STATISTICAL ANALYSIS PLAN

Study: CIDP01

Product: rozanolixizumab

A MULTICENTER, RANDOMIZED, SUBJECT-BLIND, INVESTIGATOR BLIND, PLACEBO-CONTROLLED, PARALLEL-GROUP STUDY EVALUATING THE EFFICACY, SAFETY, AND TOLERABILITY OF ROZANOLIXIZUMAB IN SUBJECTS WITH CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY (CIDP)

SAP/Amendment Number	Date
Final SAP 3.0	08 Apr 2021

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LIST OF ABBREVIATIONS

[redacted]	[redacted]
ADaM	Analysis Dataset Model
AE	Adverse event
AEoF	Adverse event of focus
ALC	Absolute lymphocyte count
ALP	Alkaline phosphatase
ALQ	Above the limit of quantification
ALT	Alanine aminotransferase
ANC	Absolute neutrophil count
ANCOVA	Analysis of covariance
AST	Aspartate aminotransferase
AUC	Area under the curve
BLQ	Below the limit of quantification
BMI	Body mass index
BP	Blood pressure
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence interval
CIDP	Chronic inflammatory demyelinating polyradiculoneuropathy
COVID-19	Coronavirus Disease of 2019
Cmax	Maximum concentration
CRO	Contract research organization
CTCAE	Common Terminology Criteria for Adverse Events
CSP	Clinical study protocol
CSR	Clinical study report
C-SSRS	Columbia Suicide Severity Rating Scale
CV	Coefficient of variation
DBP	Diastolic blood pressure
DEM	Data evaluation meeting
DMC	Data Monitoring Committee
DNA	Deoxyribonucleic acid
ECG	Electrocardiogram
eCRF	Electronic Case Report form
EFNS	European Federation of Neurological Societies
ES	Enrolled Set
EudraCT	European Union Drug Regulating Authorities Clinical Trials
FAS	Full Analysis Set

FCS	Fully conditional specification
FDA	Food and Drug Administration
FV	Final Visit
geoCV	Geometric coefficient of variation
geoMean	Geometric mean
GGT	Gamma glutamyltransferase
HDL	High density lioprotein
HIV	Human immunodeficiency virus
HLT	High level term
hsCRP	High sensitivity C-reactive protein
ICH	International Council for Harmonisation
Ig	Immunoglobulin
IgA	Immunoglobulin A
IgE	Immunoglobulin E
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IGRA	Interferon-gamma release assay
IMP	Investigational medicinal product
INCAT	Inflammatory Neuropathy Cause and Treatment
IPD	Important protocol deviation
iRODS	Inflammatory Rasch-built Overall Disability Scale
IVIg	Intravenous immunoglobulin
LDH	Lactate dehydrogenase
LDL	Low density lipoprotein
LLOQ	Lower limit of quantification
LOCF	Last observation carried forward
logit	Log odds unit
LS	Least square
MA	Markedly abnormal
MAR	Missing at random
MCID-SE	Minimum clinically important differences-standard error
MedDRA	Medical Dictionary for Regulatory Activities
MFAS	Modified full analysis set
MMRM	Mixed model repeated measures
MNAR	Missing not at random
MRC	Medical Research Council
MRD	Minimum required dilution

n	Number of participants
NF-L	Neurofilament light chain
OLE	Open-Label Extension
PD	Pharmacodynamic
PDILI	Potential drug-induced liver injury
PD-PPS	Pharmacodynamic Per-Protocol Set
PEOT	Premature end of treatment
PGIC	Patient Global Impressions of Change
PGIS	Patient Global Impressions of Severity
PK	Pharmacokinetic
PK-PPS	Pharmacokinetic Per-Protocol Set
PNS	Peripheral Nerve Society
PPS	Per-Protocol Set
PT	Preferred term
QTcF	QT corrected for heart rate using Fridericia's formula
RBC	Red blood cell
RNA	Ribonucleic acid
RT-MRC	Rasch-built, modified interval Medical Research Council scale
RS	Randomized Set
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SBP	Systolic blood pressure
sc	Subcutaneous
SCIg	Subcutaneous immunoglobulin
SD	Standard deviation
SE	Standard error
SOC	System organ class
SS	Safety Set
TEAE	Treatment-emergent adverse event
TFLs	Tables, figures and listings
ULN	Upper limit of normal
USA	United States of America
WBC	White blood cell
WHODD	World Health Organization Drug Dictionary

1 INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to provide all information that is necessary to perform the required statistical analyses of study CIDP01. It also defines the summary tables, figures and listings (TFLs) to be included in the final Clinical Study Report (CSR) according to the protocol.

This final analysis SAP is based upon, and assumes familiarity, with the following documents:

- Protocol Amendment 1: 15 Nov 2018
- Protocol Amendment 2: 09 Jul 2019
- Adverse Events of Focus (AEoF) for the rozanolixizumab Program: v1.3, 04 Aug 2020

Unless specified below, the study will be analyzed as described in the most recent version of the protocol (European Union Drug Regulating Authorities Clinical Trials [EudraCT]-Number: 2016-002411-17).

If a future protocol amendment necessitates a substantial change to the statistical analysis of the study data, this SAP may be amended accordingly. If, after database lock, additional analyses are required to supplement the planned analyses described in this SAP, those unplanned analyses will not be described in an amended SAP but they will be described in a separate statistical analysis plan. However, if analysis definitions have to be modified or updated, a SAP amendment will be required. The content of this SAP is compatible with the International Council for Harmonisation (ICH)/Food and Drug Administration (FDA) E9 Guidance documents.

UCB is the Sponsor and PAREXEL is the Contract Research Organization (CRO) for this study.

2 PROTOCOL SUMMARY

2.1 Study objectives

2.1.1 Primary objective

The primary objective of the study is:

- To evaluate the clinical efficacy of rozanolixizumab as a treatment for subjects with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)

2.1.2 Secondary objectives

The secondary objectives of the study are:

- To evaluate the safety and tolerability of rozanolixizumab subcutaneous (sc) infusion in subjects with CIDP
- To assess the pharmacodynamic (PD) effect of rozanolixizumab as measured by the total immunoglobulin G (IgG) concentrations in serum

2.1.3 Exploratory objectives

Exploratory objectives are:

- To evaluate the effects of rozanolixizumab on the concentration of total protein, albumin, α- and β-globulins, IgG subclasses, immunoglobulin M (IgM), immunoglobulin A (IgA), and immunoglobulin E (IgE), serum and plasma complement levels

- To evaluate the incidence and emergence of [redacted] with respect to immunogenicity and pharmacokinetic (PK) and PD
- To evaluate the effect of rozanolixizumab on complement and cytokines
- To assess the plasma concentrations of rozanolixizumab administered by sc infusion
- To assess the PD effect of rozanolixizumab as measured by neurofilament light chain (NF-L) in serum
- To assess the effect of rozanolixizumab on gene and protein expression, and explore the relationship between deoxyribonucleic acid (DNA), ribonucleic acid (RNA), protein, and metabolite biomarkers and cause, progression, and appropriate treatment of CIDP
- To assess the effect of rozanolixizumab on CIDP-specific auto-antibody levels
- To assess the effect of rozanolixizumab on vaccine antibody levels ([redacted]s)

2.2 Study variable(s)

2.2.1 Efficacy variable

2.2.1.1 Primary efficacy variable

The primary efficacy variable is the:

- Change from Baseline to Week 13 (Day 85) in inflammatory Rasch-built Overall Disability Scale (iRODS) score

2.2.1.2 Other efficacy variable

Preliminary definitions linked to assessment of relapse:

- **CIDP relapse (iRODS)** is defined as a clinically important deterioration from Baseline in iRODS score, ie, a MCID-SE of ≤-1.96
- **CIDP relapse (adjusted Inflammatory Neuropathy Cause and Treatment, INCAT)** is defined as an increase from Baseline of at least 1 point in the adjusted INCAT score. The adjusted score is identical to the INCAT disability score except for the exclusion of changes in upper limb function from 0 (normal) to 1 (minor symptoms) or from 1 to 0
- **CIDP relapse (maximum grip strength as assessed by site personnel)** is defined as a clinically important deterioration from Baseline in grip strength as measured by site personnel, ie, a decline of >14kPa

Other efficacy variables will include:

- Subject experienced **CIDP relapse (iRODS)** up to Week 13 (Day 85) after first treatment
- Time to **CIDP relapse (iRODS)** during the Treatment Period
- Values and change from Baseline in iRODS scores at each scheduled assessment during the Treatment and Observation Periods
- Subject experienced **CIDP relapse (adjusted INCAT)** up to Week 13 (Day 85) after first treatment
- Time to **CIDP relapse (adjusted INCAT)** during the Treatment Period
- Values and change from Baseline in adjusted INCAT score at each scheduled assessment during the Treatment and Observation Periods

- Subject experienced **CIDP relapse (maximum grip strength as assessed by site personnel)** up to Week 13 (Day 85) after first treatment
- Time to **CIDP relapse (maximum grip strength as assessed by site personnel)** during the Treatment Period
- Values and change from Baseline in maximum grip strength score (maximum of 3 assessments) taken by site personnel at each scheduled assessment during the Treatment and Observation Periods
- Values and change from Baseline in daily maximum grip strength score (maximum of 3 assessments) taken by the subject at the same time each day during the Treatment and Observation Periods
- Values and change from Baseline in Rasch-built, modified interval Medical Research Council scale (RT-MRC) sum score at each scheduled assessment during the Treatment and Observation Periods
- Values and change from Baseline in fatigue at each scheduled assessment during the Treatment and Observation Periods
- Values and change from Baseline in CIDP patient reported outcome (PRO) instrument at each scheduled assessment during the Treatment and Observation Periods
- Values and change from Baseline in Patient Global Impressions of Severity (PGIS) at each scheduled assessment during the Treatment and Observation Periods
- Patient Global Impressions of Change (PGIC) at each scheduled assessment during the Treatment and Observations Periods
- Subjects receiving rescue medication during Treatment Period
- Time to rescue medication administration during Treatment Period

2.2.2 Other variables

2.2.2.1 Pharmacokinetic variable

The PK variable is:

- Plasma concentration of rozanolixizumab at each scheduled assessment during the Treatment Period

2.2.2.2 Pharmacodynamic variables

The PD variables are:

- Minimum value and maximum decrease (absolute and percentage) from Baseline in total serum IgG concentration during the study
- Value and change (absolute and percentage) from Baseline in total serum IgG concentrations at each scheduled assessment during Treatment and Observation Periods
- Value and change (absolute and percentage) from Baseline in serum IgG subclass concentrations at each scheduled assessment during Treatment and Observation Periods
- Value and change (absolute and percentage) from Baseline in NF-L levels at each scheduled assessment during Treatment and Observation Periods

2.2.2.3 Exploratory pharmacogenetics variables

The exploratory pharmacogenetics variables are:

- Genetic and epigenetic changes that may be measured to understand the cause, progression, and appropriate treatment of CIDP

2.2.2.4 Exploratory RNA, proteins, and metabolites variables

The exploratory RNA, proteins, and metabolites variables are:

- RNA, proteins, and metabolites changes that may be measured to understand the cause, progression, and appropriate treatment of CIDP
- Exploratory biomarkers such as but not limited to [redacted]
- Change from Baseline relating to mechanism of action, disease activity, treatment response, and clinical outcome at each scheduled assessment during the Treatment and Observation Periods

These variables are not in scope of this analysis and reported separately.

2.2.3 Immunological variables

The immunological variables are:

- Values and change from Baseline in serum immunoglobulin concentrations (total IgA, IgE, and IgM) at each scheduled assessment during Treatment and Observation Periods
- Values and change from Baseline in serum complement levels (C3 and C4) and plasma complement levels (C3a and C5a) at each scheduled assessment during Treatment Period
- [redacted] status (negative or confirmed positive) and the confirmed positive titer at each scheduled assessment during Treatment and Observation Periods
- Values and change from Baseline in cytokines at each scheduled assessment during Treatment and Observation Periods
- Change in CIDP-specific auto-antibody levels in serum from Baseline during Treatment and Observation Periods (This variable is not in scope of this analysis and reported separately.)
- Values and change from Baseline in [redacted] during Treatment and Observation Periods

2.2.4 Safety variables

The safety variables for the study are:

- Occurrence of treatment-emergent adverse events (TEAEs)
- TEAEs leading to withdrawal of investigational medicinal product (IMP)
- Vital sign values and changes from Baseline (systolic and diastolic blood pressure (BP), temperature, pulse rate, and body weight) at each scheduled assessment during Treatment and Observation Periods
- 12-lead electrocardiogram (ECG) values and change from Baseline at each scheduled assessment during Treatment and Observation Periods

- Laboratory values and changes from Baseline at each scheduled assessment during Treatment and Observation Periods (hematology, clinical chemistry and urinalysis)
- Tuberculosis Signs and Symptoms Questionnaire at each scheduled assessment during Treatment and Observation Periods
- Values and change from Baseline in concentrations of total protein, albumin, α- and β-globulins at each scheduled assessment during Treatment and Observation Periods
- Serum and urine pregnancy
- Columbia Suicide Severity Rating Scale (C-SSRS)
- Headache questionnaire

2.3 Study design and conduct

This is a Phase 2A, multicenter, randomized, subject-blind, investigator-blind, placebo-controlled, parallel-group study evaluating the efficacy, safety, and tolerability of rozanolixizumab for treatment of subjects with CIDP. Eligible subjects will be adults who have a confirmed diagnosis of definite or probable CIDP according to the European Federation of Neurological Societies (EFNS)/ Peripheral Nerve Society (PNS) criteria for CIDP, have been shown to be dependent on treatment with immunoglobulin and who have remained on a stable dosing regimen of immunoglobulin therapy for at least 4 months prior to Screening.

- Treatment Arm 1: rozanolixizumab [redacted]
- Treatment Arm 2: placebo sc [redacted]

Subjects will be randomized in a ratio of 1:1 to the 2 treatment arms. The randomization will take place on the day of first treatment with investigational medicinal product (IMP). The randomization will be stratified according to previous route of administration for Ig treatment (ie, subcutaneous immunoglobulin (SCIg) and intravenous immunoglobulin (IVIg)).

The dose level of [redacted] may be reduced to [redacted] (or equivalent placebo) for an individual subject based on their tolerability.

The study consists of:

- Screening Period of between 2 and 5 weeks duration
- The 11-week Treatment Period
- The 12-week Observation Period (from 1 week up to maximum 24 weeks):
  - All subjects completing the Treatment Period (ie, all visits up to Visit 17 performed without a CIDP relapse) will be offered the possibility to enter in the Open-Label Extension (OLE) study, CIDP04, and be treated with rozanolixizumab. If they enter in the OLE, Visit 17 will be the last study visit. The Observation Period will be limited to 1 week for these subjects.

    In all other instances the subjects will perform Visits 18 to 21 for efficacy and for safety assessments. Subjects will either return to the clinic/hospital, or, if possible and agreed by both investigator and subject, have home visits conducted by certified healthcare professionals for Visits 18 and 20.

- For subjects who complete the Treatment Period without relapse but choose not to enter the OLE directly and wish to first test whether they still need treatment, they will continue the Observation Period without standard of care treatment.
- Subjects who do not wish to enter the OLE or test whether they still need treatment after having successfully completed the Treatment Period also have the opportunity to return immediately to standard of care for the duration of the Observation Period.
- All other subjects (ie, having relapsed or withdrawn from the study during Treatment Period) will complete the Observation Period. Subjects can return to their standard of care for the duration of the Observation Period.
- Stabilization: If the subject relapses during the Treatment Period or Observation Period (according to the medical judgement of the investigator supported by eg, subject's score on iRODS, Inflammatory Neuropathy Cause and Treatment (INCAT), or maximum grip strength [assessed by site personnel]), the subject will return to the standard of care (ie, Ig treatment) as rescue medication at the time of relapse and will be stabilized over a period ranging from 2 weeks up to maximum 12 weeks starting from relapse visit (eg, premature end of treatment (PEOT) [Visit 17] or later visit).

During the stabilization, visits should be performed every 1 to 3 weeks at the discretion of the investigator until the subject is stabilized. The stabilization may extend the Observation Period duration up to a maximum of 24 weeks after the last IMP dose.
At the end of the stabilization:

1. A subject who completes the Treatment Period without a CIDP relapse will be offered the possibility to enter in the OLE (CIDP04) and be treated with rozanolixizumab from that moment onwards. The subject will complete the Final Visit (FV) (V21) and enter the OLE on the same day.
2. A subject who completes the Treatment Period and does not wish to enter the OLE (CIDP04) will continue their standard of care treatment after stabilization and the stabilization visit schedule (every 1 to 3 weeks) until they have a follow-up of 12 weeks after last IMP dose. The subject will complete the FV (V21) and enter the OLE on the same day.
3. A subject who relapses during Treatment Period will continue their standard of care treatment after stabilization. They will continue the stabilization visit schedule (every 1 to 3 weeks) until they have a follow-up of 12 weeks after last IMP dose. The subject will complete the FV (V21) and end CIDP01 study participation. These subjects will be offered entry into CIDP04 only once CIDP01 study results are available, after the blind has been broken at the end of the study, and it was confirmed they received placebo.

Access to the OLE (CIDP04) is allowed for subjects completing the Treatment Period without relapse/withdrawal. Entry can occur immediately upon completion of the Treatment Period or after stabilization in case the subject relapsed during Observation Period and did not meet withdrawal criteria other than relapse. Subjects who relapse during the Treatment Period will have the opportunity to enter the OLE once all subjects have completed the study, the study is unblinded, and key results are available. In this case, only the subjects from the placebo arm will be allowed to enter the OLE study.

Further details regarding the study design are provided in Section 5 of the clinical study protocol (CSP).

2.4 Determination of sample size

Due to the pilot character of the study, the sample size is chosen based on both the statistical considerations and practical limitations (eg, to recruit sufficient subjects in a reasonable time to achieve the objectives of the study) and to establish whether a positive trend towards active treatment can be established. For this reason, a one-sided exploratory test is considered appropriate in this setting.

Since no data is currently publicly available on the primary outcome measure in this indication, the sample size is based on assumptions about the likely effect size. Thus, the sample size considerations are only based on assumptions for the effect size index (difference in group means/SD). When the sample size in each group is 15, a 1-sided 5.0% t-test for the comparison of rozanolixizumab and placebo will provide 80% power to detect a statistically significant difference in case there is a large effect of rozanolixizumab with an effect size index of 0.93. In case of a medium index (0.52) the power already decreases to 40%. It will be assumed that 10% of the randomized subjects cannot be utilized for the efficacy analysis; hence 34 subjects will be randomized.

3 DATA ANALYSIS CONSIDERATIONS

3.1 General presentation of summaries and analyses

Statistical evaluation for the final analyses will be performed by PAREXEL. The Analysis Dataset Model (ADaM) will adhere to Clinical Data Interchange Standards Consortium (CDISC) guidance documents and follow their UCB interpretation.

All analyses will be performed using SAS version 9.4 or higher (SAS Institute, Cary, North Carolina, USA). Continuous variables will be summarized by treatment group (Placebo and rozanolixizumab) and visit (where applicable) with the statistics mean, standard deviation (SD), median, minimum, and maximum. Categorical variables will be summarized by treatment group and visit (where applicable) with frequency counts and percentages. Geometric coefficient of variation (geoCV), geometric mean (geoMean) and 95% Confidence Interval (CI) for the geoMean will also be presented in the descriptive statistics for the PK concentration.

When reporting relative frequencies or other percentage values, the following rules apply:

- For values where all participants fulfill certain criteria, the percentage value will be displayed as 100
- For values where the absolute frequency is zero, there will be no percentage displayed at all
- All other percentage displays will use 1 decimal place
- Percentages displayed based on continuous data (eg, percentage changes from baseline) will be displayed to 1 decimal place.

When reporting descriptive statistics, the following rules will apply in general:

- n will be an integer
- Mean (arithmetic and geometric), SD and median will use 1 decimal place more than the original data
- Coefficient of variation and geoCV will be reported as a percentage to 1 decimal place
- Minimum and maximum will be reported using the same number of decimal places as the original value

- If no participants have data at a given timepoint, for example, then only n=0 will be presented. If n<3, then only n, minimum and maximum will be presented. If n=3, then only n, mean, median, minimum and maximum will be presented. The other descriptive statistics will be left blank.

Analyses will be performed by treatment group and for all participants where stated. The treatment groups will be displayed as follows in the TFLs:

- Treatment group 1: Placebo
- Treatment group 2: Rozanolixizumab

Participants with the reduced dose due to tolerability issues will be mapped under the same treatment groups. These participants will be flagged in the listings. For the Observation period the same treatment groups will be displayed.

Data listings containing all documented data and all calculated data, as required for the variables and analysis applicable to the final analyses, will be generated.

The visit type information (home or site visit) will be included into the listings.

3.2 General study level definitions

3.2.1 Analysis time points

3.2.1.1 Relative day

Relative day for an event will be derived with the date of the first sc infusion of IMP as reference.

Relative days for an event of measurement occurring before the date of first sc infusion are calculated as follows:

Relative Day = [(Event Date – Date of First Infusion)]

For events or measurements occurring before the date of the first sc infusion, relative day will be prefixed with '-' in the data listings.

The relative day for an event or measurement occurring on or after the reference date to the date of the last infusion is calculated as follows:

Relative Day = [(Event Date - Date of First Infusion) + 1]

For events or measurements occurring after the date of the last sc infusion, relative day will be prefixed with '+' in the data listings and will be calculated as follows:

Relative Day = + [(Event Date – Date of Last Infusion)]

There is no relative Day 0. Relative day is not calculated for partial dates in cases where relative day is shown in a participant data listing. In such cases, relative day should be presented as '- -' in the participant data listings.

3.2.2 Study periods

The total duration of the study per subject is approximately 28 weeks (up to maximum 40 weeks), consisting of:

- Screening Period of a minimum of 2 to a maximum of 5 weeks starting with Screening Visit (to occur between Day -35 and Day -14, both inclusive).

- Treatment Period (11 weeks) – from first dose of IMP to last dose of IMP. The first treatment with IMP will occur at the Randomization Visit (Visit 2) and the dosing should occur as seamlessly as possible to continue the momentum of the Baseline therapy.
- Observation Period (12 weeks up to 24 weeks) starting day after last IMP dose until study end.

In case of early withdrawal, the duration of the Treatment Period may be shortened depending on the time to withdrawal. The Observation Period may be shortened to 1 week in case a subject completes the Treatment Period and enters the OLE study immediately. In case a subject relapses during the Observation Period, the subject will be stabilized over a period of minimum 2 weeks up to 12 weeks, possibly extending the Observation Period to a maximum of 24 weeks.

The end of the study is defined as the date of the last visit of the last subject in the study.

3.3 Definition of Baseline values

Baseline will be the last available pre-dose value prior to the first infusion of study drug in the Treatment Period, or if missing, the Screening values. Assessments with the same date as the first infusion, for which time was not planned to be captured, can be acceptable as Baseline assessments. Scheduled or unscheduled measurements can be used as the Baseline value. Expected measurement-specific Baseline timepoints are presented in Table 3–1. If an unscheduled measurement occurs after the planned baseline measurement timepoint but before dosing, then the unscheduled measurement will be used.

Table 3–1: Expected Baseline

Measurement	Definition of Baseline
Safety data: • Safety Lab (Clinical chemistry, Hematology, hsCRP, Urinalysis) • ECG • Vital signs • Total protein, albumin, α- and β-globulins	Safety labs, vital signs, total protein, albumin, α- and β-globulin: Baseline visit (Day 1), if missing Screening visit. Pre-dose value at Baseline visit will be used for the vital signs. ECG: mean of triplicate values of Baseline visit. If missing Baseline visit (Day 1), mean of triplicate values of Screening visit.
Efficacy data: • iRODS • INCAT • Grip strength (assessed by site personnel and patient reported) • RT-MRC and original MRC • Fatigue score • CIDP PRO • PGIS • PGIC	Baseline visit (Day 1), if missing Screening visit For patient reported grip strength, Baseline value will be defined as the mean of three daily maximum grip strength scores taken by a participant during the last three non-missing days prior to the first IMP. Missing values will be handled as described in Section 4.2.1.

Table 3–1: Expected Baseline

Measurement	Definition of Baseline
Immunological variables: • IgA, IgE, IgM • Serum complement levels (C3, C4), • Plasma compliment (C3a, C5a) • [redacted] • Cytokines • [redacted]	Baseline visit (Day 1), except for [redacted] where baseline is Screening visit
PD variables: • Total serum IgG, • NF-L levels	Total serum IgG: Baseline visit (Day 1), if missing Screening visit NF-L: Baseline visit (Day 1)

[redacted]; C3=complement component 3; C3a=complement component 3a; C4= complement component 4; C5a= complement component 5a; CIDP=chronic inflammatory demyelinating polyradiculoneuropathy; CIDP PRO=CIDP PRO instrument; ECG=electrocardiogram; IgG=immunoglobulin G; IgA=immunoglobulin A; IgE=immunoglobulin E; IgM=immunoglobulin M; INCAT=Inflammatory Neuropathy Cause and Treatment; iRODS=inflammatory Rasch-built Overall Disability Scale; NF-L= neurofilament light chain; PGIC=Patient Global Impressions of Change ; PGIS=Patient Global Impressions of Severity; RT-MRC=Rasch-built, modified-interval Medical Research Council scale.

3.4 Protocol deviations

Important protocol deviations (IPDs) are deviations from the protocol which potentially could have a meaningful impact on study conduct or on the primary efficacy, key safety, or PK/PD outcomes (if applicable) for an individual participant. The criteria for identifying important protocol deviations will be defined in the protocol deviations specifications. Important protocol deviations will be reviewed as part of the ongoing data cleaning process and data evaluation. All important deviations will be identified and documented prior to unblinding to confirm exclusion from analysis sets.

IPDs potentially related to the Coronavirus Disease 2019 (COVID-19) were identified via a specific eCRF page "COVID-19 Impact" per visit with relationship: confirmed, suspected infection, general circumstances around or any other deviation from the protocol due to COVID-19. These deviations will also be reviewed separately as part of the ongoing data cleaning process.

3.5 Analysis sets

The following analysis sets will be defined for this study:

3.5.1 Enrolled Set

The Enrolled Set (ES) will consist of all participants who have given informed consent.

3.5.2 Randomized Set

The Randomized Set (RS) will consist of all participants randomized into the study.

3.5.3 Safety Set

The Safety Set (SS) will consist of all participants, who have received at least one dose of IMP.

Safety variables will be analyzed using the SS.

It is expected that participants will receive treatment as randomized and hence safety analyses will be based on the randomized treatment group. However, if after unblinding it is determined that a participant has received treatment different to the treatment they were randomized to, then for safety analyses the participant will be allocated to the actual treatment they received.

3.5.4 Full Analysis Set

The Full Analysis Set (FAS) will consist of all participants in the SS, who have a Baseline and at least one valid post-Baseline iRODS measurement up to Visit 17/PEOT (inclusively).

Measurements are considered invalid if the participant received rescue medication before the assessment of iRODS. Assessments collected at the same day as first intake of rescue medication are considered valid. Invalid measurements will not be used for summary tables and MMRM, but kept in listings.

The FAS is the primary analysis set for efficacy analyses. In the case of mistreatment, participants will be analyzed as treated if the participant received the incorrect treatment for the entire study period. In the case of partial mistreatment, patients should be analyzed as randomized, but considered as protocol violators. As for the SS, in the case of mistreatment participants will be primarily analyzed as treated. However, if applicable, sensitivity analyses will also be performed according to the randomized treatment group.

3.5.5 Modified Full Analysis Set

The Modified Full Analysis Set (MFAS) will consist of all participants in the FAS, excluding any participant who received a mean dose more than ±10% (ie excluding any participant who received a mean dose of IMP >10% or <-10%) from the randomized (intended) dose.

The definition of the randomized dose as well as details for calculations are provided in Section 10.1.

3.5.6 Per Protocol Set

The Per-Protocol Set (PPS) is a subset of the FAS, consisting of those participants who had no important protocol deviation affecting the primary efficacy variable, as confirmed during a preanalysis data review meeting conducted prior to study unblinding. Post-Baseline deviations will not necessarily lead to total exclusion of a participant from the PPS but may lead to exclusion of specific data.

Analysis of the primary efficacy variable will be repeated using the PPS.

3.5.7 Pharmacokinetic Per-Protocol Set

The Pharmacokinetic Per-Protocol Set (PK-PPS) is a subset of the SS, consisting of those participants who had no important protocol deviation affecting the plasma concentration of rozanolixizumab. Post-Baseline deviations will not necessarily lead to total exclusion of a participant from the PK-PPS but may lead to exclusion of specific data.

3.5.8 Pharmacodynamic Per-Protocol Set

The Pharmacodynamic Per-Protocol Set (PD-PPS) is a subset of the FAS, consisting of those participants who had no important protocol deviation affecting the serum concentrations of total IgG, IgG subclasses, or neurofilament light chain. Post-Baseline deviations will not necessarily lead to total exclusion of a participant from the PD-PPS but may lead to exclusion of specific data.

3.6 Treatment assignment and treatment groups

Safety and efficacy analyses will be based on the actual treatment participants received. Analyses will be performed by treatment groups and for all participants (if applicable) as described in Section 3.1.

3.7 Center pooling strategy

It is planned to recruit participants in Europe, United States of America and Canada in this study, with possible extension to other regions and countries. There will be no stratification by site or country performed.

3.8 Coding dictionaries

Adverse events (AEs) will be coded using version 22.0 or later of the Medical Dictionary for Regulatory Activities (MedDRA®).

Prior and concomitant medications will be coded according to version Sep 2017 or later of the World Health Organization Drug Dictionary (WHODD). Medical procedures will not be coded. If newer dictionary versions become available, data will be coded according to the approved internal standard dictionary management processes.

3.9 Changes to protocol-defined analyses

- The definition of the SS has been updated to include all subjects who received at least one dose of the IMP.
- FAS definition:
    - Study participants will be analysed as actually treated only if they received the incorrect treatment for the entire study period. In case of partial mistreatment, the participant will be analyzed as randomized.
    - The FAS definition is clarified being limited to valid primary efficacy results up to V17 only as the primary efficacy endpoint is the change in iRODS from baseline to V17.
- To prevent bias in efficacy evaluation, an efficacy assessment is considered invalid, if that assessment follows the first intake of rescue medication. Assessments on the same day as first intake of rescue medication are valid.
- The protocol specifies the primary efficacy analysis covariate “prior Ig therapy” in section 14.3.1. Prior Ig therapy is defined by the stratification factor route of administration of prior Ig therapy.
- The MFAS was included as an additional analysis set in the SAP and was not part of the final clinical study protocol (CSP). This was added as the sensitivity analysis, to ensure the robustness of the efficacy analysis results in relation to dose variation, as foreseen in the CSP.
- Hy’s Law, defined in the protocol as

  ≥3xULN ALT or AST with coexisting **≥2xULN** total bilirubin in the absence of ≥2xULN ALP

  will instead be defined as

  (ALT or AST increase **>3xULN**) and Total bilirubin **>2xULN** and ALP <2xULN

  to match program standards and general medical definitions.

- The study variable “Change in CIDP-specific auto-antibody levels in serum from Baseline during Treatment and Observation Periods” will not be analyzed in scope of this SAP. Sampling dates are captured in the CRF and will be listed. The samples’ results will not be part of this study’s database and instead analyzed and reported separately. The same is true for exploratory biomarkers RNA, proteins and metabolites variables.

3.9.1 Changes related to COVID-19

With the event of the COVID-19 pandemic, an additional protocol deviation category (related/not related to COVID-19) has been introduced as well as an eCRF page "COVID-19 Impact" to identify visits and procedures which may have been impacted. These will be presented in the analysis results as described in Section 5.2.

Protocol deviations will be presented by COVID-19 period (pre- or during). A post- COVID-19 period may be added if applicable.

3.9.2 Interim Analysis

An interim analysis was planned according to protocol section 14.7 Planned interim analysis and data monitoring:

> *“The fourth and final interim analysis will be performed once all subjects have attended Visit 17, the first visit of the Observation Period (ie, Day 85). This interim analysis will provide, at a minimum, the results for the primary variable “Change from Baseline to Week 13 (Day 85) in iRODS score.“*

The event of all participants having attended Visit 17 is expected to coincide with the event of the last participant attending his/her last visit in CIDP01, resulting in database lock and the final analysis. With both triggers resulting in similar data, the interim analysis specified in the Interim Analysis SAP is not expected to provide additional value and will not be performed.

4 STATISTICAL/ANALYTICAL ISSUES

4.1 Adjustments for covariates

The regression analysis model for efficacy evaluation will adjust for the following covariates:

- Baseline score
- Route of administration of prior Ig therapy

4.2 Handling of dropouts or missing data

4.2.1 Efficacy data

For participants who prematurely withdraw for any reason before Week 13 (Day 85), data collected during the PEOT Visit will be used to impute iRODS, INCAT and grip strength at the closest missing visit. In case a participant discontinues the study prematurely, the assessment of the PEOT visit will be mapped to closest missing visit according to the visit schedule utilizing the relative day in study to a maximum of day 85 (Visit 17). However, if a participant receives rescue medication prior to the PEOT visit, the assessment will be regarded invalid and only listed. Assessments on the same day as first intake of rescue medication is acceptable for analysis.

Since the analysis is based on the mixed model repeated measures (MMRM) approach, visits beyond the PEOT Visit will not be imputed. Missing data in-between visits will be covered by the MMRM approach.

For additional analyses of iRODS score to account for missing data, last observation carried forward (LOCF) and multiple imputation will be applied to address the issue of missing scores (see Section 8.1.3). There will be no imputation of missing individual item scores in the summaries for the iRODS; only to the overall iRODS score.

For the analysis of relapse data, participants who withdraw from the study for any reason before Week 13 (Day 85) or who have missing data at Week 13 (Day 85) will be considered as relapsed and analysed as such. The same is true for participants administered an Ig infusion rescue medication during this time interval.

Participants are asked to record three grip strength score assessments at each day. The efficacy parameter will be derived from grip strength scores taken by a participant up to five days prior to the first IMP (for Baseline value) or visit date (for post Baseline visit value):

1. Maximum of grip strength assessments available at a particular day
2. Mean of maximum grip strength over most recent three non-missing days - up to a maximum of five days
3. Missing values: In case all three assessments of a day are missing, the maximum grip strength score will be set to missing and will not be used for the derived score. In this case the preceding day's maximum grip strength score will be used instead, but no later than the fifth day prior to the first IMP or visit date respectively. In case data is entirely missing during the last five days prior to the visit, the derived score will be set to missing and the issue will be covered by the MMRM approach.

Sensitivity analyses will be performed for the primary efficacy parameter, as described in Section 8.1.3.

4.2.2 Safety Laboratory data

Measurements below the limit of quantification (BLQ) will be imputed with half of the lower limit of quantification (LLOQ) for the purpose of calculating change from Baseline and descriptive statistics.

Measurements above the limit of quantification (ALQ), if applicable, will be imputed to the upper quantification limit for the calculation of changes from baseline and descriptive statistics. These rules will be applied to all safety laboratory data including clinical chemistry and urinalysis.

Descriptive statistics will be calculated if at most 33% of the individual data points at a timepoint are missing or are either not quantifiable (<LLOQ) or ALQ. Values that are BLQ will be replaced by the numerical value of the LLOQ/2 in this instance and values that are ALQ will be imputed to the value of the upper quantification limit. If more than 33% of the individual data points at a timepoint are missing or not quantifiable (BLQ and/or ALQ), no descriptive statistics will be calculated.

4.2.3 Pharmacodynamic data

Measurements BLQ are not anticipated for the total serum IgG data. In the event that any BLQ measurements are received, these will be regarded as missing for the calculation of descriptive statistics and changes from Baseline.

Descriptive statistics will be calculated if at most 33% of the individual data points at a timepoint are missing or are either not quantifiable (<LLOQ) or ALQ as described in Section 4.2.2.

4.2.4 Immunological data

The rules for handling BLQ or ALQ measurements for all immunological data will be as described in Section 4.2.2.

Descriptive statistics will be calculated if at most 33% of the individual data points at a timepoint are missing or are either not quantifiable (<LLOQ) or ALQ as described in Section 4.2.2.

4.2.5 Rozanolixizumab concentration data

Measurements that are BLQ will be imputed with half of the LLOQ for the purpose of calculating the geoMean and its 95% CI, the geoCV, the arithmetic mean, and SD for summaries and figures. If any summary value (geoMean, arithmetic mean, lower CI level or minimum) is lower than LLOQ, then 'BLQ' will be displayed.

For the individual figures, any concentrations that are BLQ will be considered as missing, with the exception of predose BLQ measurements on Day 1, which will be imputed with zero for linear scale plots.

Additional rules for PK data summaries are provided in Section 9.1.

4.2.6 Electrocardiogram data

For the ECG data, all calculations of changes from Baseline and descriptive statistics will be based on the mean of the triplicate assessments at each timepoint. In the event that there are not 3 available measurements at a given timepoint, the mean will be calculated based on the number of measurements for which data is provided.

4.2.7 Dates and Times

Partial dates may be imputed for the following reasons:

- Classification of AEs as treatment-emergent
- Classification of medications and procedures as prior or concomitant
- Derivation of time to use of rescue medication

Imputed dates will not be shown in the listings; all dates will be displayed as reported in the database.
The following rules will be applied for partial start dates:

- If only the month and year are specified and the month and year of dosing is not the same as the month and year of the start date then use the 1st of the month, or the date of Screening if this is later
- If only the month and year are specified and the month and year of dosing is the same as the month and year of the start date, then use the date of dosing. If this results in an imputed start date that is after the specified end date, then use the 1st of the month, or the date of Screening if this is later
- If only the year is specified, and the year of dosing is not the same as the year of the start date then use January 01 of the year of the start date, or the date of Screening if this is later

- If only the year is specified, and the year of dosing is the same as the year of the start date, then use the date of dosing. If this results in an imputed start date that is after the specified end date, then use January 01 of the year of the start date, or the date of Screening if this is later
- If the start date is completely unknown, then use the date of dosing. If this results in an imputed start date that is after the specified end date, then use January 01 of the year of the end date, or the date of Screening if this is later.

Missing start times will be imputed as 00:00h or with the time of dosing for events occurring on the date of IMP administration in case of missing hour and minute. Otherwise start times with only missing minutes will be imputed with :00.

Start and end time is not recorded for concomitant medications, thus no imputations for missing times will be performed. Any medication with a start date on the first dosing date, will be assumed to be concomitant.

The following rules will be applied for partial stop dates:

- If only the month and year are specified, then use the last day of the month;
- If only the year is specified, then use December 31 of the known year;
- If the stop date is completely unknown, do not impute the stop date

Missing or partially missing date and/or times will be imputed as described in Table 4–1 for the calculation of duration of each AE. Adverse event duration is computed in and reported in day and time format: xx d hh:mm.

Table 4–1: Calculation rules for duration of AEs

Data availability	Onset date/time	Outcome date/time	Calculation rules
Complete data	D1/T1	D2/T2	Duration = [(D2 – D1)*24 + (T2 – T1)]/24 d
End time missing	D1/T1	D2/--	End time is substituted by time 23:59h (=23.98 in decimal format) Duration = <[(D2 – D1)*24 + (23.98 – T1)]/24 d
Start time missing	D1/--	D2/T2	Onset time is substituted by time 00:00h. Duration = <[(D2 – D1)*24 + T2]/24 d
Start and end time missing	D1/--	D2/--	Duration = <D2 – D1 + 1
Start day and time missing	--/--	D2/T2	Duration = <[(D2 – D0)*24 + (T2 – T0)]/24 d For a participant in the SS, D0 and T0 are the date and time of first administration of UCB7665 and for screen failures, D0 is the date of the screening visit and T0 = 00:00h

Table 4–1: Calculation rules for duration of AEs

Data availability	Onset date/time	Outcome date/time	Calculation rules
End day and time missing	D1/T1	--/--	For ongoing AE: Duration = >Discharge day – D1 d OR Duration = >Data cut-off day – D1 d For resolved AE: Duration = <Discharge day – D1 d OR Duration = < Data cut-off day – D1 d Where discharge refers to the date of the end of study visit for completed participants or the date of discontinuation for participants that were withdrawn. For any AEs with known start date/time after the date of discontinuation, the date of last contact will be used as the discharge day. For participants still ongoing in the study at the time of the data cut-off, and for whom no discharge date is available, the date of the data cut-off will be used instead of the discharge date.
Start and end date missing	--/--	--/--	For ongoing AE: Duration = >Discharge day – D0 d OR Duration = >Data cut-off day – D0 d For resolved AE: Duration = <Discharge day – D0 d OR Duration = < Data cut-off day – D0 d For a participant in the SS, D0 and T0 are the date and time of first administration of UCB7665 and for screen failures, D0 is the date of the screening visit and T0 = 00:00h. Discharge refers to the date of the end of study visit or the date of discontinuation for participants that were withdrawn. For any AEs with known start date/time after the date of discontinuation, the date of last contact will be used as the discharge day. For participants still ongoing in the study at the time of the data cut-off, and for whom no discharge date is available, the date of the data cut-off will be used instead of the discharge date.

D0/1/2=Date0/1/2; T0/1/2=Time0/1/2; d=day.

4.2.8 Handling of repeated and unscheduled measurements

All repeated and unscheduled measurements will be presented in the listings, where applicable. The following general rules will apply to all repeated and unscheduled measurements:

- For repeated or unscheduled measurements obtained prior to dosing the latest value (which may be scheduled or unscheduled) will be used in the calculation of the descriptive statistics at each visit (ie, Screening and/or Baseline);
- For repeated or unscheduled measurements obtained at the designated Baseline visit, the latest value (which may be scheduled or unscheduled) will be defined as the Baseline provided that the measurement occurred prior to dosing;
- For repeated or unscheduled measurements taken at any timepoint after dosing, the original values (if non-missing) will be used in the calculation of changes from Baseline and for the descriptive statistics (ie, in summaries by timepoint). Unscheduled and repeated measurements will generally not be included in the summaries by timepoint after dosing.

The above rules also apply to triplicate measurements obtained for the ECG data

4.3 Handling of measurements obtained at the premature end of treatment visit

Participants who withdraw from the study prematurely will be encouraged to return for the PEOT visit. The following rules will apply with regard to the inclusion of the results obtained at the PEOT in the descriptive summaries:

- Any measurements (including efficacy, safety, immunological and PD assessments) conducted at the PEOT should be included in the summaries for the respective scheduled visit, if the PEOT occurs at the time of the next scheduled visit (within the tolerance window specified in the protocol).
- If the PEOT does not correspond to the day of a scheduled visit, the efficacy, safety and other relevant assessments of the PEOT should be mapped to the nearest scheduled visit, relative to the Baseline visit date, following the last scheduled visit where assessments are available.
- If the date of the PEOT is equidistant between 2 scheduled visits at which no scheduled assessments were performed, the assessments from the PEOT will be mapped to the earliest of these visits.

Different domains from the same PEOT may be re-assigned to different study visits depending on the study schedule of assessments ie, measurements obtained at the PEOT can only be mapped to a scheduled visit at which the respective assessment was intended to be measured. Assessments from the PEOT that are mapped to scheduled visits will be flagged in the data listings.

Visits after the PEOT following the schedule of the 12-Weeks Observation period, will be mapped to the corresponding planned visit. Assessments on these visits will be flagged in the data listing.

4.4 Interim analyses and data monitoring

A Data Monitoring Commitee (DMC) will be established to monitor mainly safety data during the study. The efficacy data will be assessed during the third interim analysis. The interim analyses will be unblinded and thus the live randomization code will be utilized in the datasets and TFLs.

Details about the Interim analyses will be provided in a separate DMC SAP.

4.4.1 Timing of interim analyses

The following interim analyses are performed:

- The first interim analysis will be conducted after 8 participants have received their first 4 subcutaneous (sc) infusions and have attended the next visit (Visit 9). Based on this unblinded analysis the PK, PD and safety of rozanolixizumab will be assessed by the DMC
- The second interim analysis will be conducted after 8 participants (receiving 12 sc infusions) have attended the first visit of the Observation Period (ie, Visit 17, the visit 1 week after last dosing). Based on this unblinded analysis the PK, PD and safety of rozanolixizumab will be assessed by the DMC
- The third interim analysis will take place after data from 8 additional participants are available, ie, after 16 participants have attended the first visit of the Observation Period. Based on this unblinded analysis the PK, PD and safety of rozanolixizumab will be assessed by the DMC
  - Following DMC recommendations from the second interim analysis, listings and descriptive summary statistics for iRODS, INCAT and site personnel reported grip strength will be included in the third interim analysis
- A fourth interim analysis was planned, but will not be performed. Please see Section 3.9.2 for details.

If needed, subsequent DMC meetings will take place. The timing of further interim analyses and reviews of the data by the DMC will be decided by the DMC. Ad hoc DMC meetings can be held for reasons determined appropriate by the sponsor.

4.4.2 Data required for interim analyses

The analyses and data required for review are described in the DMC SAP and include all data specified in the DMC Charter.

4.5 Multicenter studies

Individual center results will not be displayed.

4.6 Multiple comparisons/multiplicity

Not applicable.

4.7 Use of an efficacy subset of participants

Not applicable.

4.8 Active-control studies intended to show equivalence

Not applicable.

4.9 Examination of subgroups

Not applicable.

5 STUDY POPULATION CHARACTERISTICS

5.1 Participant disposition

The number of participants who were enrolled, dosed, participants included in each analysis set, and participants who completed or prematurely discontinued the study, as well as the

reason for discontinuation, discontinuation due to AEs, will be presented by treatment group and overall. Screen failure reasons will be summarized, based on the ES.

In addition, the following listings will be presented by treatment group:

- Participant disposition (ES)
- Study discontinuation (ES)
- Visit dates (RS)
- Participant analysis sets (ES)

Participant disposition will be listed by treatment group based on the ES, and will include the date of informed consent, date of randomization, date and time of first and last dose of IMP, date of premature termination and primary reason, and date of final contact (if applicable).

The listing of study discontinuation will include the reason for discontinuation, period of discontinuation, with dose and number of days on that dose and the total number of days on study medication.

The number of days on IMP will be calculated as follows:

Number of days on IMP=(Date of Last Dose Received)-(Date of First Dose Received)+1

Time to discontinuation will be listed and plotted in a Kaplan-Meier-Curve for all discontinuations versus discontinuation due to COVID-19.

Reasons for screening failures, disposition and discontinuation reasons will also be summarized based on the respective event's date relative to the COVID-19 period.

5.2 Protocol deviations

Important protocol deviations (IPDs) will be identified and classified by the deviation types identified in the IPD document. A listing of all IPDs identified at the Data evaluation meetings (DEMs) will be presented for all participants in the RS, and will include the deviation type and description. The number and percentage of participants in the RS with IPDs will be summarized overall if appropriate. The denominator for percentages will be the number of participants in the RS

A separate listing will present the captured data from the "COVID-19 Impact" eCRF form. Frequencies of impact categories by visit will also be presented for each relatedness category (suspected, confirmed, general or other reasons). Important protocol deviations will be summarized by COVID-19 period and relationship to COVID-19 (any, related, not related). Number and percentage of participants with these protocol deviations will be summarized for the RS.

Start of the pandemic will be the date the WHO recognized COVID-19 as pandemic, 20 March 2020. The cut-off date for the post- subgroup level will be defined prior to database lock if applicable, an update to the pre-COVID-19 cut-off date may be performed. Details of the analyses will be specified in the following sections.

A date is considered pre COVID-19 up to the day before the start date, so 19 March 2020.

6 DEMOGRAPHICS AND OTHER BASELINE CHARACTERISTICS

6.1 Demographics

A by-participant listing of Baseline demographics will be presented by treatment group for the ES. This will include the year of birth (if available), age (in years), gender, race, ethnicity, height (in cm), weight (in kg) and body mass index (BMI), region and country. The age will be directly entered into the study database and will not be re-calculated for the statistical analysis.

Childbearing potential will be listed for the ES.

All demographic characteristics, except date of birth, obtained at the Screening visit will be summarized for the RS.

Body mass index in kg/m^2 is calculated based on the height (in m) and the weight (in kg) measured at the Screening visit using the following formula:

BMI (kg/m^2) = weight (kg)/[height (m)] ^{2}

The BMI will be reported to 1 decimal place.

Age will be classified into categories based on requirements for European Union Drug Regulating Authorities Clinical Trials (EudraCT) and clinicaltrials.gov reporting.

For the EudraCT reporting, the age categories will include

- 18 to <65 years
- 65 to <85 years
- ≥85 years

For the clinicaltrials.gov reporting, the age categories will include:

- ≤18 years
- 19 to <65 years
- ≥65 years

Body weight at screening will be summarized in the following categories:

- <50 kg
- 50 to <70 kg
- 70 to <100 kg
- ≥100 kg

6.2 Other Baseline characteristics

The prior Ig treatments taken four months before the Randomization visit will be listed and summarized for the RS by treatment group and for all participants. Listing will include the reported term, preferred term, dose, route of administration, frequency, formulation, start/stop dates and duration (in days). For definition of prior treatments see Section 6.4.1.

Duration will be calculated as follows:

Duration (in days) = ((End date of Ig treatment date – Start date of Ig treatment) +1)

In addition, the following variables will be listed and summarized at baseline for the RS by treatment group:

- iRODS score (raw sum score, logit locations and centile metric scores)
- INCAT
- Grip strength (assessed by site personnel and patient reported grip strength)
- Immunological variables (IgG [including total IgG and IgG subclasses], IgM, IgA, IgE)
- Cytokines
- Serum (C3 and C4) and plasma complement levels (C3a and C5a)
- Duration of disease (years)

  Duration of disease (years) will be calculated as:

$$Disease\ duration = \frac{Date\ of\ randomization - Date\ of\ initial\ CIDP\ diagnosis + 1}{365.25}$$

  If the date of initial CIDP diagnosis is partial, it should be imputed to the most recent feasible date (ie, last day of the month if only day is missing, or the last day of the year if day and month are missing). Note that if the date of randomization is missing then the duration of disease will be derived using the date of screening.

6.3 Medical and procedures history

Past medications will include any medications that started and stopped before the first administration of IMP. Medical history will be listed and summarized for the RS by treatment group and will include the MedDRA system organ class (SOC), high level term (HLT) and preferred term (PT). Procedure history and concomitant medical procedures will be listed based on the RS.

History of CIDP will be listed for RS.

6.4 Prior and concomitant medications

Prior and concomitant medications will be listed and summarized for the RS by treatment group and for all participants and will include the WHODD Anatomical Main Group [Level 1], Therapeutic Subgroup [Level 2], PT and reported term. The listing will also include the dose per intake and unit, frequency, formulation, route of administration, indication, category (prior and concomitant, prior, or concomitant) and both start and end date (or ongoing, if applicable).

- Prior medications will include any medications that started before the first administration of IMP.
- Prior and concomitant medications will include any medications that started prior to dosing and continued after.
- Concomitant medications will include any medications that have been taken at least once after the first administration of IMP during the Treatment and/or Observation Period.

6.4.1 Prior medication definition

Prior medications will include any medications that started prior to the first administration of IMP. This includes any medications that started and stopped prior to dosing as well as those

which started prior to dosing and continued after (classified as prior and concomitant medications).

6.4.2 Concomitant medication definition

Concomitant medications will include any medication that has been taken at least once (on or after the first administration of IMP) during the Dosing Period and/or the Observation Period.

Any medication that started prior to the first administration of IMP and continued after dosing will be classified as prior and concomitant. Any medication that started on or after the first administration of IMP will be classified as concomitant only.

Any medications with missing dates and/or times will be handled as described in Section 4.2.7 in order to classify them as prior or concomitant.

The following rules will be used to assign concomitant medications to the study periods:

- Treatment Period: a medication will be assigned to Treatment Period if it has been taken at least once between the first administration of IMP until Visit 17/PEOT (non inclusively). This includes medications that started prior to the first IMP and continued during Treatment Period and those that continued into the Observation Period.
- Observation Period: a medication will be assigned to Observation Period if it has been taken at least once between day 85 (Visit 17/PEOT) and the Final visit or end of study participation. This includes medications that started prior to the Observation Period.

Medications taken during both study period will be listed once, but the study period will indicate both study periods.

7 MEASUREMENTS OF TREATMENT COMPLIANCE

The study medication will be administered and monitored by the investigator or designee. Any dosing deviations (eg, incomplete infusion volume administered, infusion temporarily interrupted, infusion discontinued) will be discussed at the DEM and any actions taken regarding the analyses will be documented accordingly and discussed in the CSR.

All drug administration details (including exposure category described in Section 10.1, date, start and stop time of infusion, interruptions, discontinuations, total planned volume and actual volume delivered, planned and actual infusion rates, location of infusion site) will be listed. The reasons for any interruptions or discontinuations will be included in the listing. The duration of the infusion, in minutes, and compliance will also be calculated and presented.

Compliance, percent of planned dose administered, will be calculated based on the planned and actual volume delivered as follows:

Percent of Planned dose administered = (Total actual volume delivered (mL)/Total planned volume (mL))*100

Actual volume delivered and total planned volume (i.e. according to section 7.2 of protocol) will be captured in the eCRF. In case of interruption the sum of actual volumes delivered, and the total planned volume recorded into the eCRF will be used for the calculation.

There will be no specific analysis of compliance.

8 EFFICACY ANALYSES

All analyses of the efficacy variables will be performed on the FAS. Additional outputs may be repeated for the PPS or the MFAS where indicated. Listings will be based on the SS.

Treatment group assignment for efficacy analysis will be according to the actual treatment regimen.

All efficacy analyses are to be interpreted as exploratory analyses. No p-values will be presented.

Any efficacy measurements are considered invalid, if the participant received rescue medication before the assessment. Assessments collected at the same day as first intake of rescue medication are considered valid. Respective measurements will not be used for summary tables and MMRM, but kept in listings. This includes iRODS, INCAT, clinician reported grip strength, RT-MRC, CIDP PRO and Fatigue, PGIS, PGIC and the patient reported grip strength as derived in Section 8.2.4.

8.1 Statistical analysis of the primary efficacy variable

The primary efficacy variable described in Section 2.2.1.1 will be analyzed using the logit-transformed iRODS score to compute the change from Baseline to Week 13 (Day 85).

8.1.1 Derivations of primary efficacy variable

The iRODS is a linearly weighted patient-reported outcome measure (questionnaire) that specifically captures activity and social participation limitations in patients with CIDP. The iRODS scale was constructed based on the World Health Organization (WHO) International Classification of Functioning, Disability and Health, literature search, and patient interviews.

All 24 items of iRODS meet Rasch model expectations. The questionnaire consists of 24 items (including eating, taking a shower, walking a flight of stairs, standing for hours, etc.) and assesses a patient's perception of their ability to perform daily and social activities. Patients have 3 response options: 0=impossible to perform; 1=performed with difficulty; and 2=easily performed, performed without difficulty.

The raw sum scores of iRODS (range 0 to 48) is an ordinal scale and does not allow for easy interpretation of differences. For this reason, the ordinal scale will be translated to log odds units (logits) scale using the nomogram in Section 13.1, placing patients' estimates on the same logit scale. The primary analysis and iRODS summary will be performed on logit locations. For easier interpretation the person locations (logits) will be translated to centile metric scores changing from 0 (most severe activity and social participation restrictions) to 100 (no activity and social participation limitations). Both transformed and untransformed data will be provided in tables and key results will be presented in transformed and original units to aid interpretation based on the raw scores.

8.1.2 Analysis of the primary efficacy variable

The primary analysis will be based on a MMRM analysis (fixed effect terms: treatment group, the Baseline location iRODS score, route of administration of prior Ig therapy (as captured in the eCRF Prior and Concomitant Medication form), assessment week (at pre-specified levels determined by the visit schedule) and the treatment by week interaction and study participant as a random effect, and utilize an unstructured covariance matrix).

The Kenward-Roger approximation will be used to estimate denominator degrees of freedom. In case of non-convergence, the model will be fitted using the following covariance matrices until convergence is met: Heterogeneous Toeplitz, Heterogeneous autoregressive, Toeplitz, Autoregressive.

SAS proc MIXED will be used:

a. Subject ID, treatment group, prior Ig therapy and visit will be set as classes

b. The model will be specified with covariates baseline score, treatment group, prior Ig therapy, visit and treatment*visit
c. The repetition variable is visit.
d. Subject ID is set as random factor.
e. Covariance structure as described above.
f. LS means, differences and confidence limits for treatment*visit are requested.

An estimate for the placebo-adjusted treatment effect with 90% CI will be produced on logit location scale, on the raw scores as well as centile metric scores.

Imputation rules are given in Section 4.2.1.

8.1.2.1 Presentation of primary efficacy variable

The individual items of the iRODS and overall score will be listed by treatment group and timepoint using the SS. Overall scores will be displayed including raw sum score, logit locations and centile metric scores as well as changes from Baseline in raw sum score, logit locations and centile metric scores. Descriptive summaries will be presented by treatment group and timepoint for both absolute values and changes from Baseline based on the FAS. Raw sum score summary will show only n, median, minimum, maximum. In addition frequencies of raw scores by each iRODS questionnaire item (eating, taking a shower, walking a flight of stairs, standing for hours, etc.) will be calculated.

The summary of the primary MMRM procedure results at each week, i.e. Least Square (LS) Means along with their standard error (SE), LS Mean difference and its 2-sided 90% CI corresponding to the treatment group difference at each week, will also be presented in the descriptive statistics for raw sum score, logit location and centile metric score.

Mean change from Baseline including 90% CI of the centile metric score will be plotted against timepoint for both treatments.

8.1.3 Supportive and sensitivity analyses of the primary efficacy variable

Different sensitivity analyses to evaluate the effect of missing observations on the primary analysis findings will be performed. This applies to summary of observed results and MMRM for iRODS.

8.1.3.1 Per-protocol analysis

The first supportive analysis will be performed in the same way as the primary analysis, using the PPS.

8.1.3.2 LOCF

A further analysis will utilize the LOCF approach; a missing value will be replaced by the most recent previously observed post-Baseline value of the variable up to day 85 and the analysis will be performed for the FAS. In case a participant discontinues the study prematurely, the assessment of the PEOT visit will be mapped to next missing visit according to the visit schedule utilizing the relative day in study to a maximum of day 85 (Visit 17) before applying LOCF.

8.1.3.3 MFAS

In addition, a further exploratory sensitivity analysis to ensure the robustness of the results in relation to dose variation will be conducted for the primary endpoint, using the MFAS.

8.2 Statistical analysis of the other efficacy variables

8.2.1 CIDP relapse, MMRM and summary tables will be performed on the FAS and repeated for the PPS for iRODS, adjusted INCAT and clinician reported grip strength.CIDP relapse (iRODS)

CIDP relapse (iRODS) is defined as a clinically important deterioration from Baseline in iRODS score, i.e. a standardized change from baseline smaller than or equal to the minimum clinically important differences-standard error (MCID-SE) of ≤-1.96.
This standardized change from baseline refers to individual person-level responsiveness calculated by individual change divided by their corresponding SE of difference at a given timepoint. [Va15]

$$"MCID - SE" = \frac{Standardized\ value_{Visit} - Standardized\ value_{baseline}}{\sqrt{SE_{Visit}^2 + SE_{Baseline}^2}}$$

Values and changes from Baseline in iRODS scores will be summarized by treatment group and for all participants and listed by treatment group at each scheduled assessment during the Treatment and Observation Period.

The point estimate and the corresponding 2-sided 90% CI for the difference between placebo and rozimab CIDP relapse rates up to week 13 will be reported. The CI will be constructed using the asymptotic standard error (asymptotic Wald confidence limits).

Analyses will be performed for the FAS utilizing the observed cases.

Sensitivity analysis for relapse will be performed in the same way, however for the PPS.

The rule for handling missing data is described in Section 4.2.1.

8.2.1.1 Analysis of time to CIDP Relapse (iRODS)

The time to CIDP relapse (iRODS) is defined as the time from starting treatment (Day 1) to achievement of iRODS and will be displayed using a Kaplan-Meier curve.

Summary tables will include descriptive statistics. The point estimate for the median number of days to CIDP relapse with 90% CIs will be given if estimable. A summary including the number and percentage of censored participants, the number of relapsed participants and total participants by treatments and in total will be given. Participants withdrawing from the study will be handled as relapsed (see Section 4.2.1).

For the purpose of the analysis participants with no relapse will be censored at the end of the study.

Analyses will be performed for the FAS and repeated for the PPS.

8.2.2 Adjusted Inflammatory Neuropathy Cause and Treatment (INCAT) and CIDP relapse

The INCAT disability scale is a 10-point clinician-reported ordinal measure capturing problems in daily arm and leg activities and mobility. The measure captures daily activities such as dressing the upper part of the body, doing and undoing buttons and zips, washing and brushing hair, and handling coins. Each item is scored as being “not affected”, “affected but not prevented”, or “prevented”. The leg scale measures problems with walking, taking into account the use of aids.

The investigator (or qualified personnel) will record the participant's INCAT arm and leg disability score at each scheduled assessment.

The INCAT score is the sum of the eCRF-captured arm disability classification (from 0 to 5) and leg disability classification (from 0 to 5). The INCAT scale ranges from 0 (no signs of disability) to 10 (most severe disability score).

If there is only one point deterioration/improvement in the participant's upper limb score (arm disability score) ie, from 0 (normal) to 1 (minor symptoms) or from 1 to 0, this difference should not be considered as a significant worsening/improvement and the related difference between baseline and the respective visit should be ignored when evaluating the adjusted INCAT score for the visit in the following way:

For each visit's INCAT score, the adjusted INCAT is

(a) adjusted INCAT score = INCAT score - 1, if the arm disability score for this participant is 0 at baseline and 1 at the respective visit
(b) adjusted INCAT score = INCAT score +1, if the arm disability score for this participant is 1 at baseline and 0 at the respective visit
(c) adjusted INCAT score = INCAT score in any other case.

	Baseline score	Visit score	Total adjusted INCAT score
Arm disability score	0	1	Total adjusted INCAT score = Total visit INCAT score – 1
	1	0	Total adjusted INCAT score = Total visit INCAT score + 1
	Any other case		No adjustment

CIDP relapse (adjusted Inflammatory Neuropathy Cause and Treatment, INCAT) is defined as an increase from Baseline of at least 1 point in the adjusted INCAT score.

Values and changes from Baseline in adjusted INCAT score will be summarized by treatment group and for all participants and listed by treatment group at each scheduled assessment during the Treatment and Observation Period. For the change from Baseline at each scheduled assessment during the Treatment and Observation Period, treatment differences will be compared using the same MMRM analysis as for the primary endpoint, with the fixed categorical effects of treatment group, assessment week (at pre-specified levels determined by the visit schedule), the treatment by week interaction and the route of administration of prior Ig therapy, as well as continuous fixed covariate of the Baseline value and participant as a random effect. Analyses will be performed for the FAS utilizing the observed cases and repeated for the PPS.

INCAT score measurements will be listed by treatment group.

The statistical methods applied to CIDP relapse (adjusted INCAT) and time to CIDP relapse (adjusted INCAT) will be the same as for CIDP relapse (iRODS), see Sections 8.2.1 and 8.2.1.1.

The rule for handling missing data is described in Section 4.2.1.

Mean change from Baseline in adjusted INCAT score, including 90% CI will be plotted against timepoint for both treatments.

8.2.3 Maximum grip strength as assessed by site personnel and CIDP relapse

Grip strength is assessed by qualified site personnel each scheduled assessment. Qualified site personnel will be trained regarding obtaining and recording measurements. At each

scheduled visit, the grip strength, generated by the participant, and measured using a standardized tool, will be evaluated 3 times in the dominant hand. All 3 assessments will be recorded in the eCRF. For analyses, UCB will utilize the maximum of the 3 assessments. Efficacy will be assessed as change from Baseline in maximum grip strength score at each scheduled assessment by treatment group during the Treatment and Observation Periods.

CIDP relapse (maximum grip strength as assessed by site personnel) is defined as a clinically important deterioration from Baseline in grip strength as measured by site personnel, ie, a decline of >14kPa.

Values and changes from Baseline in maximum grip strength score taken by site personnel will be summarized by treatment group and for all participants and listed by treatment group at each scheduled assessment during the Treatment and Observation Period.

For the change from Baseline in maximum grip strength at each scheduled assessment during the Treatment and Observation Period, treatment differences will be compared using the same MMRM analysis as for the primary endpoint, with the fixed categorical effects of treatment group, assessment week (at pre-specified levels determined by the visit schedule), the treatment by week interaction and the route of administration of prior Ig therapy, as well as continuous fixed covariate of the Baseline value, and participant as a random effect. Analyses will be performed for the FAS utilizing the observed cases and repeated for the PPS.

Values of grip strength score taken by site personnel will be listed by treatment group. All 3 assessments taken at the scheduled assessments will be listed and the maximum per scheduled assessment will be flagged.

The statistical methods applied to CIDP relapse (maximum grip strength as assessed by site personnel) and time to CIDP relapse (maximum grip strength as assessed by site personnel) will be the same as for CIDP relapse (iRODS), see Sections 8.2.1 and 8.2.1.1. The rule for handling missing data is described in Section 4.2.1.

The analyses on CIDP relapse and time to CIDP relapse will be repeated with a CIDP relapse definition based on a decline of >8kPa.

Mean change from Baseline in maximum grip strength score, including 90% CI will be plotted against timepoint for both treatments.

8.2.4 Patient-reported grip strength

During the study, participants keep e-diaries to record daily grip strength from the Screening Visit until the end of study participation. Participants should be reminded to bring their diaries with them to each clinic visit and to have them available at home nursing visits. Participants will be trained by the site personnel and receive a manual describing how to assess grip strength using a standardized tool. At approximately the same time every day, the maximum grip strength, the peak pressure generated by the participant, will be assessed 3 times, with at least 30sec between measurements, using the dominant hand. Participants will be asked to complete their diaries each day and record the values for each of the 3 assessments.

For the purpose of the analysis, the mean of the maximum of the 3 daily assessments taken during the last three non-missing days prior to the scheduled visit will be used. Missing data will be handled as described in Section 4.2.1.

Values and changes from Baseline in mean daily maximum grip strength score taken by the participant will be summarized by treatment group and for all participants and listed by

treatment group at each scheduled visit during the Treatment and Observation Period. The treatment differences of change from baseline in the derived grip strength score will be compared using the same MMRM analysis as for the primary endpoint, with the fixed categorical effects of treatment group, assessment week (at pre-specified levels determined by the visit schedule), the treatment by week interaction and the route of administration of prior Ig therapy, as well as continuous fixed covariate of the Baseline value, and participant as a random effect. Analyses will be performed for the FAS utilizing the observed cases and repeated for the PPS.

Values of grip strength score taken by the participant as well as derived scores will be listed by treatment group. All 3 daily assessments taken at the scheduled assessments will be listed and the maximum per scheduled assessment will be flagged.

In addition to the above the daily maximum values will be displayed graphically over time, i.e. each treatment group's mean value and 90% CI of the maximum of the participants' three daily grip strength measurements will be displayed versus the relative day.

8.2.5 CIDP relapse

The event of CIDP relapse is defined by occurrence of either relapse across the 3 calculated criteria: iRODS relapse, adjusted INCAT relapse and maximum grip strength as assessed by site personnel (14 kPa) relapse as defined in sections 8.2.1, 8.2.2 and 8.2.3 and 'other' as captured in the CRF by the investigator. It will be described and analysed in the same way as the individual relapse definitions. This will be done for the FAS and the PPS.

8.2.6 RT-MRC sum score

The RT-MRC sum score is a summation of the RT-MRC grades in integers of the following muscles on each side: upper arm abductors, elbow flexors, wrist extensors, hip flexors, knee extensors, and foot dorsal flexors.

The RT-MRC sum score was developed based on a Rasch analysis of the original MRC grading system ([Me10]; [Me02]; [Va12]). The original MRC sum score grades from 0 to 5 (0 = No movement, no contraction; 1 = Visible contraction without movement; 2 = Movement, but only with gravity eliminated; 3 = Movement against gravity; 4 = Movement against resistance, but weaker than normal; 5 = Normal Strength). The MRC grades were rescored from 6 to 4 response options (0, paralysis; 1, severe weakness; 2, slight weakness; 3, normal strength) for the RT-MRC in order to acceptably fulfill Rasch model expectations. Sum scores range from 36 "normal" to 0 "quadriplegic".

Values and changes from Baseline in original MRC sum score and in RT-MRC sum score will be summarized by treatment group and for all participants and listed by treatment group at each scheduled assessment during the Treatment and Observation Period.

For the change from Baseline at each scheduled assessment during the Treatment and Observation Period, treatment differences will be compared using the same MMRM analysis as for the primary endpoint, with the fixed categorical effects of treatment group, assessment week (at pre-specified levels determined by the visit schedule), the treatment by week interaction and the route of administration of prior Ig therapy, as well as continuous fixed covariate of the Baseline value, and participant as a random effect. Analyses will be performed for the FAS utilizing the observed cases.

8.2.7 CIDP PRO and Fatigue scale

The **CIDP PRO instrument** consists of 2 domain scales;

- Pain Severity numeric rating scale
- Neuropathy scale.

Pain Severity consisting of 4 items assessing pain severity in the past 7 days and at the time of completion of the instrument, using 0-10 numeric rating scales. Summed total raw score will range between 0 to 40 with higher scores reflecting higher levels of pain severity.
The Neuropathy scale consists of 17 items rated within a 7-day recall period on a 6-point Likert severity scale ranging from "none" to "very severe". The summed total raw score will range from 17 to 102 with higher scores reflecting higher levels of pain and physical sensations severity.

The **Fatigue instrument** consists of 3 domain scales; Physical Fatigue comprising 16 items; Mental Fatigue comprising 18 items and Fatigability comprising 21 items. All 55 items across the 3 domain scales are rated within a 7-day recall period on a 5-point Likert frequency scale ranging from "none of the time" to "all of the time". The summed total raw scores for each of the 3 scales will range between 16 and 80; 18 to 90 and 21 to 105 points for the Physical, Mental, and Fatigability, scales respectively with a potential for an exploratory total overall score ranging from 55 to 275. Higher scores reflect higher levels of fatigue across all domain scale scores.

Values and changes from Baseline in CIDP-PRO instrument and in fatigue scores will be listed by treatment group at each scheduled assessment during the Treatment and Observation Period. Summary tables will be provided at an item level. If items are missing, the sum will be set to missing.

Following psychometric evaluation and refinement (eg, reduction in number of items) of these domain scales by using data generated in CIDP01, transformed interval 0-100 scoring will be provided for each domain score with higher scores reflecting higher levels of fatigue. A psychometric analysis plan will be created, which will detail all the exploratory and correlation analyses between the newly developed PROs and clinical variables. The PROs will also be participant to a Rasch analysis. The results of the psychometric analyses will be reported separately from the clinical study report (CSR). This analysis is not in scope of this SAP.

8.2.8 PGIS and PGIC

Participants will rate their global impression of CIDP symptom severity and fatigue severity respectively, on a 5-point Likert severity scale ranging from "none" to "very severe".

Participants will rate their global impression of change (if at all) in CIDP symptom and fatigue respectively, on a 7-point Likert severity scale ranging from "very much improved" to "very much worse" from Baseline/start of clinical study treatment to the scheduled visits.

Frequencies of subjects scoring in the respective categories in Patient Global Impressions of Severity (PGIS) and changes in frequencies from Baseline will be presented via a shift table by visit per treatment group and listed by treatment group at each scheduled assessment during the Treatment and Observation Periods.

Patient Global Impressions of Change (PGIC) will be summarized via frequencies of each response by visit and treatment group and listed by treatment group at each scheduled assessment during the Treatment and Observations Periods.

8.2.9 Use of rescue medication

The percentage of participants with concomitant medication identified as rescue medication [Yes/No] in the eCRF and time to first rescue medication administration will be summarized by treatment group and for all participants and listed by treatment group at each scheduled assessment during the Treatment and Observation Period.

If a participant receives rescue medication at multiple times, the relative day of the first occurrence is used to define the time to rescue medication.

The statistical methods applied to use of rescue medication and time to use of rescue medication will be the same as for CIDP relapse (iRODS), see Sections 8.2.1 and 8.2.1.1. The rule for handling missing data is described in Section 4.2.7 .

9 PHARMACOKINETICS AND PHARMACODYNAMICS

9.1 Pharmacokinetics

Pharmacokinetic variables of rozanolixizumab like AUC (area under the curve), C_{max} (maximum concentration) cannot be derived, since blood sampling will be performed at 1 time point post-dosing per visit only. Thus, PK is restricted to concentration data.

Concentration data will be summarized for treatment rozanolixizumab by exposure (%) categories (see section 10.1) and time point using the number of available observations, mean, median, SD, minimum, maximum, geoMean, (and associated 95% confidence intervals), and geoCV (assuming log-normally distributed data) based on the PK-PPS. Concentration data will be summarized for treatment rozanolixizumab by time point and [redacted] status (6 classifications; see Section 9.3.2) using the number of available observations, mean, median, SD, minimum, maximum, geoMean, (and associated 95% confidence intervals), and geoCV (assuming log normally distributed data) based on the PK-PPS. Individual concentrations of rozanolixizumab as well as planned and actual dose administered will be listed by treatment group for the SS and summarized for the PK-PPS, and will include the actual sampling time in days relative to the previous dose.

The following rules will apply for PK data listings and summaries:

- Values below the LLOQ will be reported as BLQ.
- Descriptive statistics of concentrations will be calculated if at most 33% of the individual data points at a timepoint are missing or are not quantifiable (<LLOQ). Values that are BLQ will be replaced by the numerical value of the LLOQ/2 in this instance. However, if n≤3, then only n, minimum and maximum will be presented as summary statistics. The other descriptive statistics will be left blank. If more than 33% of data points is missing then no summary statistics are given, irrespective of n.
- If no participants have data, only n=0 will be presented. The other descriptive statistics will be left blank.
- The 95% CI lower and 95% CI upper should be left blank if the SD (or equivalently, the geoCV) is 0
- The geoCV will be calculated using the following formula where SD is the standard deviation from the log-transformed data

$$\text{geoCV (\%)} = \text{sqrt}[(\exp(\text{SD}^2) - 1)] \times 100$$

For each participant, individual concentration versus time (week) profiles will be presented graphically in linear and semi-logarithmic scale. In addition, combined individual (spaghetti

plots) concentration versus time profiles will be presented in linear and semi-logarithmic scale with all participants overlaid on the same figure.

All figures will include the LLOQ on the semi-logarithmic plots.

9.2 Pharmacodynamics

The analysis of the PD data will be performed on the PD-PPS. All listings will be presented for the SS.

9.2.1 Total Serum IgG

Total Serum IgG concentrations and IgG subclasses will be listed by treatment group and timepoint including absolute changes from Baseline and percentage changes from Baseline. Descriptive summaries (including n, arithmetic mean, median, SD, minimum and maximum) will be presented by treatment group and timepoint for absolute values, changes from Baseline and percentage changes from Baseline.

Further descriptive summaries (including n, arithmetic mean, median, SD, minimum and maximum) will be presented by treatment group, timepoint and [redacted] status (6 categories; see Section 9.3.2) for absolute values, changes from Baseline and percentage changes from Baseline.

Participant total Serum IgG will be plotted against planned time. Mean Serum IgG, mean change from Baseline and percentage change from Baseline will be plotted against planned time by treatment group.

For each participant, the minimum value and maximum decrease (absolute and percentage) from Baseline in total serum IgG concentration during the study (using all available data up to cut-off point) will be listed. The minimum value and maximum decrease will be summarized by treatment group. In the event that a decrease from Baseline in IgG is not observed in a given participant, the maximum decrease will be reported as the smallest increase from Baseline.

9.2.2 Neurofilament light chain

NF-L levels in serum will be listed by treatment group and timepoint including changes from Baseline. Descriptive summaries will be presented by treatment group and timepoint for absolute values, changes from Baseline and percentage changes from Baseline.

Participant NF-L levels in serum will be plotted against planned time. Mean NF-L levels, mean change from Baseline and percentage change from Baseline will be plotted against planned time by treatment group.

9.3 Immunological analyses

All analyses described in this section will be based on the SS.

9.3.1 Immunoglobulins

Immunoglobulins (IgA, IgE and IgM) will be listed by treatment group and timepoint including changes from Baseline. Descriptive summaries will be presented by treatment group and timepoint for both absolute values and changes from Baseline.

Individual figures over time (absolute value) will be presented by participant, with all variables overlaid on the same plot and separate plots each participant.

Any values that are BLQ or ALQ will be handled as described in Section 4.2.4.

9.3.2 [redacted]

[redacted] will be measured using a three-tiered assay approach: screening assay, confirmatory assay and titration assay. The results for the [redacted] measurements will be listed by treatment group and timepoint based on the SS, including the Screening assay, confirmatory assay and titer (if applicable).

Samples will first be evaluated in the screening assay using a false positivity rate of 5% (reported as negative screen or positive screen), followed by analysis of screened positive samples in the confirmatory assay (which is a drug depletion assay) to confirm the true positivity of the samples (reported as negative immunodepletion or positive immunodeplet on positive). Samples that are confirmed as positive will be evaluated in a titration assay to quantify the [redacted] level and will be reported as titer (reciprocal dilution factor including minimum required dilution (MRD)).

Screening, confirmatory and titer cut points of the respective assays will be determined by the bioanalytical laboratory.

The [redacted] sample status should be determined for each visit where samples were taken for [redacted] analysis:

- Sample values that are either negative screen or positive screen and negative immunodepletion will be defined as [redacted] negative

- Sample values that are positive screen and positive immunodepletion will be defined as [redacted] positive.

There will be six [redacted] participant status classifications

(1) For participants who are negative at baseline, and antibody negative at all sampling points post treatment (including FV)- pre [redacted] negative- treatment induced [redacted] negative

(2) For participants who are negative at baseline, and antibody positive at any sampling point post treatment (including FV)- pre [redacted] negative- treatment induced [redacted] positive. If a participant has a missing pre-treatment sample (either missing or insufficient volume) at baseline with one or more [redacted] positive post-treatment samples will be also classified as pre [redacted] negative- treatment induced [redacted] positive

(3) For participants who are positive at baseline, and antibody negative at all sampling points post treatment (including FV)- pre [redacted] positive- treatment reduced [redacted]

(4) For participants who are positive at baseline, and are positive at any sampling point post treatment (including FV) with titer values of the same magnitude as baseline (i.e. ≤ then a predefined fold difference from the baseline value)- pre [redacted] positive - treatment unaffected [redacted]

(5) For participants who are positive at baseline, and are positive at any sampling point post treatment (including FV) with increased titer values compared to baseline (above a predefined fold difference increase from baseline value which will be defined within the validation of the assay and will be included in the TFLs and/or SAP when available)- pre [redacted] positive- treatment boosted [redacted] positive.

(6) For participants who have a positive pre-treatment sample and some post-treatment samples are missing, while other post-treatment samples are [redacted] negative, the participant will be classed as inconclusive.

- A participant will be classified as having treatment-induced [redacted] positivity when meeting one of the following criteria:
    1. The Baseline result is [redacted] negative and at least one post-Baseline timepoint is [redacted] positive
    2. The Baseline result is [redacted] positive and at least one post-Baseline measurement shows a pre-defined fold increase in titer from the Baseline value (the fold increase from Baseline required to meet this criterion will be defined with the development of the assay and will be included in the TFLs)

The available [redacted] sample results will be listed. The listing will include rozanolixizumab concentration, [redacted] sample result [redacted] negative or positive), together with the confirmatory result (% inhibition) and [redacted] titer for results that are [redacted] positive. In addition, the time since the previous administration of IMP will be reported (in days).

A study participant will be considered

- Overall [redacted] Positive if having at least one scheduled assessment that is confirmed positive during the treatment period (ie, classifications (2) to (6)).
- Overall [redacted] Negative if having no scheduled assessments that are confirmed positive at any time in the treatment period (ie, classification (1)).

Number and percentage of [redacted] positive and negative participants at the time of each scheduled assessment and overall will be summarized based on the SS.

The first occurrence of treatment-induced [redacted] positivity (based on the definitions above) will be summarized (number and percentage of participants) at each post-Baseline scheduled assessment, based on the SS. This tabulation will count the number of participants at each post-Baseline visit who fulfill at least one of the above defined criteria for treatment-induced positivity; participants will be counted in the numerator based on the earliest visit at which one of these criteria is fulfilled. At other visits, participants will be counted in the denominator (assuming a measurement is available). For all tabulations, percentages will be based on the number of observations at each visit.

The [redacted] status by the six categories, defined above, will be tabulated by treatment group, with an additional category "total treatment induced" combining participants who are pre [redacted] negative- treatment induced [redacted] positive, participants with a missing pre-treatment sample (either missing or insufficient volume) at baseline with one or more [redacted] positive post-treatment samples and participants pre [redacted] positive- treatment boosted [redacted] positive.

The prevalence of immunogenicity, defined as (cumulative) proportion of participants having positive immunodepletion [redacted] samples at any point up to and including that time point will be summarized by treatment group based on the SS. Missing samples will not be included in the denominator.

Individual plots of rozanolixizumab concentrations and [redacted] titer results as well as [redacted] titer results and percentage change from baseline in Total IgG by the six [redacted] classes described above will be presented. Spaghetti plots of [redacted] titer versus time will be presented for all [redacted] positive participants based on the SS.

9.3.3 Serum complement levels and plasma complement levels

Serum (C3 and C4) and plasma (C3a and C5a) complement variables will be listed by treatment group and time point including changes from Baseline. Descriptive summaries will

be presented by treatment group and time point for both absolute values and changes from Baseline.

Any values are that BLQ or ALQ will be handled as described in Section 4.2.4.

9.3.4 Cytokines

Serum cytokines will be listed by treatment group and time point, changes from Baseline will be added to the listing. Descriptive summaries will be presented by treatment group and time point for both absolute values and changes from Baseline, both for all participants and for participants experiencing infusion reactions.

Any values are that BLQ or ALQ will be handled as described in Section 4.2.4.

9.3.5 CIDP-specific auto-antibodies

CIDP-specific auto-antibody sampling information captured in the eCRF will be listed. No results will be analyzed.

9.3.6 [redacted]

[redacted] will be listed by treatment group and time point. Descriptive summaries will be presented by treatment group and time point for both absolute values and changes from Baseline.

Any values are that BLQ or ALQ will be handled as described in Section 4.2.4.

10 SAFETY ANALYSES

All safety analyses will be presented using the SS Listings will be presented by treatment group and participant; tabulations will be presented by visit/timepoint (if applicable) and treatment group.

10.1 Extent of exposure

Eligible participants will be randomized 1:1 to receive rozanolixizumab [redacted] or placebo. Randomized (intended) dose will be calculated based on participant's weight at screening as follows:

Randomized dose (mg)= weight at screening (kg)*[redacted]

The IMP solution contains [redacted] of rozanolixizumab. Actual dose in mg at Visit(i) will be calculated as follows:

Actual dose at Visit(i) (mg)= Total actual volume delivered at Visit(i) (mL)*[redacted] where actual volume delivered is collected in eCRF, and in case of interruption it should be calculated as the sum of actual volumes delivered.

Overall exposure (%) will be calculated as mean exposure (%) at each visit as follows:

Overall exposure (%) =mean([Actual dose at Visit (i) (mg)/ Randomized dose (mg) -1]*100)

Overall exposure will be categorized as follows:

- <-10%
- ≥ -10% and ≤ +10%
- > +10%

The exposure categories will be used for the definition of the MFAS (Section 3.5.5) as well as for the representation of Pharmacokinetic data (Section 9.1).

10.2 Adverse events

Adverse events will be recorded from the time of informed consent until study completion. All AEs will be coded (Section 3.8) and categorized by relationship to rozanolixizumab.

In addition, AEs will be classified according to the Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0 for severity. For any AEs where it is not possible to provide a CTCAE grading, the events will be assessed using a standard intensity classification (mild, moderate and severe).

A TEAE is defined as any event that was not present prior the first administration of IMP or any unresolved event already present before the first administration of IMP that worsens in intensity following exposure to treatment until 8 weeks following the last administration of IMP. Adverse events starting before the first administration of IMP or later than 8 weeks after the administration of the last IMP will not be considered TEAEs. Such events will be listed only.

Where dates are missing or partially missing, AEs will be assumed to be treatment-emergent unless evidence exists that does not allow the AE to be treatment-emergent. Handling of missing dates/times for classification of AEs as TEAEs is described in Section 4.2.7.

The following rules will be used to assign a TEAE to the study periods:

1. **Treatment Period:** a TEAE will be assigned to the Treatment Period for the tabulations if the start date/time of the event is at the time of or after the first administration of IMP on Day 1, up to Visit 17/PEOT (non-inclusively).
2. **Observation Period:** a TEAE will be assigned to the Observation Period for the tabulations if the start date/time of the event is at or after Visit 17/PEOT till 8 weeks after administration of the last IMP.
    - The Observation Period's TEAEs will be stratified by TEAEs of participants who received/did not receive standard of care treatment (i.e. Ig treatment) between start of the Observation Period and occurrence of the TEAE.

The number and percentage of participants who experience TEAEs will be summarized by Treatment Period, Observation Period (standard of care treatment status identified by WHODD J06BA01 and J06BA02) and Overall with respective treatment group. The following summaries will be presented:

- Incidence of TEAEs (overview including number and percentage of participants with any TEAEs, serious TEAEs, discontinuations due to TEAEs, related TEAEs, TEAEs with CTCAE Grade 3 and above [or rated as 'severe' for events with no CTCAE classification], and deaths; event counts will also be included)
- Incidence of TEAEs by SOC, HLT and PT
- Incidence of TEAEs during the Dosing Period by SOC, HLT and PT
- Incidence of serious TEAEs by SOC, HLT and PT
- Incidence of non-serious TEAEs by SOC, HLT and PT
- Incidence of AEs of special interest by SOC, HLT and PT
- Incidence of AEs of interest by SOC, HLT and PT

- Incidence of TEAEs by relationship, SOC, HLT and PT
- Incidence of TEAEs by maximum relationship, SOC, HLT and PT
- Incidence of serious TEAEs by relationship, SOC, HLT and PT
- Incidence of non-serious TEAEs by relationship, SOC, HLT and PT
- Incidence of fatal TEAEs by relationship, SOC, HLT and PT
- Incidence of TEAEs by maximum intensity (mild, moderate and severe), SOC, HLT and PT
- Incidence of non-serious TEAEs above threshold of 5% of participants by SOC and PT
- Incidence of non-serious TEAEs above threshold of 5% of participants by relationship, SOC and PT
- Discontinuation due to AEs

Summary tables will contain counts of participants, percentages of participants in parentheses and the number of events. A participant who has multiple events in the same SOC, HLT and PT will be counted only once in the participant counts but all events will be included.

Adverse event summaries will be ordered by alphabetical SOC, alphabetical HLT within SOC and decreasing frequency in the active treatment group.

In summaries including intensity, the CTCAE categories will be summarized according to the following categories:

- Grade 1: Mild
- Grade 2: Moderate
- Grade 3: Severe
- Grade 4: Severe
- Grade 5: Severe
- not gradable

In the case both category types are captured and the mapping to a standard intensity classification per above rule results in a class different from the standard intensity classification given in the eCRF, the worst case will be used.
These will be tabulated together with the AEs that were not classified according to CTCAE criteria i.e., all Grade 1 AEs as per CTCAE criteria will be included in the 'mild' category together with those AEs classified as mild as per the 'standard' intensity classification.

A listing will be presented by treatment group and participant for all AEs. This will include the onset date/time and outcome date/time of the event (including relative days), the AE duration, days since first dose of IMP, days since most recent dose of IMP, actual dose received, study period, pattern of event, severity/intensity, relationship, action taken and outcome. In addition, the listing will flag AEs that led to discontinuation, TEAEs, serious adverse events (SAEs), AEs of interest, AEs of special interest and infusion reactions.

AEs of focus (ie, TEAEs that are a review focus for rozanolixizumab or the participant population) will be summarized, in separate tables, detailing all TEAEs meeting the following criteria described below:

- Headache using the UCB-defined search criteria.
- Gastrointestinal disturbances using the UCB-defined search criteria.
- Hypersensitivity reactions using the criteria SMQ='Hypersensitivity'
- Anaphylactic reactions using the criteria SMQ='Anaphylactic reaction' and the UCB-defined search criteria.
- Injection site reactions using the UCB-defined search criteria.
- Infusion reaction collected on the eCRF AE page.
- Opportunistic infections using the UCB-defined search criteria.
- Reductions in albumin and plasma proteins using the UCB-defined search criteria.
- Effects on the kidney using the criteria SMQ='Acute renal failure'
- Drug related hepatic disorders using the criteria SMQ='Drug related hepatic disorders - comprehensive search'.

For each of the above-mentioned AEs of focus the following summaries will be presented:

- Incidence of all AEoFs by SOC, HLT and PT
- Incidence of all AEoFs by Relationship, SOC, HLT and PT
- Incidence of all serious AEoFs by SOC, HLT and PT
- Incidence of all AEoFs by Maximum Intensity, SOC, HLT and PT

UCB definitions for AEoF are found in a separate document "Adverse Events (AEs) of Focus for the rozanolixizumab Program" version 1.3, dated 04 Aug 2020.

10.3 Clinical laboratory evaluations

Laboratory data (chemistry, hematology and urinalysis) and changes from Baseline (if applicable) for numeric variables will be listed by treatment group and timepoint. Any laboratory measurements that are BLQ or ALQ will be handled as described in Section 4.2.2. Values outside the reference range for the numeric variables will be flagged in the listings. The reference ranges will also be reported in the listings. In addition, the listings will include a flag for values identified as markedly abnormal (MA) as defined by the criteria outlined in Section 13.2.

Chemistry and hematology parameters will be summarized by treatment group for both absolute values and changes from Baseline.

The laboratory variables to be included in the final analysis are presented in Table 10–1.

Table 10–1: Laboratory measurements

Category	Panel	Variable
Hematology	Red blood cell	RBC count, hemoglobin, hematocrit
	White blood cell	WBC count

Table 10–1: Laboratory measurements

Category	Panel	Variable
	White blood cell differential	Absolute counts: ANC, basophils, eosinophils, ALC, monocytes Percentages: neutrophils/leukocytes, basophils/leukocytes, eosinophils/leukocytes, lymphocytes/leukocytes, monocytes/leukocytes
	Platelet	Platelet count
Chemistry	Liver function	ALP, ALT, AST, GGT, total bilirubin[a], LDH
	Enzymes	Creatine kinase, amylase
	Proteins	Total protein, albumin, alpha- and beta- globulins, hsCRP
	Kidney Function	Urea- nitrogen, creatinine
	Lipids	Triglycerides, total cholesterol, LDL cholesterol, HDL cholesterol,
	Electrolytes	Calcium, phosphate, sodium, potassium, chloride, and magnesium
	Hormones	Procalcitonin
Urinalysis[b]	Dipstick	pH, nitrite, protein, glucose, ketones, urobilinogen, bilirubin, blood,
	Urine Sediment	Leukocytes
	Quantitative	Albumin, creatinine, protein

ALC=absolute lymphocyte count; ALP=alkaline phosphatase; ALT=alanine aminotransferase; ANC=absolute neutrophil count; AST=aspartate aminotransferase; GGT=gamma-glutamyltransferase; HDL=high density lipoprotein; hsCRP=high sensitivity C-Reactive Protein; LDH=lactate dehydrogenase; LDL=low density lipoprotein; RBC=red blood cell; WBC=white blood cell

[a] Direct bilirubin will also be measured when total bilirubin is elevated.

[b] Urine microscopy will be performed if urine is positive for protein, blood, nitrite, or leukocytes.

10.3.1 Potential drug-induced liver injury

A separate table will present participants who meet one or more of the following potential drug-induced liver injury (PDILI) criteria at any visit:

- Aspartate aminotransferase (AST): >3 x ULN, >5 x ULN, >10 x ULN, >20 x ULN
- Alanine aminotransferase (ALT): >3 x ULN, >5 x ULN, >10 x ULN, >20 x ULN
- AST or ALT: >3 x ULN, >5 x ULN, >10 x ULN, >20 x ULN
- Total bilirubin (TBL): >1.5 x ULN, >2 x ULN
- Alkaline phosphatase (ALP) >1.5 x ULN
- Alanine aminotransferase (ALT) or Aspartate aminotransferase (AST) ≥5x Upper limit of normal (ULN)
- (ALT or AST increase ≥3x ULN) and Total bilirubin ≥2x ULN
- AST or ALT ≥ 3 x ULN

- AST or ALT >3 x ULN, with TBL ≥1.5 x ULN
- AST or ALT >3 x ULN, with TBL ≥2 x ULN
- (ALT or AST increase >3x ULN) and Total bilirubin >2x ULN and ALP <2 x ULN (Hy's Law)
- (ALT or AST ≥3x ULN) and (eCRF question for "Is the subject exhibiting symptoms of hypersensitivity" = Yes or eCRF question for "Is the subject exhibiting symptoms of Hepatitis" = Yes at the same date +/-2 days)
- (ALT or AST) ≥3xULN (and ≥2x Baseline) and <5xULN and Total bilirubin <2xULN and (eCRF question for "Is the subject exhibiting symptoms of hypersensitivity"= No and eCRF question for "Is the subject exhibiting symptoms of Hepatitis"= No at the same date +/-2 days)
- (ALT or AST) ≥5xULN (and ≥2x Baseline) and Total bilirubin <2xULN (eCRF question for "Is the subject exhibiting symptoms of hypersensitivity"= No and eCRF question for "Is the subject exhibiting symptoms of Hepatitis"= No at the same date +/- 2 days)

The laboratory results listing will flag participants who are experiencing PDILI including Hy's Law.

10.4 Vital signs, physical findings, and other observations related to safety

10.4.1 Vital signs

The following vital signs measurements will be obtained:

- Pulse rate
- Systolic and diastolic blood pressure
- Body weight
- Temperature (oral preferred, ear or axillary permitted)

A by-participant listing of all vital sign measurements and change from Baseline will be presented by treatment group and timepoint. The listing will include a flag for measurements identified as markedly abnormal (MA) as calculated by the criteria outlined in Table 10–2.

Descriptive statistics will be reported for all vital sign measurements. Measured values and changes from Baseline will be summarized by vital signs variables, timepoint and treatment group.

Summarization will be as treated, participants who missed treatments will not be summarized

Table 10–2: MA Criteria for Vital Signs

Variable	Unit	Low	High
Systolic blood pressure[a]	mmHg	≤ 90 and a decrease from Baseline of ≥20	≥ 180 and an increase from Baseline of ≥20
Diastolic blood pressure[a]	mmHg	<50 and a decrease from Baseline of ≥15	>105 and an increase from Baseline of ≥ 15
Pulse rate[a]	bpm	<50 and a decrease from Baseline of ≥15	>120 and an increase from Baseline of ≥15

Table 10–2: MA Criteria for Vital Signs

Variable	Unit	Low	High
Temperature	°C		>101 0F (38.3 0C)
Body Weight	1	≥ 10% decrease from Baseline	≥ 10% increase from Baseline

Repeated and unscheduled measurements will be handled as described in Section 4.2.8.

10.4.2 Electrocardiograms

Standard 12-lead ECG recordings will be taken in triplicate with the participant resting in the supine position for at least 15 minutes and before obtaining any blood samples for assessments of laboratory variables. The following variables will be reported:

- Heart rate
- RR interval
- PQ/PR interval
- QRS duration
- QT interval
- QT corrected for heart rate using Fridericia's formula (QTcF = QT/(RR^1/3))

The individual measurements and the mean of the triplicate measurements will be reported in the by-participant listings. The listing will also include the change from Baseline (based on the mean of the triplicate measurements at each timepoint) and will be presented by treatment group and timepoint. The listing will also include a flag for values identified as MA/PCS as defined by the following criteria.

Table 10–3: MA/PCS criteria for Electrocardiograms

Parameter	Abnormality Criteria
QT interval (ms)	>=500ms
	>=60ms increase from Baseline
QTc(F) (ms)	>=500ms
	>=60ms increase from Baseline
PR interval (ms)	Treatment-emergent value >200ms
QRS interval (ms)	Treatment-emergent value >100ms
Heart rate (bpm)	<50bpm
	>120bpm

Measured values and changes from Baseline will be summarized by treatment group at each timepoint and by ECG variable (based on the mean of the triplicate values at each timepoint).

Summarization will be as treated, participants who missed treatments will not be summarized.

The following cut-points in QTcF (raw data and change from Baseline) will be summarized categorically by treatment group (number and percentage of participants) and visit/timepoint. The denominator for the percentages will be the number of participants with a non-missing measurement for the variable at the specific visit/timepoint.

Raw QTcF data:

• <450msec

• ≥450msec to <480msec

• ≥480msec to <500msec

• ≥500msec

Change from Baseline QTcF:

• <30msec

• ≥30ms to <60msec

• ≥60msec

Electrocardiogram findings for the individual triplicate measurements will be listed separately.

Repeated and unscheduled measurements will be handled as described in Section 4.2.8.

In the event that the complete set of triplicate measurements is not available at a specified timepoint the data will be handled as described in Section 4.2.6.

10.4.3 Suicidality

A full Columbia Suicide Severity Rating Scale (C-SSRS) assessment will be performed only when participant has a positive response to the suicidal ideation query. Results of suicidal ideation and C-SSRS will be listed by treatment group, participant and time point.

10.4.4 Other safety variables

Results of Serum and Urine pregnancy test will be listed.

Results of tuberculosis signs and symptoms questionnaire will be listed.

Results of Chest X-Ray will be listed.

Results of interferon-gamma release assay (IGRA) tuberculosis test will be listed.

Physical and neurological examination findings will be listed.

Results of serology testing for human immunodeficiency virus (HIV), Hepatitis B and Hepatitis C will be listed.

Participants experiencing severe headache will complete the Headache Questionnaire daily until resolution (ie, if headache becomes moderate or mild, normal collection of AEs should apply). At the clinic visit when the severe headache is reported, the Headache Questionnaire will be followed by a neurological assessment (including fundoscopy). If the severe headache is initially reported at a home visit or during a telephone call, the participant should be reviewed at the study site as soon as is practically possible for further investigations. Further workup will be performed at the discretion of the investigator and may include, eg, a computed tomography scan, magnetic resonance imaging and/or a lumbar puncture for cerebral spinal fluid collection. In addition, samples for exploratory biomarkers should be taken for participants experiencing severe headache (Table 5-2 of the protocol). These investigations will be performed to further understand the mechanism of headache in these participants.

The results of the headache questionnaire, neurological examination and any additional tests performed (CT scan, fundoscopy and LP for CSF collection) will be listed for each

participant having experienced severe headache. No summary tabulations will be provided for these assessments

Stool collection and analysis will be performed for participants reporting moderate or severe diarrhea. Results of the analysis will be listed for each participant. No summary tabulation will be provided for this assessment.

11 OTHER ANALYSES

Exploratory pharmacogenetics variables samples date/timepoint collection will be listed.

Exploratory RNA, proteins, and metabolites variables samples date collection will be listed.

For the presentation of the data for the interim analyses, each participant will be presented separately in the form of a patient profile which will include the following information:

- Participant demographics (age, gender, race, BMI, body weight at Screening)
- Treatment group
- Medical history (including procedure history)
- Prior and concomitant medication
- Drug administration (including whether performed at site or at home)
- AEs
- Safety laboratory variables (individual figures over time by panel [hematology, clinical chemistry, coagulation] and variable)
- Vital signs variables (individual figures over time by variable)
- ECG variables (individual figures over time by variable)
- IgG (individual figures over time for observed values and changes from Baseline)

12 REFERENCES

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13 APPENDICES

13.1 Conversion of iRODS scores

Table 13–1: Nomogram

R-ODS summed raw score	Rasch person location (logits)	centile metric	Corresponding SE SE= 0.4248 – 0.0016*location + 0.0140*location^2
0	-6.95	0	1.11
1	-6.03	6	0.94
2	-5.36	11	0.84
3	-4.87	14	0.76
4	-4.48	16	0.71
5	-4.14	19	0.67
6	-3.84	21	0.64
7	-3.57	22	0.61
8	-3.32	24	0.58
9	-3.09	26	0.56
10	-2.87	27	0.54
11	-2.66	28	0.53
12	-2.46	30	0.51
13	-2.26	31	0.5
14	-2.07	32	0.49
15	-1.88	34	0.48
16	-1.70	35	0.47
17	-1.52	36	0.46
18	-1.33	37	0.45
19	-1.15	39	0.45
20	-0.97	40	0.44
21	-0.79	41	0.43
22	-0.61	42	0.43
23	-0.42	43	0.43
24	-0.24	45	0.43
25	-0.05	46	0.42
26	0.14	47	0.42
27	0.34	48	0.43
28	0.53	50	0.43
29	0.73	51	0.43
30	0.94	52	0.44
31	1.15	54	0.44
32	1.36	55	0.45
33	1.58	57	0.46

R-ODS summed raw score	Rasch person location (logits)	centile metric	Corresponding SE SE= 0.4248 – 0.0016*location + 0.0140*location^2
34	1.81	58	0.47
35	2.04	60	0.48
36	2.28	61	0.49
37	2.54	63	0.51
38	2.80	65	0.53
39	3.09	67	0.55
40	3.40	69	0.58
41	3.74	71	0.61
42	4.11	73	0.65
43	4.54	76	0.71
44	5.03	80	0.77
45	5.59	83	0.85
46	6.25	88	0.96
47	7.07	93	1.11
48	8.11	100	1.33

13.2 Marked abnormality criteria for Rozanolixizumab program

The following criteria will be applied in the determination of marked abnormalities for laboratory assessment values for the clinical studies within the Rozanolixizumab clinical development program. These values are based on the CTCAE criteria version 5, grade 3 or higher criteria unless otherwise noted.

Table 13-2: MA Values for Rozanolixizumab Clinical Development Program Based on CTCAE Grades

Domain	Parameter	Unit (conventional)	Unit (standard)	Marked Abnormality criteria
Chemistry	AST (SGOT)	U/L	U/L	>5.0 x ULN
Chemistry	ALT (SGPT)	U/L	U/L	>5.0 x ULN
Chemistry	ALP (Alkaline Phosphatase)	U/L	U/L	>5.0 x ULN
Chemistry	GGT (Gamma Glutamyl Transferase)	U/L	U/L	>5.0 x ULN
Chemistry	Bilirubin (Total)	mg/dL	umol/L	>3.0 x ULN if Baseline value is normal; >3.0 x Baseline value if Baseline is abnormal
Chemistry	Albumin	g/dL	g/L	<2 g/dL; <20 g/L
Chemistry	Creatinine	mg/dL	umol/L	>3.0 x ULN
Chemistry	Estimate glomerular filtrate rate (eGFR)[1]	mL/min/1.73 m^2	mL/min/1.73 m^2	eGFR <29 mL/min/1.73 m^2
Chemistry	C reactive protein (CRP)[2]	mg/L	mg/L	>10 mg/L
Chemistry	Calcium	mg/dL	mmol/L	Low: Corrected serum calcium of <6.0 mg/dL; <1.5 mmol/L
Chemistry				High: Corrected serum calcium of >12.5 mg/dL; >3.1 mmol/L
Chemistry	Potassium	mmol/L	mmol/L	Low: <2.5 mmol/L
				High: >6.0 mmol/L
Chemistry	Sodium	mmol/L	mmol/L	Low: <125 mmol/L
				High: >155 mmol/L
Chemistry	Glucose	mg/dL	mmol/L	<40 mg/dL; <2.2 mmol/L
Chemistry	Total Cholesterol	mg/dL	mmol/L	>400 /dl; >10.34 mmol/L
Chemistry	Triglycerides	mg/dL	mmol/L	>500 mg/dl; >5.7 mmol/L

Table 13-2: MA Values for Rozanolixizumab Clinical Development Program Based on CTCAE Grades

Domain	Parameter	Unit (conventional)	Unit (standard)	Marked Abnormality criteria
Chemistry	Immunoglobulin G (IgG)	g/L	g/L	≤ 1 g/L
Hematology	Hemoglobin	g/dL	g/L	<8.0 g/dL; <80 g/L
Hematology	WBC (Leukocytes)	10^9/L	10^9/L	Low: <2.0 x 10^9/L
				High: >100 x 10^9/L
Hematology	Lymphocytes Absolute	10^9/L	10^9/L	Low: <0.5 x 10^9/L
				High: >20 x 10^9/L
Hematology	Neutrophils Absolute	10^9/L	10^9/L	<1.0 x 10^9/L
Hematology	Platelets	10^9/L	10^9/L	<50.0 x 10^9/L

14 AMENDMENT(S) TO THE STATISTICAL ANALYSIS PLAN (SAP)

14.1 Amendment 1

14.1.1 Rationale

Following the clinical study protocol amendment 2, the SAP was updated to reflect these changes and add detail to some analysis descriptions in this document. Changes were made to harmonize safety results across the IMP's program.

14.1.2 Changes

Change #1

Section 3.4, 3.9, 4.9, 5.2, 6:

COVID-19 protocol deviations were introduced and will be listed and summarized. Demographics, baseline characteristics and prior and concomitant medical conditions will be summarized by COVID-19 period.

Change #2

Section 3.5.3:

The Safety Set has been updated to include all subjects who received at least one dose of the IMP.

Change #3
Section 3.5.4, 3.9:
FAS definition: Study participants will be analysed as actually treated only if they received the incorrect treatment for the entire study period. In case of partial mistreatment, the participant will be analyzed as randomized.

Change #4

Section 3.5.5 and 8.1.4:

A modified full analysis set has been introduced to analyze the sensitivity to IMP dose variations.

Change #5

Section 4.2.1 and 8.2.4:

Patient reported grip strength at a visit is calculated as the mean of three daily maximum grip strength scores so data can be analyzed by visit and will be analyzed using MMRM.

Change #6

Section 6.1:

Region, country, body weight categories at screening added to demographics.

Change #7

Section 6.2:

Duration of disease (years) has been added to baseline characteristics.

Change #8

Section 7:

Treatment compliance is determined by percent of actual to planned dose administered

Change #9

Section 8.1.2:

Definition of fixed effects of the MMRM have been clarified. In case of non-convergence of the model, a sequence for alternative covariance matrix assumptions has been defined.

Change #10

Section 8.1.2.1:

The MMRM estimates will be summarized.

Change #11

Section 8.1.3:

The description of MI and LOCF sensitivity analyses have been detailed. P-values will not be displayed for sensitivity analyses.

Change #12

Section 8.2.2:

The adjusted INCAT score derivation has been detailed and is also analyzed using MMRM. A graphic representation will be created.

Change #13

Section 8.2.3:

Maximum grip strength as assessed by site personnel is also analyzed using MMRM. A graphic representation will be created.

Change #14

Section 8.2.6:

RT-MRC ANCOVA model was aligned with primary MMRM.

Change #15

Section 8.2.7:

"Following psychometric evaluation and refinement (eg, reduction in items) of these domains scales by using data generated in CIDP01, transformed interval 0-100 scoring will be provided for both domain scores with higher score reflecting higher severity" has been deleted, as this is not in scope of this analysis. Sum scores will be set to missing, in case of missing individual items.

Change #16

Section 8.2.9:

Identification of rescue medication has been clarified and time to first administration will be summarized.

Change #17

Section 10.1:

The extent of exposure to study treatment is categorized by percent deviation from randomized dose.

Change #18

Section 10.2:

TEAEs occurring in the observation period will not be stratified by stabilization period, but by participants being under standard of care treatment when the TEAE occurs.

Specific AEs of focus will be summarized separately.

Change #19

Section 10.3.1:

The instructions for assessment of PDILI were made clearer.

Change #20

Section 10.4.1:

Blood pressure MA/PCS definitions were changed to be in harmony with other Rozanolixizumab studies.

Change #21

Section 11:

A description of contents of patient profiles was added.

14.2 Amendment 2

14.2.1 Rationale

Adaptations reflect findings in a blinded data evaluation meeting and review of planned outputs.

14.2.2 Changes

14.2.2.1 Change 1

Sections 3.5.4 and 3.9, 4.2.1 and 8:

The FAS definition was clarified and efficacy assessments following intake of rescue medication are not eligible for analysis.

14.2.2.2 Change 2

Some COVID-19 related analyses were considered not valuable and removed. This includes removal of potentially COVID-19 impacted data and subgroup assessments based on COVID-19 period.

14.2.2.3 Change 3

Definition of Hy's Law updated.

14.2.2.4 Change 4

The fourth interim analysis was canceled not providing additional value.

14.2.2.5 Change 5

Exploratory statistical inference tests were removed to prevent overinterpretation of potential statistical significance. No p-values will be reported.

14.2.2.6 Change 6

Sensitivity analysis via multiple imputation was removed due to the low sample size.

14.2.2.7 Change 7

It was clarified that relapse, MMRM and summary tables for iRODS, adjusted INCAT and clinician reported grip strength will be performed for the FAS and PPS.

14.2.2.8 Change 8

Efficacy listings will be based on the SS, not the FAS, to present all relevant data available.

14.2.2.9 Change 9

Summary presentation of CIDP PRO Fatigue, PGIS and PGIC were corrected to reflect the scales of the assessments adequately.

14.2.2.10 Change 10

A PDILI criterion has been corrected (text for symptoms missing).

14.2.2.11 Change 11

ECG MA criteria table has been corrected (missing text). An IgG MA criterion has been added.

14.2.2.12 Change 12

CIDP-specific auto-antibodies will not be analyzed in scope of this SAP.

STATISTICAL ANALYSIS PLAN SIGNATURE PAGE

This document has been reviewed and approved per the Review and Approval of Clinical Documents Standard Operating Procedures. Signatures indicate that the final version of the Statistical Analysis Plan (SAP) or amended SAP is released for execution.

Approval Signatures

Name: cidp01-sap-final analysis

Version: 3.0

Document Number: CLIN-000135428

Title: CIDP01 SAP Final

Approved Date: 12 Apr 2021

Document Approvals	
Approval Verdict: Approved	Name: [redacted] Capacity: Clinical Date of Signature: 09-Apr-2021 15:03:34 GMT+0000
Approval Verdict: Approved	Name: [redacted] Capacity: Document Author Date of Signature: 12-Apr-2021 13:18:40 GMT+0000
Approval Verdict: Approved	Name: [redacted] Capacity: Subject Matter Expert Date of Signature: 12-Apr-2021 14:46:20 GMT+0000