CELLTRION Inc.

CT-P10 3.4

A Phase 3, Randomised, Parallel-Group, Active-Controlled, Double-Blind Study to Compare Efficacy and Safety between CT-P10 and Rituxan in Patients with Low Tumour Burden Follicular Lymphoma

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Statistical Analysis Plan

Version 1.2

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Upon review of this document, including table, listing and figure shells, the undersigned approves the final statistical analysis plan. The analysis methods and data presentation are acceptable, and the table, listing and figure production can begin.

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List of Abbreviations

Abbreviation	Definition
ADA	Anti-Drug Antibodies
AE	Adverse Event
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Chemical
B-cell	B-Lymphocyte
BLQ	Below The Lower Limit Of Quantification
BOR	Best Overall Response
BP	Blood Pressure
BSA	Body Surface Area
CI	Confidence Interval
CTCAE	Common Terminology Criteria for Adverse Events
CR	Complete Response
CRu	Unconfirmed Complete Response
CSR	Clinical Study Reports
CT	Computed Tomography
CV%	Percent Coefficient of Variation
DRM	Data Review Meeting
DSMB	Data Safety Monitoring Board
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic Case Report Form
EOT	End of Treatment
FISH	Fluorescence In Situ Hybridization
FL	Follicular Lymphoma
FLIPI	Follicular Lymphoma International Prognostic Index
GCP	Good Clinical Practice
GELF	Groupe d'Etudes des Lymphomes Folliculaires
HBcIg	Hepatitis B Core Immunoglobulin
HBsAb	Hepatitis B Surface Antibody
HBsAg	Hepatitis B Surface Antigen
HIV	Human Immunodeficiency Virus
ICF	Informed Consent Form
IgA	Immunoglobulin A
IgG	Immunoglobulin G
IgM	Immunoglobulin M

IQR	Interquartile Range
IRR	Infusion-Related Reactions
ITT	Intent-to-Treat
IV	Intravenous
IVRS	Interactive Voice Response System
IWRS	Interactive Web Response System
LDH	Lactate Dehydrogenase
LLoQ	Lower Limit of Quantification
LTBFL	Low Tumour Burden Follicular Lymphoma
MNAR	Missing Not at Random
MP1	The 1st Year of Maintenance Period
MP2	The 2nd Year of Maintenance Period
MRI	Magnetic Resonance Imaging
Nab	Neutralizing Antibody
ORR	Overall Response Rate
OS	Overall Survival
PD	Progressive Disease
PFS	Progression Free Survival
PK	Pharmacokinetics
PML	Progressive Multifocal Leukoencephalopathy
PP	Per-Protocol Population
PPD	Product of The Perpendicular Diameters
PR	Partial Response
PT	Preferred Term
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
[redacted]	[redacted]
SD	Stable Disease
SE	Standard Error
SOC	System Organ Class
SPD	Sum of Product Of The Perpendicular Diameters
TB	Tuberculosis
TEAE	Treatment-Emergent Adverse Event
TESAE	Treatment-Emergent Serious Adverse Event
TLF	Table, Listing and Figure
TTP	Time to Progression
WHO DD	World Health Organization Drug Dictionary

1. ADMINISTRATIVE STRUCTURE

This study is being conducted under the sponsorship of CELLTRION, Inc. The clinical monitoring, medical writing and pharmacokinetic parameter calculation are being performed under contract with [redacted], in collaboration with CELLTRION, Inc. The data management and statistical analysis are being performed by CELLTRION, Inc.

2. INTRODUCTION

This Statistical Analysis Plan (SAP) defines the statistical methods and data presentations to be used by CELLTRION Clinical Statistics team in the analysis and presentation of data from CELLTRION study number CT-P10 3.4, entitled as "A Phase 3, Randomised, Parallel-Group, Active-Controlled, Double-Blind Study to Compare Efficacy and Safety between CT-P10 and Rituxan in Patients with Low Tumour Burden Follicular Lymphoma".

There are two clinical study reports (CSRs) planned for the following time points, with provision of additional CSRs if required for regulatory or academic purposes:

- After all eligible patients have completed the 7 month assessment (prior to Cycle 3 of the Maintenance Study Period)
- After all patients have completed or terminated from the study

This SAP covers full study analyses and data presentation and is based on the following documents:

- Study Protocol Version 4.0 – 28th June 2017
- Unique Case Report Form Version 6.0 – 7th July 2017

Table, Listing and Figure (TLF) mock shells will be provided as an addendum to this document.

2.1. Data Cut-off for Analysis

The 1st CSR will include all analysis results, except for the secondary efficacy endpoint analyses, using data up to 7 months (prior to Cycle 3 of the Maintenance Study Period) of each patient. For the data being collected on 'Adverse Events' and 'Concomitant Medications' eCRF pages, the data reported prior to the visit date of the Maintenance Cycle 3 will be included. In case of patients who have discontinued the study treatment before the Maintenance Cycle 3, all collected data will be included.

The final CSR will report all analysis results up to the completion or termination of all patients from study.

3. STUDY OBJECTIVES

3.1. Primary Objective

- To demonstrate that CT-P10 is similar to Rituxan in terms of efficacy as determined by overall response rate (ORR, complete response [CR] + unconfirmed complete response [CRu] + partial response [PR]) at 7 months (Prior to Cycle 3 of Maintenance Study Period) according to the Modified Response Criteria for Malignant Lymphoma

3.2. Secondary Objectives

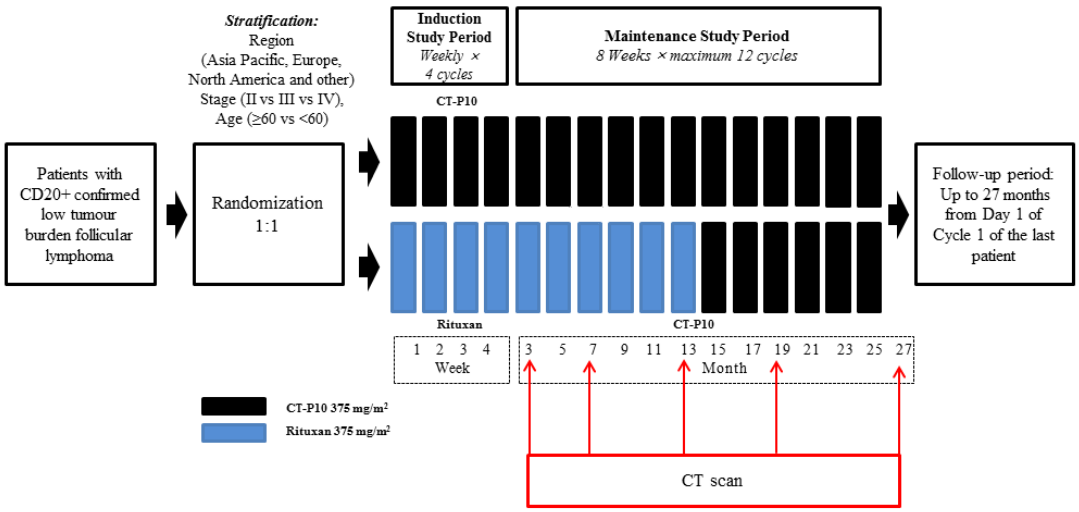
- To evaluate ORR (CR + CRu + PR) according to the Modified Response Criteria for Malignant Lymphoma during the study period
- To evaluate additional efficacy parameters (progression free survival [PFS], time to progression [TTP] and overall survival [OS] according to the Modified Response Criteria for Malignant Lymphoma)
- To evaluate pharmacokinetics (PK), pharmacodynamics (B-lymphocyte [B-cell] kinetics), overall safety including immunogenicity, and biomarkers of CT-P10 in comparison with Rituxan

4. OVERALL STUDY DESIGN AND PLAN

This is a Phase 3, prospective, randomized, parallel-group, active-controlled, double-blind, multicenter, international study to evaluate the similarity of efficacy and safety of CT-P10 to Rituxan in patients with Grade 1 to 3a (Ann Arbor stage II-IV) low tumour burden follicular lymphoma (LTBFL) based on Groupe d'Etudes des Lymphomes Folliculaires (GELF) criteria. The study will include study centers in Europe, Africa, the Middle East, Asia Pacific, and Latin and North America.

The study will consist of 4 periods: Screening Period, Induction Study Period, Maintenance Study Period, and Follow-up Period. The overview of study design is shown in Figure 1.

Figure 1: Schematic of Study Design



- Screening Period (up to 6 weeks)
- Induction Study Period (up to 4 weeks):
  - Study drug will be administered weekly for 4 weeks (at a dose of 375 mg/m^2 by an intravenous [IV] infusion).
  - The End of Treatment (EOT) 1 visit will occur 1 week (±1 day) after the last dose of study drug administration in the Induction Study Period.
  - Patients will be assessed 8 weeks (±7 days) after the last dose of study drug administration in the Induction Study Period, and the investigator will determine whether patients qualify to continue in the Maintenance Study Period.
    - Patients who experienced CR, CRu, PR, or stable disease (SD) in this assessment will qualify for the Maintenance Study Period and the assessment visit will be called the Maintenance 1 visit.
    - Patients who experienced progressive disease (PD) or unknown status of disease will not enter into the Maintenance Study Period. These patients will be withdrawn from the study treatment and will enter the Follow-up Period, provided patient consent has not been withdrawn. For these patients, the assessment visit will be called the EOT2 visit.

- If a patient withdraws before the completion of the Induction Study Period, this patient will not enter the Maintenance Study Period. However, the patient will enter the Follow-up Period, provided patient consent has not been withdrawn.

- Maintenance Study Period (up to maximum 12 cycles for 2 years):

  - The first dose in the Maintenance Study Period will be administered 8 weeks (±7 days) after the last dose of study drug administration in the Induction Study Period.

  - Study drug will be administered every 8 weeks up to maximum 12 cycles for 2 years (at a dose of 375 mg/m^2 by an IV infusion).

  - The first year of Maintenance Period (MP1) consists of 6 cycles of maintenance therapy (Maintenance Cycles 1 to 6) and the second year of Maintenance Period (MP2) consists of 6 cycles of maintenance therapy (Maintenance Cycles 7 to 12). After MP1, once the similarity between study drugs is confirmed, additional treatment with CT-P10 will be offered to all patients who have completed MP1 at discretion of the investigator.

  - The EOT3 visit will occur 8 weeks (±7 days) after the last dose of study drug administration in the Maintenance Study Period.

  - Patients who complete the Maintenance Study Period will enter the Follow-up Period. A patient will be considered as having completed the study treatment if:

    - The patient could have entered but did not continue on the MP2 and completed all visits of the MP1 (total 6 cycles).

    - The patient continued on the MP2 and completed all visits of the MP1 and MP2 (total 12 cycles).

  - If a patient withdraws before the completion of the Maintenance Study Period, the patient will enter the Follow-up Period, provided patient consent has not been withdrawn.

    - If a patient is terminated within 6 months from Day 1 of Cycle 1 of the Induction Study Period, the EOT3 visit will occur within 4 to 8 weeks (±7 days) after the last dose of study drug administration in the Maintenance Study Period.

- Follow-up Period (up to 27 months from Day 1 of Cycle 1 of the Induction Study Period for the last enrolled patient):

  - During the Follow-up Period, patients will be monitored every 6 months (±2 weeks) for disease status until treatment with new anticancer therapy or disease progression, and

every 3 months (±2 weeks) for survival and salvage treatment until death or study termination.

The end of study is defined as the date of the database is locked. The schedule of events is presented in APPENDIX 1.

5. GENERAL STATISTICAL CONSIDERATIONS

Continuous data will be summarized using descriptive statistics: n, mean, standard deviation, minimum, median, and maximum, unless otherwise specified. Minimum and maximum will be presented to the same number of decimal places as reported, mean and median will be presented to one more decimal place than the reported. Standard deviation will be presented to two more decimal places than the raw data. If the geometric mean and percent coefficient of variation (CV%) are to be presented, geometric mean will be set to the same decimal places as the mean and CV% will be set to the one less decimal places than the standard deviation. If interquartile range (IQR) is to be presented, it will be displayed along with 25th and 75th quartile in same decimal place with median. Confidence interval (CI) obtained from statistical procedures will be displayed to two decimal places. P-values will be presented to three decimal places. If a p-value is less than 0.001, it will be reported as "< 0.001". If a p-value is greater than 0.999 it will be reported as "> 0.999".

Categorical data will be summarized using numbers and percentages of patients. Percentages will be presented to one decimal place and will be suppressed when the count is zero. The denominator for all percentages will be the number of patients within each treatment group for the population of interest, unless otherwise specified.

Tables summarized by visit will be conducted for all scheduled visits including EOT1, EOT2, EOT3 and excluding Follow-up visits. EOT2 and Maintenance Cycle 1 will be combined.

All data will be displayed in listings. Unless otherwise specified, listings will be sorted by the treatment group, patient number, and assessment date or visit date, if applicable. In cases where more ordering is required, other variables will be included in the sort order as applicable.

When combining data from electronic Case Report Form (eCRF) and analytical facilities such as [redacted], discrepancy will be handled as following:

1) Recorded as sample collected in eCRF but no corresponding results from analytical facility – listing will display only the sample collection date/time from eCRF and the data will be summarized in 'Missing' category, if applicable.

2) No records in eCRF which corresponds to the results from analytical facility – listing will display sample collection date/time and results from analytical facility.

3) Discrepancy in sample collection date/time from eCRF and analytical facility – listing will display sample collection date/time from eCRF, and results from analytical facility.

All available results from analytical facilities will be included in the summary table.

5.1. Software

All analyses will be conducted using [redacted] The exact binomial method will be applied using [redacted]. PK parameters will be computed using the appropriate validated software.

5.2. Sample Size

Sample size calculations for the primary efficacy endpoint are based on the proportion of patients with a CR, CRu, or PR response (the "responders") at 7 months (Prior to Cycle 3 of the Maintenance Study Period).

A sample size of 174 patients (87 patients in each treatment group of CT-P10 and Rituxan) leads to 91% statistical power for the demonstration of similarity of ORR at 7 months (Prior to Cycle 3 of the Maintenance Study Period) based on ORR of 88% and an equivalence margin of ±17% using a 2-sided 90% CI approach corresponding to 5% significance level of an equivalence test. The intent-to-treat (ITT) population will be the primary analysis population for the efficacy analysis. A supportive analysis for the efficacy analysis will be conducted using the per-protocol (PP) population for response rate. In the PP population with a 13% drop-out rate, 86% statistical power is expected.

The equivalence margin of ±17% preserves at least 77% efficacy based on the lower bound of 95% CI of the estimated difference of ORRs of patients received rituximab 6 doses (88%, 162/184) and of patients in "watch-and wait" group (6%, 9/155) in Ardeshna et al (2014). The historical efficacy of rituximab based on the difference of ORR between the patients treated with rituximab and patients in "watch-and wait" group is 82% with the 95% CI of (0.75, 0.88). Therefore, the historical treatment efficacy of rituximab for the equivalence margin is estimated as 75% conservatively and by applying 77% preservation rate, the equivalence margin is proposed as ±17%.

The actual drop-out rate and ORR will be assessed in a blinded manner at data safety monitoring board (DSMB) when the primary endpoint evaluation is available from 50%-60% of patients. A reassessment of sample size accounting the actual drop-out rate and the observed ORR in blinded

manner will be made in order to achieve an adequate statistical power for the primary endpoint; at least 80% power in PP population. The sample size will not be decreased from the initial 174 total sample size but could be increased up to 250 patients.

5.3. Randomization, Stratification and Blinding

Patients will be randomly assigned to each treatment group using a computer-generated randomization schedule prepared prior to the study commencing. Patients will be randomized and assigned a kit using an interactive web response system (IWRS) or interactive voice response system (IVRS). The randomization will be balanced by using permuted blocks and will be stratified by region (Asia Pacific, Europe, or North America and Other), Ann Arbor stage (II, III or IV) and age (≥60 or <60 years).

This study will be double-blind and will remain blinded to study patients, investigators, and study center staffs (except for the unblinded staffs) until all patients have completed the study and the database has been finalized for study termination. The randomization code will be broken for the statistical analyses and reporting of primary endpoint for the 1st CSR. Only the relevant study personnel of CELLTRION and [redacted] will be unblinded. The study blind will not be broken except in a medical emergency (where knowledge of the study drug received would affect the treatment of the emergency) or regulatory requirement (e.g. for SAEs or death).

5.4. Population of Analysis

There will be five populations and seven subsets of analysis: Intent-to-treat population, Intent-to-treat population – ADA negative/positive subset, Intent-to-treat population – 2nd Maintenance Period subset, Per-protocol population, Per-protocol population – ADA negative/positive subset, Per-protocol population – 2nd Maintenance Period subset, Safety population, Safety population – 2nd Maintenance Period subset, Pharmacokinetic population and Pharmacodynamic population.

The number of patients in each population and subset will be tabulated by treatment group for the ITT population. A listing will also be provided displaying this data.

5.4.1. Intent-to-treat Population

The ITT population will consist of all patients enrolled and randomly assigned to receive a study drug, regardless of whether or not any study drug dosing was completed. Patients in the ITT population will be analyzed according to the treatment group to which they were randomized by IWRS or IVRS, and not according to what they actually received. The ITT population will be the primary population for the efficacy analyses.

5.4.1.1. Intent-to-treat Population – ADA Negative/Positive Subset

For analyses of efficacy primary endpoint, the ITT population – ADA negative subset will be defined consisting of all patients in the ITT population who have only "Negative" result in immunogenicity anti-drug antibody (ADA) test obtained after receiving at least one dose (full or partial) of study drug and up to Maintenance Cycle 3 (up to 7 months), including unscheduled visit result. Other patients in the ITT population who show at least one "Positive" result in ADA tests obtained after receiving at least one dose (full or partial) of study drug and before Maintenance Cycle 3 will be considered as ITT population – ADA positive subset.

5.4.1.2. Intent-to-treat Population – 2nd Maintenance Period Subset

The ITT population – 2nd Maintenance Period subset will consist of all patients in the ITT population who have answered 'Yes' on the eCRF page of '2nd Year Maint Therapy Y/N'. For the ITT population – 2nd Maintenance Period subset, patients who have been randomized into Rituxan treatment group will be analyzed under 'Switched to CT-P10' treatment group, and who have been randomized into CT-P10 treatment group will be analyzed as 'CT-P10 Maintenance' treatment group.

5.4.2. Per-protocol Population

The PP population will consist of all patients who are randomly assigned and have at least one response evaluation after receiving at least one dose (full) of study drug in the Induction Study Period without any major protocol violation or deviation that may affect the interpretation of study results of efficacy. A list of Inclusion and Exclusion criteria which has impact on PP population is presented in APPENDIX 4. Patients in the PP population will be analyzed according to the treatment group to which they were randomized by IWRS or IVRS, and not according to what they actually received. Supportive efficacy analyses will be conducted using the PP population.

5.4.2.1. Per-protocol Population – ADA Negative/Positive Subset

For analyses of efficacy primary endpoint, the PP population – ADA negative subset will be defined consisting of all patients in the PP population who have only "Negative" result in immunogenicity anti-drug antibody (ADA) test obtained after receiving at least one dose of study drug and up to Maintenance Cycle 3, including unscheduled visit result. Other patients in the PP population who show at least one "Positive" result in ADA tests obtained after receiving at least one dose of study drug and before Maintenance Cycle 3 will be considered as PP population – ADA positive subset.

5.4.2.2. Per-protocol Population – 2nd Maintenance Period Subset

The PP population – 2nd Maintenance Period subset will consist of all patients in the PP population who have at least one response evaluation after receiving at least one (full) dose of CT-P10 on or

after Maintenance Cycle 7. For the PP population – 2nd Maintenance Period subset, patients who have been randomized into Rituxan treatment group will be analyzed under 'Switched to CT-P10' treatment group, and who have been randomized into CT-P10 treatment group will be analyzed as 'CT-P10 Maintenance' treatment group.

5.4.3. Safety Population

The Safety population will consist of all patients who received at least one dose (full or partial) of study drug. For the Safety population, patients who have received at least one dose (full or partial) of CT-P10 up to MP1 will be analyzed under CT-P10 treatment group, and all the other patients will be analyzed as Rituxan treatment group. A patient will be considered to have received each study drug if the patient's actual administered dose and kit number dispensed is recorded on 'Study Drug Administration CT-P10/RITUXAN' eCRF page. All safety analyses will be conducted on the Safety population.

5.4.3.1. Safety Population – 2nd Maintenance Period Subset

The Safety population – 2nd Maintenance Period subset will consist of all patients in the Safety population who have received at least one (full or partial) dose of CT-P10 on or after Maintenance Cycle 7 (i.e. during MP2). For the Safety population – 2nd Maintenance Period subset, patients who have been analyzed as Rituxan treatment group in the Safety population will be analyzed under 'Switched to CT-P10' treatment group, and who have been analyzed in CT-P10 treatment group in the Safety population will be analyzed as 'CT-P10 Maintenance' treatment group.

5.4.4. Pharmacokinetic Population

The PK population will consist of all patients who received at least one dose (full) of study drug and have at least one post-treatment PK concentration result. Patients in the PK population will be analyzed according to the treatment group to which they actually received. All PK analyses will be conducted based on the PK population.

5.4.5. Pharmacodynamic Population

The Pharmacodynamic population will consist of all patients who received at least one dose (full) of study drug and have at least one post-treatment pharmacodynamic result. Patients in the Pharmacodynamic population will be analyzed according to the treatment group to which they actually received. The Pharmacodynamic population will be the primary population for all pharmacodynamic analyses.

5.5. Definition of Baseline

The baseline value will be considered to be the last non-missing value before the first administration of study drug. Post-baseline values will be considered to be all values collected after the first administration of study drug.

5.6. Protocol Violations and Deviations

A major protocol violation or deviation may affect the interpretation of study results or the patient's rights, safety or welfare. Major violations and deviations are defined as follows:

- Mis-randomizations (defined as patients who received the opposite treatment)
- Non-compliance of Inclusion and Exclusion criteria (to be identified through review of data sourced from the site monitoring database)
- Significant Good Clinical Practice (GCP) non-compliance sites (to be identified by [redacted] as sites which have been closed due to scientific misconduct and/or serious GCP non-compliance)

Patients with Non-compliance of Inclusion and Exclusion criteria or Significant Good Clinical Practice (GCP) non-compliance sites could be excluded from PP population. Also, Mis-randomizations will be excluded from PP, PK and Pharmacodynamic population. The major protocol violations and deviations will be summarized by treatment group for the ITT population and will also be presented in a listing.

5.7. Missing Values

In order to evaluate the impact of missing data on the efficacy primary endpoint results, additional analyses with tipping point analyses will be conducted for the primary efficacy endpoint for ITT population.

Tipping point analyses will be conducted under Missing Not at Random (MNAR) scenarios. Imputed values (patients with no response evaluation result or 'Unable to assess') as responder will be shifted gradually by treatment groups to make MNAR scenarios. 90% CI of the difference between two proportions (CT-P10 group and Rituxan group) will be calculated using asymptotic methods, and scenarios will be displayed by shift table.

All the scenarios will be also provided using 2-dimensional plot.

6. PATIENT DISPOSITION

The number of patients who were screened will be displayed. The number of screening failures and the primary reason for screening failure will also be summarized.

The number of patients who have been randomized, the number and percentage of patients who have initiated study treatment, have discontinued the study treatment, and have completed the study treatment will also be displayed for prior to Maintenance Cycle 3 and up to MP1 in the ITT population, and MP2 in the ITT population – 2nd Maintenance Period subset.

- A patient will be considered to have failed the Screening if the date is recorded on the 'Screening Failure' page of eCRF.

- A patient will be considered to be randomized if the date of randomization is recorded on the 'Randomization' page of eCRF. The randomization date recorded in this eCRF page will be used as the date of randomization for further analyses described in this document.

- A patient will be considered to have initiated study treatment if actual administered dose or the kit number of study drug are recorded on the 'Study Drug Administration CT-P10/RITUXAN' page of eCRF of the Induction Study Period. MP2 will be considered to be initiated if actual administered dose or the kit number of study drug is recorded on eCRF at Cycle 7 of the Maintenance Study Period.

- A patient will be considered to have completed study treatment prior to Maintenance Cycle 3 if the patient has initiated treatment in the Induction Study Period and not recorded to have discontinued study treatment prior to Maintenance Cycle 3 visit date on 'Study Termination' page of eCRF. A patient will be considered to have completed up to MP1 if the patient recorded 'Yes' was collected in question 'Did the patient complete the 1st year Maintenance Study Period' on the eCRF page of 'Study Treatment Termination'. A patient will be considered to have completed MP2 if the patient has initiated MP2 and recorded to have completed all study periods on 'Study Treatment Termination' page of eCRF.

- A patient will be considered to have discontinued study treatment prior to Maintenance Cycle 3 if it is recorded that the patient did not complete prior to Maintenance Cycle 3 visit date on the 'Study Treatment Termination' page of eCRF. A patient will be considered to have discontinued study treatment up to MP1 if the patient did not answer 'Yes' to question 'Did the patient complete the 1st year Maintenance Study Period' on the 'Study Treatment Termination' page of eCRF. A patient who have discontinued after completion of MP1 and before initiation of MP2 will be considered separately. A patient

will be considered to have discontinued study treatment in MP2 if the patient have initiated MP2 and 'No' is recorded to question 'Was the patient offered additional treatment by 12 cycle in 2nd year Maintenance Period?' on 'Study Treatment Termination' page of eCRF.

The number and percentage of patients who have completed MP1 and not entered MP2, who discontinued each period (for prior to Maintenance Cycle 3, up to MP1, and MP2) will also be displayed by primary reason for discontinuation. Time on study drug prior to discontinuation in each category which is calculated as (Last dose date – First dose date + 1) will also be summarized with descriptive statistics.

The number and percentage of patients who entered the Follow-up Period will be summarized. A patient will be considered to have entered the Follow-up Period if the patient has visited at the first Follow-up visit schedule. Reason for ending participation in the study will also be summarized, as evidenced in the 'End of Study Participation' page of eCRF. Deaths will be summarized by reasons using the data reported on 'Study Treatment Termination' page or 'Survival Status' page of eCRF.

The patient disposition data collected will be listed for the ITT population. A listing of patients reported as screening failures will also be provided.

7. DEMOGRAPHICS, BASELINE AND BACKGROUND CHARACTERISTICS

7.1. Demographics

The following patient demographic measures recorded in eCRF will be tabulated for the ITT population: age (years); sex (Male, Female); race (American Indian or Alaska native, Asian, Black or African American, Native Hawaiian or other pacific islander, White or Caucasian, Not Allowed by Investigator Country Regulations, or Other); fertility status (Pre-Menarche, Surgically Sterilized, Post-Menopausal [last menstrual period more than 1 year], Potentially Able to bear Children, or Other); region (Asia Pacific, Europe, North America, or Other); Ethnicity (Hispanic or Latino, Not Hispanic or Latino, Not Reported, or Unknown); and height (cm), weight (kg) , body surface area (BSA [m^2]) and Eastern Cooperative Oncology Group (ECOG) performance status as recorded at the Screening.

Age will be automatically calculated in the eCRF system based on the date of the informed consent signed, the year of birth and information on date of birth passed or not. All demographics data will be listed for the ITT population.

7.2. Medical History

Medical history is captured at the Screening and will be coded using Medical Dictionary for Regulatory Activities (MedDRA Version 18.1 or later). Medical history will be summarized by treatment group, system organ class (SOC) and preferred term (PT) displaying the number and percentage of patients for the ITT population.

A listing of medical history will be provided by treatment group for the ITT population.

7.3. Pathological Diagnosis, Ann Arbor Staging and FLIPI Score

At the Screening, information related to patients' disease status will be collected. All data related to disease status will be analyzed for the ITT population.

7.3.1. Pathological Diagnosis

Pathological diagnosis assessment results will be obtained from independent central pathologic review, and additional results from local assessment may be available. Pathological diagnosis data from central independent review will include following: Follicular CD20+ Lymphoma Diagnosis; Follicular Lymphoma Grade at Screening; CD3, CD10, CD20, B-cell Lymphoma (BCL)-2 and BCL-6; Fluorescence In Situ Hybridization (FISH) result and comments if applicable. Local assessment result will include following: Disease duration of lymphoma; Follicular CD20+ Lymphoma Diagnosis; Follicular Lymphoma Grade examined both at initial diagnosis and Screening; and spleen size (cm) obtained at Screening by CT scan for organ enlargement assessment.

Disease duration (Months) will be calculated as: (First dose date – Initial diagnosis date + 1) / 30.4. Incomplete initial diagnosis date will be imputed using the latest possible date. If the day is missing (i.e. XXMAR2017) the date will be set to the last day of the month (i.e. 31MAR2017). If the day and the month are missing (i.e. XXXXX2017) the date will be set to 31st December (i.e. 31DEC2017). If the imputed initial diagnosis date is later than first study drug administration date, it will be imputed as the first study drug administration date. If the whole date is missing, the date will not be imputed and disease duration will not be calculated.

Pathological diagnosis data will be summarized in a table by treatment group. All central and local assessment results will be presented in separate listings. FISH results and comments from central review will only be presented in listings separately.

7.3.2. Ann Arbor Staging

Ann Arbor stage, the principal stage and modifiers, from both at initial and screening diagnosis will be summarized and listed by treatment group. If a patient has more than one modifier, the patient will be counted in each modifier category.

7.3.3. FLIPI Score

Follicular Lymphoma International Prognostic Index (FLIPI) Score (0 to 5) will be tabulated along with each component by treatment group. All FLIPI Score data will also be listed.

7.4. Inclusion and Exclusion Criteria

Details of inclusion and exclusion criteria can be found in Sections 4.1.1 and 4.1.2 of the protocol (CT-P10 3.4) respectively. Inclusion and exclusion criteria for each patient will be presented in separate listings for the ITT population. A number of inclusion and exclusion criteria may be modified during protocol revisions. The listing will indicate which version of protocol the subject was recruited under and hence which criteria applied.

7.5. Other Baseline Characteristics

At the Screening, assessments for following viral serology parameters will be conducted:

- Hepatitis B Surface Antigen (HBsAg)
- Hepatitis B Surface Antibody (HBsAb)
- Hepatitis B Core Immunoglobulin (HBcIg)
- Hepatitis B Virus DNA test
    - DNA test will be conducted for patients with negative HBsAg, negative or positive HBsAb, and positive HBcIg.
- Hepatitis C Antibody
- Human Immunodeficiency Virus 1 (HIV-1) and HIV-2

A listing will present viral serology data for the ITT population. Screening results of viral serology tests will be summarized in a table for the ITT population. For HIV-1 and HIV-2, summarization will be combined as following: ‘Positive (at least one positive)’, ‘Negative (at least one negative with no positive)’, and ‘Both Not Done’.

8. BIOMARKERS

A blood sample for evaluation of FcγR genotype (FcγRIIa, FcγRIIIa and/or any necessary genotypes) will be collected according to the APPENDIX 1. The FcγR genotype will be evaluated as secondary endpoints.

The number and percentage of patients per genotype will be tabulated by treatment group for the ITT population. The denominator for all percentages will be the number of patients who agreed to collect blood samples for biomarker assessment. A listing will also be presented.

9. MEDICATIONS AND TREATMENTS

9.1. Prior and Concomitant Medications

All medications will be coded according to the World Health Organization drug dictionary (WHO DD September, 2015 or later). All prior anticancer therapies and concomitant medications should be recorded in the eCRF. For the purpose of inclusion in prior and/or concomitant medication tables, incomplete medication start and stop dates will be imputed as follows:

If the stop date is partial or missing, the following rules will be applied.

- If the day is missing (e.g. XXFEB2017), the last day of the month (e.g. 28FEB2017) will be assumed.
- If the day and month are missing (e.g. XXXXX2017), December 31st will be assumed.
- If the stop date is missing (e.g. XXXXXXXXX), the date will be considered as 'Continuing'.

In the case of the death of a patient, the stop date will be imputed as the date of death if the imputed stop date is after the date of death.

If the start date is partial or missing, the following rules will be applied. If the stop date is incomplete, imputed stop date will be used instead of reported stop date.

- If the day is missing (e.g. XXFEB2017), the month and year of the partial date will be compared to the date of the first infusion.
    - If the month and the year are equal for both dates, the start date will be imputed as the earlier date of: (i) the date of the first infusion, or (ii) the recorded/imputed stop date

of the medication. If the recorded/imputed stop date is missing, the start date will be imputed as the date of the first infusion.

- If the month or year is not equal for both dates, the start date will be imputed as the first day of the month (e.g. 01FEB2017).

- If the day and month are missing (e.g. XXXXX2017), the year of the partial date will be compared to the date of the first infusion.
  - If the years are equal for both dates, the start date will be imputed as the earlier date of: (i) the date of the first infusion, or (ii) the recorded/imputed stop date of the medication. If the recorded/imputed stop date is missing, the start date will be imputed as the date of the first infusion.
  - If the years are not equal for both dates, the start date will be imputed as the first day of January of the year (e.g. 01JAN2017).
- If the start date is missing (e.g. XXXXXXXXX), the start date will be imputed as the earlier date of: (i) the date of first infusion, or (ii) the recorded/imputed stop date of the medication. If the recorded/imputed stop date is missing, the start date will be imputed as the date of first infusion.

Medications will be classed as either prior or concomitant medication. A prior medication is defined as any medication where the start and stop dates or imputed start and stop dates are before the date of first infusion. A concomitant medication is defined as any medication that has an actual or imputed stop date on or after the date of first infusion or missing. The start date of a concomitant medication can be before or after the date of the first infusion.

Prior and concomitant medications will be tabulated separately by treatment group, drug class (using Anatomical Therapeutic Chemical [ATC] level 2), and preferred term, for the Safety population. The total number of prior or concomitant medications and the number and percentage of patients with at least one prior or concomitant medication will be summarized.

Concomitant medications will be presented for Overall, up to MP1 and MP2, defined as follows: a concomitant medication with a start date prior to the date of first infusion in MP2, or concomitant medication for those patients who did not enter MP2 will be included up to MP1. Otherwise, concomitant medication for those patients who have entered MP2 will be summarized in MP2 for the Safety population – 2nd Maintenance Period subset if the concomitant medication has a start date on or after the date of first infusion in MP2.

All prior and concomitant medications will be presented in separate listings by treatment group for

the Safety population. Patients who are included in the Safety population – 2nd Maintenance Period subset will be flagged in listings.

9.2. Exposure to Study Drug

The number and percentage of patients with dose administered at each treatment visit will be tabulated by treatment group for the Safety population. For patients who are not administered, reason why the dose was not administered will be also displayed. Planned dose per BSA (mg/m^2), actual administered dose per BSA (mg/m^2), actual dose intensity (actual administered dose per BSA / actual duration of dose) (mg/m^2/week) and relative dose intensity (actual dose intensity / planned dose intensity * 100) (%) will be summarized using descriptive statistics by visit.

Actual duration of dose is given by the following formula:

Actual duration of dose (Weeks) = (Next cycle date – Current cycle date) / 7

For the last cycle within each study period, the duration of dose is assumed to be 1 week for the Induction Study Period and 8 weeks for the Maintenance Study Period.

For those patients action taken, the number and percentage of patients with each reason (AE or Other) will be displayed by visit. The proportion of patients who are administered incorrect dose will be summarized on the table. Incorrect dose is defined as an actual dose level which is 5% over than planned dose (mg/m^2) * BSA (m^2). Moreover, for those patients delaying study drug, the number and percentage of patients with each reason (Nonhematological toxicity, Hematological toxicity, Cardiac toxicity, Other adverse event, Disease evaluation and Other) will be displayed.

Total number of patients with at least one dose (Full/Partial) of study drug during Overall will be summarized. Descriptive statistics of the total amount of planned dose per BSA (mg/m^2) and actual administered dose per BSA (mg/m^2), actual dose intensity (mg/m^2/week) and relative dose intensity (%) will also be provided displaying.

The total actual duration of dose will be based on the following calculation:

Duration of dose for Overall (Weeks) = Duration of dose for up to MP1 (Weeks) + Duration of dose for MP2 (Weeks)

Duration of dose for up to MP1 (Weeks) = (([Last infusion date during Induction Study Period + 7] – First infusion date during Induction Study Period) / 7) + (([Last infusion date during MP1 + 56] – First infusion date during MP1) / 7)

Duration of dose for MP2 (Weeks) = ([Last infusion date during MP2 + 56] – First infusion date

during MP2) / 7

In addition, a listing will be provided by treatment group for the Safety population showing the details of study drug exposure for each patient including BSA.

9.3. Salvage Treatment

During the Follow-up Period, salvage treatment (e.g., including chemotherapy, immunotherapy, radiotherapy or surgery) will be monitored every 3 months until death or study termination. Chemotherapy and immunotherapy will be coded according to the WHO DD September, 2015 or later, and surgery will be coded using MedDRA version 18.1 or later.

Therapy details will be listed and tabulated by therapy category and treatment group for the Safety population. Drug class (using ATC level 2) and PT will be used for chemotherapy and immunotherapy. Type of radiotherapy and purpose of surgery will be summarized for radiotherapy and surgery respectively. SOC and PT will be used for surgery.

10. EFFICACY ANALYSES

Efficacy will be assessed by response evaluation, and time-to-event analyses. Sensitivity analysis for response evaluation will also be performed.

Response evaluation will be based on the tumour assessment using image, bone marrow involvement, organ enlargement, lactate dehydrogenase (LDH) level and B-symptoms according to the Modified Response Criteria for Malignant Lymphoma. Tumour assessments will be performed at the time points specified in the APPENDIX 1.

Images for tumour assessment will be reviewed twice by central and local, and both image review results from central (central independent reviewer) and local (eCRF) will be analyzed and listed separately.

Listings based on central independent review and local review including target lesions, non-target lesions and new lesions will be presented by treatment group and visit for ITT population respectively. Patients who are included in the PP population will be flagged in listings. The target lesions listing collected from central review will include following: Information of lesion number, tumour type, location, laterality, methods of measurement, days of assessment, shortest and longest axis (mm), product of the perpendicular diameters (PPD) of target lesions (mm^2), sum of product of the perpendicular diameters (SPD) of target nodal lesions (mm^2), percent change from baseline of target nodal SPD (%), percent change from nadir of target nodal SPD (%). SPD, percent change

from baseline of SPD and percent change from nadir of SPD for target extra-nodal and both (target nodal and target extra-nodal) also will be listed. The target lesions listing from local review will include following: Information of lesion number, location, site code, days of assessment, methods of measurement, shortest and longest axis, PPD and SPD

Listings for response evaluation results from central and local will be presented separately. Both listings will include best overall response (BOR) and BOR date (prior to MC3). For central response evaluation results, most recent date will be derived as the date of response evaluation based on the following considerations:

Overall Response Evaluation	Radiologic Response[1]	Bone Marrow	B-symptom	LDH Level
CR	V	V	V	V
CRu	V	V	V	V
PR	V	V[2]	V[3]	V[3]
SD	V	V[2]		

Note: Date of progression disease and relapsed disease will be determined as recorded date of oncologist evaluation.
1 Date of target lesion, non-target lesion and new lesion assessment will be included.
2 For PD case exclusion.
3 It will be considered when overall response is downgrade from CR or CRu.

Response date of central review will be used for BOR date of central. Also, date of evaluation recorded on the 'Response Evaluation' eCRF page will be used for BOR date of local response evaluation results. If BOR of two or more assessment visits are same, then the BOR of the earliest assessment date will be used. Listings will be produced for the ITT population including PP population flag.

10.1. Primary Efficacy Endpoint

The primary efficacy endpoint is the ORR (CR + CRu + PR) at 7 months (Prior to Cycle 3 of the Maintenance Study Period) according to the Modified Response Criteria for Malignant Lymphoma.

10.1.1. Overall Response Rate

Overall response rate (ORR) is defined as the proportion of patients whose BOR is CR, CRu or PR (the 'responders'). For the primary analysis, the BOR will be derived from the overall responses according to the Modified Response Criteria for Malignant Lymphoma across all time points up to 7 months assessment (Prior to Cycle 3 of the Maintenance Study Period). When CR, CRu, PR or SD is believed to be the best response, it must also meet the minimum 8 weeks from randomization. If the minimum duration is not met in case of CR, CRu, PR or SD, the patient's BOR will be decided as the best response among subsequent assessments fulfilled the minimum

duration. For example, a patient who has SD at first assessment, progressive disease at second and does not meet minimum duration for SD, will have a best response of progressive disease. If the patient lost to follow-up after the first SD assessment, the patient's overall response would be considered to be unevaluable. In the case when a patient has an assessment result of PD within the minimum duration of 8 weeks from randomization, the patient's BOR will be considered as PD.

ORR up to 7 months will be compared between CT-P10 group and Rituxan group for the ITT population and PP population. A point estimate and 90% CI of the difference between two proportions will be presented using an exact binomial method. Similarity will be demonstrated if the two-sided 90% CI for the difference in proportion between CT-P10 and Rituxan is within the equivalence margin of ±17%. Additional exact binomial test will be conducted for ITT population – ADA Negative/Positive subset and PP population – ADA Negative/Positive subset. If the number of ADA Positive subset is very small (≤ 5% of ITT population or PP population) then the subset will not be summarized since it is not statistically meaningful.

A table presenting ORR and the analysis result will be provided. The number and percentage of patients in each response category will also be presented by treatment group separately. Patients without any response evaluation data will be included as 'Missing'. A supportive analysis will be conducted in the PP population and also be provided in the table. The table will be generated by using data from the central review and the local review separately. Additional table presenting ORR will be shown for ITT population – ADA Negative/Positive subset and PP population – ADA Negative/Positive subset. If the number of ADA Positive subset is very small (≤ 5% of ITT population or PP population) then the subset will not be summarized since it is not statistically meaningful.

10.1.2. Sensitivity Analysis

As the exact binomial method does not allow for stratification, a sensitivity analysis will be performed on the primary efficacy endpoint, utilizing a logistic regression model with treatment as a fixed effect and region (Asia Pacific vs. Europe vs. North America and Other), Ann Arbor stage (Lower than or equal to II vs. III vs. IV) and age (≥60 vs. <60 years) as covariates. The resulting odds ratio and 90% CI will be converted into difference of proportions using the Delta method for the purpose of comparison of proportions. The sensitivity analysis will be conducted in the ITT population and the PP population supportively.

Difference of proportions using the Delta method is explained in the following process.

1) The individual odds and standard errors (SEs) for both treatments will be obtained from the model. For the purposes of this algorithm, let the estimate of the odds of being a responder in the CT-P10 group be denoted by θ_a and the estimate of the odds of being a

responder in the Rituxan group be denoted by θ_b

2) Calculate the variances of these estimates, $\mathrm{Var}(\theta_a)$ and $\mathrm{Var}(\theta_b)$ respectively from the SEs obtained from the model.

3) Calculate the estimates of the corresponding proportions, denote p_a and p_b respectively, for each of the treatment groups, from the estimated odds using the following formula:

$$p_a = \frac{\theta_a}{1+\theta_a}, \qquad p_b = \frac{\theta_b}{1+\theta_b}$$

And hence calculate the estimate of the difference of proportions $(p_a - p_b)$.

4) Using Taylor expansions and the Delta method, the following formula for approximation can be obtained:

$$\mathrm{Var}[\mathrm{f(X)}] \approx (f'(E[X])^2 \, Var[X]$$

Applying this approximation specifically to this case, and using the formula specified in step (3) we obtain the formula

$$Var(p_a) = \frac{Var(\theta_a)}{(1+\theta_a)^4}, \qquad Var(p_b) = \frac{Var(\theta_b)}{(1+\theta_b)^4}$$

Which should be used to calculate $\mathrm{Var}(p_a)$ and $\mathrm{Var}(p_b)$.

5) Calculate the variance of the difference in proportions $\mathrm{Var}(p_a\text{-}p_b)$ as the sum of $\mathrm{Var}(p_a)$ and $\mathrm{Var}(p_b)$. Use this to obtain the SE of the difference, and hence calculate the 90% CI using the formula:

$$\text{90\% Confidence Interval} = (p_a - p_b) \pm 1.64\ [\mathrm{SE}(p_a - p_b)]$$

Note: this method assumes that the estimate ORR of CT-P10 group is independent of the estimate ORR of the Rituxan group.

10.2. Secondary Efficacy Endpoint

The following efficacy parameters for the study drug will be analyzed as secondary endpoints:

- Overall response rate (CR + CRu + PR) during the study period according to the Modified Response Criteria for Malignant Lymphoma

- Progression-free survival, defined as the interval between randomization and disease progression/relapse, or death from any cause, whichever occurs first

- Time to progression, defined as the interval between randomization and disease progression/relapse or death as a result of lymphoma, whichever occurs first

- Overall survival, defined as the interval between randomization and death from any cause

All time-to-event analyses excluding overall survival will be performed only for the final CSR for the central (up to MP2) and local (up to Follow-up) review. Time to overall survival analysis will be only conducted in the local review in the final CSR. Records on 'Survival Status', 'Response Evaluation' or 'Study Treatment Termination' eCRF page will be used.

For the Progression-free survival, Time to Progression and Overall Survival, the number of patients with events and censoring will be summarized on the ITT population. The reasons for events or censoring will be also presented on the table. The 25th percentile, 50th percentile (median) and 75th percentile of each time-to-event parameter and 95% CI for each treatment group will be displayed using the Kaplan-Meier method. The survival rates per 6 months will be estimated by the Kaplan-Meier method and presented along with their corresponding 95% CI. A Kaplan-Meier curve will also be provided for each the time-to-event analyses for the ITT population.
Descriptive Statistics including the 25th percentile and 75th percentile of Follow-up Duration will be provided for the ITT population.
Time-to-event analyses, event or censoring information (e.g., Date of Event, Reason for Event) will be listed by treatment group for the ITT population.

All secondary efficacy endpoint analyses will be conducted only for final CSR.

10.2.1. Overall Response Rate

For the secondary efficacy endpoint, the ORR during the study period (Overall and up to MP1) according to Modified Response Criteria for Malignant Lymphoma will be analyzed.

ORR during study period and the number and percentage of patients within each response category will be summarized by treatment group for the ITT population and the PP population. The table will be generated twice by using data from the central review and the local review.

Moreover, ORR and the number and percentage of patients will be summarized by visit for the ITT population and PP population. The table will be also generated twice by using data from the central and local review.

10.2.2. Progression-Free Survival

Progression-free survival (PFS) is defined as the interval between randomization and disease progression/relapse or death from any cause, whichever occurs first (Cheson et al 2007).

Censoring will be defined as following:

Reason for Censoring	Censoring date
No tumour assessments	Randomization date
Ongoing without event	Last tumour assessment date
Study termination for any reason without documented progression/relapse or death	Last tumour assessment date before study termination
New anticancer treatment started	Last tumour assessment date before salvage treatment
Death or progression after more than one missed visit[1]	Last tumour assessment date if there are missing visits before PD or death

1 If there is only one missed visit, then it will be considered as an event case. Otherwise, it will be considered as a censoring case.

Time-to-event for PFS will be calculated as follows:

Time-to-event for PFS (Months) = (Date of Event/Censoring – Date of Randomization + 1) / 30.4

10.2.3. Time to Progression

Time to progression (TTP) is defined as the interval between randomization and disease progression/relapse or death as a result of lymphoma, whichever occurs first (Cheson et al 2007).

Censoring will be defined as following:

Reason for Censoring	Censoring date
No tumour assessments	Randomization date
Ongoing without event	Last tumour assessment date
Study termination for any reason without documented progression/relapse or death	Last tumour assessment date before study termination
New anticancer treatment started	Last tumour assessment date before salvage treatment
Death due to lymphoma or progression after more than one missed visit[1]	Last tumour assessment date if there are missing visits before PD or death
Death due to reason other than lymphoma	Last tumour assessment date before death due to reason other than lymphoma

1 If there is one missed visit, then it will be considered as an event case. Otherwise, it will be considered as a censoring case.

Time-to-event for TTP is calculated as follows:

Time-to-event for TTP (Months) = (Date of Event/Censoring – Date of Randomization + 1) / 30.4

10.2.4. Overall Survival

Overall survival (OS) is defined as the interval between randomization and death from any cause (Cheson et al 2007). For patients whose status with no death recorded or lost to follow-up, data will be censored at the time when the patient was last known to be alive.

Time-to-event for OS is formulated as follows:

Time-to-event for OS (Months) = (Date of Event/Censoring – Date of Randomization + 1) / 30.4

10.2.5. Follow-up Duration

Follow-up duration is defined as the interval between randomization date and last information date. Event in the following order (No censored cases):

1) Patient withdrew consent
2) Patient lost to follow-up
3) Death
4) Study is closed
5) Other

Follow-up duration is formulated as follows:

Follow-up duration (Months) = (Date of Event – Date of Randomization + 1) / 30.4

10.3. Bone Marrow

Bone marrow testing will be done according to APPENDIX 1.

The number and percentage of patients with each bone marrow assessment result will be tabulated by treatment group and visit for the ITT population. The results will be listed by treatment group for ITT population including PP population flag.

10.4. B-symptoms

B-symptoms in lymphoma patients are disease-related clinical symptoms that are not caused by

anticancer therapy (or drug toxicity), and are defined as follows:

- Significant unexpected fever (>38 ºC)
- Unexplained, recurrent drenching night sweats
- Unexplained loss of more than 10% of body weight within the previous 6 months, as assessed and reported (present versus absent) by the investigator.

The number and percentage of patients with at least one B-symptom and patients per symptom will be tabulated by treatment group and visit for the ITT population. The results will be listed by treatment group for ITT population including PP population flag.

10.5. β-2 microglobulin

Blood samples for β-2 microglobulin will be assessed at the time points specified in APPENDIX 1.

The number and percentages with β-2 microglobulin results will be presented by treatment group and visit for the ITT population. All β-2 microglobulin data will be listed by treatment group and visit.

11. PHARMACOKINETIC ANALYSES

All pharmacokinetic analysis will be performed on the PK population unless otherwise specified. Blood samples for pharmacokinetic analysis will be obtained according to APPENDIX 1.

11.1. Serum concentrations

Serum concentrations of rituximab will be summarized using descriptive statistics by treatment group at each scheduled collection time for PK population. Serum concentrations below the lower limit of quantification (BLQ) at baseline (predose at Induction Study Cycle 1) will be set as zero. Serum concentrations BLQ after study drug exposure will be set as the lower limit of quantification (LLoQ). Descriptive statistics will consist of n, mean, standard deviation, geometric mean, CV%, minimum, median and maximum. Geometric mean will not be reported if the dataset includes zero values, CV% will not be reported if the mean is zero.

Mean serum concentration-time profiles of rituximab will be plotted by treatment on linear and semi-logarithmic scales based on scheduled sample times for PK population. Individual linear

concentration-time plots based on scheduled time by treatment group will also be conducted for PK population.

Serum concentrations of rituximab will be presented for the Safety population by treatment in a listing.

11.2. Pharmacokinetic Parameters

The secondary pharmacokinetic endpoints are Maximum serum concentration (C_{max}) and Trough serum concentration (C_{trough}) at each dose. C_{max} is the observed maximum serum concentration following drug administration, and C_{trough} is the observed trough serum concentration following drug administration; calculated from the predose concentration of the next dose. If the patient discontinued before next dose, concentration at EOT1 (for Cycles 1 to 3 in Induction Study Period) or EOT2 (for Cycle 4 in the Induction Study Period where there is no predose for Cycle 1 Maintenance) will be used. Serum concentrations BLQ at baseline (predose at Induction Study Cycle 1) will be set as zero. Serum concentrations BLQ after study drug exposure will be set as LLoQ. Missing values for any PK parameters will not be imputed.

The table will summarize the PK parameters using descriptive statistics by treatment group: n, mean, standard deviation, geometric mean, CV%, minimum, median and maximum. Geometric mean will not be reported if the dataset includes zero values, CV% will not be reported if the mean is zero.

Pharmacokinetic parameters for the PK population will be listed.

12. PHARMACODYNAMIC ANALYSES

All pharmacodynamic tables and listings will be generated based on the Pharmacodynamic population by treatment group unless otherwise specified. Blood samples for B-cell kinetics will be obtained according to APPENDIX 1. The secondary pharmacodynamic endpoint is B-cell kinetics.

A summary table presenting actual values and changes from baseline along with descriptive statistics will be presented for B-cell values by treatment group and time-point for all scheduled visits, including the records at predose and 1 hour after the end of infusion. Descriptive statistics will consist of n, mean, standard deviation, geometric mean, CV%, minimum, 25th percentile, median, 75th percentile, maximum and IQR. Geometric mean will not be reported if the dataset includes zero values. Any values recorded below the lower limit or above the upper limit of quantification will be set to the respective limit for all summary tables.

13. SAFETY ANALYSES

All analysis of safety data will be conducted for the Safety population and displayed by treatment group in 1st CSR. For the final CSR, all analysis of safety data will be conducted for the Safety population and Safety population – 2nd Maintenance Period subset and displayed by treatment group. The safety endpoints will be assessed using the following: AEs, SAEs, concomitant medications, hypersensitivity (via vital signs and ECG), physical examination findings, vital signs measurements, clinical laboratory analyses, chest x-ray findings, ECG findings, infection, infusion-related reactions, immunogenicity testing, immunoglobulin testing, tuberculosis (TB) assessment, ECOG status and pregnancy.

The analyses of concomitant medication are described in Section 9.1.

Unscheduled results will not be summarized, but will be listed only, with the exception of the Common Terminology Criteria for Adverse Events (CTCAE) analysis of laboratory data detailed in Section 13.2.

13.1. Adverse Events

An adverse event (AE) is defined as any untoward medical occurrence in a patient enrolled (i.e., when the 'Informed Consent' page of eCRF is recorded) into the study regardless of its causal relationship to study drug.

A treatment-emergent AE (TEAE) is defined as any event not present before exposure to study treatment or any event already present that worsens in intensity or frequency after exposure to study treatment.

The MedDRA version 18.1 or later will be used to code all AEs. AEs will be graded for intensity according to CTCAE version 4.03.

All AEs occurring during the study will be listed by treatment group. Listings for AEs will include following information: Study period (Induction to MP1, MP2, and Follow-up); SOC, PT and verbatim term; start and stop date; duration (days from start date until stop date of an AE); frequency (intermittent, continuous); outcome (recovered/resolved, recovering/resolving, recovered/resolved with sequelae, not recovered/not resolved, fatal, unknown); any treatment required (no, yes with specified treatment); intensity (CTCAE grade 1 to 5); action taken by investigator (no action taken, dose decreased, dose interruption [or prolonged], permanently discontinued, dose delay); relationship to study drug (unrelated, possible, probable, definite); whether the event is serious (yes, no); and whether patient is terminated from the study due to AE

(yes, no).

In summaries, AEs will be considered to be related if the relationship is possible, probable or definite. If relationship or intensity is missing, it will be summarized separately under a missing category.

Combined PTs using APPENDIX 5 will be summarized in AE tables. Listings will include PTs as coded without applying the PT combining rule.

Summaries related AEs will be presented in overall and by each study period (Induction to MP1, MP2 and Follow-up). Any AE having a start date on or after Induction Cycle 1 visit date and before Maintenance Cycle 7 visit date or Follow-up 1 visit date (in case a patient with discontinuation before Maintenance Cycle 7) will be included in the Induction to MP1 Period. Any AE having a start date on or after the Maintenance Cycle 7 visit date and before Follow-up 1 visit date will be included in the MP2 Period. Any serious adverse drug reaction (SADR) reported in the eCRF having a start date on or after the Follow-up 1 visit date and up to last Follow-up visit date will be included in the Follow-up Period.

The number and percentage of patients with at least one event including TEAE, TESAE, TEAE leading to permanent discontinuation of the study drug and TEAEs of special interest will be presented by relationship to study drug, intensity, SOC and PT for the Safety population and Safety population – 2nd Maintenance Period subset. At each level of summarization for the number of patients, a patient is counted only once if they reported one or more events and only the most severe event recorded will be counted. Percentages will be calculated out of the number of patients in each population. The total number of events and number of patients with at least one event will also be displayed.

All AE related tables will be also displayed without relationship to study drug.

If the stop date of an AE is partial or missing, the following rules will be applied. The imputed stop date will be only used to impute start date.

- If the day of an AE is missing (e.g. XXFEB2017), the last day of the month (e.g. 28FEB2017) will be assumed.
- If the day and month are missing (e.g. XXXXX2017), December 31st will be assumed.
- If the stop date of an AE is missing (e.g. XXXXXXXXX), the date will be considered as ‘Missing’.

In case a patient is dead, the stop date will be imputed as the date of death if the imputed stop date

is after the date of death.

If the start date of an AE is partial or missing, the following rules will be applied.

- If the day of an AE is missing (e.g. XXFEB2017), the month and year of the partial date will be compared to the date of the first exposure to study drug.
    - If the month and the year are equal for both dates, the AE start date will be imputed as the earlier date of: (i) the date of the first exposure to study drug, or (ii) the recorded/imputed stop date of the AE. If the recorded/imputed stop date of the AE is missing, the start date will be imputed as the date of the first exposure to study drug.
    - If the month or year is not equal, the AE start date will be imputed as the first day of the month (e.g. 01FEB2017).
- If the day and month are missing (e.g. XXXXX2017), the year of the partial date will be compared to the date of the first exposure to study drug.
    - If the years are equal for both dates, the AE start date will be imputed as the earlier date of: (i) the date of the first exposure to study drug, or (ii) the recorded/imputed stop date of the AE. If the recorded/imputed stop date of the AE is missing, the start date will be imputed as the date of the first exposure to study drug.
    - If the years are not equal, the start date will be imputed as the 1st day of January of the year (e.g. 01JAN2017).
- If the start date of an AE is missing (e.g. XXXXXXXXX), the start date will be imputed as the earlier date of: (i) the date of the first exposure to study drug, or (ii) the recorded/imputed stop date of the AE. If the recorded/imputed stop date of the AE is missing, the start date will be imputed as the date of the first exposure to study drug.

The recorded/imputed dates of AEs will be used for decision whether the event is TEAE and classification of study periods.

13.1.1. Incidence of Treatment-Emergent Adverse Events

Treatment-Emergent Adverse Events and TEAEs reported for at least 3% and 5% of patients in either treatment group will be summarized. For the Summary of TEAE reported for at least 3% and 5% of patients in either treatment group, it will be only presented with relationship to study drug.

All TEAEs will be flagged in the listing for AEs described in Section 13.1.

13.1.2. Adverse Event Leading to Death

All patients who have an outcome of AE as 'Death' will be only listed including following information: SOC, PT, verbatim term, cause of death, date of death, days from the first dose until death, date of last visit, days on study and relationship to study drug.

13.1.3. Serious Adverse Events

A serious adverse event (SAE) is defined as any event that results in death, is immediately life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, important medical event based on appropriate medical judgment or is a congenital anomaly/birth defect.

If a patient is hospitalized purely for convenience, the hospitalization does not qualify as an SAE. If a patient is hospitalized solely due to disease progression, the hospitalization does not qualify as an SAE.

All SAEs will be listed including variables detailed in Section 13.1. Additional information of SAE will also be provided based on the 'Serious Adverse Event' page of eCRF.

13.1.4. Treatment-Emergent Adverse Events leading to Permanent Study Drug Discontinuation

All TEAEs which led to permanent discontinuation of study drug will be summarized and listed including variables detailed in Section 13.1.

13.1.5. Treatment-Emergent Adverse Events of Special Interest

The following will be considered as AEs of special interest: infusion-related reactions (IRR), infections and progressive multifocal leukoencephalopathy (PML).

TEAEs of IRR will be determined if the information is recorded as IRR in the 'Adverse Events' page of the eCRF. TEAEs of infections will be determined if a SOC is 'Infections and infestations'. Although PML is an AE of special interest, it is captured only by a PT 'Progressive multifocal leukoencephalopathy'. Therefore, TEAEs of PML will be included in the summary of TEAEs instead of generating an additional table.

All TEAEs of IRR and infections will be listed separately including variables detailed in Section 13.1. With variables detailed in Section 13.1, the listing will include information recorded on the 'Adverse Events' and 'Infusion related/Anaphylactic Reaction' page of eCRF will be included: start/stop time of IRR; signs and symptoms; whether symptoms are experienced (no, yes with

specified intensity NCI CTCAE); the lowest blood pressure (BP) level after study drug exposure [mmHg] and date/time of BP assessment (if BP is decreased after study drug exposure); comments on IRR.

13.2. Clinical Laboratory Evaluations

Clinical laboratory assessments of hematology, clinical chemistry and urinalysis will be performed at the local laboratory. Since reported units and normal ranges are various among sites, results will be converted to standard unit. Results of the assessment will be collected at the time points specified in the APPENDIX 1.

Descriptive statistics for actual values and changes from baseline of each hematology or clinical chemistry parameter will be presented by visit for the Safety population.

All possible numeric parameters will be labeled and graded by CTCAE. Grades that require clinical input only will not be evaluated. Grades which are part numeric and part clinical input will be assigned based on the numeric portion only. CTCAE terms and ranges for applicable parameters are listed in APPENDIX 3. The CTCAE grades for this analysis will be Grade 1 (Mild), Grade 2 (Moderate), Grade 3 (Severe) and Grade 4 (Life-threatening). The CTCAE Grade 5 (Death) will not be applied in this analysis since death cannot be determined from a numeric laboratory result. If the result for a patient does not satisfy any CTCAE grade, it will be classified as “No Grade”.

Results of unscheduled visits will be included for CTCAE grade. In summary, unscheduled visit and EOT visit results will be used in the related cycle. For example, C1D5 (Day 5 of Cycle 1 result will be summarized in Cycle 1; EOT1 result will be summarized in the last cycle of the Induction Study Period. In addition, C2D1 result should be summarized in Cycle 1 result because laboratory blood sample for C2D1 is taken before Cycle 2 dose administration. The same rule will be applied to subsequent cycles.

The number and percentage of patients who have a result for each grade will be summarized by laboratory category, CTCAE term, visit, grade and treatment group for the Safety population and Safety population – 2nd Maintenance Period subset. The summary will be presented in Overall and by each study period (up to MP1, MP2). Only the most severe case during unscheduled and scheduled visits will be included.

The number and percentage of patients with CTCAE grade greater than or equal to 3 will be summarized by laboratory category, CTCAE term, grade and treatment group for the Safety population and Safety population – 2nd Maintenance Period subset. The summary will be presented in Overall and by each study period (up to MP1, MP2). Only the most severe case of the post-baseline during unscheduled and scheduled visits will be included.

The number and percentage of patients with CTCAE grade will be provided, by laboratory category, CTCAE term, grade and treatment group for the Safety population and Safety population – 2nd Maintenance Period subset, in the form of a shift table to detect changes from baseline. The summary will be presented in Overall and by each study period (up to MP1, MP2). Only the most severe case during unscheduled and scheduled visits will be included for the post-baseline result.

All hematology and clinical chemistry data will be listed by treatment group. Results of CTCAE will be presented by separate listing.

Result interpretation for all urinalysis parameters will be collected as {'Normal', 'Abnormal, not clinically significant' and 'Abnormal, clinically significant'}. The number and percentage of patients with urinalysis results will be provided, by parameter, visit and treatment group for the Safety population, in the form of a shift table to detect changes from baseline.

All urinalysis data will be listed by treatment group, visit and parameter.

13.2.1. Hematology

Following hematology laboratory tests will be included: Absolute neutrophil count (*10E9/L), Hemoglobin (g/dL), Platelet count (*10E9/L) and White blood cell count (*10E9/L).

13.2.2. Clinical Chemistry

The following chemistry laboratory tests will be included: Alanine aminotransferase (ALT) (U/L), Albumin (g/L), Alkaline phosphatase (U/L), Aspartate aminotransferase (AST) (U/L), Blood urea nitrogen (mmol/L), Calcium (mmol/L), Creatinine (μmol/L), Glucose (mmol/L), Lactate dehydrogenase (IU/L), Potassium (mmol/L), Sodium (mmol/L), Total bilirubin (μmol/L), Total protein (g/L) and Uric acid (mmol/L).

13.2.3. Urinalysis

All relevant categorical urinalysis parameters will be included: Bilirubin, Blood, Glucose, Ketones, and Protein. Microscopic examination of Bacteria count, Red blood cell count and White blood cell count will be done if urinalysis dipstick results for any of the analytes are 2+ or greater.

13.3. Immunogenicity

Blood samples for assessment of immunogenicity (Anti-drug antibodies [ADA] and Neutralizing antibody [NAb]) will be collected at the time points specified in the APPENDIX 1. Immunogenicity assessment consists of both ADA and NAb assay.

The ADA assay will be performed using the single labelled antibody with CT-P10 tag. NAb will

be determined using a single antibody.

The ADA assay will follow three tiered approach consisting of (i) screening assay, (ii) specificity/confirmatory assay and (iii) titration. The test outcome for the screening assay will be: {'Potential Positive' or 'Negative'}. Samples that are 'Potential Positive' in the screening assay will be spiked with excess study drug to determine if samples are a true positive. The test outcome for the specificity/confirmatory assay will be: {'Reactive', 'Negative', or 'N/A'}. 'Reactive' indicates a true positive test outcome and will be labeled as 'Positive' in outputs, 'Negative' is considered negative, and 'N/A' indicates the assay was negative at the screening phase of the process. Patients with a 'Negative' test outcome for either the screening or specificity/confirmatory assay will be considered 'Negative' for the overall ADA assessment. For further characterization, the antibody level will be assessed by titration in confirmed positive samples.

Samples that are positive in the ADA assay will be analyzed further to conduct a NAb assessment. The test outcome for the screening assay will be: {'Reactive', 'Rejected for Hemolysis (HEM)', 'Insufficient Sample Volume (ISV)' or 'Negative'}. Samples that are 'Reactive' in the screening assay will be undergone further testing in the confirmatory (immunodepletion) assay to determine if samples are a true positive. The test outcome for the confirmatory assay will be: {'Positive', 'Negative' or 'N/A'}. 'Positive' indicates a true positive test outcome, 'Negative' is considered negative, and 'N/A' indicates the assay was negative at the screening phase of the process. Patients with a 'Negative' test outcome for either the screening or confirmatory assay will be considered 'Negative' for the overall NAb assessment. For further characterization, the antibody level will be assessed by titration in confirmed positive samples.

Both ADA and NAb test will be performed on samples obtained at all relevant visits. The results of the final ADA assay and the final NAb assay will be summarized. The number and percentage of patients will be provided by treatment group and visit for the Safety population.

The ADA and NAb titer values of the CT-P10 tagged assay will be transformed using a $[\log_2 X] + 1$ and $[\log_8 X]$ transformation respectively. If the values in the data are forms of inequality, the sign of inequality will be removed and then the values will be transformed. Descriptive statistics of transformed ADA titer will be displayed by treatment group and visit for the Safety population.

All immunogenicity test results including actual and transformed results of ADA/NAb titer will be listed by treatment group and visit.

13.4. Immunoglobulin

Blood samples for assessment of immunoglobulins (IgM, IgG and IgA) will be collected at the time points specified in the APPENDIX 1. Descriptive statistics for actual values and changes

from baseline to each scheduled post-baseline visit will be presented by immunoglobulin tests and treatment group for the Safety population. Any values BLQ will be set to this limit for analysis. All data of immunoglobulin will be listed by treatment group, visit and test. In the case when duplicated measurements of immunoglobulins are recorded within the same visit, the highest value will be used for analysis in a conservative approach.

13.5. Vital Signs

Vital signs, BSA and weight will be measured at the time points specified in the APPENDIX 1. Vital signs (including systolic and diastolic BP, heart rate, respiratory rate and body temperature) will be measured by the investigator or the designee. Body temperature recorded in Fahrenheit (^oF) will be converted to Celsius (^oC). Height will be collected once in Screening Period and will be listed with demographics in Section 7.1. BSA will be calculated based on Mosteller method (Mosteller et al 1987) with two decimal places in each cycle:

$$BSA(m^2) = ([Height(cm) \times Weight(kg)]/3600)^{1/2} \text{ or } ([Height(in) \times Weight(lb)]/3131)^{1/2}$$

Descriptive statistics for actual values and changes from baseline of vital signs, weight and BSA will be presented by treatment group and visit for the Safety population. All vital signs, weight and BSA data will be listed by treatment group and visit.

13.6. Electrocardiogram

A 12-lead ECG will be performed at the time points specified in the APPENDIX 1. All scheduled 12-lead ECGs must be performed after the patient has rested quietly for at least 5 minutes in the supine position.

Findings will be classified as {'Normal', 'Abnormal, not clinically significant' and 'Abnormal, clinically significant'}. The number and percentage of patients will be provided, by treatment group and visit for the Safety population, in the form of a shift table to detect changes from baseline. All ECG data will be listed by treatment group and visit.

13.7. Hypersensitivity Monitoring

Hypersensitivity will be assessed by vital sign monitoring (including systolic and diastolic BP, heart rate, respiratory rate and body temperature) within 15 minutes before the study drug infusion, within 15 minutes after the end of the study drug infusion and at 60 minutes (± 15 minutes) after the end of the study drug infusion on each dosing day.

The number and percentage of patients with a clinically notable vital sign hypersensitivity result will be presented by treatment group, visit, time point and parameter for the Safety population.

The criteria for clinically notable results are defined as follows:

Parameter	Low	High
Systolic blood pressure (mmHg)	≤ 90	≥ 160
Diastolic blood pressure (mmHg)	≤ 50	≥ 90
Heart rate (beats per minute)	≤ 50	≥ 100
Respiratory rate (breaths per minute)	≤ 12	≥ 20
Body temperature (°C)	≤ 35.0	≥ 38.0

In addition, hypersensitivity should be monitored by routine continuous clinical monitoring including ECG (3-lead or 12-lead) monitoring at 60 minutes (± 15 minutes) after the end of the study drug infusion. Findings will be classified as {'Normal', 'Abnormal, not clinically significant' and 'Abnormal, clinically significant'}. The number and percentage of patients will be provided by treatment group and visit for the Safety population in the form of a shift table to detect changes from baseline. All hypersensitivity data will be listed by treatment group, visit and time point.

13.8. Tuberculosis Assessment

During the Screening Period, a current diagnosis of active TB or examination findings indicating the presence of active TB will result in patient exclusion from the study. TB assessment will be performed at the time points specified in the APPENDIX 1. Findings will be classified as {'Normal', 'Abnormal, not clinically significant' and 'Abnormal, clinically significant'}.

The number and percentage of patients who have TB assessment results will be summarized by treatment group and visit for the Safety population. All TB data will be listed by treatment group and visit.

13.9. Physical Examination

Physical examinations with particular attention to infections and PML will be performed at the time points specified in the APPENDIX 1. Information of physical examination will be recorded in the 'Physical Examination' or the 'Adverse Event' page of the eCRF in case any new abnormality in post-screening is detected.

Findings will be classified as {'Normal', 'Abnormal, not clinically significant' and 'Abnormal, clinically significant'}. The number and percentage of patients will be provided, by treatment group and visit for the Safety population, in the form of a shift table to detect changes from baseline. All physical examination data will be listed by treatment group and visit.

13.10. ECOG Status

Eastern Cooperative Oncology Group (ECOG) performance status is to assess health of oncology patients with score running from 0 (a measure of perfect health) to 5 (death). The grade of performance status is defined as follows:

Grade	Performance Status
0	Fully active, able to carry on all predisease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of light or sedentary nature, e.g. light house work, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of walking hours
3	Capable of only limited self-care; confined to bed or chair more than 50% of walking hours
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair
5	Dead

ECOG performance status ('Grade 0' to 'Grade 5') will be summarized by treatment group and visit for the Safety population. All ECOG performance status data will be listed by treatment group and visit.

13.11. Pregnancy

Serum pregnancy test and Urine pregnancy test in women of childbearing potential will be performed at the time points specified in the APPENDIX 1. Both serum and urine pregnancy tests will be performed at a local laboratory.

Results of serum pregnancy test data will be summarized and listed by treatment group and visit for the Safety population. Results of urine pregnancy dipstick test will also be summarized and listed by treatment group and visit for the Safety population.

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15. APPENDICES

APPENDIX 1: Schedule of Events

EOT2/C1*

	Screening Period	Induction Study period[1]						Maintenance Study Period[1]													Follow-Up Period[2]	
Study Visit	**Screening**	**C1**	**C2**	**C3**	**C4**	**EOT 1[3]**	**EOT 2[3]**	**C1**	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C8**	**C9**	**C10**	**C11**	**C12**	**EOT 3[3]**	**Every 3M**	**Every 6M**
Week		1	2	3	4	5	12	12	20	28	36	44	52	60	68	76	84	92	100	108		
Month							3	3	5	7	9	11	13	15	17	19	21	23	25	27		
Timing Window	**Day –42 to Day 0**		**±1 day**	**±1 day**	**±1 day**	**±1 day**	**±7 day**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±14 days**	**±14 days**
Procedure**																						
Informed consent[4]	X																					
Demographics	X																					
Medical history, height	X																					
Ann Arbor staging	X																					
FLIPI score	X‡																					
Pathological diagnosis[5]	X																					
Inclusion/exclusion criteria	X	X[6]																				
Randomisation		X[7]																				
Physical examination	X	X[8]	X[8]	X[8]	X[8]	X	(X)	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X		
BSA[9]		X[8]	X[8]	X[8]	X[8]			X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]			
Vital signs[10] and weight	X	X[8]	X[8]	X[8]	X[8]	X	(X)	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X		
ECOG performance status	X	X[8]	X[8]	X[8]	X[8]	X	(X)	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X		
Haematology[11,12] (local)	X‡		X[8]	X[8]	X[8]	X	(X)	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X		
Clinical chemistry[12,13] (local)	X‡		X[8]	X[8]	X[8]	X	(X)	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X		
Urinalysis[12,15] (local)	X‡		X[8]	X[8]	X[8]	X	(X)	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X		
Serum pregnancy test[16] (local)	X‡					X	X													X		
Urine pregnancy test[16] (local)		X[8]	X[8]	X[8]	X[8]			X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]			

								EOT2/C1*													
	Screening Period	**Induction Study period[1]**						**Maintenance Study Period[1]**												**Follow-Up Period[2]**	
Study Visit	**Screening**	**C1**	**C2**	**C3**	**C4**	**EOT 1[3]**	**EOT 2[3]**	**C1**	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C8**	**C9**	**C10**	**C11**	**C12**	**EOT 3[3]**	**Every 3M**	**Every 6M**
Week		**1**	**2**	**3**	**4**	**5**	**12**	**12**	**20**	**28**	**36**	**44**	**52**	**60**	**68**	**76**	**84**	**92**	**100**	**108**		
Month							**3**	**3**	**5**	**7**	**9**	**11**	**13**	**15**	**17**	**19**	**21**	**23**	**25**	**27**		
Timing Window	**Day –42 to Day 0**		**±1 day**	**±1 day**	**±1 day**	**±1 day**	**±7 day**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±14 days**	**±14 days**
Hepatitis B and C and HIV[17] (local)	X																					
Immunogenicity testing[18] (central)		X[8]					(X)	X[8]		X[8]			X[8]			X[8]				X	(X)	
Immunoglobulin testing[18] (central)		X[8]				X	(X)	X[8]	X[8]	X[8]												
Chest x-ray[19]	X						(X)	X[8]		X[8]			X[8]			X[8]				X		
Tumour response assessment[23]																						
- Radiography(CT ± MRI)[20]	X						(X)	X[8]		X[8]			X[8]			X[8]				X		X
- Physical examination on tumour site[21]	X‡						(X)	X[8]		X[8]			X[8]			X[8]				X		X
- LDH[14](local)	X‡		X	X	X	X	(X)	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X		X
- B-symptoms[21]	X‡						(X)	X[8]		X[8]			X[8]			X[8]				X		X
- Bone marrow examination[22] (local)	X						(X)	(X)		X[8]			(X)			(X)				(X)		(X)
PK sampling (central)[24]		X	X	X	X	X	(X)	X	X	X												
B-cell kinetics[25] (central)		X	X	X	X	X	(X)	X	X	X												
Study drug administration[26]		X	X	X	X			X	X	X	X	X	X	X	X	X	X	X	X			
12-Lead ECG[27] (local)	X					X	(X)	X[8]		X[8]			X[8]			X[8]				X		
Hypersensitivity monitoring[27]		X	X	X	X			X	X	X	X	X	X	X	X	X	X	X	X			
TB monitoring[28]	X	X[8]	X[8]	X[8]	X[8]	X	(X)	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X		
Concomitant medications[29]	X	X	X	X	X	X	(X)	X	X	X	X	X	X	X	X	X	X	X	X	X		
AE reporting[30]	X	X	X	X	X	X	(X)	X	X	X	X	X	X	X	X	X	X	X	X	X		

	Screening Period	Induction Study period[1]						Maintenance Study Period[1]													Follow-Up Period[2]	
Study Visit	**Screening**	**C1**	**C2**	**C3**	**C4**	**EOT 1[3]**	**EOT 2[3]**	**C1**	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C8**	**C9**	**C10**	**C11**	**C12**	**EOT 3[3]**	**Every 3M**	**Every 6M**
Week		**1**	**2**	**3**	**4**	**5**	**12**	**12**	**20**	**28**	**36**	**44**	**52**	**60**	**68**	**76**	**84**	**92**	**100**	**108**		
Month							**3**	**3**	**5**	**7**	**9**	**11**	**13**	**15**	**17**	**19**	**21**	**23**	**25**	**27**		
Timing Window	**Day –42 to Day 0**		**±1 day**	**±1 day**	**±1 day**	**±1 day**	**±7 day**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±7 days**	**±14 days**	**±14 days**
Blood samples for FcγR genotype (FcγRIIa, IIIa, and/or any necessary genotypes)[31]		X[8]																				
β-2 microglobulin[32] (central)	X‡						(X)	X[8]		X[8]			X[8]			X[8]				X		
Survival status and salvage treatment[33]																					X	

Abbreviations: AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; B-cell, B-lymphocyte; BSA, body surface area; C, cycle; CR, complete response; CRu, unconfirmed complete response; CT, computed tomography; ECG, electrocardiogram; ECOG, Eastern Cooperative Oncology Group; EOT; End of Treatment; FLIPI, Follicular Lymphoma International Prognostic Index; HBcIg, hepatitis B Induction immunoglobulin; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HIV, human immunodeficiency virus; Ig, immunoglobulin; LDH, lactate dehydrogenase; MRI, magnetic resonance imaging; PK, pharmacokinetic; PR, partial response; RBC, red blood cell; SD, stable disease; TB, tuberculosis; ULN, upper limit of normal; WBC, white blood cell.

1. Each treatment cycle in the Induction Study Period is 7 days (± 1 day) and each subsequent cycle begins the day after the previous cycle ends. For maintenance therapy, each treatment cycle will be administered once every 8 weeks (±7 days) from the previous dose date of study drug (either CT-P10 or Rituxan). The maintenance Study Period will be continued up to maximum 12 cycles for 2 years, with study drug administrated every 8 weeks for a maximum of 6 cycles for 1 year. Subsequently all patients will be allowed to receive CT-P10 every 8 weeks interval for 1 additional year upon investigator's discretion. A month consists of 4 weeks for this study.
2. After the latest EOT visit, each follow-up visit will occur every 3 months (±14 days) for up to 27 months from the first administration of the study drug of the last enrolled patient.
3. The EOT1 visit for the Induction Study Period will occur 1 week (±1 days) after the last dose of study drug administration for safety assessment, the EOT2 visit will occur 8 weeks (±7 days) after the last dose of study drug administration for the Induction Study Period for efficacy assessment, and the EOT3 visit will occur 8 weeks (±7 days) after the last dose of study drug administration for the Maintenance Study Period. If a patient is terminated within 6 months from Day 1 of Cycle 1 of Induction Study Period, The EOT3 visit will occur within 4 to 8 weeks (±7 days) after the last dose of study drug administration in the Maintenance Study Period. Patients who experienced progressive or unknown status of disease during the EOT2 visit assessment (at 3 months) will not be entered into the Maintenance Study Period and the assessment visit will be called 'EOT2'. Patients who experienced CR, CRu, PR or SD in this assessment (at 3 months) will qualify for the Maintenance Study Period and the assessment visit will be called Maintenance 1 visit.
4. Informed consent must be obtained before any protocol-required procedures are performed.

5. During the Screening Period, CD20+ FL grade 1 to 3a according to the World Health Organization 2008 classification should be tested by central independent review for eligibility evaluation from all sites. Local assessment can be done for eligibility if it is discussed and arranged with the sponsor or the sponsor's designee. Tissue obtained within 6 months before the first infusion of the study drug will be used. Pathological review will be performed as per the site guideline which will be provided by the sponsor.
6. The inclusion and exclusion criteria need to be confirmed prior to randomisation.
7. Patients will be randomly assigned to study drug before dosing. Study drug will be administered on the day of randomisation.
8. Assessed prior to study drug infusion.
9. Body surface area will be calculated for actual dose using the Mosteller formula within 3 days before study drug administration of each cycle. Other formula can be used if it is agreed with the sponsor or sponsor's designee in advance.
10. Vital signs (including systolic and diastolic blood pressure, heart rate, respiratory rate, and body temperature) will be measured after 5 minutes of rest.
11. Haematology assessments will consist of WBC count, absolute neutrophil count, haemoglobin, and platelet count.
12. All screening laboratory safety assessments must be completed within 14 days before the first administration of the study drug. All laboratory safety assessments (haematology, clinical chemistry and urinalysis) must be completed within 3 days before Day 1 of each cycle during the Induction Study Period (except Cycle 1) and within 7 days before Day1 of each cycle during the Maintenance Study Period. Testing will be performed at the local laboratory.
13. Clinical chemistry assessments will consist of sodium, potassium, blood urea nitrogen, creatinine, glucose, AST, ALT, alkaline phosphatase, total bilirubin, calcium, total protein, albumin, and uric acid.
14. Lactate dehydrogenase will be evaluated within 3 days before Day 1 of each cycle during the Induction Study Period (except Cycle 1) and within 7 days before Day 1 of each cycle during the Maintenance Study Period. Testing will be performed at the local laboratory. This should be performed at the time of response evaluation during the follow-up Study Period.
15. Urinalysis will consist of protein, blood, glucose, ketones, and bilirubin. If any of the dipstick analytes are 2+ or greater, a microscopic examination of urine will be performed with determinations of WBC, RBC, and bacteria counts.
16. Serum pregnancy tests in women of childbearing potential will be performed during the Screening Period (within 14 days before Day 1 of Cycle 1), at the EOT1 visit (within 3 days), the EOT2 visit (within 3 days), and the EOT3 visit (within 3 days). Serum pregnancy testing will be performed at the local laboratory. At Day 1 of each cycle during the Induction Study Period and the Maintenance Study Period, a urine pregnancy test will be performed. Urine pregnancy testing will be performed at the local laboratory.
17. HBsAg, HBsAb, and HBcIg should be assessed within 42 days before the first drug administration in all patients (mandatory). If the result is HBsAg (positive), the patient should be excluded from the study. For patients whose HBsAg is negative, HBsAb is negative or positive, and HBcIg is positive, a DNA test should be performed within 42 days before the first drug administration. If the DNA test result is positive, the patient should be excluded from the study and if the DNA test result is negative, the patient can be included. For the patients enrolled based on the DNA test, the DNA test will be done every 24 weeks (±8 weeks) for monitoring purposes until the patient receives new anticancer therapy. If hepatic symptoms are suspicious (ie, AST ≥3 times the ULN, ALT ≥3 times the ULN, or total bilirubin ≥2 times the ULN) during the Induction Study Period and Maintenance Study Period, then HBsAg, HBsAb, HBcIg, and DNA should be tested. Hepatitis C virus antibody and HIV antibody must be obtained within 42 days before the first study drug administration for all patients. Hepatitis and HIV testing will be performed at the local laboratory.
18. Immunoglobulin (IgG, IgM, IgA) testing and immunogenicity (antirituximab antibodies) testing will be obtained prior to the beginning of study drug of the Induction Study Period. Immunoglobulin testing will also be obtained at the EOT1 visit and before administration on Day 1 of Cycle 1 (Month 3; EOT2), Cycle 2 (Month 5), and Day 1 of Cycle 3 (Month 7) during the Maintenance Study Period. Immunogenicity testing will also be obtained prior to Day 1 of Cycle 1 (Month 3; EOT2), Cycle 3 (Month 7), and Cycle 6 (Month 13) and Cycle 9 (Month 19) during the Maintenance Study Period and at the EOT3 visit. Immunoglobulin and Immunogenicity testing must be completed before administration of the study drug at each planned visit and any time during the EOT visit. Immunoglobulin and Immunogenicity testing will be performed at the central laboratory. If a patient is terminated within 6 months from Day 1 of Cycle 1 of Induction Study Period, immunogenicity should be assessed at EOT2 (Month 3), EOT3 and the first follow-up visit.

19. A chest x-ray will be obtained within 6 weeks before the first administration of the study drug. During the Maintenance Study Period, chest x-ray will be obtained prior to (within 7 days before each visit) Cycle 1 (Month 3; EOT2), Cycle 3 (Month 7), Cycle 6 (Month 13) and Cycle 9 (Month 19) and at the EOT3 visit. During the study period, a chest x-ray will be performed whenever an assessment is needed, at the investigator's discretion. If a CT or proper image has been taken, a chest x-ray could not be performed at the investigator's discretion.
20. Tumour assessments will be performed using CT (neck, chest, abdomen, and pelvis) with contrast with or without magnetic resonance imaging. The baseline measurement will be obtained within 6 weeks before Day 1 of Cycle 1 of the Induction Study Period. The same methods of assessment using CT with or without MRI should be used for all subsequent evaluations. A CT scan will be obtained prior to (within 7 days before each visit) at Cycle 1 (Month 3; EOT2), Cycle 3 (Month 7), Cycle 6 (Month 13), Cycle 9 (Month 19) and the EOT3 visit during the Maintenance Study Period. During the Follow-up Period, the tumour assessment (within 7 days before the next visit) will be performed every 6 months in patients. Clinical suspicion of disease progression at any time will require a physical examination and prompt radiological confirmation, rather than waiting for the next scheduled tumour assessment. In case of an additional or delayed tumour assessment for any reason, subsequent tumour assessments should be performed according to the originally planned schedule unless a scan has been performed within the past 21 days. If an investigator considers disease progression before EOT2 (Month 3), tumour assessment can be done at any time. If this tumour assessment is done within 21 days from suggested time-point of assessment (3 months from Cycle 1 of Induction Study Period), tumour assessment at EOT2 (Month 3) will not be performed. If an investigator considers discontinuation of study treatment based on safety reason before EOT2 (Month 3), tumour assessment can be done at any time. If a patient discontinue from the study treatment before Month 7 without disease progression, tumour assessment will be performed at Month 7. If the previous tumour assessment is done within 21 days from Month 7, tumour assessment at month 7 will not be performed.
21. B-symptoms (significant unexpected fever [>38℃]; unexplained, recurrent drenching night sweats; unexplained loss of more than 10% of body weight within the previous 6 months, as assessed and reported [present versus absent] by the investigator) and physical examination on the tumour site will be assessed at the time of response evaluation.
22. A bone marrow examination should not be performed at screening for patients with a prior history of marrow involvement. If bone marrow involvement is positive the result of the bone marrow examination will be used as baseline information regardless of when the bone marrow involvement is confirmed. If bone marrow involvement is negative or unknown, the bone marrow examination should be performed within 90 days before the first administration of the study drug. Bone marrow examinations should be performed to confirm CR prior to Cycle 3 (Month 7) in the Maintenance Study Period per bone marrow involvement as follows: (a) if bone marrow involvement is positive before study treatment biopsy should be performed for CR confirmation; (b) if bone marrow involvement is negative before study treatment biopsy is not mandatory for CR confirmation; (c) if bone marrow involvement is positive and CR is confirmed by biopsy, biopsy is not mandatory at next assessment. At other time points during the Maintenance Study Period and the Follow-up Period, no further bone marrow examinations are planned but bone marrow examination can be performed at the investigator's discretion at any visit. Bone marrow examination will be performed by unilateral trephine biopsy. No bone marrow aspiration will be performed.
23. Response evaluation will use the Modified Response Criteria for Malignant Lymphoma. All response results must be recorded in the electronic case report form. Response results by the investigator will be used to determine the eligibility and treatment practice. In addition, tumour assessment images will be evaluated centrally during Induction Study Period and Maintenance Study Period by an independent reviewer for reporting purposes. During the Follow-up period, tumour assessment images will be reviewed at the local level only. Response evaluation will be performed prior to Cycle 1 (Month 3; EOT2), Cycle 3 (Month 7), Cycle 6 (Month 13) and Cycle 9 (Month 19) and at the EOT3 visit in the Maintenance Study Period, and every 6 months during the Follow-up Period until treatment with new anticancer therapy or disease progression.
24. Pharmacokinetic (PK) samples will be collected at predose (before the study drug infusion within the day), and at 1 hour (±15 minutes) after completing the study drug infusion for each Induction Study Period cycle. At the EOT 1 and EOT 2 visits, PK samples will be obtained anytime during the day. Blood samples for PK analysis will be obtained at predose, and 1 hour (±15 minutes) after the end of study drug infusion (EOI) on Day 1 of Cycle 1 (Month 3) and Cycle 2 (Month 5) during the Maintenance Study Period. On Day 1 of Cycle 3 (Month 7), PK analysis will be obtained at predose. Testing will be performed at the central laboratory. Details of blood sampling schemes are provided in APPENDIX 2.

25. Blood samples for assessment of B-cell kinetics will be collected at predose (before the study drug infusion within the day) study drug on Day 1 of each treatment cycle in the Induction Study Period; at predose, and 1 hour after the end of infusion during Cycle 1 in the Induction Study Period. At the EOT1 and EOT2 visits, Pharmacodynamics samples will be obtained anytime during the day. In addition, blood samples for Pharmacodynamics analysis will be obtained at predose, and 1 hour after the end of study drug infusion on Day 1 of Cycle 1 (Month 3) and Cycle 2 (Month 5), at predose on Day 1 of Cycle 3 (Month 7) during Maintenance Study Period. Testing will be performed at the central laboratory.
26. Study drug (either CT-P10 or Rituxan), 375 mg/m^2 of BSA, will be administered on Day 1 of each cycle at 1 week intervals during Induction Study Period, and 8 weeks intervals during Maintenance Study Period. The first dose of study drug is to be administered at the same date with randomisation. Antipyretic (eg, paracetamol), antihistaminic (eg, H1 antihistamine), and glucocorticoid medications will be administered 30 minutes before each study drug infusion.
27. 12-lead ECG will be obtained within 42 days before the first drug administration, EOT1, prior to Cycle 1 (Month 3; EOT2), Cycle 3 (Month 7), Cycle 6 (Month 13), Cycle 9 (Month 19) and the EOT3 visit during the Maintenance Study Period. Additional vital signs including systolic and diastolic blood pressure, heart rate, respiratory rate, and body temperature (before beginning the study drug infusion on Day 1 of each cycle [within 15 minutes before the beginning of the study drug infusion], at the end of study drug infusion [within 15 minutes after the end of the study drug infusion], and 60 minutes [±15 minutes] after the end of the study drug infusion) will be assessed to monitor for possible hypersensitivity reactions. In addition, hypersensitivity should be monitored by routine continuous clinical monitoring including ECG (3-lead or 12-lead) monitoring 60 minutes (±15 minutes) after the end of the study drug infusion. Emergency equipment, such as adrenaline, antihistamines, corticosteroids, and respiratory support (including inhalational therapy, oxygen, and artificial ventilator), must be available.
28. Throughout the study, patients should be monitored for the clinical signs and symptoms of TB. Chest x-rays could also be used as a TB monitoring method. Patients with active TB will be excluded during the Screening Period. Chest x-rays for TB screening and clinical monitoring will be reviewed at the local level. Chest x-ray can be replaced by CT or proper image.
29. All medications used during the study, as well as all medications taken from the signed date of the ICF until 30 days after the last dose of study drug administration or an EOT Visit, whichever is longer, will be recorded.
30. Adverse events will be assessed from the date the informed consent form is signed until up to 30 days after the last dose of study drug or an EOT visit (whichever occurs later), regardless of the relationship to the study drug. The related AEs will be followed until resolution or improvement to baseline, relationship reassessed as unrelated, death, start of new anticancer therapy, confirmed by the investigator that no further improvement could be expected, no more collection of clinical or safety data, or final database closure. Adverse events of special interest (i.e. infusion-related reaction, infection and PML) should be closely monitored. Any SAEs experienced after 30 days of the last dose of study drug or an EOT visit (whichever occurs later), should only be reported if the investigator suspects a causal relationship to the study treatment.
31. Only for patients who sign a separate informed consent form for the biomarker assessment (genotypes). Blood samples for FcγR genotype (FcγRIIa, IIIa, and/or any necessary genotypes) will be collected after randomisation and before study drug administration on Day 1 of Cycle 1 during the Induction Study Period only. FcγR genotyping will be performed at the central laboratory.
32. β-2 microglobulin will be assessed within 14 days before the first drug administration, prior to Cycle 1 (Month 3; EOT2), Cycle 3 (Month 7), Cycle 6 (Month 13), Cycle 9 (Month 19) and the EOT3 visit during the Maintenance Study Period at the central laboratory. β-2 microglobulin assessments will be performed on the date of the planned visit. Testing will be performed at the central laboratory.
33. During the Follow-up Period, patients will be monitored every 6 months for disease status until treatment with new anticancer therapy or disease progression. Survival and salvage treatment (e.g., including chemotherapy, immunotherapy, surgery, or radiotherapy) will be monitored every 3 months until death or study termination. For patients with confirmed disease progression or treatment with new anticancer therapy, survival and salvage treatment may be followed up via the telephone contact.

‡ must be assessed within 14 days before the first administration of the study drug.

* Patients who experience progressive or unknown status of disease during the Induction Study Period will not be entered into the Maintenance Study Period and the assessment visit will be called the EOT2 visit. Patients who experienced CR, CRu, PR or SD in this assessment will qualify for the Maintenance Study Period and the assessment visit will be called the Maintenance 1 visit.

** If a study centre is not equipped to perform the specified tests, this will be discussed and arranged with the sponsor or the sponsor's designee.

APPENDIX 2: Sampling Times for Central Laboratory Analysis

Cycle	Week	Pharmaco-kinetic	Pharmaco-dynamic	Immuno-globulin	Immuno-genicity	Efficacy	β-2 micro-globulin	Tumour tissue/ CD20 lymphoma cell	Biomarker
Screening	-	-	-	-	-	Any time	Any time	Any time	-
Induction 1	1	Predose, after 1 hour	Predose, after 1 hour	Predose	Predose	-	-	-	Before infusion
Induction 2	2	Predose, after 1 hour	Predose	-	-	-	-	-	-
Induction 3	3	Predose, after 1 hour	Predose	-	-	-	-	-	-
Induction 4	4	Predose, after 1 hour	Predose	-	-	-	-	-	-
EOT 1	5	Anytime during the day	Anytime during the day	Anytime during the day	-	-	-	-	-
Maintenance 1 (EOT 2)	12 (M3)	Predose, after 1 hour (If EOT 2, anytime during the day)	Predose, after 1 hour (If EOT 2, anytime during the day)	Predose (If EOT 2, anytime during the day)	Predose (If EOT 2, anytime during the day)	Radiological assessment (Patient who is PD has to be excluded from the maintenance therapy)	Before infusion (If EOT 2, anytime during the day)	-	-
Maintenance 2	20 (M5)	Predose, after 1 hour	Predose, after 1 hour	Predose	-	-	-	-	-
Maintenance 3	28 (M7)	Predose	Predose	Predose	Predose	Radiological assessment	Before infusion	-	-

Cycle	Week	Pharmaco-kinetic	Pharmaco-dynamic	Immuno-globulin	Immuno-genicity	Efficacy	β-2 micro-globulin	Tumour tissue/ CD20 lymphoma cell	Biomarker
Maintenance 6	52 (M13)	-	-	-	Predose	Radiological assessment	Before infusion	-	-
Maintenance 9	76 (M19)	-	-	-	Predose	Radiological assessment	Before infusion	-	-
EOT 3	108 (M27)	-	-	-	Anytime during the day	Radiological assessment	Anytime during the day	-	-
Follow-Up	-	-	-	-	(First follow-up visit)	Every 6 months	-	-	-

Abbreviations: EOT = End of Treatment, M = month, PD = progressive disease

Notes:
Predose/Before infusion: before the study drug infusion within the day
After 1 hour: 1 hour (±15 minutes) after the end of the study drug infusion
If a patient discontinues from the study drug at EOT 2, blood sampling for PK, Pharmacodynamics, immunoglobulin, immunogenicity and β-2 microglobulin will be conducted any time during the EOT 2 visit.
Efficacy: Tumour assessment during the Induction/Maintenance Study Period will be reviewed by central laboratory for reporting purpose.
If patient is terminated within 6 months from Day 1 of Cycle 1 of Induction Study Period, immunogenicity should be assessed at EOT2 (Month 3), EOT3 and the first Follow-up visit

APPENDIX 3: Table of CTCAE Terms and Grades

CTCAE Term	Laboratory Parameter	Level	Grade 1	Grade 2	Grade 3	Grade 4
Anemia	Hemoglobin	Low	<LLN - 10.0 g/dL; <LLN - 100 g/L	<10.0 - 8.0 g/dL; <100 - 80g/L	<8.0 g/dL; <80 g/L;	-
Alanine aminotransferase increased	Alanine Aminotransferase (ALT)	High	>ULN - 3.0 x ULN	>3.0 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN
Alkaline phosphatase increased	Alkaline phosphatase	High	>ULN - 2.5 x ULN	>2.5 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN
Aspartate aminotransferase increased	Aspartate Aminotransferase (AST)	High	>ULN - 3.0 x ULN	>3.0 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN
Blood bilirubin increased	Total Bilirubin	High	>ULN - 1.5 x ULN	>1.5 - 3.0 x ULN	>3.0 - 10.0 x ULN	>10.0 x ULN
Creatinine increased[1]	Creatinine	High	>1 - 1.5 x baseline; >ULN - 1.5 x ULN	>1.5 - 3.0 x baseline; >1.5 - 3.0 x ULN	>3.0 baseline; >3.0 - 6.0 x ULN	>6.0 x ULN
Hemoglobin increased[1]	Hemoglobin	High	Increase in >0 - 2 gm/dL above ULN or above baseline if baseline is above ULN	Increase in >2 - 4 gm/dL above ULN or above baseline if baseline is above ULN	Increase in >4 gm/dL above ULN or above baseline if baseline is above ULN	-
Hypercalcemia	Calcium	High	>ULN - 11.5 mg/dL; >ULN - 2.9 mmol/L	>11.5 - 12.5 mg/dL; >2.9 - 3.1 mmol/L	>12.5 - 13.5 mg/dL; >3.1 - 3.4 mmol/L	>13.5 mg/dL; >3.4 mmol/L
Hyperkalemia	Potassium	High	>ULN - 5.5 mmol/L	>5.5 - 6.0 mmol/L	>6.0 - 7.0 mmol/L	>7.0 mmol/L
Hypernatremia	Sodium	High	>ULN - 150 mmol/L	>150 - 155 mmol/L	>155 - 160 mmol/L;	>160 mmol/L

Hyperuricemia	Uric Acid	High	>ULN - 10 mg/dL (0.59 mmol/L) without physiologic consequences	-	>ULN - 10 mg/dL (0.59 mmol/L) with physiologic consequences	>10 mg/dL; >0.59 mmol/L
Hypoalbuminemia	Albumin	Low	<LLN - 3 g/dL; <LLN - 30 g/L	<3 - 2 g/dL; <30 - 20 g/L	<2 g/dL; <20 g/L	-
Hypocalcemia	Calcium	Low	<LLN - 8.0 mg/dL; <LLN - 2.0 mmol/L	<8.0 - 7.0 mg/dL; <2.0 - 1.75 mmol/L	<7.0 - 6.0 mg/dL; <1.75 - 1.5 mmol/L	<6.0 mg/dL; <1.5 mmol/L
Hypoglycemia	Glucose	Low	<LLN - 55 mg/dL; <LLN - 3.0 mmol/L	<55 - 40 mg/dL; <3.0 - 2.2 mmol/L	<40 - 30 mg/dL; <2.2 - 1.7 mmol/L	<30 mg/dL; <1.7 mmol/L
Hypokalemia	Potassium	Low	<LLN - 3.0 mmol/L	<LLN - 3.0 mmol/L	<3.0 - 2.5 mmol/L	<2.5 mmol/L
Hyponatremia	Sodium	Low	<LLN - 130 mmol/L	-	<130 - 120 mmol/L	<120 mmol/L
Neutrophil count decreased	Total Neutrophils	Low	<LLN - 1500/mm3; <LLN - 1.5 x 10e9 /L	<1500 - 1000/mm3; <1.5 - 1.0 x 10e9 /L	<1000 - 500/mm3; <1.0 - 0.5 x 10e9 /L	<500/mm3; <0.5 x 10e9 /L
Platelet count decreased	Platelet count	Low	<LLN - 75,000/mm3; <LLN - 75.0 x 10e9 /L	<75,000 - 50,000/mm3; <75.0 - 50.0 x 10e9 /L	<50,000 - 25,000/mm3; <50.0 - 25.0 x 10e9 /L	<25,000/mm3; <25.0 x 10e9 /L
White blood cell decreased	White Blood Cells	Low	<LLN - 3000/mm3; <LLN - 3.0 x 10e9 /L	<3000 - 2000/mm3; <3.0 - 2.0 x 10e9 /L	<2000 - 1000/mm3; <2.0 - 1.0 x 10e9 /L	<1000/mm3; <1.0 x 10e9 /L

Note: The LLN and ULN values will be the normal ranges as provided by the local laboratory at each relevant transfer.

1 The most severe grade is counted if the CTCAE grade is discrepant by multiple definitions

APPENDIX 4: List of Inclusion and Exclusion Criteria which has Impact on Efficacy Analysis

Criteria No.		Criteria
Inclusion Criteria	#2	Patient has histologically confirmed CD20+ FL grade 1 to 3a according to the World Health Organization 2008 classification (Jaffe et al 2009); biopsy within 6 months before the first administration of the study drug.
	#3	Patient has at least 1 measurable tumour mass in 2 dimensions, and the mass must be: • Nodal lesion >15 mm in the longest dimension; or • Nodal lesion >10 mm to ≤15 mm in the longest dimension and >10 mm in the shortest dimension; or • Extranodal lesion with both long and short dimensions ≥10 mm.
	#4	Patient has Ann Arbor stage II, III, or IV disease.
	#5	Patient has low tumour burden, defined as based on Groupe d'Etudes des Lymphomes Folliculaires (GELF) criteria: • No B symptoms, • LDH < upper limit of normal (ULN), • Largest nodal or extra mass < 7 cm, • < 3 nodal sites with a diameter ≥3 cm, • No significant serous effusions detectable clinically or on CT (small, clinically non-evident effusions on CT scan are not deemed significant), • Spleen ≤16 cm by CT, and • No clinical organ failure or organ compression (e.g. ureteric obstruction)

	#6	Patient has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1 (Oken et al 1982).
Exclusion Criteria	#1	Patient has received rituximab (or a rituximab proposed biosimilar product).
	#3	Patient has evidence of histological transformation to high-grade or diffuse large B-cell lymphoma.
	#4	Patient has known central nervous system involvement or any evidence of spinal cord compression by lymphoma.
	#5	Patient has received previous treatment for NHL: • Previous treatment including chemotherapy, radiotherapy, immunotherapy, and/or surgery (except previous biopsy). • All doses of corticoid therapy for treatment of NHL. • Corticoid therapy within 4 weeks before the first administration of the study drug, with prednisone >20 mg per day (or equivalent doses of other steroid medications) for any purpose except NHL.
	#9	Patient has any malignancy other than NHL, except adequately treated squamous or basal cell carcinoma of the skin or cervical carcinoma in situ, within the 5 years before the first administration of the study drug.
	#10	Patient has a current or recent treatment (within 42 days before the first administration of the study drug or 5 times the half-life, whichever is longer, prior to screening) with any other investigational medicinal product or device.

APPENDIX 5: Rule of combining Preferred Terms

SOC	PT	Combined PT
Gastrointestinal disorders	Abdominal pain Abdominal pain lower Abdominal pain upper	Abdominal pain
Infections and infestations	Abscess oral Subcutaneous abscess	Abscess
Blood and lymphatic system disorders	Anaemia Iron deficiency anaemia	Anaemia
Psychiatric disorders	Anxiety Anxiety disorder Anxiety disorder due to a general medical condition	Anxiety
Musculoskeletal and connective tissue disorders	Arthritis reactive Arthritis	Arthritis
Infections and infestations	Bacterial vaginosis Vaginitis bacterial	Bacterial vaginosis
Infections and infestations	Asymptomatic bacteriuria Bacteriuria	Bacteriuria
Cardiac disorders	Bradycardia	Bradycardia

	Sinus bradycardia	
Cardiac disorders	Cardiac failure Cardiac failure chronic	Cardiac failure
General disorders and administration site conditions	Chest pain Non-cardiac chest pain	Chest pain
Hepatobiliary disorders	Bile duct stone Cholelithiasis	Cholelithiasis
Infections and infestations	Conjunctivitis Conjunctivitis bacterial	Conjunctivitis
Respiratory, thoracic and mediastinal disorders	Cough Productive cough	Cough
Skin and subcutaneous tissue disorders	Dermatitis Dermatitis allergic Dermatitis atopic Stasis dermatitis Dermatitis contact Seborrhoeic dermatitis Solar dermatitis	Dermatitis
Metabolism and nutrition disorders	Diabetes mellitus	Diabetes mellitus

	Type 2 diabetes mellitus Type 1 diabetes mellitus	
Skin and subcutaneous tissue disorders	Drug eruption Toxic skin eruption	Drug eruption
Skin and subcutaneous tissue disorders	Dyshidrotic eczema Eczema Eczema nummular	Eczema
Injury, poisoning and procedural complications	Ankle fracture Facial bone fracture Femur fracture Foot fracture Hand fracture Humerus fracture Lower limb fracture Lumbar vertebral fracture Rib fracture Tibia fracture Tooth fracture Ulna fracture	Fracture

	Upper limb fracture Wrist fracture Patella fracture	
Infections and infestations	Fungal infection Fungal skin infection Genital infection fungal Oral candidiasis Oral fungal infection Vulvovaginal candidiasis Balanitis candida Aspergillus infection Onychomycosis	Fungal infection
Nervous system disorders	Headache Tension headache	Headache
Infections and infestations	Helicobacter gastritis Helicobacter infection	Helicobactor infection
Infections and infestations	Herpes simplex Herpes zoster Oral herpes	Herpes virus infection

	Genital herpes simplex	
Metabolism and nutrition disorders	Glucose tolerance impaired Hyperglycaemia Impaired fasting glucose	Hyperglycaemia
Immune system disorders	Drug hypersensitivity Hypersensitivity	Hypersensitivity
General disorders and administration site conditions	Catheter site pain Injection site haematoma Injection site pain Puncture site pain	Injection site reaction
Injury, poisoning and procedural complications	Chest injury Cartilage injury Craniocerebral injury Concussion Contusion Eye contusion Fall Injury Limb injury	Injury

	Meniscus injury Skin injury Tendon rupture Wound Bone contusion Back injury Ear injury Limb crushing injury Muscle injury Muscle rupture Radiation skin injury Skin abrasion Laceration	
Musculoskeletal and connective tissue disorders	Intervertebral disc disorder Intervertebral disc protrusion	Intervertebral disc disorder
Infections and infestations	Bacterial infection Localised infection Pulpitis dental Skin infection	Localised infection

	Tooth infection Tonsillitis bacterial Staphylococcal infection Eczema infected Nail infection Infected dermal cyst	
Infections and infestations	Bronchiolitis Bronchitis Lower respiratory tract infection Lung infection Respiratory tract infection Respiratory tract infection viral	Lower respiratory tract infection
Nervous system disorders	Neuropathy peripheral Peripheral sensory neuropathy Toxic neuropathy	Neuropathy peripheral
General disorders and administration site conditions	Face oedema Generalised oedema Localised oedema Oedema peripheral	Oedema

	Peripheral swelling Swelling	
Infections and infestations	Otitis externa Otitis media Otitis media acute Otosalpingitis	Otitis
Infections and infestations	Pneumocystis jirovecii pneumonia Atypical mycobacterial pneumonia Pneumonia	Pneumonia
Skin and subcutaneous tissue disorders	Pruritus Pruritus generalised Pruritus allergic	Pruritus
Skin and subcutaneous tissue disorders	Rash Rash erythematous Rash generalised Rash macular Rash maculo-papular Rash pruritic	Rash
Infections and infestations	Rhinitis	Rhinitis

	Viral rhinitis	
Infections and infestations	Acute sinusitis Sinusitis Sinusitis bacterial	Sinusitis
Gastrointestinal disorders	Mouth ulceration Stomatitis Aphthous ulcer	Stomatitis
Cardiac disorders	Sinus tachycardia Supraventricular tachycardia Tachycardia Ventricular tarchycardia	Tachycardia
Infections and infestations	Body tinea Tinea capitis Tinea infection Tinea pedis	Tinea infection
Infections and infestations	Laryngitis Nasopharyngitis Pharyngitis Pharyngitis bacterial	Upper respiratory tract infection

	Viral pharyngitis Pharyngotonsillitis Tonsillitis Tracheitis Tracheobronchitis Sinobronchitis Upper respiratory tract infection Viral upper respiratory tract infection Upper respiratory tract infection bacterial	
Infections and infestations	Cystitis Urinary tract infection Urethritis	Urinary tract infection
Skin and subcutaneous tissue disorders	Mechanical urticaria Urticaria	Urticaria
Vascular disorders	Venous thrombosis Venous thrombosis limb Jugular vein thrombosis	Venous thrombosis
Ear and labyrinth disorders	Vertigo Vertigo positional	Vertigo

Infections and infestations	Gastrointestinal viral infection Gastroenteritis viral Gastroenteritis norovirus	Gastroenteritis viral
Nervous system disorders	Dizziness Dizziness postural	Dizziness
Nervous system disorders	Dysaesthesia Paraesthesia	Paraesthesia
Respiratory, thoracic and mediastinal disorders	Oropharyngeal pain Oropharyngeal discomfort	Oropharyngeal pain
Nervous system disorders	Anosmia Hyposmia	Anosmia
Gastrointestinal disorders	Intestinal polyp Large intestine polyp	Intestinal polyp
Hepatobiliary disorders	Cholecystitis Cholecystitis chronic	Cholecystitis
Musculoskeletal and connective tissue disorders	Tenosynovitis Tenosynovitis stenosans	Tenosynovitis
Psychiatric disorders	Depressed mood Depression	Depression

	Depressive symptom	
Renal and urinary disorders	Calculus ureteric Calculus urinary	Calculus ureteric