STATISTICAL ANALYSIS PLAN

Study: CIDP04

Product: Rozanolixizumab

AN OPEN-LABEL EXTENSION STUDY TO INVESTIGATE THE LONG-TERM SAFETY, TOLERABILITY, AND EFFICACY OF ROZANOLIXIZUMAB IN SUBJECTS WITH CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY (CIDP)

SAP/Amendment Number	Date
Final SAP 1.0	08 Jun 2021

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LIST OF ABBREVIATIONS

ADA	Anti-drug antibody
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
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
C_{max}	Maximum concentration
CRO	Ccontract research organization
CTCAE	Common Terminology Criteria for Adverse Events
CSP	Cclinical study protocol
CSR	Clinical study report
C-SSRS	Columbia Suicide Severity Rating Scale
CV	Ccoefficient of variation
DBP	Diastolic blood pressure
DMC	Data Monitoring Committee
ECG	Eelectrocardiogram
eCRF	Eelectronic Case Report Form
EFNS	European Federation of Neurological Societies
ES	Enrolled Set
EudraCT	European Union Drug Regulating Authorities Clinical Trials
FAS	Full Analysis Set

FDA	Food and Drug Administration
FV	Final Visit
geoCV	Geometric coefficient of variation
geoMean	Geometric mean
GGT	Gamma glutamyltransferase
HDL	High density lioprotein
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
logit	Log odds unit
MA	Markedly abnormal
MCID-SE	Minimum clinically important differences-standard error
MedDRA	Medical Dictionary for Regulatory Activities
MFAS	Modified full analysis set
MRC	Medical Research Council
MRD	Minimum required dilution
n	Number of study 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
PT	Preferred term
QTcF	QT corrected for heart rate using Fridericia's formula
RBC	Red blood cell
RNA	Ribonucleic acid
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 necessary to perform the required statistical analyses of study CIDP04. It defines the summary tables, figures, and listings (TFLs) to be included in the Clinical Study Report (CSR).

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

- Final Protocol: 14 Dec 2018
- Protocol Amendment 2: 12 Jul 2019
- Protocol Amendment 3: 16 Mar 2020

Unless otherwise 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: 2018-004392-12).

If a future protocol amendment necessitates a substantial change to the statistical analysis of the study data, this SAP may be amended accordingly. Changes to the analysis from the protocol are documented in section 3.9.

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 assess long-term safety and tolerability of weekly doses of rozanolixizumab in study participants with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).

2.1.2 Secondary objective

The secondary objective of the study is to assess long-term clinical efficacy of weekly doses of rozanolixizumab.

2.1.3 Exploratory objectives

The exploratory objectives of the study are to assess the PD, PK, and immunological variables in the treatment course with rozanolixizumab and to assess whether long-term dosing of rozanolixizumab improves patient-reported outcomes (PROs). These include:

- The PD effect of rozanolixizumab as measured by the total immunoglobulin G (IgG) concentrations in serum
- The effects of rozanolixizumab on the concentrations of total protein, albumin, α- and β globulins, IgG subclasses, immunoglobulin M (IgM), immunoglobulin A (IgA), immunoglobulin E (IgE), and serum and plasma complement levels
- The incidence and emergence of anti-drug antibody (ADA) with respect to immunogenicity and PK and PD

- The effect of rozanolixizumab on complement and cytokines
- The plasma concentrations of rozanolixizumab administered by subcutaneous (sc) infusion
- The PD effect of rozanolixizumab as measured by neurofilament light chain (NF-L) in serum
- The effect of rozanolixizumab on CIDP-specific auto-antibody levels
- The effect of rozanolixizumab on vaccine antibody levels (influenza A and tetanus)
- The effect of rozanolixizumab on exploratory biomarkers, and explore the relationship between protein and metabolite biomarkers and cause, progression, and appropriate treatment of CIDP

2.2 Study variables

For all study variables, the Baseline values for study participants who enroll directly into CIDP04 will be the Baseline values from the parent study (eg, CIDP01). For study participants with a gap period prior to enrollment in CIDP04, details of the analyses of specific Baseline are defined in Section 3.3.

2.2.1 Safety variables

2.2.1.1 Primary safety variable

The primary safety variable is:

Occurrence of treatment-emergent adverse events (TEAEs)

2.2.1.2 Other safety variables

The other safety variables are:

- TEAEs leading to permanent withdrawal of investigational medicinal product (IMP)
- Vital sign values and changes from Baseline (systolic and diastolic blood pressure (BP), pulse rate (PR), body temperature, and body weight) at each scheduled assessment during Treatment and Observation Periods
- Physical examination findings
- Neurological examination findings
- 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

2.2.2 Other variables

2.2.2.1 Efficacy variables

Preliminary definitions linked to assessment of relapse are:

- CIDP relapse (Inflammatory Rasch-Built Overall Disability Scale [iRODS]) is defined as a clinically important deterioration from Baseline in iRODS score, ie, a minimum clinically important differences-standard error (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

The other efficacy variables are:

- Values and absolute change from Baseline in iRODS scores at each scheduled assessment during the Treatment and Observation Periods
- Study participant experienced CIDP relapse (iRODS) up to Week 25 and Week 77 (where applicable) from Baseline
- Time to CIDP relapse (iRODS) during the Treatment Period from Baseline
- Study participant experienced CIDP relapse (adjusted INCAT) up to Week 25 and Week 77 (where applicable) from Baseline
- Time to CIDP relapse (adjusted INCAT) during the Treatment Periods from Baseline
- Values and absolute change from Baseline in adjusted INCAT score at each scheduled assessment during the Treatment and Observation Periods
- Study participant experienced CIDP relapse (maximum grip strength as assessed by site personnel) up to Week 25 and Week 77 (where applicable) from Baseline
- Time to CIDP relapse (maximum grip strength as assessed by site personnel) during the Treatment Periods from Baseline
- Values and absolute change from Baseline in maximum grip strength score (maximum of assessments) taken by site personnel at each scheduled assessment during the Treatment and Observation Periods
- Values and absolute change from Baseline in RT-MRC sum score at each scheduled assessment during the Treatment and Observation Periods
- Study participants receiving rescue medication during Treatment Periods
- Time to rescue medication administration during Treatment Periods

2.2.2.2 Patient-reported outcome variables

- Values and change from Baseline in fatigue domain scores at each scheduled assessment during the Treatment and Observation Periods
- Values and change from Baseline in CIDP patient-reported outcome (PRO) instrument domain scores 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) value at each scheduled assessment during the Treatment and Observations Periods

2.2.2.3 Pharmacokinetic variable

Plasma concentration of rozanolixizumab at each scheduled assessment during the Treatment Periods.

2.2.2.4 Pharmacodynamic variables

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

2.2.2.5 Immunological variables

- 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
- ADA (anti-rozanolixizumab antibodies) 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 Tetanus- and influenza A virus-specific IgG antibodies during Treatment and Observation Periods

2.2.2.6 Exploratory biomarkers

The exploratory biomarkers are:

- Protein 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, B-cell activating factor and Circulating Immune Complexes may be measured to evaluate the effect of rozanolixizumab
- Absolute 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.

2.3 Study design and conduct

This is a Phase 2A, multicenter, single-arm, open-label extension OLE study to evaluate the safety, tolerability, and efficacy of rozanolixizumab during long-term treatment of study participants with CIDP from a previous study with rozanolixizumab.

Access to CIDP04 for study participants coming from CIDP01: Study participants from CIDP01 who have completed the Treatment Period (ie, all visits up to Visit 17) without a relapse of CIDP will be offered the opportunity to be directly enrolled into this OLE study. Study participants will enter CIDP04 on the same day as the last study visit in CIDP01: Visit 17. Study participants from CIDP01 who have experienced a relapse of CIDP (during either the Treatment Period or the Observation Period), have been successfully rescued and stabilized with SOC medication and have consented to enter this OLE study, may be assessed for eligibility. The study participants who relapsed during the Treatment Period of CIDP01 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 is confirmed they received placebo in CIDP01.

In case the study participants have a gap period between the end of the parent study and the start of this OLE study (ie, last visit in the parent study does not take place on the same day as entry of study CIDP04), a Screening Period of 2 to 5 weeks will be applicable to confirm that the study participant still meets the eligibility criteria for entry in the OLE study and allow for a smooth transition between the treatment used by the study participants during the gap period and the initiation of rozanolixizumab. The CIDP04 study includes a first 24-week Treatment Period (Part 1) followed by a second Treatment Period (Part 2) of up to 52 weeks (or until an Access Program or equivalent is in place, whichever comes first). Entry to the Treatment Period (Part 2) will be contingent to a favorable individual benefit-risk after careful individual assessment has been performed for each study participant completing Treatment Period (Part 1). An 8-week Observation Period will be followed in case of premature termination or after completion of the Treatment Periods (either at end of Part 1 for study participants not continuing in Part 2 or at end of Part 2). The Observation Period will not be performed in the event of a study participant continuing treatment with rozanolixizumab after the end of the study (ie, in case of an Access Program), in which case only the premature end of treatment (PEOT) (Visit 26) Visit will be performed.

During the Treatment Periods (Part 1 and Part 2), study participants will have weekly visits (either on site or at home) during which they will be dosed with a sc infusion of rozanolixizumab up to [redacted]. The initial dose in the study will be based on the dose the study participant has received at the completion of the parent study (eg, CIDP01). For study participants who were

known to be on placebo in the parent study, a starting dose of [redacted] will be used. The maximum dose will be [redacted]. See Section 7.2 in the protocol for details on treatment to be administered.

During the first 4 weeks of the Treatment Period (Part 1), all visits will be on site. During Weeks 5 to 8, home visits and on-site visits will be alternating (Weeks 5 and 7 will be on site; Weeks 6 and 8 will be at home). Starting at Week 9 and through the end of the Treatment Period (Week 24 and if applicable, Week 76), study participants will have 1 visit on site followed by 3 visits at home for every 4-week period.

After the completion of the Treatment Period(s) (starting at Week 25 for study participants only completing Part 1 or from Week 77 for study participants completing both Part 1 and Part 2 or at any early timepoint in case of PEOT), study participants will enter the 8-week Observation Period where no IMP will be administered. During the Observation Period, study participants will have on-site visits at the entry and exit of the Observation Period (Weeks 25/77, and 32/84, and home visits at Weeks 27/79 and 29/81). Study participants can return to their SOC during the Observation Period. In case the study participant enters an Access Program, no Observation Period will be performed with the exception of the PEOT (Visit 26) Visit which will be immediately completed.

At the discretion of the investigator and/or study participant, home visits can be changed to site visits (eg, for safety reasons). In case an on-site visit cannot be performed, the next visit will be performed at site instead of at home, and all safety assessments that should have been completed at the missed visits will be performed.

The assessments to be completed during each visit are presented in Table 5.1 in the protocol.

2.4 Determination of sample size

No formal sample size calculation has been performed since this is an open label extension study. All study participants from the parent study (eg, CIDP01) eligible for the OLE will be included.

3 DATA ANALYSIS CONSIDERATIONS

3.1 General presentation of summaries and analyses

Statistical evaluation for the analyses will be performed by PAREXEL. 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 (newly treated in CIPD04 or previously treated in CIPD01) and by visit (where applicable) with the statistics mean, standard deviation (SD), median, minimum, and maximum. Categorical variables will be summarized by treatment group and by 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 study 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 study 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.

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

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

If entry in CIDP04 (Visit 2) is done on the same day as the last visit of the parent study (CIDP01) and in case an assessment was performed at last visit of the parent study, data from the parent study will be used in the TFLs for Visit 2/Week 1.

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. For study participants treated with rozanolixizumab in parent study (eg CIDP01) the date of the first sc infusion of IMP administered at the parent study will be used as reference and be considered as the date of the first intake of IMP. For study participants treated with placebo during the parent study, date of first intake of IMP will be date of first IMP in CIDP04.

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. Relative day 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 study participant data listing. In such cases, relative day should be presented as '- -' in the study participant data listings.

3.2.1.2 Study periods

The total duration of the study for an individual study participant will be up to 89 weeks; this includes a 2- to 5-week Screening Period, a 24-week Treatment Period (Part 1), an optional maximum 52-week Treatment Period (Part 2), or until an Access Program or equivalent is in place whichever comes first, and an 8-week Observation Period in case the participant does not enter in an Access Program (or equivalent). Detailed definitions of those periods are as follows:

- Screening Period is applicable only for study participants with a gap period (ie, last visit in the parent study does not take place on the same day as entry of study CIDP04) between CIDP01 and CIDP04. It will start from the Screening visit to the day before Visit 2, when the first IMP is administered.
- Treatment Period Part 1 will start from the IMP administered at Visit 2 to the last IMP administered in Treatment Period Part 1, ie. Visit 25 (Weeks 1 to 24).
- The optional Treatment Period Part 2 will start after Visit 25 (non-inclusively) and last up to 52 weeks (Weeks 25 to 76) to the last IMP administration visit in Treatment Period Part 2.
- The Observation Period will start after the last IMP administration before Visit 26/PEOT (non-inclusively) and end with the Final Visit (FV/Visit 29).

Please note that Visit 26 can either refer to week 25, if a participant participates only in Treatment Period part 1, or week 77, if a participant also completes Treatment Period part 2.

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

3.3 Definition of Baseline values

For all study variables, the Baseline values for study participants treated with rozanolixizumab in the parent study (ie, CIDP01) will be the Baseline values from the parent study. For study participants treated with placebo in the parent study, the Baseline values will be the ones present at Baseline in CIDP04 (Visit 2 or if missing, the Screening Visit value (if applicable)). Note this Visit 2 value may be corresponding to the last value registered into CIDP01 as these may be the same visit.

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 as the baseline value.

Table 3–1: Expected Baseline

Measurement	Definition of Baseline
Safety data: • Safety Lab (Clinical chemistry, Hematology, Urinalysis) • ECG • Vital signs • Total protein, albumin, α- and β-globulins	For study participants treated with rozanolixizumab in parent study CIDP01: Safety labs, vital signs, total protein, albumin, α- and β-globulin: Baseline visit (Day 1) of parent study, if missing Screening visit of parent study (pre-dose value , if applicable). For study participants treated with placebo in the parent study: Safety labs, vital signs, total protein, albumin, α- and β-globulin: Baseline visit (Day 1) in CIDP04, if missing Screening visit (if applicable) (pre-dose value, if applicable). ECG: mean of triplicate values of Baseline visit (Day 1) in CIDP04. If missing Baseline visit, mean of triplicate values of Screening visit (if applicable).
Efficacy data • iRODS • INCAT • Grip strength (assessed by site personnel) • RT-MRC and original MRC • Fatigue score • CIDP PRO • PGIS • PGIC	For study participants treated with rozanolixizumab in parent study CIDP01: Baseline visit (Day 1) in CIDP01, if missing Screening visit For study participants treated with placebo in the parent study: Baseline visit (Day 1) in CIDP04, if missing Screening visit (where applicable)
Immunological variables: • IgA, IgE, IgM • Serum complement levels (C3, C4), • Plasma complement (C3a, C5a) • ADA • Cytokines • Tetanus- and influenza A virus-specific IgG antibodies	For study participants treated with rozanolixizumab in parent study CIDP01, refer to baseline definition in SAP for the parent study (ie Baseline visit (Day 1) of parent study, except for Tetanus- and influenza A virus-specific IgG antibodies where baseline is Screening visit of parent study). For study participants treated with placebo in the parent study : Baseline visit (Day 1) in CIDP04, except for Tetanus- and influenza A virus-specific IgG antibodies where baseline is Screening visit if applicable

Table 3–1: Expected Baseline

Measurement	Definition of Baseline
Pharmacodynamical variables: • Total serum IgG • NF-L levels	For study participants treated with rozanolixizumab in parent study CIDP01, refer to baseline definition in SAP for the parent study (ie for Total serum IgG: Baseline visit (Day 1) of parent study, if missing Screening visit of parent study. For study participants treated with placebo in the parent study: Total serum IgG: Baseline visit (Day 1) in CIDP04, if missing Screening visit (where applicable) NF-L: Baseline visit (Week 1) in CIDP04

ADA=anti-drug antibody; 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 IPDs will be identified and documented prior to unblinding to confirm exclusion from analysis sets.

IPDs potentially related to the Coronavirus Disease 2019 (COVID-19) will be 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

3.5.1 Enrolled Set

The Enrolled Set (ES) will consist of all study participants who have signed the informed consent form.

3.5.2 Safety Set

The Safety Set (SS) will consist of all enrolled study participants who were administered at least one dose of rozanolixizumab in CIDP04.

All safety variables will be analyzed using the SS.

3.5.3 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 26/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, but kept in listings.

3.5.4 Modified Full Analysis Set

The Modified Full Analysis Set (MFAS) will consist of all participants in the FAS, excluding any participant who either:

- received a mean actual dose of IMP deviating >10% or <-10% from the total planned dose
- missed more than two administrations in a period of three months.

The definition of the dose as well as details for calculations are provided in Section **Error! Reference source not found.**.

3.5.5 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.

3.5.6 Pharmacodynamic Per-Protocol Set

The Pharmacodynamic Per-Protocol Set (PD-PPS) is a subset of the SS, 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

All study participants will receive rozanolixizumab in the OLE.

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

- Treatment group 1: Newly treated (ie, study participants treated with placebo in parent study)
- Treatment group 2: Previously treated (ie, study participants treated with rozanolixizumab in parent study)

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

It is expected that study participants will have received treatment as randomized in CIDP01 and hence safety and efficacy analyses will be based on the randomized treatment group in CIDP01. However, if after unblinding of CIDP01 it is determined that a study participant has received

treatment different to the treatment they were randomized to, then for safety analyses the study participant will be allocated according to the actual treatment they received.

3.7 Center pooling strategy

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

3.8 Coding dictionaries

Adverse events (AEs) will be coded using version 23.1 or later of the Medical Dictionary for Regulatory Activities (MedDRA®).

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

- 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. Additionally, relapses defined by decline of >8kPa will be investigated.
- The FAS definition is clarified to include at least one valid post baseline iRODS assessment result.
- The PD-PPS will be handled as a subset of the SS instead of the FAS as defined in the protocol to not exclude data due to missing efficacy results.
- 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 considered valid.
- The MFAS is included as an additional analysis set in the SAP and was not part of the final clinical study protocol (CSP). This was added as a sensitivity analysis, to ensure the robustness of the efficacy results in relation to dose variation.
- Elevated liver function tests and potential drug induced liver injury criteria are harmonized across the rozanolixizumab program. Protocol-defined criteria are updated to match UCB's standard evaluations. Please refer to Section 10.3.1 for a list of the criteria that will be evaluated.

  ≥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

3.9.2 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.Interim Analysis

Per protocol section 14.7:

> *“Two interim analyses will be conducted. Firstly at the time of the lock of the parent study CIPD01 and additionally once all study participants have completed Part 1 of the Treatment Period in CIDP04 and have either entered into the Treatment Period Part 2 or the Observation Period. Details of the planned analyses will be fully outlined in the respective SAPs.”*

The events "lock of the parent study" and "all study participants have completed Part 1 of the Treatment Period in CIDP04" are expected to be close together and not differ enough in presented data to provide benefit by additional analysis. Therefore, these two interim analyses will not be performed.

4 STATISTICAL/ANALYTICAL ISSUES

4.1 Adjustments for covariates

Not applicable.

4.2 Handling of dropouts or missing data

4.2.1 Efficacy data

For study participants who prematurely withdraw for any reason before Visit 26, data collected during the PEOT Visit will be mapped to the closest missing visit according to the visit schedule utilizing the relative day in study to a maximum of Visit 26 (end of treatment period). However, if a participant receives rescue medication prior to the PEOT visit, any efficacy assessment post intake will be regarded invalid and only listed. Assessments on the same day as first intake of rescue medication are acceptable for analysis.

Study participants administered an Ig infusion rescue medication during the treatment phase will be considered relapsed even in case no relapse was documented. Missing relapse data, i.e. data for any relapse event definition, will be considered missing. In case of drop-out, if no relapse occurs or rescue medication is taken until PEOT visit (inclusively), the subject will be censored for time-to-event analysis at the date of PEOT visit.

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.

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 the respective 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 displayed 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 presented.

4.2.3 Pharmacodynamic data

Measurements BLQ are not anticipated for the total serum IgG data. If any BLQ measurements are received, these will be regarded as missing for the presentation 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 Week 1/ Visit 2 for study participants treated with placebo in the parent study, 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. If 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 first 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 study 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 study participants or the date of discontinuation for study 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 study 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 study 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 study 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 study 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 first original value (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 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

Study 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 (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 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 8-Weeks Observation period, will be mapped to the corresponding planned visit. Assessments on these visits will be flagged in the data listing.

4.4 Data monitoring committee (DMC)

A DMC will systematically monitor and report on the progress, safety, and/or critical efficacy endpoints of this study by convening to review the ongoing safety and efficacy data. The DMC

will also review the impact of infusion rate on local and systemic tolerability during the first 2 doses.

4.4.1 Timing of DMC

DMC meetings for CIDP04 will take place in conjunction with CIDP01 DMC meetings. Once CIDP01 is completed, additional meetings for CIDP04 may be organized as agreed with the DMC members.

4.4.2 Data required for DMC

The analyses and data required for DMC review are described in a separate 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 study 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 Study 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, and discontinuation due to AEs (categorised as fatal, non-fatal, other) 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 (SS)
- Participant analysis sets (ES)

Study participant disposition will be listed based on the ES by treatment group, and will include the date of informed consent, 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 first dose of IMP will be the first IMP infusion in CIDP01 for study participants treated with rozanolixizumab in CIDP01 or the first dose of rozanolixizumab in CIDP04 for the study participants under placebo in CIDP01.

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 of study participation will be listed and plotted in a Kaplan-Meier-Curve for all discontinuations versus discontinuation due to COVID-19. The plot will be based on the randomized set.

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 SS, and will include the deviation type and description. The number and percentage of participants in the SS with IPDs will be summarized overall if appropriate. The denominator for percentages will be the number of participants in the SS.

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 COVID-19 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 SS.

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

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-study 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 or at Visit 2 in case of missing values will be summarized for the SS.

Body mass index in kg/m^2 is calculated based on the height (in m) and the weight (in kg) measured either at the Screening visit (Visit 1) or baseline visit (Visit 2) of CIDP04 using the following formula:

$$BMI\ (kg/m^2) = weight\ (kg)/[height\ (m)]^2.$$

The BMI will be rounded 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 or Visit 2 of CIDP04 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 Baseline visit in CIDP04 will be listed for the SS by treatment group for all study participants and will include the reported term, preferred term (PT), dose, route of administration, frequency, formulation, start/stop dates and duration (in days) and if it was a rescue treatment in the parent study or not. For definition of prior treatments see Section 6.4.1.

Duration will be calculated as follows:

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

In addition, the following variables will be listed and summarized at baseline for the SS 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)

6.3 Medical and procedures history

Medical history updates, not reported in CIDP01, will be listed for the SS by treatment group and will include the MedDRA system organ class (SOC), high level term (HLT) and preferred term (PT).

Procedure history updates (not reported in CIDP01) and concomitant medical procedures will be listed based on the SS.

6.4 Prior and concomitant medications

Prior and concomitant medications will be listed for the SS by treatment group and for all study 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).

6.4.1 Prior medication definition

Prior medications will include any medications that started prior to the first administration of IMP for study participants with a gap period between the study CIDP01 and CIDP04. This includes any medications that started and stopped prior to dosing in CIDP04 as well as those which started prior to dosing and continued after (classified as prior and concomitant medications) if a gap period was present. For study participants who entered the study on the last visit day of CIDP01 prior medications will not be defined.

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 of CIDP04 study) during the Treatment 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 26/PEOT (non-inclusively).

This includes medications that started prior to the first IMP and continued during Treatment Period.

- Observation Period: a medication will be assigned to Observation Period if it has been taken at least once between Visit 26/PEOT (inclusively) and the FV. 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 (where applicable), 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 (ie, 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 summaries of efficacy data will be performed on the FAS. Additional outputs are repeated for the MFAS where indicated. Listings will be based on the SS. Treatment group assignment for efficacy data presentation will be according to the actual treatment regimen.

8.1 iRODS

8.1.1 iRODS scores

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 listed and summarized by treatment group for each scheduled assessment during the Treatment and Observation Period.

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.

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

The summary tables will be repeated based on the MFAS.

8.1.2 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]

$$"MCID-SE" = \frac{Logit\ location_{Visit} - Logit\ location_{baseline}}{\sqrt{SE^2_{Visit} + SE^2_{Baseline}}}$$

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).

The time to CIDP relapse (iRODS) is defined as the time from Baseline (Visit (Day 1) in CIDP01 for study participants treated with rozanolixizumab in the parent study or Baseline Visit (Day 1) in CIDP04 if study participants received placebo in the parent study) to achievement of iRODS and will be displayed using a Kaplan-Meier curve. Study participants withdrawing from the study will be censored unless relapsed or receiving rescue medication, which also is

interpreted as relapse. 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 who did not experience a relapse and are ongoing at the time of a data snapshot will be censored at the time of their last available assessment.

Relapse and time to relapse will be listed. Analyses will be performed for the FAS utilizing the observed cases. The relapse tables and figures will be generated for relapses up to Treatment Period Part 1 and for the entire Treatment Period (Part 1 and Part 2).

8.2 Adjusted INCAT

8.2.1 Adjusted INCAT score

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, considering the use of aids.

The investigator (or qualified personnel) will record the participants’ 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 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

Raw and adjusted INCAT scores will be listed. Adjusted INCAT scores will be summarized by treatment group for each scheduled assessment during the Treatment and Observation Period together with changes from baseline.

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

8.2.2 CIDP relapse (INCAT)

CIDP relapse (adjusted INCAT) is defined as an increase from Baseline of at least 1 point in the adjusted INCAT score.

The statistical methods and presentations applied to CIDP relapse (adjusted INCAT) and time to CIDP relapse (adjusted INCAT) will be the same as for CIDP relapse and time to CIDP relapse (iRODS), see Section 8.1.2.

8.3 Maximum Grip Strength (Assessed by Site Personnel)

8.3.1 Maximum Grip Strength (Assessed by Site Personnel)

Grip strength is assessed by qualified site personnel at 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 and listed. For analyses, UCB will utilize the maximum of the 3 assessments, which will be flagged in listings.

Maximum grip strength as assessed by site personnel will be listed and summarized by treatment group for each scheduled assessment during the Treatment and Observation Period together with changes from baseline.

8.3.2 CIDP relapse (Maximum Grip Strength, 14 kPa)

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

The statistical methods and presentations applied to CIDP relapse (Maximum Grip Strength, 14 kPa)) and time to CIDP relapse (Maximum Grip Strength, 14 kPa) will be the same as for CIDP relapse and time to CIDP relapse (iRODS), see Section 8.1.2.

8.3.3 CIDP relapse (Maximum Grip Strength, 8 kPa)

CIDP relapse (maximum grip strength as assessed by site personnel, 8 kPa) is defined as a clinically important deterioration from Baseline in grip strength as measured by site personnel, ie, a decline of >8 kPa.

The statistical methods and presentations applied to CIDP relapse (Maximum Grip Strength, 8 kPa) and time to CIDP relapse (Maximum Grip Strength, 8 kPa) will be the same as for CIDP relapse and time to CIDP relapse (iRODS), see Section 8.1.2.

8.4 CIDP Relapse

The event of CIDP relapse is defined by first 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 8.1.2, 8.2.2 and 8.3.2 and "other" as captured in the eCRF by the investigator. It will be described and analyzed in the same way as the individual relapse definitions.
The specified reason for "other" relapse will be included in the listing of CIDP relapse.

A listing will present if a participant experienced a CIDP relapse, CIDP relapse (iRODS), CIDP relapse (INCAT), CIDP relapse (Maximum Grip Strength, 14 kPa), CIDP relapse (Maximum Grip Strength, 8 kPa) or any other relapse reported by the investigator.

8.5 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) summary tables.

8.6 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.

8.6.1 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.

8.6.2 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 study participants 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.

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 rozanolixizumab by exposure (%) categories and time point using the number of available observations, mean, median, SD, minimum, maximum,

geoMean, (and associated 95% CI), and geoCV% (assuming log-normally distributed data) based on the PK-PPS. Definitions and rules for the exposure (%) categories are provided in Section 10.1.

Concentration data will be summarized for treatment rozanolixizumab by time point and ADA 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 study 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 study 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 study participants overlaid on the same figure.

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

9.2 Pharmacodynamics

The analysis of 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 and ADA status (6 categories; see Section 9.3.2) for absolute values, changes from Baseline and percentage changes from Baseline.

Study 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 study 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. If a decrease from Baseline in IgG is not observed in a given study participant, the maximum decrease will be reported as the smallest increase from Baseline.

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 timepoint including changes from Baseline. Descriptive summaries will be presented by timepoint for both absolute values and changes from Baseline.

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

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

9.3.2 Anti-drug antibodies

Anti-rozanolixizumab antibodies will be measured using a three-tiered assay approach: screening assay, confirmatory assay and titration assay. The results for the ADA 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 immunodepletion). Samples that are confirmed as positive will be evaluated in a titration assay to quantify the ADA 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 ADA status should be determined for each visit where samples were taken for ADA analysis:

- Sample values that are either negative screen or positive screen and negative immunodepletion will be defined as ADA negative
- Sample values that are positive screen and positive immunodepletion will be defined as ADA positive.

There will be six study participant classifications:

1. For study participants who are negative at baseline, and antibody negative at all sampling points post treatment (including FV)- pre ADA negative- treatment induced ADA negative

2. For study participants who are negative at baseline, and antibody positive at any sampling point post treatment (including FV)- pre ADA negative- treatment induced ADA positive. If a study participant has a missing pre-treatment sample (either missing or insufficient volume) at baseline with one or more ADA positive post-treatment samples will be also classified as pre ADA negative- treatment induced ADA positive
3. For study participants who are positive at baseline, and antibody negative at all sampling points post treatment (including FV)- pre ADA positive- treatment reduced ADA
4. For study 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. ≤ than a predefined fold difference from the baseline value)- pre ADA positive - treatment unaffected ADA
5. For study 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 ADA positive- treatment boosted ADA positive.
6. For Study participants who have a positive pre-treatment sample and some post-treatment samples are missing, while other post-treatment samples are ADA negative, the study participant will be classed as inconclusive.

A study participant will be classified as having treatment-induced ADA positivity when meeting one of the following criteria:

1. The Baseline result is ADA negative and at least one post-Baseline timepoint is ADA positive
2. The Baseline result is ADA 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)

A study participant will be considered:

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

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

Number and percentage of ADA positive and negative study participants at the time of each visit and overall will be summarized by treatment group based on the SS.

The first occurrence of treatment-induced ADA positivity (based on the definitions above) will be summarized (number and percentage of study participants) at each post-Baseline visit, based

on the SS. This tabulation will count the number of study participants at each post-Baseline visit who fulfill at least one of the above defined criteria for treatment-induced positivity; study participants will be counted in the numerator based on the earliest visit at which one of these criteria is fulfilled. At other visits, study 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 ADA status by the six categories, defined above, will be tabulated by treatment group, with an additional category "total treatment induced" combining study participants who are pre ADA negative- treatment induced ADA positive, study participants with a missing pre-treatment sample (either missing or insufficient volume) at baseline with one or more ADA positive post-treatment samples and study participants pre ADA positive- treatment boosted ADA positive.

The prevalence of immunogenicity, defined as (cumulative) proportion of study participants having positive immunodepletion ADA 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 ADA titer results as well as ADA titer results and percentage change from baseline in Total IgG by the six ADA classes described above will be presented. Spaghetti plots of ADA titer versus time will be presented for all ADA positive study 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. Summaries using descriptive statistics will be presented by treatment group and by 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 by time point, changes from Baseline will be added to the listing. Summaries using descriptive statistics will be presented by treatment group and by time point for both absolute values and changes from Baseline, both for all study participants and for study 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 Tetanus-and influenza A virus-specific IgG antibodies

Tetanus-and influenza A virus-specific IgG antibodies will be listed by treatment group and time point. Summaries using descriptive statistics 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 study participant; tabulations will be presented by treatment group and visit/timepoint (if applicable).

10.1 Extent of exposure

The initial dose administered will be based on the dose at the time of completion of the Treatment Period from the parent study (eg, CIDP01). For study participants who had a gap period between the parent study (eg, CIDP01) and CIDP04, a starting dose of [redacted] will be used (see protocol Table 7-1).
The intended dose will be calculated based on the study participant's weight at screening (where applicable) or Baseline in CIDP04 for Treatment Period Part 1. For Treatment Period Part 2, body weight is collected every 6 months starting at first visit in this period and the most recent weight will be used to select the correct volume for dose infusion from these timepoints. The calculation is done as follows for the applicable weight:

Intended dose (mg) = weight (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 as well as 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 in CIDP04 study or any unresolved event already present before the first administration of IMP in CIDP04 study that worsens in intensity following exposure to treatment until 8 weeks following

the last administration of IMP in CIDP04 study. Adverse events starting before the first administration of IMP in CIDP04 study 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:

- **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 in CIDP04 study on Week 1, up to Visit 26/PEOT (non-inclusively).
- **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 26/PEOT till 8 weeks after administration of the last IMP in CIDP04 study.
  - The Observation Period's TEAEs will be stratified by TEAEs of study 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 study 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 study 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 study participants, percentages of study participants in parentheses and the number of events. A study participant who has multiple events in the same SOC, HLT and PT will be counted only once in the study 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 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 study 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**Error! Reference source not found.**.

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 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
	White blood cell differential	Absolute counts: ANC, basophils, eosinophils, ALC, monocytes Percentages: neutrophils/leukocytes, basophils/leukocytes, eosinophils/leukocytes, lymphocytes/leukocytes, monocytes/leukocytes

Table 10–1: Laboratory measurements

Category	Panel	Variable
	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 study 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, >8 x ULN, >10 x ULN, >20 x ULN
- Alanine aminotransferase (ALT): >3 x ULN, >5 x ULN, >8 x ULN, >10 x ULN, >20 x ULN
- AST or ALT: >3 x ULN, >5 x ULN, >8 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
- 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 >3 x ULN) and Total bilirubin >2 x ULN and ALP <2 x ULN (Hy's Law)

- Incidence of potential hepatotoxicity with symptoms potentially associated with hepatitis or hypersensitivity (participants meeting laboratory criteria for pDILI for at least 1 visit and reporting at least 1 symptom potentially associated with hepatitis or hypersensitivity according to the Investigator on the pDILI CRF.)
- Incidence of potential hepatotoxicity with no symptoms potentially associated with hepatitis or hypersensitivity (participants meeting laboratory criteria for pDILI for at least 1 visit and not reporting any symptom potentially related to hepatitis or hypersensitivity according to the Investigator pDILI CRF.)

The laboratory results listing will flag study 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-study 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 Section 13.2**Error! Reference source not found.**.

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, study participants who missed treatments will not be summarized. 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 study 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 ($QTcF = QT/\sqrt[3]{RR}$)

The individual measurements and the mean of the triplicate measurements will be reported in the by-study 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 by timepoint. The listing will also include a flag for values identified as MA as defined by the criteria outlined in Section 13.2**Error! Reference source not found.**.

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

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).

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 study participant has a positive response to the suicidal ideation query. Results of suicidal ideation and C-SSRS will be listed by treatment group, study 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 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.

Study 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). The results of the headache questionnaire will be listed for each study participant.

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

12 REFERENCES

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Adverse Events of Focus (AEoF) for the rozanolixizumab Program, version 1.3, 04 Aug 2020

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
e	-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

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
32	1.36	55	0.45
33	1.58	57	0.46
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 MA criteria for Rozanolixizumab program

The following criteria will be applied in the determination of marked abnormalities for laboratory assessment values. They are based on Version 5 of the Common Terminology Criteria for Adverse Events (CTCAE) 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

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

Domain	Parameter	Unit (conventional)	Unit (standard)	Marked Abnormality criteria
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	IgG	g/L	g/L	≤ 1 g/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	Low: <40 mg/dL; <2.2 mmol/L
				High: > 250 mg/dL; >13.9 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
Hematology	Hemoglobin	g/dL	g/L	<8.0 g/dL; <80 g/L
Hematology	WBC (Leukocytes)[4]	10^9/L	10^9/L	Low: <2.0 x 10^9/L
				High: >30 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

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

Domain	Parameter	Unit (conventional)	Unit (standard)	Marked Abnormality criteria
Hematology	Platelets	10^9/L	10^9/L	<50.0 x 10^9/L
Vital Signs	Pulse Rate	bpm	bpm	≤50 and a decrease from Baseline of ≥15 ≥120 and an increase from Baseline of ≥15
Vital Signs	Systolic Blood Pressure	mmHg	mmHg	≤ 90 and a decrease from Baseline of ≥20 ≥ 180 and an increase from Baseline of ≥20
Vital Signs	Diastolic Blood Pressure	mmHg	mmHg	≤50 and a decrease from Baseline of ≥15 ≥105 and an increase from Baseline of ≥ 15
Vital Signs	Temperature	°F	°C	>101 °F (38.3 °C)
Vital Signs	Body Weight			≥ 10% decrease from Baseline ≥ 10% increase from Baseline
ECG	QT interval	ms	ms	≥500ms
				≥60ms increase from Baseline
ECG	QTc(F)	ms	ms	≥500ms
				≥60ms increase from Baseline
ECG	PR interval	ms	ms	Treatment-emergent value >200ms
ECG	QRS interval	ms	ms	Treatment-emergent value >100ms
ECG	Heart rate	bpm	bpm	<50bpm
				>120bpm

Abbreviations: ALT= alanine aminotransferase; AST = aspartate aminotransferase; dL = deciliter; GGT: gamma-glutamyltransferase; L = liter; mg = milligram; mmol = millimoles; µg = microgram; U = unit; ULN = upper limit of normal

Note: Marked abnormality criteria are defined by Grade 3 or higher events according to the Common Terminology for Adverse Events (CTCAE), Version 5.0, November 17, 2017 unless otherwise noted.

[1]eGFR is calculated using the Chronic Kidney Disease Epidemiology Collaboration or CKD-EPI formula (https://qxmd.com/calculate/calculator_251/egfr-using-ckd-epi) which is eGFR = 141 * min(Scr/κ,1)$^{\alpha}$ * max(Scr/κ, 1)$^{-1.209}$ * 0.993^{Age} * 1.018 [if female] * 1.159 [if black]; where Scr is serum creatinine (mg/dL), κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1. For derivation from values in standard units (umol/L) the κ values are 61.9 for females and 79.6 for males.

[2]Includes CRP and High Sensitivity (HS) CRP. Reference for marked abnormality criteria: Nehring, S.M.; Goyal, A.; Patel, B.C. (2020). StatPearls Publishing, web link: https://www.ncbi.nlm.nih.gov/books/NBK441843/.

[3]Immunoglobulin G criterion based on immunodeficiency literature and noted in RLZ study protocols.

[4]WBC (Leukocytes) markedly abnormal high criterion is not based on Version 5 CTCAE Grade 3 or higher criteria. Due to the mechanism of action of RLZ, the safety alert is related to infection risk which would be identified by a

lower cut-point than the standard which is related to acute leukemias. A markedly abnormal high cut-point >30 x 109/L is applied to flag leukocytosis (George 2012).

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.

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