

For all laboratory parameters, SI units are used as default.

When a variable collected in the eCRF is linked to another variable, one or both variables will be presented in the same column of the listing or in adjacent columns if space permits this.

For example:

- 'Setting'='OTHER' and 'Other, specify'='Lung'
  "OTHER: Lung" will be displayed in the column as 'Setting'.
- 'Dose'='120' and Dose unit ='mg'
  '120 mg' will be displayed in the column as 'dose (unit)'.

- If Date = "2012-05-12" and Study day ="5", then "12MAY2012 / 5" will be displayed in the column as 'Date / Study Day'.
- If End date = " " and ongoing is ticked, then "Ongoing" will be displayed in the column as 'End date / Study Day'.

13.4 Presentation of analysis sets

The outputs to be produced based on this document will use 'Screened Patients', 'FAS', 'PPS', 'SAF', "PKAS', 'IAS" in the table/figure/listing titles.

13.5 General rules for presenting frequencies and percentages

If a summary table displays only categorical variables then the convention illustrated in the following example will be used:

Preferred Term	**Tafasitamab + R-CHOP N=xx n (%)**	**Tafasitamab + Lenalidomide + R-CHOP N=xx n (%)**	**Overall N=xx n (%)**
Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
Fatigue	xx (xx.x)	xx (xx.x)	xx (xx.x)
Nausea	xx (xx.x)	xx (xx.x)	xx (xx.x)
Anemia	xx (xx.x)	xx (xx.x)	xx (xx.x)

However, if a summary table displays both continuous and categorical variables then the convention illustrated in the following example will be used:

	Tafasitamab + R-CHOP N=xx	**Tafasitamab + Lenalidomide + R-CHOP N=xx**	**Overall N=xx**
Sex, n (%)			
Male	xx (xx.x)	xx (xx.x)	xx (xx.x)
Female	xx (xx.x)	xx (xx.x)	xx (xx.x)
Age (Years)			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
StD	xx.xx	xx.xx	xx.xx

Median	xx.x	xx.x	xx.x
Minimum	xx.x	xx.x	xx.x
Maximum	xx.x	xx.x	xx.x

13.6 Presentation of dates

Calendar dates and times (optional) in all the listings will be displayed in the format:

DDMONYYYY hh:mm e.g. 15JAN2019 08:20.

Note: If time is not collected, calendar dates will be displayed as: DDMONYYYY.

14. REFERENCES

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3. ICH E9 (R1): addendum on estimands and sensitivity analysis in clinical trials to the guideline on statistical principles for clinical trials. 17 February 2020 EMA/CHMP/ICH/436221/2017.
4. EMA Guidance: Points to consider on implications of Coronavirus disease (COVID-19) on methodological aspects of ongoing clinical trials. 26 June 2020, EMA/158330/2020 Rev. 1.
5. ICH Topic E10: Choice of Control Group and Related Issues in Clinical Trials, adopted by CPMP, 20 July 2000, issued as CPMP/ICH/364/96.
6. Guidance for Industry Providing Regulatory Submissions in Electronic Format – Standardized Study Data Verson 4.1, March 2018
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8. Salles, G, et al (2018) 'Single-Arm Phase II Study of MOR208 Combined with Lenalidomide in Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma: L-Mind', in ASH.
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10. Brookmeyer R, Crowley JJ. A confidence interval for the median survival time. Biometrics 1982, 38:29-41.