STATISTICAL ANALYSIS PLAN

AMENDMENT 2

Study: MG0007

Product: Rozanolixizumab

AN OPEN-LABEL EXTENSION STUDY TO EVALUATE ROZANOLIXIZUMAB IN STUDY PARTICIPANTS WITH GENERALIZED MYASTHENIA GRAVIS

SHORT TITLE:

A Phase 3, open-label extension (OLE) study to evaluate 6-week treatment cycles of rozanolixizumab in study participants with gMG.

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Regulatory Agency Identifier Number(s):

Registry	**ID**
Eudra CT Number	2020-003230-20
IND Number	132407

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VERSION HISTORY

SAP Version	Approval Date	Change	Rationale
1.0	27 Mar 2021	Not Applicable	Original version
Amendment 1	24 Jun 2022	See details in Section 14.1	To address DEM1 and DEM2 comments
Amendment 2	22 Feb 2024	See details in Section 14.2	To implement the changes in Protocol Amendment 3 and address DEM3 comments

LIST OF ABBREVIATIONS

AChE	Acetylcholinesterase
AChR	Acetylcholine Receptor
ADA	Antidrug Antibody
ADD	Average Daily Dose
AE	Adverse Event
AEOF	Adverse Event of Focus
AESI	Adverse Event of Special Interest
AESM	Adverse Event of Special Monitoring
ALP	Alkaline Phosphatase
ALQ	Above the Upper Limit of Quantification
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Chemical
BLQ	Below the Lower Limit of Quantification
BMI	Body Mass Index
BUN	Blood Urea Nitrogen
CI	Confidence Interval
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
COVID-19	Coronavirus Disease 2019
CRF	Case Report Form
CSR	Clinical Study Report
C-SSRS	Columbia-Suicide Severity Rating Scale
CTCAE	Common Terminology Criteria for Adverse Events

CV	Coefficient of Variation
DILI	Drug-Induced Liver Injury
ECG	Electrocardiogram
eCRF	electronic Case Report Form
eGFR	estimated Glomerular Filtration Rate
EOS	End of Study
EQ-5D-5L	5-Level European Quality of Life 5 Dimensions
ES	Enrolled Set
ER	Emergency Room
FAS	Full Analysis Set
FDA	Food and Drug Administration
geoCV	Geometric Coefficient of Variation
GI	Gastrointestinal
gMG	Generalized Myasthenia Gravis
HbA1c	Hemoglobin A1C
hCG	Human Chorionic Gonadotropin
HLGT	High Level Group Term
HLT	High Level Term
ICH	International Council for Harmonisation
ICU	Intensive Care Unit
IDMC	Independent Data Monitoring Committee
IEC	Independent Ethics Committee
Ig	Immunoglobulin
IGRA	Interferon Gamma Release Assay

IMP	Investigational Medicinal Product
INR	International Normalized Ratio
IPD	Important Protocol Deviation
IRB	Institutional Review Board
IVIg	Intravenous Infusion of Immunoglobulin G
LDH	Lactate Dehydrogenase
LLOQ	Lower Limit of Quantification
LPFD	Last Patient First Dose
LPLV	Last Patient Last Visit
MA	Markedly Abnormal
MAP	Managed Access Program
MedDRA	Medical Dictionary for Regulatory Activities
MG	Myasthenia Gravis
MG-ADL	MG-Activities of Daily Living
MG-C	MG-Composite
MG-QOL15r	Myasthenia Gravis-Quality of Life
MuSK	Muscle-specific Kinase
Nab	Neutralizing Antibody
OLE	Open-label Extension
PD	Pharmacodynamics
pDILI	Potential Drug-Induced Liver Injury
PEOT	Premature End of Treatment
PEX	Plasma Exchange
pIDMC	Program Independent Data Monitoring Committee

PK	Pharmacokinetic
PMDA	Pharmaceuticals and Medical Devices Agency
PRO	Patient-Reported Outcome
PT	Preferred Term
PTT	Partial Prothrombin Time
QMG	Quantitative Myasthenia Gravis
QW	Weekly
RBC	Red Blood Cell
RLZ	Rozanolixizumab
SAP	Statistical Analysis Plan
SC	Subcutaneous
SCIg	subcutaneous immunoglobulin
SD	Standard Deviation
SGOT	Serum Glutamic-Oxaloacetic Transaminase
SGPT	Serum Glutamic-Pyruvic Transaminase
SOC	System Organ Class
SS	Safety Set
SU	Safety Update
TB	Tuberculosis
TEAEs	Treatment-Emergent Adverse Events
TEMA	Treatment-Emergent Markedly Abnormal
TFLs	Tables, Figures and Listings
ULN	Upper Limit of Normal
VAS	Visual Analogue Scale

WBC	White Blood Cell
WHODD	World Health Organization Drug Dictionary

1 INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to provide all information that is necessary to perform the statistical analyses of study MG0007, including three interim cuts and final analysis. It also defines the summary tables, figures and listings (TFLs) to be included in the final Clinical Study Report (CSR) according to the protocol.

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

- Protocol Amendment 3: 03 Oct 2022
- Rozanolixizumab Program Safety Analysis Plan: 16 Nov 2023

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.

2 PROTOCOL SUMMARY

2.1 Study objectives

2.1.1 Primary objective

To assess the safety and tolerability of additional 6-week treatment cycles with rozanolixizumab in study participants with generalized myasthenia gravis (gMG)

2.1.2 Secondary objective

To assess the efficacy of 6-week treatment cycles with rozanolixizumab in study participants with gMG

2.1.3 Other objectives

- To assess the pharmacokinetics (PK) of rozanolixizumab
- To evaluate the incidence and emergence of antidrug antibody (ADA) of rozanolixizumab
- To assess the pharmacodynamics (PD) of rozanolixizumab
- To assess the effects of rozanolixizumab on the concentration of [redacted]
- To assess the need for gMG medications including changes in type and doses
- To assess the effect of rozanolixizumab on [redacted]

2.2 Study endpoints

2.2.1 Safety endpoints

2.2.1.1 Primary safety endpoints

- Occurrence of treatment-emergent adverse events (TEAEs)
- TEAEs leading to withdrawal of investigational medicinal product (IMP)

2.2.1.2 Other safety endpoints

- Occurrence of serious TEAEs
- Occurrence of treatment-emergent adverse events of special monitoring (AESM)
- Vital sign values and changes from Baseline (Day 1) (systolic and diastolic blood pressure [BP] and pulse rate at each scheduled assessment during Treatment and Observation Periods)
- 12-lead electrocardiogram (ECG) values and change from Baseline at each scheduled assessment during the Treatment and Observation Periods
- Laboratory values and changes from Baseline at each scheduled assessment during the Treatment and Observation Periods (hematology, clinical chemistry, and urinalysis)

2.2.2 Efficacy endpoints

2.2.2.1 Secondary efficacy endpoints

For each of the first 3 x 6-week treatment cycle, change from Baseline (Day 1) to Day 43[a]:

- In MG-Activities of Daily Living (MG-ADL) score within one treatment cycle
- In Quantitative MG (QMG) score within one treatment cycle
- In MG-Composite (MG-C) score within one treatment cycle
- In MG Symptoms patient-reported outcomes (PRO) 'Muscle Weakness Fatigability' score within one treatment cycle
- In MG Symptoms PRO 'Physical Fatigue' score within one treatment cycle
- In MG Symptoms PRO 'Bulbar symptoms' score within one treatment cycle
- In MG-ADL responder (≥2.0-point improvement) within one treatment cycle
- Time to MG-ADL response (≥2.0-point improvement from Baseline [Day 1]) within one treatment cycle

For consecutive treatment cycles:

- Time between consecutive treatment cycles

2.2.2.2 Other efficacy endpoints

For each 6-week treatment cycle and Observation Period (where applicable), improvement from Baseline (Day 1) to each scheduled assessment:

- MG-ADL responder (≥2.0-point) within one treatment cycle
- QMG responder rate (≥3.0-point) within one treatment cycle
- MG-C responder rate (≥3.0-point) within one treatment cycle
- Time to MG-ADL response (≥2.0-point) within one treatment cycle
- Minimal symptom expression (MG-ADL score of 0 or 1) at any time during Treatment and Observation Periods

For each 6-week treatment cycle and Observation Period (where applicable), change from Baseline (Day 1) to each scheduled assessment:

- In MG-ADL score within one treatment cycle
- In QMG score within one treatment cycle
- In MG-C score within one treatment cycle
- In MG Symptoms PRO 'Muscle Weakness Fatigability' score within one treatment cycle
- In MG Symptoms PRO 'Physical Fatigue' score within one treatment cycle
- In MG Symptoms PRO 'Bulbar symptoms' score within one treatment cycle

For each 6-week treatment cycle and Observation Period (where applicable), change from Baseline (Day 1) to Day 43[a]:

- In 5-level European quality of life 5 dimensions (EQ-5D-5L) within one treatment cycle
- In Myasthenia Gravis-Quality of Life (MG-QOL15r) within one treatment cycle

Note:

[a] Day 43 = Visit 8 for the initial fixed cycle and Visit 7 for the subsequent cycles.

2.2.3 Pharmacokinetic and pharmacodynamic

2.2.3.1 Pharmacokinetic endpoints

Plasma concentrations of rozanolixizumab at each scheduled assessment

2.2.3.2 Pharmacodynamic endpoints

For each 6-week treatment cycle and Observation Period (where applicable):

- Minimum value and maximum decrease from Baseline (Day 1) in total serum IgG and IgG subclasses concentration over time
- Change from Baseline (Day 1) in serum IgG subclasses concentration over time
- Change (absolute and percentage) from Baseline (Day 1) in MG-specific autoantibodies at each scheduled assessment during the Treatment and Observation Periods

2.2.4 Anti-drug antibody endpoints

- ADA at each scheduled assessment

2.2.5 Immunological endpoints

- Change from Baseline (Day 1)[b] in [redacted] in participants experiencing infusion reactions

For initial fixed treatment cycle only:

- Change from Baseline (Day 1) in serum Ig concentrations [redacted]) at each scheduled assessment during Treatment and Observation Periods

Note:

[b] Baseline will be used from the sample collected at Day 1 (Visit 2) in MG0003. Other exploratory safety biomarkers may be assessed.

2.2.6 Rescue therapy and healthcare endpoints

- Use of rescue therapy (yes/no)
- Time to rescue therapy
- Healthcare resource utilization, including hospitalization (type: intensive care unit [ICU]/non-ICU and duration in each respective type of care)

2.2.7 COVID-19 related endpoint

- [redacted]

2.3 Study design and conduct

2.3.1 Overall design

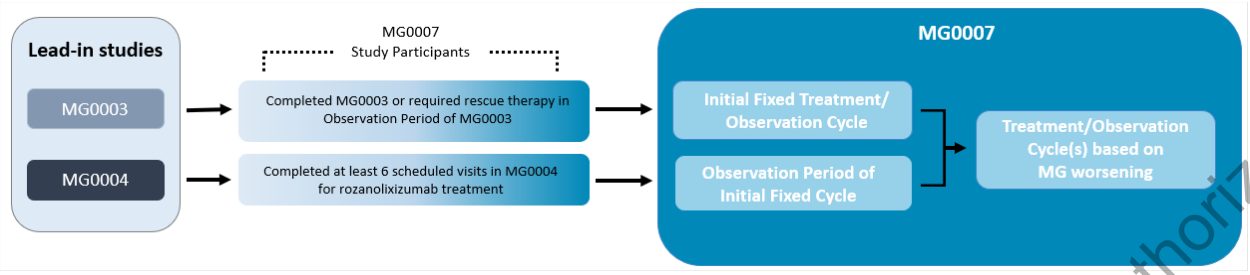
This is a Phase 3, multicenter, 2-arm, OLE study to evaluate 6-week treatment cycles of rozanolixizumab in study participants with gMG. MG0007 is an extension study of MG0003. The study is open to study participants from MG0003 and MG0004.

Eligible study participants from MG0003 will be randomized to receive an initial fixed 6-week treatment cycle of a subcutaneous dose of rozanolixizumab equivalent to approximately 7mg/kg or 10mg/kg weekly (QW) (see Figure 2–1 and Figure 2–2), followed by an Observation Period that begins after the last dose of that treatment cycle as per assessments described in the Schedule of Activities in protocol.

Eligible study participants from MG0004 who have completed at least 6 scheduled visits for rozanolixizumab treatment and the Premature End of Treatment (PEOT) visit can move directly into the Observation Period in MG0007. Additionally, eligible study participants from MG0004 who are in the Observation Period can complete the End of Study (EOS) visit and move directly into the Observation Period in MG0007 (see Figure 2–1 and Figure 2–2). If IMP treatment was withheld for low IgG in MG0004, study participant's missed dose(s) can be counted as part of the total 6 visits for completion of MG0004 and meet eligibility requirements for MG0007. These study participants will undergo their first MG0007 treatment with rozanolixizumab upon worsening of gMG symptoms. Participants will continue on their last treatment dose from MG0004. Dose adjustments may be applied in future cycles as per description below.

The rollover into MG0007 must be completed within 4 weeks after the EOS visit from MG0003, or the PEOT or EOS (as appropriate) visit from MG0004. In the event a study participant has a gap period (>4 weeks) between the EOS or PEOT visit from the lead-in study and the start of MG0007, a Screening Period of up to 4 weeks will be applicable to confirm that the study participant still meets the eligibility criteria for entry into MG0007.

Figure 2–1: MG0007 entry schema



In case of symptom worsening (eg, an increase of 2.0 points on the MG-ADL or 3.0 points on the QMG scale) between assessments, resulting in a need for additional treatment, study participants will undergo another 6-week treatment cycle followed by an Observation Period, based on the Investigator's discretion. The dose may be adjusted to 7mg/kg or 10mg/kg at the beginning of each treatment cycle based on the Investigator's discretion. The minimal time to start the next treatment cycle is 4 weeks following the last dose of the treatment period of the previous cycle. If a study participant requires treatment earlier than 4 weeks, IgG levels from the previous cycle should be considered and discussed with the Medical Monitor. A new treatment cycle **should not** be initiated until total IgG level is ≥2g/L.

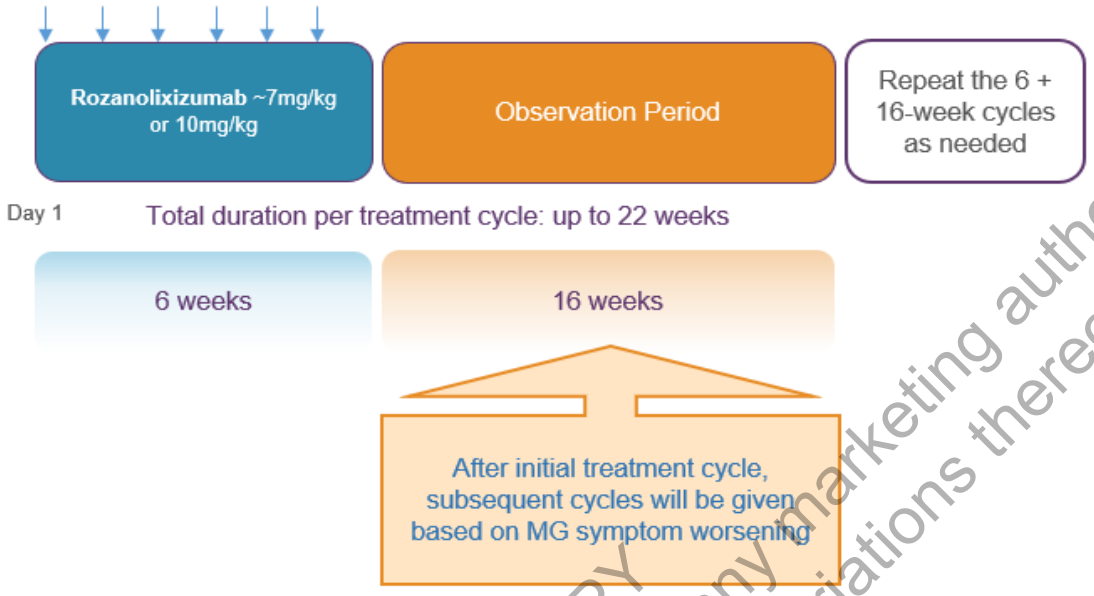
Participants in MG0007 will remain on their gMG background medications. With the exception of corticosteroids and acetylcholinesterase (AChE) inhibitors, all gMG medication doses should be maintained during each respective 6-week treatment cycle and efforts should be made to maintain a stable dose during the first 8 weeks of the Observation Period.

Study participants who receive rescue therapy (intravenous immunoglobulin [IVIg], plasma exchange [PEX], subcutaneous immunoglobulin [SCIg], or iv corticosteroid) during the Treatment Period are not eligible to receive any further treatment with rozanolixizumab. These participants must complete the first 8 weeks of the Observation Period after the last dose of rozanolixizumab prior to completing the EOS visit assessments, and subsequently will be withdrawn from the study.

Those patients who received rescue therapy (IVIg, PEX, SCIg, or iv corticosteroid) during the observation or no treatment with rozanolixizumab periods may continue in the study at the Investigator's discretion and after discussion with Medical Monitor and/or UCB Study Physician. The following cycle of rozanolixizumab should in general not start earlier than 4 weeks following the last dose of IVIg, SCIg, or iv corticosteroids or the last PEX session, unless there is a medical reason, and an earlier treatment initiation is being considered [redacted] for the study participant as agreed upon with the Medical Monitor and/or UCB Study physician.

Study participants (not withdrawn from the study) will continue in the study and until product approval or until transition to a managed access program (MAP), if available, as indicated per the Sponsor, and according to local guidance.

Figure 2–2: MG0007 study schema



2.3.2 Dosing

This OLE study will continue treatment with rozanolixizumab subcutaneous (sc) fixed doses across body weight tiers equivalent to approximately 7mg/kg and 10mg/kg administered QW for 6-week treatment cycle (Table 2–1). Weight-based dose adjustments should be limited to a maximum of every 6 months during the study.

If one of the doses described in Table 2–1 is determined to be futile and is discontinued in MG0003, then that dose arm will be dropped from MG0007, and study participants in the affected dose arm will be transferred to an adjusted dose.

Dose modifications from 10mg/kg to 7mg/kg equivalent and vice versa are permitted at the beginning of the treatment cycles at the Investigator's discretion, and if the benefit-risk remains favorable for the study participant. Recommended dose modifications from 10mg/kg to 7mg/kg equivalent due to drug-related adverse events may include but are not limited to:

- Moderate to severe headaches that are considered to be related to rozanolixizumab
- Moderate to severe gastrointestinal (GI) disturbances that are considered to be related to rozanolixizumab
- Moderate to severe toxicities (≥Grade 2 as defined by Common Terminology Criteria for Adverse Events [CTCAE], version 5.0) for which rozanolixizumab cannot be excluded as a cause
- Recurrent hypogammaglobulinemia with a serum total IgG level of <2g/L.

Table 2–1: MG0007 dose levels and weight tiers

Bodyweight	Rozanolixizumab dose equivalent	
	7mg/kg Dose 1	10mg/kg Dose 2
≥35 to <50kg	280mg	420mg
≥50 to <70kg	420mg	560mg
≥70 to <100kg	560mg	840mg
≥100kg	840mg	1120mg

2.4 Determination of sample size

No formal sample size calculation can be performed. All eligible study participants from MG0003 and MG0004 will be invited to participate in MG0007. Approximately 200 study participants will be enrolled into MG0007.

The number of 200 study participants is assuming a drop-out rate from the lead-in study of approximately 15% (including participants who opt not to continue in MG0007).

3 DATA ANALYSIS CONSIDERATIONS

3.1 General presentation of summaries and analyses

For safety analyses, data will be summarized by dose levels of rozanolixizumab at the time of the event or measurement. For efficacy analyses, data will be summarized by the dose first received in the study. Additionally, efficacy data will be summarized by dose levels of rozanolixizumab received in each treatment cycle.

Statistical analysis and generation of tables, figures, participant data listings, and statistical outputs will be performed using SAS® Version 9.3 or higher. All tables and listings will use Courier New font size 9.

Descriptive statistics will be displayed to provide an overview of the study results. For continuous variables, descriptive statistics will include number of participants with available measurements (n), mean, standard deviation (SD), median, minimum, and maximum.

For categorical variables, the number and percentage of participants in each category will be presented. Unless otherwise noted, the denominator for percentages will be based on the number of participants included in the respective analysis set. Participants with missing data can generally be accounted for using the following approaches:

- For summaries of demographics and Baseline characteristics: summarize percentages based on all participants in the analysis set and include a "Missing" category (corresponding to participants with missing data for the variable being summarized) as the last row in the list of categories being summarized.
- For summaries of efficacy and safety endpoints, unless otherwise specified: summarize percentages based only on those participants with observed data for the variable being summarized. As the denominator may be different from the number of participants in the

analysis set being considered, the denominator should be displayed in the table. The general format for displaying this will be "n/Nsub (%)."

Unless otherwise noted, all percentages will be displayed to one decimal place. No percentage will be displayed for zero counts, and no decimal will be presented when the percentage is 100%.

For the purpose of the tabulations the lower and upper confidence limits for the percentages will be truncated at 0 and 100% respectively.

For PK concentration data, summary statistics will include geometric mean, geometric coefficient of variation (geoCV), 95% confidence interval (CI) for geometric mean, arithmetic mean, SD, median, minimum, and maximum.

Decimal places for descriptive statistics will always apply the following rules:

- "n" will be an integer;
- Mean (arithmetic, geometric), SD, and median will use one additional decimal place compared to the original data;
- geometric CV [%] will be presented with one decimal place;
- Minimum and maximum will have the same number of decimal places as the original value.

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

Derived variables in general will display the mean and median to 1 more decimal place, SD to 2 more decimal places and same decimal place to minimum and maximum than the variables used in the derivation. If the number of decimal places reported in the raw data is varied, then use either the maximum raw number of reported decimal places or 3, whichever is the lowest, as a guide for the descriptive statistics.

3.2 General study level definitions

3.2.1 Analysis visits

All data will be analyzed based on the visits identified per the Schedule of Activities in protocol. Mapping to analysis visit windows is not applied, except for PEOT visit (specified in Section 3.2.3).

3.2.1.1 Relative day

Relative day for an event will be derived with the date of the first sc infusion of Investigational Medicinal Product (IMP) in MG0007 as reference.

Relative days for an event of measurement occurring before the date of first sc infusion will be prefixed with '-' and are calculated as follows:

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

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

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

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

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

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

3.2.2 Study periods

The study cycle consists of the following:

- Treatment Period: 6 weeks
- Observation Period: 16 weeks
- Non-treatment period

The following definitions for starting and entering the study periods for each cycle will be applied:

- **Treatment Period** starts with the first day of IMP in each cycle in MG0007 and ends after Day 43 or PEOT assessments. All participants in the Safety Set will be considered to have started the Treatment Period. A participant is considered to have completed the Treatment Period of each cycle if assessments from Treatment Period Day 43 are completed.
- **Observation Period** starts with one day after the end of the Treatment Period of each cycle and ends after the final assessments at Day 155 visit. Participants with assessment on any Observation Period day are considered to have started the Observation Period.
- **Non-treatment period** starts with one day after the end of the Observation Period of each cycle and ends before the start of next cycle or the EOS assessment.

A study participant is considered to have completed the study if he/she has completed all phases of the study including the Observation Period and the EOS visit assessments. The end of the study is defined as the date of the last visit of the last participant in the study.

3.2.3 Mapping of assessments performed at Premature End of Treatment Visit

PEOT assessments will be assigned to the next scheduled site visit (following the last scheduled visit that the participant completed prior to PEOT) where each assessment is evaluated as per protocol. This approach means that there is a chance that PEOT data will be mapped to different visits according to the schedule of assessments.

3.3 Definition of Baseline values

For the analyses done by entire study, Baseline values will be the last available value prior to or on the same date of first administration of IMP in MG0007. Scheduled or unscheduled measurements can be used as the Baseline value.

For the analyses done by study cycle, Baseline values will be defined as the last available value prior to or on the same date (and same time if time is collected for the individual assessment) of first administration of IMP at each cycle (ie Baseline [Day 1]) value for that cycle.

In case of baseline of specific cycle is missing, values from previous cycle or previous studies EOS visit will be considered as baseline for that cycle.

For [redacted] Baseline values will be the Baseline values determined in MG0003.

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 key efficacy, key safety, or PK/PD outcomes (if applicable) for an individual participant. The criteria for identifying important protocol deviations will be defined within the appropriate protocol-specific document. Important protocol deviations will be reviewed as part of the ongoing data cleaning process and data evaluation.

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 Full Analysis Set

The Full Analysis Set (FAS) will consist of all study participants in the ES who were randomized in this study or in MG0004. Study participants enrolling from MG0004 will utilize their last assigned dose level from MG0004 as their planned dose in MG0007.

3.5.3 Safety Set

The Safety Set (SS) will consist of all study participants in the FAS who received at least one dose of IMP in MG0007.

3.6 Treatment assignment and treatment groups

For the analyses using SS, FAS and ES by entire study and first dose received, study participants will be grouped according to the highest dose levels of IMP participants received in MG0007 first cycle (7mg/kg or 10mg/kg). If participants switched dose in first cycle of MG0007, then they will be assigned to IMP 10mg/kg group. For example, if a participant's highest dose in first cycle of MG0007 is IMP 10 mg/kg and then changed to 7 mg/kg in the next cycle, then the participant will still be allocated to 10 mg/kg for these analyses.

For the safety analyses using SS by entire study and most recent dose received (summary of adverse events), participants will be grouped according to the most recent dose level of IMP participants received prior to the onset of AEs. For example, if a participant's last dose prior to an AE is 10 mg/kg, then the participant will be allocated to 10 mg/kg for this AE.

For the analyses performed using SS and FAS by treatment cycle, participants will be grouped according to the highest dose levels of IMP participants received (7mg/kg or 10mg/kg) within

each cycle. If participants switched dose within one cycle, then they will be assigned to IMP 10mg/kg group for that cycle. For example, if for a participant, the highest does in first cycle is 10 mg/kg and the highest dose received in second cycle is 7 mg/kg, then the participant will be allocated to IMP 10 mg/kg and 7mg/kg respectively.

For participants who were not treated in FAS and ES, they will be assigned to 'Not Treated' group.

3.7 Center pooling strategy

The study participants from MG0003 and MG0004 will be invited to participate in this study. The data from all sites will be pooled for analyses purposes.

3.8 Coding dictionaries

Adverse events (AEs) and medical histories will be coded using version 24.0 of the Medical Dictionary for Regulatory Activities (MedDRA®).

Medications will be coded according to B3 version Mar 2021 of the World Health Organization Drug Dictionary (WHODD).

3.9 Changes to protocol-defined analyses

In the protocol section 9.2.1, the intercurrent events to be considered are the use of rescue therapy prior to Day 43 and permanent treatment discontinuation (or withdrawal from study) due to TEAEs. In the SAP, we consider use of rescue therapy prior to Day 43 and permanent treatment discontinuation due to TEAEs as intercurrent events.

In the protocol, the treatment policy strategy is described for the analysis meaning that all data was planned to be analyzed regardless of study participants receiving treatment with rescue therapy. Summaries will also be presented for the efficacy endpoints where participants will be censored at the time that they take rescue medication. In the SAP, time to MG-ADL response will be analyzed censoring the data at the time of the use of rescue therapy and all other efficacy endpoints will be summarized following treatment policy.

Protocol amendment 3 did not mention how to treat IgG when participants receive rescue therapy. In the SAP, the IgG values up to and including 8 weeks after start date of rescue therapy will be excluded from the analysis.

In the protocol section 8.3.1, Hy's law is defined as >3xULN ALT or AST with coexisting >2xULN total bilirubin in the absence of <2xULN ALP, with no alternative explanation for the biochemical abnormality (ie, without waiting for any additional etiologic investigations to have been concluded). In this SAP, Hy's law is defined as (AST or ALT ≥ 3 x ULN) and TBL ≥ 2 x ULN and ALP < 2 x ULN to be consistent with Rozanolixizumab program SAP.

4 STATISTICAL/ANALYTICAL ISSUES

4.1 Adjustments for covariates

Statistical testing is not planned for this study, hence adjustment for covariates will not be required.

4.2 Handling of dropouts or missing data

4.2.1 Efficacy data

The rules for handling missing data of individual items in the calculation of the QMG, MG-C, MG-ADL, MG Symptom PRO, and MG-QOL15r scores are described in Section 13.1, Section 13.2, Section 13.3, Section 13.4, and Section 13.5, respectively.

For ordinal endpoints (eg EQ-5D-5L), the observed case method will be applied. No further imputation is used.

4.2.2 Dates and times

Partially or completely missing dates may be imputed for the following reasons:

- Classification of AEs as TEAEs;
- Classification of medications as past, prior, or concomitant medications;
- Durations of AEs.

Imputed dates will not be shown in listings. All dates will be displayed as reported in the database.

The following rules will be applied for partially or completely missing start dates:

- If year, month and day are all missing then assign the date of first dose of IMP. If an imputed start date is after the specified end date, then assign January 01 of the year of the end date, or the date of screening if this is later (if the latter imputation results in an end date that is earlier than the start date, then use January 01).
- If month and day are missing, and year is:
  - the same as the year of the first dose of IMP then assign the month-day of first dose of IMP. If the imputed start date is after the specified end date, then assign January 01, or the month-day of screening date if this is later (if the latter imputation results in an end date that is earlier than the start date, then assign January 01);
  - not the same as the year of the first dose of IMP then assign January 01.
- If only day is missing, and month-year is:
  - the same as the month-year of the first dose of IMP then assign the day of first dose of IMP. If the imputed start date is after the specified end date, then assign first day of the month, or the day of screening date if this is later (if the latter imputation results in an end date that is earlier than the start date, then assign first day of the month);
  - not the same as the month-year of the first dose of IMP then assign the first day of the month.

The following rules will be applied for partially or completely missing stop dates:

- If only the month and year are specified, then use the last day of the month. If an imputed stop date is after last contact date and last contact date is before the data cut-off date, then

assign last contact date as the stop date. If an imputed stop date is after last contact date and last contact date is after the data cutoff date, then assign data cutoff date as the stop date.

- If only the year is specified, then use December 31 of the known year. If an imputed stop date is after last contact date and last contact date is before the data cutoff date, then assign last contact date as the stop date. If an imputed stop date is after last contact date and last contact date is after the data cutoff date, then assign data cut-off date as the stop date.
- If the stop date is completely unknown, then use discharge date or data cut-off date. Discharge date refers to the date of the end of study visit for completed participants or the date of discontinuation for participants that were withdrawn. For any AEs with known start date after the date of discontinuation, the date of last contact will be used as the discharge date. For participants still ongoing in the study at the time of the data cut-off, and for whom no discharge date is available, the date of the data cut-off will be used instead of the discharge date.

Any medication with a start date on the first dosing date and time unknown, will be assumed to be concomitant.

Imputed AE dates will be used for the calculation of duration of AEs as described in Table 4–1.

Table 4–1: Calculation rules for duration of AEs

Data availability	Onset date	Outcome date	Calculation rules
Complete data	D1	D2	Duration = D2 – D1 + 1 d
Start date partially or completely missing	--	D2	Duration ≤ D2 – D0 + 1 d Notes: D0 is imputed start date per above rules.
End date partially or completely missing	D1	--	For ongoing AE: Duration ≥ D3 – D1 d For resolved AE: Duration ≤ D3 – D1 d Notes: D3 is imputed end date per above rules.
Start and end date partially or completely missing	--	--	For ongoing AE: Duration ≥ D3 – D0 d For resolved AE: Duration ≤ D3 – D0 d Notes: D0 is imputed start date and D3 is imputed end date per above rules.

4.2.3 Impact of the coronavirus disease 2019 (COVID-19) on study data

Missing data is expected to be one of the major implications of the COVID-19 pandemic. The following approaches/strategies will be applied to assess the impact of COVID-19 in this study.

- Added an electronic Case Report Form (eCRF) page "COVID-19 Impact", including impacted visits, impact categories and relationship to COVID-19;
- Additional fields were added in protocol deviation specification documents to record protocol deviations relationship to COVID-19;
- Included additional summary analyses based on the timing of COVID-19 impact [during/post COVID-19 pandemic based on COVID-19 start date 20-Mar-2020 and COVID-19 end date 05-May-2023 (WHO, 2023)].

4.3 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 the first dose of IMP the latest non-missing value (scheduled or unscheduled) will be used in the calculation of descriptive statistics (ie Screening);
- For repeated or unscheduled measurements obtained at any time point after the first dose of IMP, the scheduled values (if non-missing) will always be used in the calculation of changes from Baseline and for the descriptive statistics (ie, in summaries by time point). If repeated scheduled values are obtained at any time point, the latest non-missing values will be used.

See Section 8.4.2 for the rules applied to ECG triplicate measurements.

4.4 Interim analyses and data monitoring

Submission Cut and Day 120 cut will be conducted during the study. For Submission Cut, all the analyses specified in the SAP will be performed using all the data of all participants till 08 July 2022 for submission purposes. For Day 120 cut, only selected analyses of safety in the SAP will be performed using all the data till 07 October 2022.

An overarching Rozanolixizumab program IDMC (pIDMC) will oversee the safety of this study by reviewing safety data at periodic timepoints with other Rozanolixizumab studies. The scope and role of the overarching pIDMC will be described in overarching IDMC charter and its study specific attachment.

Data requirements for each interim cut are summarized below:

- Submission Cut: PK, NAb, and ADA are required. PK and ADA data will be transferred to PXL 7 weeks after the MG0003 database lock. Bioanalysis of PK and ADA samples takes around 10 weeks. In order to meet the timelines for the PK/ADA data transfer to PXL, PK and ADA samples will need to be sent to the LGC lab around 10 weeks before the data transfer.
- Day 120 cut: PK, NAb, and ADA are required. Available samples transferred to Lab around 10 weeks before data transfer, data transfer around 1.5 weeks before the review.

4.5 Multicenter studies

Individual center results will not be displayed.

4.6 Multiple comparisons/multiplicity

Adjustment for multiplicity will not be required since all analyses will be descriptive in nature.

4.7 Use of an efficacy subset of subjects

All efficacy data will be summarized only, and there is no sensitivity analysis planned.

4.8 Active-control studies intended to show equivalence

Not applicable.

4.9 Examination of subgroups

4.9.1 General subgroups

The continuous secondary efficacy endpoints will be evaluated for subgroups of interest including:

- Age (18-<65, ≥65 years)
- Age (18-<65, 65-<85, ≥85 years)
- Sex (male, female)
- Region (North America, Europe, and Asia [excluding Japan], Japan)
- Stratification factor in MG0003 - MG-specific autoantibody (muscle-specific kinase [MuSK]+ or acetylcholine receptor [AChR]+)

  Notes: Region as specified for MG0003 will be used. The stratification factors MuSK(+/-) and AChR(+/-) will be based on the derived values from MG0003 subgroup analysis.

The MG-ADL scores and change from Baseline will be summarized in the five subgroups as above and additional subgroups as follow:

- Duration of disease at MG0003 Baseline (<median, ≥median)
- MGFA disease class at MG0003 Baseline
- Thymectomy at MG0003 Baseline (yes, no)
- MG0007 Baseline MG-ADL category (<5, ≥5).

These evaluations will be descriptive; no statistical testing of treatment-by-subgroup interactions nor statistical testing of treatment effects within subgroups will be carried out.

Subgroup analyses will only be performed for cases where there are at least 5 study participants in a specific category.

4.9.2 Examination of weight subgroups and administered doses

To support the goal of a fixed dosing strategy for Rozanolixizumab, additional subgroup analyses will be performed by administered dose group for each weight subgroup below:

- Weight (< 50kg, 50 - <70 kg, 70 - <100kg, ≥100kg, total)
- Administered dose (RLZ 280mg, RLZ 420mg, RLZ 560mg, RLZ 840mg, RLZ 1120mg, RLZ Total)

4.9.3 Manual push analysis

Additionally, participants who have used manual push will be flagged in all listings. Separate listings for treatment-emergent adverse events and total IgG will be provided.

5 STUDY POPULATION CHARACTERISTICS

For analysis using FAS and ES, the first cycle treatment group includes 'Not Treated' group.

5.1 Subject disposition

The following outputs will be created.

Summaries:

- **Reasons for screen failures** (as collected on the Study Termination Screen Failure CRF page) will be tabulated using the ES for overall. Additionally, the reasons for screen failures will be summarized by during and post- the COVID-19 pandemic based on the screen failure date relative to the pandemic cut-off date.
- **Disposition of study participants screened** will be tabulated using the ES for overall, by region and by site. In this summary, the site number, principal investigator name, first participant in date and last participant out date, will be captured by first actual treatment and by each analysis set (FAS and SS).
- **Disposition of analysis sets** will be summarized by the first cycle treatment group, RLZ total, total and analysis sets (ES, FAS and SS) using the ES.
- **Disposition and discontinuation reasons** will be tabulated using the FAS and SS, and will contain the number and percentage of study participants by treatment group, overall and by during and post- the COVID-19 pandemic who:
    - Started Study
    - Completed Study
    - Discontinued Study with primary reason for discontinuation (primary reason for premature study termination as collected in the Study Termination Enrolled CRF)

  Note: The summary by during and post- the COVID-19 pandemic will be based on the start, completed and discontinuation date relative to the pandemic cut-off date which will be presented in the same table. The discontinuation reason in each period will also be summarized. Discontinuation due to COVID-19 pandemic as well as discontinuation due to transition to MG0020 study will be summarized as sub-category under "Other" reason.
- **Discontinuation due to AEs** will be presented using the FAS and SS to display the total number of study participants who discontinued the study due to AEs by treatment group, RLZ total, total and the categories: AE serious fatal, AE non-fatal and other (AE non-serious fatal).
- **Count of participant by visit** using SS will summarize the number of participants at each visit by treatment group.

– **Impact of COVID-19** will be presented using the FAS to display the number and percentage of participants in each impact category by treatment group, RLZ total, total and visit.

Listings of study participant disposition using ES, study discontinuation using FAS, study participants who did not meet study eligibility criteria using ES, and participant analysis sets using ES will be provided.

5.2 Important protocol deviations

A summary of number and percentage of study participants with an important protocol deviation by relationship to COVID-19, first actual treatment group, RLZ total and total will be provided for the FAS. Additionally, the summary will be repeated by during and post- the COVID-19 pandemic based on the deviations start date relative to the pandemic cut-off date.

A listing of important protocol deviations will be provided based on the FAS.

6 DEMOGRAPHICS AND OTHER BASELINE CHARACTERISTICS

For analysis using FAS and ES, the first cycle treatment group includes 'Not Treated' group.

6.1 Demographics

Demographic variables will be summarized on the FAS and SS, by categories mentioned below using descriptive statistics by first actual treatment group, RLZ total and total. Additional subgroup summary will be presented by during and post- the COVID-19 pandemic based on the enrolled date relative to the pandemic cut-off date using FAS.

Categories for continuous variables (including n, mean, SD, Median, Min and Max):

- Age at the time of study MG0003 entry (years)

  Notes: Missing age will be calculated as year of informed consent signed – year of birth
- Height (cm)
- Weight (kg)
- Body mass index (BMI, kg/m^2), to be calculated as: BMI = Weight (kg) / $(\text{Height (m)})^2$

Categorical variables (using frequency counts and percentages):

- Age (18-<65, 65-<85, ≥85 years)
- Age (≤18,19-<65, ≥65 years)
- BMI (<30 kg/m^2, ≥30 kg/m^2)
- Weight (<50kg, 50kg-<70 kg, 70-<100kg, ≥100kg)
- Weight (<50kg, ≥50kg)
- Weight (<70kg, ≥70kg)
- Sex (Male, Female)

- Race (American Indian or Alaskan native, Asian, Black, Native Hawaiian or Other Pacific Islander, White, Other/Mixed)
- Ethnicity (Hispanic or Latino, Not Hispanic or Latino)
- Region (North America, Europe, Asia [excluding Japan], Japan)
- Country
- Study where the study participant comes from: MG0003 or MG0004
- Worsening of disease (yes, no)
- Needed additional therapies in the observation period of MG0003 and entered MG0007 (yes, no)

Note: Worsening of disease is defined as the worsening of gMG symptoms (eg, an increase of 2 points on the MG-ADL or 3 points on the QMG scale) between two consecutive visits based on the Investigator's discretion.

A by-participant listings of demographics will be provided using the FAS. Childbearing potential and lifestyle will be listed using the ES separately.

6.2 Baseline characteristics

The following variables will be summarized by treatment group and RLZ total for the SS. The baseline values are derived according to Section 3.3.

- MG0003 Baseline MuSK antibody status (positive, negative)
- MG0003 Baseline AChR antibody status (positive, negative)
- MG0007 Baseline MuSK antibody status (positive, negative)
- MG0007 Baseline AChR antibody status (positive, negative)
- Baseline MG-ADL score
- Baseline MG-ADL category (<5, ≥5)
- Baseline QMG score
- Baseline MG-C score
- Baseline total IgG value
- Age at initial MG diagnosis
- Duration of disease at MG0003 Baseline (<median, ≥ median)
- MGFA disease class at MG0003 Baseline
- Thymectomy at MG0003 Baseline (yes, no)

Note: Duration of disease at MG0003 Baseline = (Date of Randomization in MG0003-Date of Initial MG Diagnosis+1)/365.25; MG0003 MuSK and AChR antibody status are based on the derived values from MG0003 model analysis.

6.3 Medical history and concomitant diseases

Any medical conditions that were not reported in MG0003/MG0004 will be captured on CRF of this study and listed using the FAS.

6.4 Prior and concomitant medications

The number and percentage of participants taking Prior or Concomitant medications will be summarized using the SS by Anatomical Therapeutic Chemical (ATC) class, presenting as Anatomical Main Group (ATC Level 1), Pharmacological Subgroup (ATC level 3), Preferred Term (PT), actual treatment group, and RLZ total for entire study.

Additionally, rescue medications are those that are mentioned in Protocol section 6.5.3 and identified:

- if Rescue Medication is ticked as yes on CRF Concomitant Medication page
- Or PEX as procedure entered on CRF Concomitant Medical Procedure page

The start date of rescue medication should be on or after Baseline. All rescue medications will be summarized using the SS.

Medications classified as Prior or Concomitant will be listed using the FAS. A by-participant listing of concomitant procedures will also be listed using the FAS. Originally reported dates will be used for listings.

6.4.1 Categories of prior and concomitant medications

Medications will be classified as follow based on imputed start and stop dates & times as outlined in Section 4.2.2.

- **Prior** medications will include any medications that started before the first administration of MG0007 IMP.
- **Concomitant** medications will include any medications that have been taken at least once after the first administration of MG0007 IMP during the Treatment and/or Observation Period.

Medication Started	Medication finished	Classification
Before 1st Dose IMP	Any time	Prior
Any time	After 1st Dose IMP	Concomitant

6.4.2 Assignment of medications to study period

The following rules will be used to assign a medication to a study period:

- **Treatment Period:** a medication will be assigned to the Treatment Period if it has been taken at least once between the first administration of IMP on Day 1 of each study cycle, up to Day 43 or PEOT assessments.

- **Observation Period:** a medication will be assigned to the Observation Period if it has been taken at least once from the day after Treatment Period to the Day 155 visit of each study cycle.

The prior or concomitant medications out of the 2 periods above will be displayed as 'NA' in the listing.

7 MEASUREMENTS OF TREATMENT COMPLIANCE

Not applicable. The number of infusions will be recorded as detailed in Section 8.1.

8 SAFETY ANALYSES

All safety analyses tables and figures will be presented using the SS. All listings will be presented using FAS. Listings will be presented by treatment group, study cycle, and participant; tabulations will be presented by treatment group, RLZ total and/or study cycle. Unless otherwise specified, safety analyses will be presented by actual dose received as defined in Section 3.6.

8.1 Extent of exposure

The following dosing information for entire study will be summarized using SS by RLZ total:

- Number of participants receiving 7mg/kg or 10mg/kg initially and the treatment sequence (eg 7mg/kg-7mg/kg, 7mg/kg-10mg/kg, etc.)

The following dosing information for entire study will be summarized using SS by the first cycle treatment and RLZ total:

- Total number of study cycles (regardless of the first cycle being mandatory or not) as a continuous variable (n, sum, mean, sd, median, min, max will be provided)
- Number of study cycles (1, 2, 3, …, until the maximum number of study cycles)
- Number of cycles per participant year rate
- Time in study [<3 months (90 days), >=3 to <6 months (180 days), >=6 to <9 months (270 days), >=9 to <12 months (360 days),>=12 to <24 months (720 days), >=24 months to <30 months (900 days), >=30 to <36 months (1080 days), >=36 months (1080 days)]
- Time in study (months) and time in study (days) as continuous variables (n, sum, mean, sd, median, min, max will be provided)

Note:

- Time in study=Date of last visit or withdrawal–Date of first visit+1. Time in study last category will be adjusted based on data to have non-zero count in last category.
- Number of cycles per participant year rate=(Sum of number of cycles)/(Sum of participant year), where Participant year=Time in study /365.25.
- 1 month=30 days.

The following dosing information will be summarized using SS by entire study, study cycle, actual dose received within each cycle and RLZ total:

- Number of infusions received as a continuous variable (n, sum, mean, sd, median, min, max will be provided)
- Number of infusions received by the following categories:
  - For each study cycle: 1, 2, 3, 4, 5, 6
  - For entire study: 1-6, 7-12, 13-18, 19-24, 25-30, 31-36, 37-42, 43-48, …, until last interval where the maximum number of infusions falls into.

Notes:

- Values for entire study will be the summation from study cycles;

A figure for actual dose received in all study cycles by participant will be provided. Figures of exposure by time, by number of cycles, by drug free time for participants from MG0004, and by drug free time for participants from MG0003 will also be provided.

All IMP administration details will be listed.

8.2 Adverse events

8.2.1 Data considerations

Adverse events will be recorded from the time of informed consent until study completion. All AEs will be coded (Section 3.8).

In addition, AEs will be classified according to the Common Terminology Criteria for Adverse Events (CTCAE) Version 5 or later 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). For the purpose of reporting severe AEs, all CTCAE severity classifications will be mapped to a standard intensity classification as described below:

- Grade 1 - Mild
- Grade 2 - Moderate
- Grade 3, 4, 5 - Severe

These will be tabulated together with the AEs that were not classified according to CTCAE criteria (ie, 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). In the case a mapped standard intensity classification per above rule is different from the standard intensity classification on CRF, the worst case will be used as the standard intensity classification (ie, an AE with Grade 1 and moderate as intensity classification will be classified into moderate) .

Any AE that occurred during the study will be defined as "**any AE**".

For each cycle, a **TEAE** is defined as any event that was not present prior to the first administration of rozanolixizumab of each treatment cycle or any unresolved event already present before the first administration of rozanolixizumab that worsens in intensity following exposure to treatment up to and including 8 weeks (56 days) after the last dose of each treatment cycle.

The following rules will be used to assign a TEAE to a study period in each study cycle:

- **Treatment Period:** a TEAE will be assigned to the Treatment Period for the tabulations if the start date of the event is on or after the date of the first administration of MG0007 IMP on Day 1, up to 7 days after the last dose of IMP in each cycle;
- **Observation Period:** a TEAE will be assigned to the Observation Period for the tabulations if the start date of the event is greater than the day after Treatment Period until 8 weeks (56 days) following the final dose in each study cycle.

An intermittent period AE is defined as AEs occurring after the 8-week (56-day) TEAE period, prior to the next cycle.

A persistent AE is defined as an unresolved AE that extends continuously from MG0003 /MG0004 to MG0007 and does not worsen in intensity following exposure to IMP in MG0007. Persistent AEs will be recorded in MG0007 database.

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 for classification of AEs as TEAEs is described in Section 4.2.2.

A TEAE will be counted as a TEAE related to IMP if the response to the question "Relationship to Study Medication" is "Related".

AEs will be presented as "number of participants (percentage of participants) [number of events]". In this style of output, "[number of events]" will include all cases of an AE including repeat occurrences in individual participants, while "number of participants" will count each participant only once.

Persistent AEs, intermittent period AEs and other non-TEAEs will be listed only.

8.2.2 Adverse events summaries

TEAEs will be summarized by the most recent dose level prior to onset of TEAEs for entire study analysis or the highest dose within a cycle for by-cycle analysis and RLZ total including the number and percentage of study participants and frequency. Additional details are described below:

1. Overview of TEAEs by entire study and study cycle will include following categories: any TEAEs, serious TEAEs, participant discontinuation due to TEAEs, permanent withdrawal of IMP due to TEAEs, temporary withdrawal of IMP due to TEAEs, TEAEs requiring dose change, treatment-related TEAEs, severe TEAEs, TEAEs leading to death, all deaths (AEs leading to death). Additionally, summary of TEAEs by study cycle, fixed dose and weight subgroups will be conducted as specified in Section 4.9.2.

2. Incidence of TEAEs will be summarized for entire study by SOC, HLT, PT for:
   - Any TEAEs
   - Any TEAEs during Treatment Period
   - Any TEAEs by maximum intensity (mild, moderate and severe)
   - Any TEAEs by relationship
   - Severe TEAEs

- Non-serious TEAEs above reporting threshold of 5% of study participants
- Fatal TEAEs
- Fatal TEAEs by relationship
- Serious TEAEs
- Serious TEAEs by relationship
- Participant discontinuation due to TEAEs
- TEAEs leading to permanent withdrawal of IMP
- TEAEs leading to temporary withdrawal of IMP
- TEAEs requiring dose change
- Treatment-emergent AESM
- Treatment-emergent AESI

3. Incidence of any TEAEs by entire study and study cycle will be summarized by decreasing participant count of PT in RLZ total. Same analysis will be repeated by fixed dose and weight subgroups as specified in Section 4.9.2.

4. Incidence of TEAEs will also be summarized by SOC, HLT, PT, and the highest dose level prior to onset of TEAEs and RLZ total for each study cycle, including the number and percentage of study participants and frequency for:

- Any TEAEs
- Severe TEAEs
- Serious TEAEs
- Participant discontinuation due to TEAEs
- TEAEs leading to permanent withdrawal of IMP

5. Overview of non-TEAEs by entire study will include following categories: any non-TEAEs, serious non-TEAEs, participant discontinuation due to non-TEAEs, permanent withdrawal of IMP due to non-TEAEs, temporary withdrawal of IMP due to non-TEAEs, severe non-TEAEs, non-TEAEs leading to death.

6. Incidence of non-TEAEs will be summarized for entire study by SOC, HLT, PT for:

- Any non-TEAEs
- Severe non-TEAEs
- Serious non-TEAEs
- Fatal non-TEAEs
- Incidence of Non-TEAEs leading to discontinuations

AESMs include severe and/or serious headache and suspected aseptic meningitis.

AESIs are the cases of potential Hy's Law (see Section 8.3.1).

AESMs and AESIs will be identified based on the assessment by the Investigator as recorded in the CRF. An AE will be counted as an AESM if there is a 'yes' response to the question "Adverse event of Special Monitoring?" and 'no' otherwise. An AE will be counted as an AESI if there is a 'yes' response to the question "Adverse Event of Special Interest?" and 'no' otherwise.

When applicable adverse event summaries will be ordered by alphabetical SOC, alphabetical HLT within SOC and decreasing frequency of PT in the RLZ total column for tables.

Listings of all TEAEs, all non-serious TEAEs, serious TEAEs, permanent withdrawal of IMP due to TEAEs, study participant discontinuation from study due to TEAEs, AEs leading to death, AESIs, AESMs, intermittent period AEs, persistent AEs, non TEAEs and TEAEs for participants who used manual push will be presented by treatment group, study cycle and participant. Most recent dose will be presented in listing even when the AE start date is partial. A flag will be added in those listings to highlight whether the AE occurred on manual push or not.

8.2.3 Adverse events of focus

Rozanolixizumab adverse events of focus (AEOF) include the following categories:

- Headaches
- Aseptic meningitis
- Gastrointestinal disturbances
- Hypersensitivity reactions
- Anaphylactic reactions
- Injection site reaction
- Infections
- Opportunistic infections
- Reductions in albumin and plasma proteins
- Effects on the kidney
- Drug related hepatic disorders
- Effects on lipids

1. The number and percentage of study participants who experience each category of the AEOF will be summarized by most recent dose level prior to onset of the AEOF and RLZ total treatment group. The following summaries will be presented for entire study by SOC, HLT, and PT:

- Treatment-emergent AEOF
- Serious Treatment-emergent AEOF
- Treatment-emergent AEOF by maximum intensity (mild, moderate and severe)

- Treatment-emergent AEOF hypersensitivity reactions, anaphylactic reactions and injection site reactions by ADA
- Severe Treatment-emergent AEOF

2. Incidence of TEAEs will also be summarized by SOC, HLT, PT, and the highest dose level prior to onset of TEAEs and RLZ total for each study cycle, including the number and percentage of study participants and frequency for:

- Treatment-emergent AEOF
- Severe Treatment-emergent AEOF

3. Graphs for AEOF headache in Treatment Period by time of onset (relative to infusion and cycle), severity, causality and duration for each study participant will also be provided. A graph for AEOF headache by participant for participants with at least two headaches in this study will also be provided.

A by-subject listing of all AEOF by category (as listed above) will be provided by treatment group, study cycle and participant. Most recent dose will be presented in listing even when the AE start date is partial. Further details related to the statistical analysis of the above mentioned treatment-emergent AEOFs are provided in Section 13.7.

8.3 Clinical laboratory evaluations

The following table (Table 8–1) lists safety laboratory assessments that are collected throughout the study:

Table 8–1: Clinical Laboratory Parameters

Laboratory Assessments	Parameters			
Hematology	Platelet Count Red Blood Cell (RBC) Count Hemoglobin Hematocrit		RBC Indices: Mean corpuscular volume Mean corpuscular hemoglobin %Reticulocytes	White Blood Cell (WBC) Count with Absolute Count and Differential: Neutrophils Lymphocytes Monocytes Eosinophils Basophils
Clinical Chemistry[a]	Blood Urea Nitrogen (BUN)	Potassium	Aspartate Aminotransferase (AST) / Serum Glutamic-Oxaloacetic	Total and direct bilirubin

Table 8–1: Clinical Laboratory Parameters

Laboratory Assessments	Parameters			
			Transaminase (SGOT)	
	Creatinine	Sodium	Alanine Aminotransferase (ALT)/ Serum Glutamic-Pyruvic Transaminase (SGPT)	Total Protein Albumin
	Glucose (fasting state, preferred)	Calcium	Alkaline phosphatase	C-reactive protein (CRP)
	Lactate dehydrogenase (LDH)	Triglycerides	Low-density lipoprotein (LDL) High-density lipoprotein (HDL)	Total Cholesterol
Routine Urinalysis	• Specific gravity • pH, glucose, protein, ketones, albumin, bilirubin, urobilinogen, nitrite, leukocyte esterase, hemoglobin by dipstick, albumin/creatinine ratio, creatinine • Microscopic examination (if blood or protein is abnormal)			
Other Screening Tests	• Follicle-stimulating hormone and estradiol (as needed in women of non-childbearing potential only) • Urine drug screen (to include at minimum: amphetamines, barbiturates, cocaine, opiates, cannabinoids and benzodiazepines) • Serum or urine human chorionic gonadotropin pregnancy test (as needed for women of childbearing potential)[b] • PTT and INR • Serology testing (for Hepatitis B, Hepatitis C, and HIV) • All study-required laboratory assessments will be performed by a central laboratory. The results of each test must be entered into the eCRF.			

NOTES:
For additional assessments that may be required in case of AESM, see protocol Table 1-6.
[a] Details of liver chemistry stopping criteria and required actions and follow-up assessments after liver stopping or monitoring event are given in protocol Section 7.1.1 and Appendix 6 (Section 13.6). PDILI criteria are given in the SAP Section 8.3.1.

Table 8–1: Clinical Laboratory Parameters

Laboratory Assessments	Parameters
[b] Local urine testing will be standard for the protocol unless serum testing is required by local regulation or Institutional Review Board (IRB)/Independent Ethics Committee (IEC).	

Chemistry, hematology and quantitative urinalysis (observed value, absolute change from Baseline) will be summarized in standard unit using descriptive statistics for each study cycle by actual dose received within the study cycle at each scheduled visit and RLZ total.

The central lab data will be used for the summary tables. Repeated lab measurements will be handled per Section 4.3.

Measurements below the lower limit of quantification (BLQ) will be imputed with half of the lower limit of quantification (LLOQ), and measurements above the upper limit of quantification (ALQ) will be imputed to the upper quantification limit for the purpose of quantitative summaries.

An assessment is markedly abnormal (MA) if it meets the MA criteria outlined in Section 13.6.

A **treatment-emergent (TE)** assessment is defined as any assessment that was not present prior to the first administration of rozanolixizumab of each treatment cycle or 8 weeks (56 days) after the last dose of each treatment cycle. **TE period** for each cycle is from first administration of rozanolixizumab and 8 weeks (56 days) after last dose of rozanolixizuman of each cycle.

The following rules will be used to assign a TE assessment to a study period in each study cycle:

Treatment Period: a TE assessment will be assigned to the Treatment Period for the tabulations if the start date of the assessment is on or after the date of the first administration of MG0007 IMP on Day 1, up to 7 days after the last dose of IMP in each cycle;

Observation Period: a TE assessment will be assigned to the Observation Period for the tabulations if the start date of the assessment is greater than the day after Treatment Period until 8 weeks (56 days) following the final dose in each study cycle;

An **intermittent period** assessment is defined as any assessment occurring after the 8-week (56-day) TE period, prior to the next cycle.

The number and percentage of participants who have TE MA chemistry and hematology assessment will be summarized for entire study by initial dose level and RLZ total, and for each study cycle by actual dose received within the study cycle and RLZ total at any visit (including unscheduled visit). The number and percentage of participants who have MA chemistry and hematology assessment during Intermittent Period will also be summarized for entire study by initial dose level and RLZ total, and for each study cycle by actual dose received within the study cycle and RLZ total at any visit (including unscheduled visit).

The laboratory variables that are categorized as normal, high or low based on the reference range supplied by the analytical laboratory will be presented in shift tables from Baseline to any post-Baseline visit (including unscheduled visit) for entire study by RLZ total only, and for each study cycle by actual dose received within the study cycle and RLZ total. All laboratory test results

will be listed, including Baseline, scheduled and unscheduled visits with results in standard unit. Values outside the reference range for the continuous variables will be flagged in the listings. The reference ranges will also be reported in the listings.

Mean values in albumin, C-reactive protein, White Blood Cell Count with absolute count and differential (neutrophils, lymphocytes, monocytes, eosinophils and basophils) and platelets will be plotted over time by study cycle and actual dose level received within study cycle and RLZ total with all treatments overlaid on the same plot.

In addition, the listings will include a flag for values identified as MA. Additional lab test, including pregnancy testing, will also be listed.

8.3.1 Potential drug-induced liver injury

The number and percentage of study participants who meet one or more of the following potential drug-induced liver injury (pDILI) criteria during TE period will be summarized by entire study, actual treatment group at the time of meeting the following criteria and RLZ total:

- Participants with at least one post-Baseline liver laboratory assessment
- Incidence of potential hepatotoxicity with symptoms potentially associated with hepatitis or hypersensitivity
- Incidence of potential hepatotoxicity with no symptoms potentially associated with hepatitis or hypersensitivity
- Laboratory criteria for pDILI:
  - (AST or ALT ≥ 3 x ULN) and TBL ≥ 1.5 x ULN
  - (AST or ALT ≥ 3 x ULN) and TBL ≥ 2 x ULN
  - (AST or ALT ≥ 3 x ULN) and TBL ≥ 2 x ULN and ALP < 2 x ULN (Hy's Law)

In order to meet the above criteria, a study participant must experience the elevation in bilirubin and ALT or AST (and the absence of the ALP elevation) at the same visit. For example, a study participant who experiences a ≥2xULN elevation of bilirubin at one visit and a ≥3xULN elevation in ALT (or AST) at a subsequent visit has not fulfilled the Hy's law criteria. If participant meets part of one criterion but at least one parameter is unknown, then he/she should not be considered for meeting the criterion.

Additional analyses for liver function tests (LFTs) will be performed to assess the potential for liver toxicities in accordance with the United States Food and Drug Administration guidelines. Per guidelines, the following criteria will be used to define levels of LFT elevation:

- 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

The number and percentage of study participants who meet one or more of the above LFT elevation criteria during TE period will be summarized by entire study, actual treatment group at the time of meeting the above criteria and RLZ total.

A listing will also be provided for study participants who meet at least one of the above criteria. All results obtained at that visit for the specified parameters will be displayed.

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

8.4.1 Vital signs

Observed values and changes from Baseline of vital signs variable (pulse rate, systolic and diastolic blood pressure, and temperature) will be summarized for each study cycle by actual dose received within the study cycle and RLZ total.

The number and percentage of participants who meet each of the markedly abnormal (MA) criteria outlined in Section 13.6 during TE period will be summarized for entire study by the initial dose level and RLZ total, and for each study cycle by actual dose received within the study cycle and RLZ total at any visit (including unscheduled visit).

Additionally, the vital signs variables that are categorized as normal or TE MA based on the MA criteria will be presented in shift tables from Baseline to any post-Baseline visit (including unscheduled visit) for entire study by RLZ total only, and for each study cycle by actual dose received within the study cycle and RLZ total.

A by-participant listing of all vital sign measurements and change from Baseline will be presented by treatment group, study cycle, and visit. The listing will include a flag for values identified as MA. Unscheduled measurements will be presented in the listings.

8.4.2 Electrocardiograms

The following ECG variables will be reported:

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

Observed values and changes from Baseline will be summarized for each study cycle by actual dose received within the study cycle and RLZ total, at scheduled visit and by ECG variable. The number and percentage of participants with normal, abnormal not clinically significant and abnormal clinically significant ECG results by investigator will be provided in a shift table from Baseline to worst post-Baseline interpretation for each study cycle by actual dose received within the study cycle and RLZ total and for entire study by RLZ total only.

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 visit. In the event that there are not 3 available measurements at a given visit, the mean will be calculated based on the number of measurements for which data are provided.

The number and percentage of study participants who meet each of the MA criteria outlined in Section 13.6 during TE period will be summarized for entire study by the initial dose level and RLZ total, and for each study cycle by actual dose received within the study cycle and RLZ total at any visit (including unscheduled visit).

A listing of electrocardiogram data will be presented, including repeated and unscheduled measurements.

8.4.3 Other safety endpoints

8.4.3.1 Physical examination

Results of abnormalities in physical examination are not collected in MG0007 therefore no listing or table will be provided for physical examination abnormal results.

8.4.3.2 Suicidal risk monitoring

Suicidal ideation is defined as an event in any of the following 5 categories:

[redacted]

Suicidal behavior is defined as an event in any of the following 5 categories:

[redacted]

Suicidal behavior or ideation is defined as an event in any of the above 10 categories.

Self-injurious behavior without suicidal intent is corresponding to the response to [redacted] in questionnaire.

A by-participant listing of the C-SSRS questionnaire data will be provided by treatment group and study cycle.

8.4.3.3 Assessment and management of Tuberculosis (TB)

By-participant listings of interferon gamma release assay (IGRA) TB test, chest X-ray and TB signs and symptoms questionnaire for TB will be provided.

9 EFFICACY ANALYSES

All efficacy analyses tables and figures will be performed based on the SS by study cycle and highest dose level received within the cycle and RLZ total as described in Section 3.6. All listings will be presented using FAS. No statistical testing will be performed for efficacy analyses. All efficacy endpoints will be summarized descriptively, unless specified otherwise.

9.1 MG-ADL score

The complete list of MG-ADL items and scores are provided in Table 13–3. The total score will be calculated according to the rules set down in Section 13.3.

The MG-ADL total score and change from Baseline will be summarized by study cycle, actual dose level received within study cycle, and RLZ total using descriptive statistics.

The above MG-ADL summaries will be repeated for COVID-19 free study participants, where COVID-19 free participants for this SAP exclude:

- Study participants who discontinue treatment due to suspected/confirmed COVID-19 infection ("Confirmed COVID-19" or "Suspected COVID-19" as the relationship to COVID-19 in the COVID-19 Impact eCRF);
- Study participants who discontinue treatment due to non-infection related COVID-19 issues ("General circumstances around COVID-19 without infection" or "other" as the relationship to COVID-19 in the COVID-19 Impact eCRF);
- Study participants have visits affected in treatment period (eg visit performed by video call) due to COVID-19 pandemic.

The subgroup summaries will be performed as specified in Section 4.9.1. Additional summary by fixed dose and weight subgroups will also be conducted as specified in Section 4.9.2.

The MG-ADL total score (excluding ocular items) with associated change from Baseline will be summarized by study cycle, actual dose level received within study cycle, and RLZ total using descriptive statistics.

The mean change from Baseline in MG-ADL over time will be plotted by study cycle and treatment group.

A boxplot of change from Baseline in MG-ADL at Day 43 will be generated by study cycle and administered dose as specified in Section 4.9.2.

By-participant listings of MG-ADL values will be provided. In addition, listing of MG-ADL by study cycle and dose will also be provided.

9.2 QMG score

The complete list of QMG items and scores are provided in Table 13–1. Partially missing total scores will be imputed according to the rules set down in Section 13.1.

The QMG total score and QMG total score (excluding ocular items) with associated change from Baseline will be summarized by study cycle, actual dose level received within study, and RLZ total using descriptive statistics.

The subgroup summaries (by MuSK+ or AChR+ only) will be performed as specified in Section 4.9.1. Additional summary by fixed dose and weight subgroups will also be conducted as specified in Section 4.9.2.

The mean change from Baseline in QMG over time will be plotted by study cycle and treatment group.

A boxplot of change from Baseline in QMG at Day 43 will be generated by study cycle and administered dose as specified in Section 4.9.2.

By-participant listings of QMG scores will be provided.

9.3 MG-C score

The complete list of MG-C items and scores are provided in Table 13–2. The MG-C total score and MG-C total score (excluding ocular items) will be calculated according to the rules set down in Section 13.2.

The MG-C total score and total score (excluding ocular items) with associated change from Baseline will be summarized by study cycle, actual dose level received within study, and RLZ total using descriptive statistics.

The subgroup summaries (by MuSK+ or AChR+ only) will be performed as specified in Section 4.9.1. Additional summary by fixed dose and weight subgroups will also be conducted as specified in Section 4.9.2.

The mean change from Baseline in MG-C over time will be plotted by study cycle and treatment group.

A boxplot of change from Baseline in MG-C at Day 43 will be generated by study cycle and administered dose as specified in Section 4.9.2.

By-participant listings of MG-C scores will be provided.

9.4 MG Symptoms PRO

The MG Symptoms PRO scale scores will be calculated according to the rules set down in Section 13.4.

The MG Symptoms PRO 'Muscle Weakness Fatigability', 'Physical Fatigue' and 'Bulbar Symptoms' scale scores and changes from Baseline will be summarized by study cycle, actual dose level received within study cycle, and RLZ total using descriptive statistics.

The subgroup summaries (by MuSK+ or AChR+ only) will also be performed as specified in Section 4.9.1.

The mean change from Baseline in MG Symptoms PRO over time will be plotted by study cycle and treatment group.

By-participant listings of MG Symptoms PRO scale scores will be provided separately.

9.5 MG-ADL responder rate (≥2.0 points improvement from Baseline)

Study participants will be classified as MG-ADL total score responders at a scheduled visit if there is an improvement (decrease of at least a 2-points) from Baseline in the MG-ADL total score.

The number and percentage of observed MG-ADL responders at each scheduled post-Baseline visit will be summarized by study cycle, actual dose level received within study cycle, and RLZ total using descriptive statistics.

Additional summary of observed MG-ADL responders by fixed dose and weight subgroups will also be conducted as specified in Section 4.9.2.

9.6 Time to first MG-ADL response

Time to First MG-ADL response (in days) by study cycle is defined as Date of First post-Baseline MG-ADL Response (≥2.0 points improvement from Baseline) within study cycle - Date of first IMP within study cycle + 1. Participants will be excluded from the survival analysis for a cycle if they did not have IMP in that cycle.

Study participants who use rescue therapy within study cycle before achieving first MG-ADL response within study cycle will be censored at time of rescue intake. For non-responders who take rescue therapy, they will be censored at the date taken rescue therapy, or last non-missing post Baseline MG-ADL visit, whichever is earlier. For non-responders who do not take rescue therapy, they will be censored at the last non-missing post-Baseline MG-ADL visit date.

The survival estimates of 1, 8, 15, 22, 29, 36, 43, 71, 99, 127, 155, 180, 300, 400, 500, 600, 700, 800, 900 and 1000 days to first MG-ADL response, median times to MG-ADL response with 95% CI, and cumulative number of events by study cycle will be calculated using Kaplan-Meier method for RLZ dose level received within study cycle and RLZ total. Number of censored study participants will be reported as well. A Kaplan-Meier plot will also be generated by study cycle and treatment group.

9.7 QMG responder rate (≥3.0 points improvement from Baseline)

Participants will be classified as QMG total score responders at a scheduled visit if the QMG total score is at least a 3-point improvement (decrease) from Baseline.

The number and percentage of observed QMG responders at each scheduled post-Baseline visit will be summarized by study cycle, actual dose level received within study cycle, and RLZ total using descriptive statistics.

Additional summary of observed QMG responders by fixed dose and weight subgroups will also be conducted as specified in Section 4.9.2.

9.8 MG-C responder rate (≥3.0 points improvement from Baseline)

Participants will be classified as MG-C total score responders at a scheduled visit if the MG-C total score is at least a 3-point improvement (decrease) from Baseline.

The number and percentage of observed MG-C responders at each scheduled post-Baseline visit will be summarized by study cycle, actual dose level received within study cycle, and RLZ total using descriptive statistics.

Additional summary of observed MG-C responders by fixed dose and weight subgroups will also be conducted as specified in Section 4.9.2.

9.9 EQ-5D-5L

The EQ-5D-5L essentially consists of 2 pages: the EQ-5D descriptive system and the EQ visual analogue scale (EQ VAS).

A frequency table will be produced to summarize answers provided to each of the 5 dimensions of the EQ-5D descriptive system at each scheduled visit by study cycle, actual dose level received within study cycle, and RLZ total.

The observed value of EQ VAS and change from Baseline will be summarized by study cycle, actual dose level received within study cycle, and RLZ total using descriptive statistics. No imputation will be applied on missing item in EQ-5D descriptive system and EQ VAS.

A by-participant listings of EQ-5D-5L will be provided.

9.10 MG-QOL15r

The MG-QOL15r total score is calculated by adding all the individual items described in Section 13.5.

The MG-QOL15r total score and change from Baseline to Day 43 will be summarized by study cycle, actual dose level received within study cycle, and RLZ total.

The mean change from Baseline in MG-QOL15r over time will be plotted by study cycle and treatment group.

A by-participant listings of MG-QOL15r will be provided.

9.11 Time between consecutive treatment cycles

The time between treatment cycles is calculated as: date of first sc infusion in consecutive cycle - date of last sc infusion before new cycle + 1 (or date of censoring - date of last sc infusion before potential new cycle + 1).

Discontinued participants will be censored at their discontinuation date and completers will be censored at their last visit date.

The number and percentage of study participants with <=21, >21-<=28, >28-<=60, >60-<=90, >90-<=120, >120-<=150, >150-<=180, >180-<=300, >300-<=400, >400-<=500, ... , >900-<=1000 days between study cycles will be summarized by treatment group in the proceeding cycle and RLZ total. Mean, SD, median, min and max will also be calculated for time between consecutive treatment cycles by treatment groups in the proceeding cycle and RLZ total. The same summaries will be repeated but participants who had no event in a specific cycle will be excluded from that cycle analysis.

Survival estimates for day 1, 28, 60, 90, 120, 150, 180, 300, 400, 500, 600, 700, 800, 900 and 1000 will be calculated using Kaplan-Meier method by treatment group in proceeding cycle and

RLZ total. The median times (with 95% CI) between study cycles and cumulative number of events by study cycle will also be reported. The survival event is defined as the start of subsequent cycle since last sc infusion of preceding cycle. Number of censored participants will be reported as well.

9.12 Minimal Symptom Expression

The Minimal Symptom Expression is defined as MG-ADL score of 0 or 1 (Vissing et al. 2020). The complete list of MG-ADL items and scores are provided in Table 13–3. The total score will be calculated according to the rules set down in Section 13.3.

The number and percentage of participants achieving Minimal Symptom Expression at any time during the Treatment and Observation Periods will be summarized by study cycle, actual dose level received within study cycle, and RLZ total using descriptive statistics.

10 PHARMACOKINETICS AND PHARMACODYNAMICS

All PK and PD analyses tables and figures described in this section will be performed on the SS by study cycle and dose level received within the cycle and RLZ total as described in Section 3.6. All listings will be presented using FAS.

10.1 Pharmacokinetics

Individual plasma concentrations of rozanolixizumab will be summarized by study cycle, actual dose level received within study cycle, RLZ total, actual dose (in mg) and scheduled sampling day using n, arithmetic mean, median, SD, minimum, maximum, geometric mean (geomean) with associated 95% CI, and geometric coefficient of variation (geoCV) (assuming log-normally distributed data).

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 1/3 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. If more than 1/3 of the individual data points at a timepoint are missing or are not quantifiable, then only n, minimum, median and maximum will be presented. The other descriptive statistics will be left blank.
- If n<3, then only the n, minimum and maximum will be presented. If no study participants have data at a given timepoint, then only n=0 will be presented.
- 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

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

Individual concentrations of rozanolixizumab will be listed by treatment group for each cycle and will include the actual sampling time in days relative to the previous dose, the IgG observed at the same visit, the ADA titer observed for the binding assay and the NAb titer for the same visit, IgG and IgG subclasses, and MG-ADL change from baseline for the corresponding visit.

10.2 Pharmacodynamics

10.2.1 Total serum IgG and IgG subclasses

Total serum IgG concentrations and IgG subclasses will be summarized by study cycle, actual dose level received within study cycle, overall, and time point for observed values, change from Baseline, and percentage change from Baseline for each cycle. For the analysis of the IgG data, in case rescue therapies are taken, the data up to (not including) the start date of rescue therapy and the data 8 weeks after the start date of rescue therapy will be utilized for the summary tables, ie the data from (including) start date of rescue therapy, to 8 weeks after start date of rescue therapy will be excluded from summary analysis. In cases where a study participant drops out, no missing value imputation will be performed for the IgG.

The maximum change from Baseline in total serum IgG (absolute and percentage change) will be reported in the listing and summarized by study cycle, actual dose level received within study cycle, and RLZ total. If there is no decrease from Baseline in total serum IgG in a given study participant, the maximum change will be reported as the smallest increase from Baseline.

Additionally, summary of total IgG by fixed dose and weight subgroups will be conducted as specified in Section 4.9.2.

Median and median percentage change from Baseline values in total serum IgG will be plotted over time by study cycle, actual dose level received within study cycle, and RLZ total with Baseline bodyweight groups (<50kg, 50kg-<70 kg, 70kg-<100kg, ≥100kg) overlaid on the same plot.

Spaghetti plots will be provided for absolute IgG and percentage change from baseline in IgG over time stratified by treatment group and Baseline bodyweight group (<50kg, 50kg-<70 kg, 70kg-<100kg, ≥100kg) where the Baseline bodyweight group is multipaneled or overlaying with different colors within each treatment group for each cycle.

A boxplot of maximum percentage from Baseline in total IgG up to Day 43 will be generated by study cycle and administered dose as specified in Section 4.9.2.

A subject plot for MG-ADL, QMG, and IgG over time for participants with weight below 50kg will also be provided.

Serum concentrations of total IgG and IgG subclasses will be listed together with concentrations of rozanolixizumab, ADA and NAb sample status and titer, MG-specific autoantibodies, MG-ADL change from Baseline, as specified in Section 10.3.2. The IgG values that were excluded from summary analysis will be flagged in listing. A separate listing of total IgG for participants who used manual push will also be provided.

10.2.2 MG-specific autoantibodies

Participants with <0.05 nmol/L in the MuSK assay at Baseline visit will be assigned to MuSK Negative.

MG-specific autoantibodies [anti-MuSK/anti-AChR v1 (determined with reagent 1)/anti-AChR v2 (determined with reagent 2)] will be summarized by study cycle, actual dose level received within study cycle, and RLZ total, at scheduled visit for observed values and absolute changes from Baseline by the participants who are anti-MuSK or anti-AchR autoantibody-positive at the MG0003 Baseline visit. For anti-AChR, if both anti-AChR v1 and anti-AChR v2 exist in one cycle, only anti-AChR v2 will be used in the summary table.

Anti-MuSK will also be summarized by study cycle, actual dose level received within study cycle, and RLZ total, at scheduled visit for observed values and percentage changes from Baseline by the participants who are anti-MuSK autoantibody-positive at the MG0003 Baseline visit.

Anti-AChR (values determined either with reagent 1 or 2) will be summarized by study cycle, actual dose level received within study cycle, and RLZ total, at scheduled visit for percentage changes from Baseline by the participants who are anti-AchR autoantibody-positive at the MG0003 Baseline visit.

The maximum change from Baseline in MG-specific autoantibodies [absolute (anti-MuSK, anti-AChR v1, anti-AChR v2) and percentage change (anti-MuSK, anti-AChR v1&v2 combined)] will be reported in the listing and summarized for each treatment. If there is no decrease from Baseline in MG-specific autoantibodies in a given study participant, the maximum change will be reported as the smallest increase from Baseline.

Median absolute and median percentage change from Baseline values in MG-Specific autoantibodies will be plotted over time by study cycle, RLZ dose level received within study cycle, and RLZ total with all treatments overlaid on the same plot for positive participants at MG0003 Baseline. Additionally, median percentage change from Baseline in anti-MuSK and median percentage change from Baseline of total IgG, and MG-ADL, QMG, MG-C mean change from Baseline will be plotted by study cycle, actual dose level received within study cycle and RLZ total for positive participants at MG0003 Baseline. The same plot will be repeated for median percentage change from Baseline values in anti-AChR for positive participants at MG0003 Baseline.

MG-specific autoantibodies will be listed, together with total IgG, IgG subclasses for all participants, and MG-ADL, QMG, MG-C change from Baseline.

10.3 Anti-drug antibody and neutralizing antibody (NAb) status

The ADA of rozanolixizumab will be measured using a three-tiered assay approach: screening assay, confirmatory assay and titration assay. Any sample confirmed positive for ADA will be assayed to determine whether there is neutralizing potential.

Evaluation of rozanolixizumab immunogenicity will be performed using data from all evaluable study participants in the SS, defined as all study participants who have an evaluable pretreatment (baseline) sample (negative or positive ADA sample status), and at least 1 evaluable post-Baseline value.

Study participants with an evaluable pretreatment (baseline) sample but without a single evaluable sample taken post-Baseline will be included in the reporting of pre-existing ADA but excluded from all other immunogenicity analyses.

10.3.1 Data consideration

ADA Sample Status

The ADA sample status will be determined for each pre-treatment (Baseline) and post-treatment (post-Baseline) visit where samples are taken for ADA analysis.

- Sample values that are either 'negative screen' or 'positive screen' and 'negative immunodepletion' will be defined as **ADA negative** if corresponding rozanolixizumab concentrations are equal or below the validated drug tolerance limit of the ADA assay (200µg/mL rozanolixizumab) allowing detection of 100ng/mL ADA
- Sample values that are either 'negative screen' or the combination of 'positive screen' and 'negative immuno-depletion', but with corresponding rozanolixizumab concentrations above the validated drug tolerance limit of the ADA assay, will be defined as ADA inconclusive
- Sample values that are 'positive screen' and 'positive immunodepletion' will be defined as **ADA positive**
- Samples that could not be tested for ADA status due to inadequate sample volume, mishandling, or errors in sample collection, processing, storage, etc, will be defined as **Missing**.

Neutralizing antibody (NAb) sample status (positive/negative/missing) will be determined for ADA positive samples. Samples that are NAb positive will be evaluated in a titration assay to quantify the NAb level and will be reported as titer.

Definition of ADA Baseline

Baseline for anti-drug antibody (ADA) for MG0007 should be the last measurement prior to receiving the very first rozanolixizumab (RLZ) infusion across all MG studies. Specifically, baseline for ADA is define as:

- MG0003 ADA baseline if participants randomized to RLZ groups in MG0003;
- MG0004 ADA baseline if participants randomized to placebo in MG0003 and enrolled in MG0004 before entering MG0007;
- MG0007 ADA baseline of first study cycle if participants randomized to placebo in MG0003 and enrolled straight into MG0007.

If the ADA sample status for the visit prior to the first dose of RLZ is missing, the last non missing sample will be used.

ADA/NAb Participant Status

The ADA participant status will be classified on study participant and group level as outlined below (Shankar et al. 2014; Rup et al, 2015). A description of how study participants will be categorized for the immunogenicity assessment is provided in Table 10–1.

Individual study participants will be assessed for ADA participant status, composed of 6 categories: ADA negative, inconclusive, and ADA positive, whereby a positive participant's

status is determined as originating from a treatment-induced, boosted, reduced or unaffected ADA response.

Study participants who are identified as being treatment-induced or treatment-boosted ADA-positive will be grouped as treatment-emergent (TE)-ADA positive participants. Study participants who are identified as being treatment-reduced or treatment-unaffected ADA-positive will be grouped as non-TE-ADA positive participants. Both TE-ADA positive and non-TE–ADA positive participants will be further classified as NAb negative or NAb positive.

The individual and combined ADA participant categories will be derived and summarized through each scheduled assessment visit (Day 1, Day 22, Day 43, Day 99 for Cycle 1, Day 1 and Day 43 for subsequent cycle, up to the last visit, and EOS visit), unless specified otherwise. Post-Baseline time points where no ADA sample was collected, will be ignored for the categorization.

Table 10–1: Terms and Definitions for ADA Status Evaluation in Study Participant

Classification	Classification Label	Definition
Individual participant categories		
1	Pre-ADA negative – treatment induced ADA negative (ADA-NEG)	Study participants who have an ADA negative sample at Baseline and at all sampling points post-Baseline up to the timepoint of interest.
2	Inconclusive	Study participants who have an ADA positive or negative Baseline sample and some post-Baseline samples are missing or inconclusive, while other post-Baseline samples are ADA negative up to the timepoint of interest.
3	Pre-ADA negative – treatment induced ADA positive (TI-POS)	Study participants who have an ADA negative sample at Baseline and have at least one ADA positive sample at any sampling point post-Baseline up to the timepoint of interest.
4	Pre-ADA positive – treatment boosted ADA positive (TB-POS)	Study participants who have an ADA positive sample at Baseline and at least one ADA positive sample at any sampling point post-Baseline up to the timepoint of interest, with increased titer values compared to Baseline (greater than a predefined fold difference increase from Baseline value which will be defined within the validation of the assay ie MSR of the assay).
5	Pre-ADA positive – treatment reduced ADA positive (TR-POS)	Study participants with an ADA positive sample at Baseline, and ADA negative samples at all sampling points post-Baseline up to the timepoint of interest.
6	Pre-ADA positive – treatment unaffected ADA positive (TU-POS)	Study participants with an ADA positive sample at Baseline and an ADA positive sample at any sampling point post-Baseline up to the timepoint of

Table 10–1: Terms and Definitions for ADA Status Evaluation in Study Participant

		interest, with titer values of the same magnitude as Baseline (less than a predefined fold difference from the Baseline value which will be defined within the validation of the assay, ie MSR of the assay[1]).
Combined participant categories		
7	Treatment emergent ADA positive (TE-POS)	Includes study participants who are treatment induced ADA positive (category 3) or treatment boosted ADA positive (category 4).
8	Non-treatment emergent ADA positive (Non-TE-POS)	Includes study participants who are treatment reduced ADA positive (category 5) or treatment unaffected ADA positive (category 6).
9	Treatment emergent ADA positive – NAb positive (TE-POS, NAb-POS)	Includes study participants who are treatment emergent positive (category 7) and have at least one NAb positive sample.
10	Treatment emergent ADA positive – NAb negative (TE-POS, NAb-NEG)	Includes study participants who are treatment emergent positive (category 7) and have no NAb positive samples.
11	Non-treatment emergent ADA positive - NAb positive (Non-TE-POS, NAb-POS)	Includes study participants who are non-treatment emergent positive (category 8) and have at least one NAb positive sample.
12	Non-treatment emergent ADA positive - NAb negative (Non-TE-POS, NAb-NEG)	Includes study participants who are non-treatment emergent positive (category 8) and have no NAb positive samples.

Note: if a participant has no baseline ADA, then she/he can't be treated as "Inconclusive".
[1] The fold difference increase from baseline value, ie the minimum significant ratio (MSR=1.36) determined during assay validation, will be reported in the relevant tables, listings and figures. It reflects the fold difference in titer level that considered higher than the assay variation in titer determination.

10.3.2 ADA summaries

The following outputs will be presented on the SS.

Tables:

- Number and percentage of study participants with ADA (positive, negative, inconclusive, missing sample) and NAb (positive, negative, missing) sample status at the time of each visit will be summarized by study cycle, actual dose level received within study cycle and RLZ total. Denominator is the number of study participants having a non-missing result at that visit.
- Number and percentage of study participants in each of the individual and combined ADA participant status categories presented in Table 10–1 will be summarized by entire study (for Baseline up to EOS and Baseline up to Last Visit), study cycle (for Baseline up to Day 1 and Baseline up to Day 43), actual dose level received within study cycle and RLZ total. The

table will be repeated by prior treatment immediately before entering MG0007 (RLZ or placebo) at Last Visit only.

- Total prevalence of pre-existing ADA and NAb, defined as number and percentage of participants having an ADA/NAb positive sample status at baseline, with the denominator being the total number of study participants having an evaluable sample result at baseline. Missing samples will not be included in the denominator. The table will be repeated by prior treatment immediately before entering MG0007 (RLZ or placebo).
- The first occurrence of treatment-emergent ADA positivity: cumulative number and percentage of TE-ADA positive participants (category 7) who are ADA positive for the first time at each visit by treatment group and RLZ total. The table will be repeated by prior treatment immediately before entering MG0007 (RLZ or placebo).
- Summary table of mean maximum percentage CFB in total IgG up to Day 43 and mean CFB in MG-ADL at Day 43, summarized by ADA participant categories 1, 2, 9, 10, 11 and 12 by treatment group and RLZ total and by study cycle (for Baseline up to Day 43).
- Overall summary table of TEAEs at Last Visit summarized by ADA participant categories 1, 2, 7 and 8 for the corresponding time period of interest by the most recent treatment group and RLZ total.
- Summary table of incidence of TEAE at Last Visit by ADA participant category 1, 2, 7 and 8 for the corresponding time period of interest by the most recent treatment group and RLZ total.
- Summary table of AEOF hypersensitivity reactions, anaphylactic reactions and injection site reactions (defined as AEOF in Section 13.7) at Last Visit by ADA participant category 1, 2, 7 and 8 for Baseline up to Last Visit by the most recent treatment group and RLZ total.

Figures:

- Individual time course plots for ADA positive study participants with at least one ADA positive sample, representing ADA and NAb titers (on log-scale), percentage CFB for total IgG and MG-specific autoantibodies, and CFB for MG-ADL total score. The sub-title of the graph will include the study participant number, bodyweight category, treatment group (including prior treatment group in MG0003), study cycle, and individual ADA participant category (3, 4, 5, 6) up to last assessment of each cycle. The dosing will be represented in the x-axis with bars/arrows at the time of dose.
- A box-and-whisker plot of maximum postdose ADA titer (on log-scale) through Day 43 of each cycle versus ADA participant category for categories 9, 10, 11 and 12 (determined for the corresponding time period of interest) by study cycle. The same plot will be repeated for NAb titer for ADA participant categories 9 and 11.
- Time course plot of mean CFB in MG-ADL total score, summarized by ADA participant category 1, 2, 9, 10, 11 and 12. Categories will be determined for the time period from baseline up to Day 43 for each cycle. Separate plots for each treatment group and by study cycle.

- Spaghetti plots of individual time course of percentage CFB for total IgG, for each of the ADA participant categories 1, 2, 9, and 10 and time period of interest (Baseline up to Last Visit) whereby the ADA participant categories are multipaneled. Separate plots for each treatment group. Individual samples that tested positive for ADA will be visualized using a symbol and/or color. Dosing time points should be indicated below the x-axis.
- Scatter dot plot of individual CFB in MG-ADL total score categorized by ADA titer tertile (including category ADA not present) for each scheduled assessment (Day 22, Day 43, Day 99 for Cycle 1, Day 1 and Day 43 for subsequent cycle). The same plot will be repeated for NAb titer.
- Scatter dot plot of individual percentage CFB for total IgG categorized by ADA titer tertile (including category ADA not present) for each scheduled assessment (Day 22, Day 43, Day 99 for Cycle 1, Day 1 and Day 43 for subsequent cycle). The same plot will be repeated for NAb titer.

Listings:

- By-subject listing by study cycle, treatment group, and timepoint, of ADA and NAb sample status, ADA titer, NAb titer, rozanolixizumab plasma concentration, percentage CFB for total IgG and IgG subclasses, CFB for MG-specific autoantibodies, CFB for MG-ADL total score, QMG and MG-C. In addition, the time since administration of IMP will be reported (in days).
- By-subject listing by study cycle, treatment group, and timepoint, of ADA and NAb sample status, ADA titer, NAb titer, and AEs.

10.4 Immunology

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

10.4.1 [redacted]

[redacted] variables will be listed by treatment group, visit and time point including changes from Baseline for each cycle.

10.4.2 Serum cytokines

Cytokines results will be listed by treatment group, visit and time point for each cycle.

10.4.3 [redacted]

[redacted]

11 OTHER ANALYSES

The tables and figures described in this section will use SS. All listings will be presented using FAS unless otherwise noted.

11.1 Dose change in use of concomitant medications over time

The following summaries will be produced by study cycle using SS in all participants:

- The number and percentage of participants with dose change (dose increase, dose decrease) in use of steroids (ATC3 code: [redacted]), immunosuppressants (ATC3 code: [redacted]) or AChE Inhibitor (ATC3 code: [redacted]) during the study;
- Average daily dose (ADD) of above medications by preferred term (PT) at Baseline and last study visit (in general EOS visit);

Note: ADD of above medications will be calculated for each PT according to the dose and dose frequency on Prior and Concomitant Medications CRF (eg ADD of a participant taking steroid 20 mg QOD is 10 mg). Baseline ADD will follow the same Baseline definition in Section 3.3, which will be calculated using the steroid dose taken prior to first IMP in MG0007. ADD at last study visit is calculated using the dose taken at last available visit.

- The change from Baseline of average daily dose (ADD) at last study visit, calculated as

  ADD at last study visit – Baseline ADD;

- A listing will be provided for study participants in SS with dose change of steroids, including MG-ADL total score at Baseline and last study visit (EOS visit), last MG-ADL score prior to first steroid dose change, maintenance dose of RLZ, Baseline steroid ADD and steroid ADD at last study visit.

  Note: Maintenance dose of RLZ is the most recent dose of RLZ when last steroid dose is given.

11.2 Use of rescue therapy

The use of rescue therapy will be identified as a 'yes' response to the "Rescue Medication?" question on the Prior and Concomitant Medications CRF, or plasma exchange as collected on concomitant medical procedure CRF".

The number and percentage of study participants who used of rescue therapy by study cycle and the actual dose received in that cycle will be summarized using SS.

Data from study participants who used rescue therapy will be listed using the FAS.

11.3 Time to first rescue therapy

Time to first rescue therapy (in days) is defined as: Date of first post-baseline rescue therapy use - Date of first IMP in the study + 1.

For participants who do not take rescue therapy, discontinued participants will be censored at their discontinuation date and completers will be censored at their last visit date.

The survival estimates of 1, 29, 43, 71, 99, 127,155, 180, 300, 400, 500, 600,700, 800, 900, and 1000 days to rescue therapy and the median times (with 95% CI) to rescue therapy will be

calculated using Kaplan-Meier method by initial RLZ dose level and RLZ total. Number of censored participants will be reported as well.

The median times to rescue therapy by study cycle will be calculated using Kaplan-Meier method for RLZ dose level received within study cycle and RLZ total. 95% CI of median times will be reported as well.

The time to rescue therapy will be listed using FAS.

11.4 Healthcare resource utilization, including hospitalization

The following summaries will be produced using descriptive statistics by entire study, study cycle, actual dose level received within study cycle and RLZ total using the SS:

- Number of study participants with hospitalization/ emergency room (ER) visit
- Total number of hospitalization/ ER visit
- Reason of hospitalization/ ER visit
- Number of study participants discharged from hospitalization/ ER visit
- Total number of days in hospitalization/ ER visit

Note:

- Total number of days in hospitalization/ ER visit for each hospitalization/ER visit= Discharge date – hospitalization/ ER visit date +1
- Total number of days in hospitalization/ ER visit for each cycle = sum of total number of days in hospitalization/ ER visit for all hospitalization/ER visit within the cycle
- Total number of days in hospitalization/ ER visit during study = sum of total number of days in hospitalization/ ER visit for all cycles
- Only hospitalization started after first IMP and before last visit will be considered in the summary
- In case of completely missing discharge date, the following imputation rules will be applied for the discharge date:
  - Hospital start date of next hospital stay – 1 as end date of this hospital stay;
  - Death date in case participant died and the end date of hospital stay is missing;
  - Last visit date if the end date of hospital stay is missing and the participant did not die.
- In case that discharge date is partially missing (day missing) then impute to last day of the month unless this date is after the hospital start date of a next stay (then impute to 1 day before) or it becomes after death date (then impute to death date).

A listing will be provided for the hospitalization/ ER visit. The data from Health Care Provider Consultations Not Foreseen by the Protocol CRF form will also be listed.

11.5 COVID-19 Test and [redacted]

The results of COVID-19 test and [redacted] will be listed for those study participants who had COVID-19 test or received [redacted] either before or during MG0007 by the [redacted]. The number of a cycle associated with the assessment will be indicated (ie, cycle 1 (initial), cycle 2, etc.).

11.6 Specific analyses for PMDA

The following endpoints will be summarized for study participants in Japan only using SS unless otherwise specified:

- Study participant characteristics, including important PDs (as specified in Section 5):
  - Disposition of Analysis Sets using ES
  - Disposition and Discontinuation Reasons
  - Discontinuation due to AEs
  - Impact of COVID-19 for Any Reason
  - Important Protocol Deviations by COVID-19 Period
- Demographics and other baseline characteristics, including medical history, prior and concomitant medications and rescue medications (as specified in Section 6):
  - Demographics
  - Baseline Characteristics
  - Prior Medications
  - Concomitant Medications
  - Rescue Medications
- Extent of exposure (as specified in Section 8.1)
- TEAE Summaries (as specified in Section 8.2.2 and Section 8.2.3)
  - TEAE overview
  - The number, percentage of participants and frequency of the following TEAEs will be summarized by SOC, HLT, PT, and by most recent dose prior to onset of TEAEs and RLZ total for entire study:
    - Any TEAEs
    - Any TEAEs during Treatment Period
    - Any TEAEs by maximum intensity (mild, moderate and severe)
    - Any Severe TEAEs
    - Any TEAEs by relationship
    - Fatal TEAEs

- Fatal TEAEs by relationship
- Serious TEAEs
- Serious TEAEs by relationship
- Participant discontinuation due to TEAEs
- TEAEs leading to permanent withdrawal of IMP
- TEAEs leading to temporary withdrawal of IMP
- TEAEs requiring dose change
- Treatment-emergent AESIs

– The number, percentage of participants and frequency of any TEAEs will be summarized by SOC, HLT, PT, and by most recent dose prior to onset of TEAEs and RLZ total for each study cycle

- MG-ADL total score and change from Baseline (as specified in Section 9.1)
- QMG total score and change from Baseline (as specified in Section 9.2)
- MG-C total score and change from Baseline (as specified in Section 9.3)
- MG Symptoms PRO 'Muscle Weakness Fatigability', 'Physical Fatigue' and 'Bulbar Symptoms' scale scores and changes from Baseline (as specified in Section 9.4)
- EQ VAS observed value and change from Baseline (as specified in Section 9.9)
- MG-QOL15r observed results and change from Baseline (as specified in Section 10.10)
- MG-ADL responder rates (as specified in Section 9.5)
- QMG responder rates (as specified in Section 9.7)
- MG-C responder rates (as specified in Section 9.8)
- ADA summaries (as specified in Section 10.3.2):
  – Number and percentage of study participants with positive, negative, missing or inconclusive sample ADA status at the time of each visit and RLZ total will be summarized by study cycle, actual dose level received within study cycle and RLZ total.
  – Number and percentage of study participants in each of the ADA classifications presented in Table 10–1 will be summarized by study cycle, actual dose level received within study cycle and RLZ total.
  – Total prevalence of pre-existing ADA and NAb, defined as number and percentage of participants having an ADA/NAb positive sample status at baseline, with the denominator being the total number of study participants having an evaluable sample result at baseline. Missing samples will not be included in the denominator.
  – The first occurrence of treatment-emergent ADA positive will be summarized using frequency and percentage at each post-Baseline visit by study cycle, actual dose level received within study cycle and RLZ total.

- Use of rescue therapy (as specified in Section 11.2)

The following figures will be provided for Japanese participants only:

- Spaghetti plot of individual change from Baseline in MG-ADL, QMG, MG-C, and percentage change from Baseline in total IgG, AChR and MuSK over time by study cycle and treatment group
- Mean change from Baseline in MG-ADL, QMG, MG-C, MG Symptom PRO and MG-QOL15r by Study Cycle and Treatment Group

11.7 Headache questionnaire

The results of the headache questionnaire will be listed for study participants for whom data were collected using ES. No summary tabulations will be provided for these assessments.

11.8 History of headache

The history of headache will be listed for study participants for whom data were collected using FAS. No summary tabulations will be provided for these assessments.

11.9 Myasthenia Gravis Foundation of America (MGFA)

The MGFA classes will be listed by visit using FAS. No summary tabulations will be provided for these assessments.

12 REFERENCES

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13 APPENDICES

13.1 Quantitative Myasthenia Gravis scale

The QMG scale comprises 13 items, including ocular and facial movement, swallowing, speech, limb strength and forced vital capacity. Scoring for each item ranges from no weakness (0) to severe weakness (3), with an overall score range from 0 to 39, ie, a higher score indicates more severe disease. A 3-point change in the overall score is considered to be clinically relevant.

The QMG testing form is provided in Table 13–1. The total score is obtained by summing the responses to each individual item. Thus, the score ranges from 0 to 39.

[redacted] The score ranges from 0 to 33.

In the event of missing data, the following rules will be applied:

- If 1 or 2 items are not answered, the overall score will be obtained by imputing the missing items with the average score across the remaining items at the specific visit. The imputed value will be rounded to one decimal place
- If more than 2 items are missing the overall score will not be calculated at the specific visit

Table 13–1: Quantitative myasthenia gravis testing form

[redacted]

Table 13–1: Quantitative myasthenia gravis testing form

F=female; M=male.

13.2 Myasthenia Gravis-Composite scale

The MG-C score items and associated scores are provided in Table 13–2.

The MG-C score comprises 10 items, each of which is weighted differently in the calculation of the overall score. The overall score ranges from 0 to 50, with a higher score indicating more severe disease.

The total score is obtained by summing the responses to each individual item.

The total score (excluding ocular items) is calculated by summing the last 7 items, excluding ptosis, double vision, and eye closure. The score ranges from 0 to 41.

In the event of missing data at a particular visit, the MG-C score will not be calculated. Due to the different weighting applied to each item it is not possible to impute the missing data with the average score across the remaining items. If baseline total score of a cycle is missing, the previous last non-missing total score (from previous cycle or study) will be considered as baseline.

Table 13–2: MG-C score items and scoring algorithm

Item	Result/Grade	Result/Grade	Result/Grade	Result/Grade
Ptosis, upward gaze (physician examination)	>45 seconds/0	11-45 seconds/1	1-10 seconds/2	Immediate/3
Double vision on lateral gaze, left or right (physician examination)	>45 seconds/0	11-45 seconds/1	1-10 seconds/3	Immediate/4
Eye closure (physician examination)	Normal/0	Mild weakness (can be forced open with effort)/0	Moderate weakness (can be forced open easily)/1	Severe weakness (unable to keep eyes closed)/2
Talking (patient history)	Normal/0	Intermittent slurring or nasal speech/2	Constant slurring or nasal but can be understood/4	Difficult to understand speech/6
Chewing (patient history)	Normal/0	Fatigue with solid food/2	Fatigue with soft food/4	Gastric tube/6
Swallowing (patient history)	Normal/0	Rare episode of choking or trouble swallowing/2	Frequent trouble swallowing eg, necessitating changes in diet/5	Gastric tube/6
Breathing (thought to be caused by MG)	Normal/0	Shortness of breath with exertion/2	Shortness of breath at rest/4	Ventilator dependence/9
Neck flexion or extension (weakest) (physician examination)[a]	Normal/0	Mild weakness/1	Moderate weakness (ie, 50% weak, +/-15%)/3	Severe weakness/4
Shoulder abduction (physician examination) [a]	Normal/0	Mild weakness/2	Moderate weakness (ie, 50% weak, +/-15%)/4	Severe weakness/5
Hip flexion (physician examination) [a]	Normal/0	Mild weakness/2	Moderate weakness (ie, 50% weak, +/-15%)/4	Severe weakness/5

[a] Moderate weakness for head and neck items should be construed as weakness that equals roughly 50%+/-15% of expected normal strength. Any weakness milder than that would be mild and any weakness more severe than that would be classified as severe.

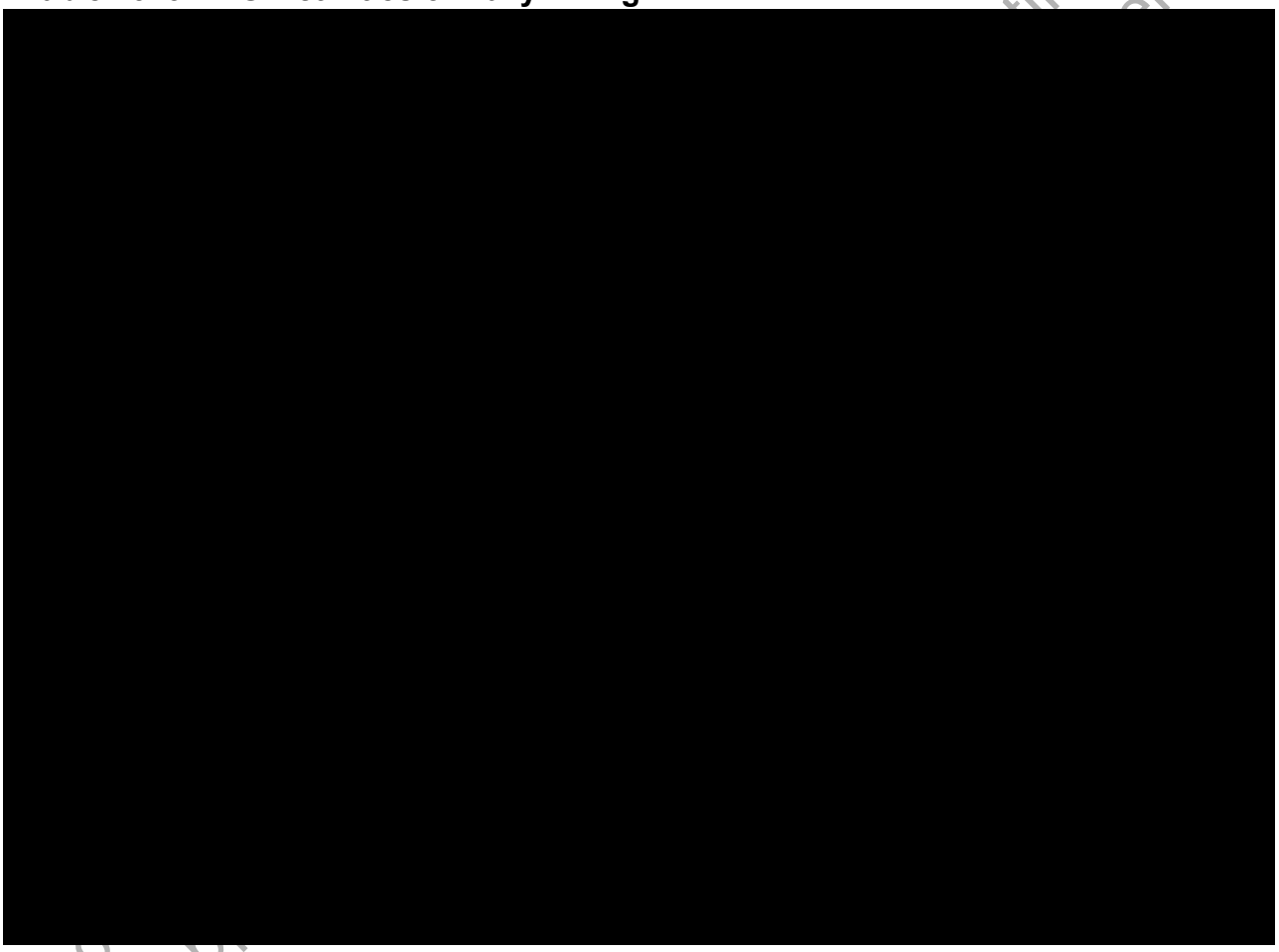
13.3 Myasthenia Gravis-Activities of Daily Living

The MG-ADL score comprises 8 items, each with a score of 0 to 3. The total score is obtained by summing the responses to each individual item. Thus, the score ranges from 0 to 24 with a higher score indicating more disability. The MG-ADL testing form is provided in Table 13–3.

In the event of missing data, the following rules will be applied:

- If 1 or 2 items are not answered, the overall score will be obtained by imputing the missing items with the average score across the remaining items at the specific visit. The imputed value will be rounded to one decimal place
- If more than 2 items are missing the overall score will not be calculated.

Table 13–3: MG-Activities of Daily Living



13.4 Myasthenia Gravis Symptoms PRO

The MG Symptoms PRO instrument consists of 42 items across 5 scales: ocular symptoms (items 1 to 5); bulbar symptoms (items 6 to 15); respiratory symptoms (items 16 to 18); physical fatigability (items 19 to 33) and muscle weakness fatigability (items 34 to 42).

The MG Symptoms PRO calculation includes two steps: 1) rescoring the item responses; and 2) calculation of the final scores. Details of the scoring is found in the Myasthenia Gravis Symptoms PRO Instrument Scoring Manual, dating of 28 February 2019.

Step 1: Rescoring the item responses. The item responses should be rescored so as the lowest item-level score is 0. Rescoring rules are provided in Table 13–4.

Step 2: Calculation of the MG Symptoms PRO Scores

- MG Symptom PRO scale scores

The MG symptom PRO scale scores are calculated using the formula below, ie the sum of item scores is linearly transformed to have all domain scores ranging from 0 to 100:

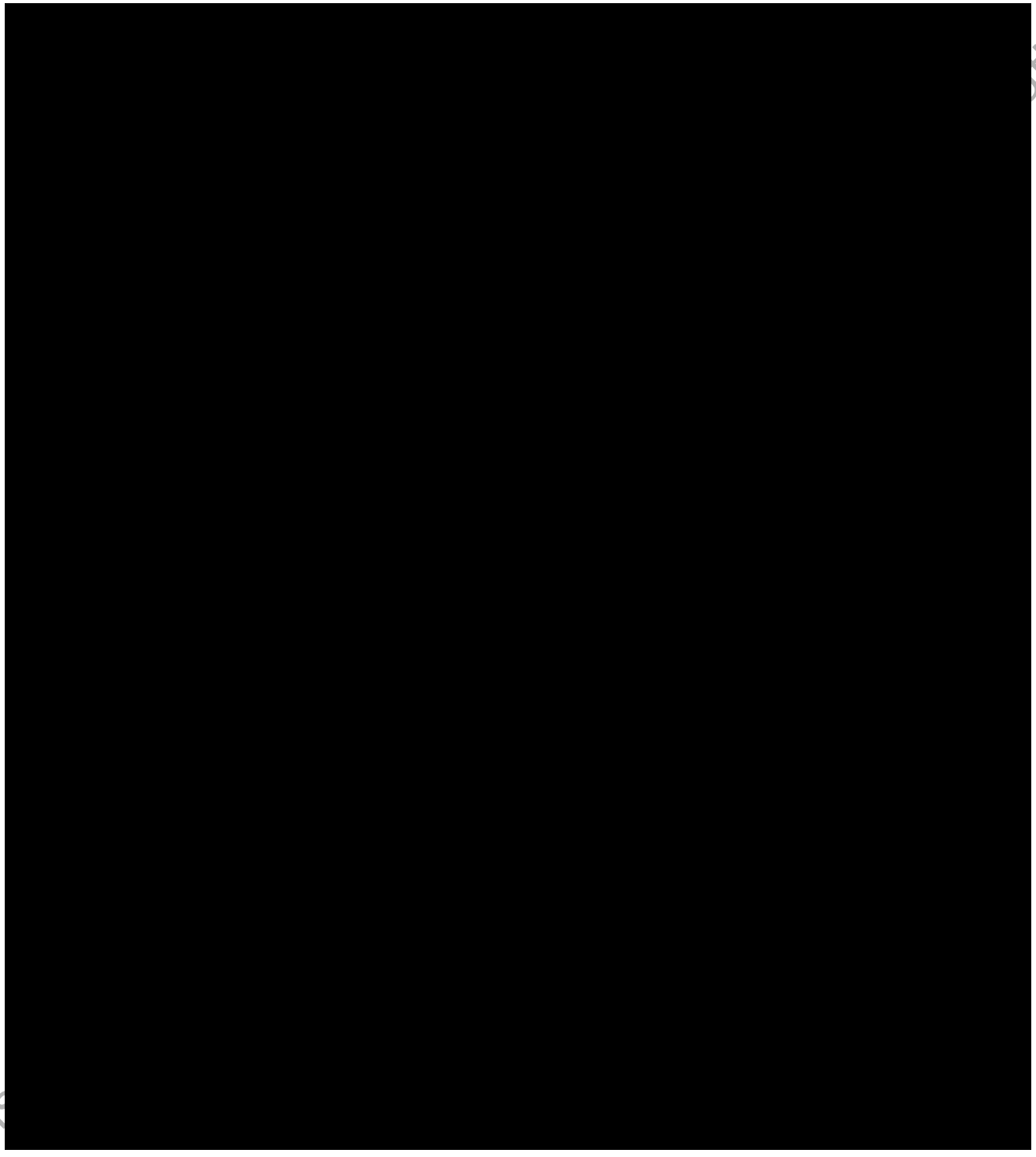
$$MG\ Symptom\ PRO\ scale\ score = \frac{Sum\ of\ item\ scores\ within\ the\ scale}{Raw\ score\ range} \times \frac{Total\ number\ of\ items\ in\ the\ scale}{Number\ of\ non\ missing\ items\ in\ the\ scale} \times 100$$

The score for each scale is calculated only when at least 70% of the items are completed. Details on the minimum number of items needed for score calculation and the range of raw score are provided in Table 13–5.

Table 13–4: Myasthenia Gravis Symptoms PRO

[redacted]

Table 13–4: Myasthenia Gravis Symptoms PRO



[redacted]

Table 13–5: Description of the MG Symptoms PRO Scale Scores

Scale	Number of Items	Number of items needed for score	Raw score range	Listing of items included (MG Symptoms PRO item number)
Ocular symptoms	5	4	0-15	1-5
Bulbar symptoms	10	7	0-30	6-15
Respiratory symptoms	3	3	0-9	16-18
Physical fatigue	15	11	0-60	19-33
Muscle weakness fatigability	9	7	0-36	34-42

13.5 MG-QOL15r

The MG-QOL15r is a brief survey, completed by the study participant, that is designed to assess some aspects of "quality of life" related to MG. The total score is calculated by summing all 15 individual items.

In the event of missing data, the following rules will be applied:

- In the case where at least 70% of the items (ie 11 items out of the 15) are answered, the total score will be generated after imputing the missing responses by the average of available (ie non-missing) responses, by adding all item scores.
- In the case where more than 30% (ie 5 items or more) are missing, the total score will not be generated.

Table 13–6: MG-QOL15r

Please indicate how true each statement has been (over the past few weeks).

	Not at all	Somewhat	Very much
	0	1	2
1. I am frustrated by my MG			
2. I have trouble using my eyes because of my MG (e.g. double vision)			
3. I have trouble eating because of MG			
4. I have limited my social activity because of my MG			
5. My MG limits my ability to enjoy hobbies and fun activities			
6. I have trouble meeting the needs of my family because of my MG			
7. I have to make plans around my MG			
8. I am bothered by limitations in performing my work (include work at home) because of my MG			
9. I have difficulty speaking due to MG			
10. I have lost some personal independence because of my MG (e.g. driving, shopping, running errands)			
11. I am depressed about my MG			
12. I have trouble walking due to MG			
13. I have trouble getting around public places because of my MG			
14. I feel overwhelmed by my MG			
15. I have trouble performing my personal grooming needs due to MG			

MG-QOL15r
Muscle and Nerve 2016 Dec;54(6):1015-1022.

Total MG-QOL15r score

MG-QOL15r - United States/English
MG-QOL15r_AU1.0_engUSort.doc

13.6 Markedly abnormal 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. If both high and low criteria are shown for a parameter, the criteria should be summarized separately in tabular or graphical data summaries.

Table 13–7: Hematology

Parameter	Unit (conventional)	Unit (standard)	Marked Abnormality Criteria
Hemoglobin	g/dL	g/L	<8.0 g/dL; <80 g/L
WBC (Leukocytes)[1]	10^9/L	10^9/L	Low: <2.0 x 10^9/L
			High: >30 x 10^9/L
Lymphocytes Absolute	10^9/L	10^9/L	Low: <0.5 x 10^9/L
			High: >20 x 10^9/L
Neutrophils Absolute	10^9/L	10^9/L	<1.0 x 10^9/L
Platelets	10^9/L	10^9/L	<50.0 x 10^9/L

[1]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 10^9/L is applied to flag leukocytosis (George 2012).

Table 13–8: Chemistry

Parameter	Unit (conventional)	Unit (standard)	Marked Abnormality Criteria
AST (SGOT)	U/L	U/L	>5.0 x ULN
ALT (SGPT)	U/L	U/L	>5.0 x ULN
ALP (Alkaline Phosphatase)	U/L	U/L	>5.0 x ULN
GGT (Gamma Glutamyl Transferase)	U/L	U/L	>5.0 x ULN
Bilirubin (Total)	mg/dL	umol/L	>3.0 x ULN if Baseline value is normal; >3.0 x Baseline value if Baseline is abnormal
Albumin	g/dL	g/L	<2 g/dL; <20 g/L
Creatinine	mg/dL	umol/L	>3.0 x ULN or >3 x baseline
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
C reactive protein (CRP)[2]	mg/L	mg/L	>100 mg/L
Calcium[3]	mg/dL	mmol/L	Low: Corrected serum calcium of <7.0 mg/dL; <1.75 mmol/L
			High: Corrected serum calcium of >12.5 mg/dL; >3.1 mmol/L
Immunoglobulin G[4]	(g/L)	(g/L)	≤1 g/L
Potassium	mmol/L	mmol/L	Low: <3.0 mmol/L
			High: >6.0 mmol/L
Sodium	mmol/L	mmol/L	Low: <125 mmol/L
			High: >155 mmol/L
Glucose[5]	mg/dL	mmol/L	Low: <40 mg/dL; <2.2 mmol/L
			High: > 250 mg/dL; >13.9 mmol/L

Table 13–8: Chemistry

Total Cholesterol	mg/dL	mmol/L	>400 mg/dl; >10.34 mmol/L
Triglycerides	mg/dL	mmol/L	>500 mg/dl; >5.7 mmol/L

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]; 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 61.88 for females and 79.56 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/. A moderate elevation of CRP level per referred reference is used for the marked abnormality criteria for RLZ to ensure a change suggestive of inflammatory process is captured. Standard CRP test should be used. In case high sensitivity CRP (hs-CRP) test have been used in any ongoing studies apply same value (>100 mg/L) as markedly abnormal criteria.

[3]Corrected Calcium (mmol/L) =0.02 * (40 – Albumin (g/L)) + Calcium (mmol/L).

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

[5]Glucose high criterion defined by Grade 3 and higher events according to CTCAE, Version 4.03, June 14, 2010.

Table 13–9: Vital Signs

Parameter	Abnormality Criteria
Pulse Rate (beats/minute)	≤50 and a decrease from Baseline of ≥15 ≥120 and an increase from Baseline of ≥15
Systolic Blood Pressure (mmHg)	≤ 90 and a decrease from Baseline of ≥20 ≥ 180 and an increase from Baseline of ≥20
Diastolic Blood Pressure (mmHg)	≤50 and a decrease from Baseline of ≥15 ≥105 and an increase from Baseline of ≥ 15
Temperature	>101 ^{0}F (38.3 ^{0}C)
Body Weight	≥ 10% decrease from Baseline ≥ 10% increase from Baseline

Table 13–10: Electrocardiogram

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

Abbreviations: bpm = beats per minute; ms = milliseconds; QTc(F) = Fridericia corrected QT interval;
Note: Treatment-emergent is defined as meeting the criteria at any post-Baseline visit after the first infusion of study medication and within 56-days of the last infusion and not meeting the same criteria during Baseline

13.7 AEs of focus for Rozanolixizumab program

The AEOF selection criteria is specified in the Rozimab Safety AEs of Focus document developed by UCB. The purpose of this document is to detail the approach to identifying TEAEs meeting criteria for AEOF for the Rozanolixizumab (also called RLZ) program.

Following Events are AEOFs for Rozimab for MG studies:

No	Event (also included in Title of TFL output)	Selection criteria
1	Headache (Note: also included in AESM if severe and/or serious)	TEAE with HLGT='Headaches'
2	Possible aseptic meningitis (Note: also included in AESM)	SMQ=' Noninfectious meningitis' narrow search
3	Gastrointestinal disturbances	TEAE with HLT='Gastrointestinal and abdominal pains (excl oral and throat)' or -HLT='Nausea and vomiting symptoms' or HLT='Diarrhoea (excl infective)' or HLT='Gastritis (excl infective)' or PT = 'Abdominal discomfort'
4	Hypersensitivity reactions	SMQ='Hypersensitivity' narrow search
5	Anaphylactic reactions	SMQ='Anaphylactic reaction' and TEAEs that either emerged on the **same day** as when a study medication injection reaction was received, or that emerged **one day after** a study medication injection was received, and

		which fulfill <u>any</u> of the following 3 criteria should be included in the summary table: 1. If a subject reports any TEAE which codes to a PT included in Category A, then the event will be flagged as an anaphylactic reaction. 2. If a subject reports any TEAE which codes to a PT included in Category B **AND** reports any TEAE which codes to a PT included in Category C, **and both TEAEs have the same start date**, then both events will be flagged as anaphylactic reactions. 3. If a subject reports any TEAE which codes to a PT included in Category D **AND** reports (either a TEAE which codes to a PT included in Category B **OR** a TEAE which codes to a PT included in Category C), **and both TEAEs have the same start date**, then both events will be flagged as anaphylactic reactions.
6	Injection site reactions	TEAE with HLT='Injection site reactions' or HLT='Infusion site reactions' or HLT='Administration site reactions NEC'
7	Infections	TEAE with SOC ="Infections and infestations" Note: This was added as a reminder for safety that infections are considered as AE of focus and require assessment. No programming of this topic is required as TEAEs can be found in general AE Tables.
8	Opportunistic infections (Note: also included in AESM)	TEAEs in MedDRA SMQ = 'Opportunistic infections' narrow search
9	Reductions in albumin and plasma proteins	TEAEs with PT='Blood albumin decreased' or PT='Protein albumin ratio' or LLT='Plasma protein abnormal' or LLT='Proteins serum plasma low'
10	Effects on the kidney	TEAEs in SMQ= 'Acute renal failure' narrow search
11	Drug related hepatic disorders	TEAEs in SMQ='Drug related hepatic disorders - comprehensive search' narrow and broad search
12	Effect on lipids	TEAEs with PT= 'Blood cholesterol increased' or PT= 'Low density lipoprotein increased' or PT= 'Blood triglycerides increased' or PT= 'Hypercholesterolaemia' or PT= 'Hypertriglyceridaemia' or PT= 'Hyperlipidaemia' or PT= 'Dyslipidaemia' or

		PT= 'Lipids increased'

14 AMENDMENT(S) TO THE STATISTICAL ANALYSIS PLAN

14.1 Amendment 1

Rationale for the amendment

This amendment is to apply following changes:

- Update definitions of ADA participant categories, and update related analyses
- Minor cosmetic changes
- To be consistent with MG0003 and MG0004

Modifications and changes

Section # and Name	Description of Change	Brief Rationale
General	All listings using SS were changed to use FAS.	To include full data in listings
2.2.2.2 Other efficacy endpoints	The MG-C responder was changed to be at least 3-point decrease from Baseline instead of 5-point decrease.	To be consistent across MG studies
3.3 Definition of Baseline values	Removed ADA Baseline definitions	ADA Baseline definitions were moved to Section 10.3
3.6 Treatment assignment and treatment groups	Added a rule for actual treatment group in analysis: "If participant switched dose within one cycle, then they will be assigned to IMP 10mg/kg group for that cycle."	To be consistent with MG0003
3.9 Changes to protocol-defined analyses	Previously deleted lab variables were added back so the related changes to protocol defined analyses were not applicable and therefore deleted from this section; Added rule for excluding data in time to MG-ADL response when there is an intercurrent event.	To explain the discrepancy between SAP and protocol
4.2.2 Dates and times	Modified imputation rules for missing dates	To consider the case when data cutoff and data extract dates are different
4.4 Interim analyses and data monitoring	Updated data requirements for two interim cuts	For clarity
4.9.1 General subgroups	Updated MG-specific autoantibody stratification factors definition; Added more subgroups	For consistency with MG0003 and MG0004
4.9.2 Examination of weight subgroups and administered doses	Added new section for fixed dose analyses	To be consistent with MG0003
5.1 Subject disposition	Added count of participant by visit analysis	For consistency with MG0003 and MG0004

Section # and Name	Description of Change	Brief Rationale
6.2 Baseline characteristics	Added some Baseline characteristics	To be consistent with MG0003
6.4 Prior and concomitant medications	Added definition of rescue therapy	For clarity
8.1 Extent of exposure	Added definition of number of cycles per participant year and study IMP duration of entire study; Added a figure for actual dose received in all study cycles by participant	For clarity
8.2.2 Adverse events summaries	Removed TEAEs relative to ADA analysis; added summary of TEAEs by fixed dose and weight subgroup summary	First part is covered by TEAE by ADA participant category in Section 10.3 and second part is for fixed dose analysis
8.2.3 Adverse events of focus	Updated AEOF categories; Removed incidence of AEOF by relationship and incidence of AEOF headache and gastrointestinal disturbances by intensity; Added a graph for AEOF by participant	For consistency with MG0003 and MG0004 and also requested during DEM2
8.3 Clinical laboratory evaluations	Added albumin and C-creative protein to Table 8.3 and added definition of TEMA laboratory assessment; Added figure for the platelets count	To capture all measured parameters and identify treatment-emergent MA values in laboratory evaluations
8.3.1 Potential drug-induced liver injury	Changed the summary to be for treatment-emergent only; Changed the LFT level summary table to be for entire study only	To include only treatment-emergent pDILI
8.4.1 Vital signs	Changed the summary of MA results to be for treatment-emergent only; The entire study summary was changed to by the initial dose level	To include only treatment-emergent results
8.4.2 Electrocardiograms	Changed the summary of MA results to be for treatment-emergent only; The entire study summary was changed to by the initial dose level	To include only treatment-emergent results
8.4.3.1 Physical examination	Removed physical examination abnormal results listing	Data were not collected
9.1 MG-ADL score	Added MG-ADL excluding ocular items analysis, listing of MG-ADL by study cycle and dose, mean change from Baseline over time figure, boxplot of change from Baseline in MG-ADL at Day 43, and summary of MG-ADL by fixed dose and weight subgroups; removed MG-ADL by ADA status figure	For consistency with MG0003 and MG0004
9.2 QMG score	Added mean change from Baseline over time figure, boxplot of change from Baseline in QMG at Day 43, and	For consistency with MG0003

Section # and Name	Description of Change	Brief Rationale
	summary of QMG by fixed dose and weight subgroups	
9.3 MG-C score	Added mean change from Baseline over time figure, boxplot of change from Baseline in MG-C at Day 43, and summary of MG-C by fixed dose and weight subgroups	For consistency with MG0003
9.4 MG Symptoms PRO	Added mean change from Baseline over time figure	For consistency with MG0003
9.5 MG-ADL responder rate (≥2.0 points improvement from Baseline)	Added summary by fixed dose and weight subgroups; Removed summary analysis for imputed responders	For consistency with MG0003
9.6 Time to MG-ADL response	Added Kaplan-Meier plot for time to MG-ADL response	For data visualization
9.7 QMG responder rate (≥3.0 points improvement from Baseline)	Added summary by fixed dose and weight subgroups; Removed summary analysis for imputed responders	For consistency with MG0003
9.8 MG-C responder rate (≥3.0 points improvement from Baseline)	Added summary by fixed dose and weight subgroups; Removed summary analysis for imputed responders	For consistency with MG0003
9.10 MG-QOL15r	Added mean change from Baseline over time figure	For consistency with MG0003
9.11 Time between consecutive treatment cycles	Updated the definition for time between consecutive treatment by changing the starting point from Day 43 to last sc infusion date	To consider last infusion date and account for missing visit
10 PHARMACOKINETICS AND PHARMACODYNAMICS	Updated definitions of ADA participant categories and related analyses	For consistency with MG0003 and MG0004
10.2.1 Total serum IgG and IgG subclasses	Added summary by fixed dose and weight subgroups and a boxplot of maximum percentage from Baseline in total IgG up to Day 43.	For consistency with MG0003
10.2.2 MG-specific autoantibodies	Added a threshold for MuSK assay at Baseline to be considered as positive; For figures of MG-specific autoantibodies, changed to median from mean	For data accuracy and consistency with MG0003
10.3 Anti-drug antibody and neutralizing antibody (NAb) status	Updated definitions of ADA participant categories and ADA related analyses	To be consistent with MG0003 and MG0004
10.3.2 ADA summaries	The maximum PCFB of IgG and mean CFB of MG-ADL by ADA participant category summary table was changed to consider Baseline up to Day 43 in each cycle only; Removed RLZ total in all figures; Changed time period of interest	For clarity and to be consistent with MG0003

Section # and Name	Description of Change	Brief Rationale
	to Baseline up to Day 43 of each cycle for by box-and-whisker plot of maximum post-dose ADA and NAb titer and time course plot of mean MG-ADL by ADA participant category; Removed Day 1 timepoint in scatter dot plots; Added injection site reactions to AEOF summary by ADA category	
11.1 Dose change in use of concomitant medications over time	Removed figure of CFB in MG-ADL with dose change	For consistency with MG0004
11.6 Specific analyses for PMDA	Updated some analysis set to SS; Added MG Symptoms PRO score, EQ VAS, and MG-C responder rates summary, two TEAE tables, and two figures	Per PMDA request
11.8 History of headache	Added a listing for history of headache	To present the data
11.9 Myasthenia Gravis Foundation of America (MGFA)	Added a listing for MGFA	To present the data
13.6 Markedly abnormal criteria for Rozanolixizumab program	Added corrected calcium algorithm and updated the marked abnormality criteria for corrected calcium and eGFR formula parameters.	For clarity
13.7 AEs of focus for Rozanolixizumab program	Updated definitions of AEOF	To be consistent across MG studies

14.2 Amendment 2

Rationale for the amendment

This amendment is to apply following changes:

- To align with changes made in Protocol Amendment 3

Modifications and changes

Section # and Name	Description of Change	Brief Rationale
2.1 Study objectives	Cytokine was removed.	Protocol amendment 3 change
2.3.1 Overall design	Added rules for participants who received rescue therapy during the observation or no treatment with rozanolixizumab periods.	Protocol amendment 3 change
3.9 Changes to protocol-defined analyses	MG-C changes were removed; Updated the definition of Hy's law to be consistent with program SAP. Added rule for excluding IgG data in summary when patients take rescue therapy.	MG-C responder definition were updated in Protocol amendment 3 and to be consistent with rozanolixizumab program SAP

Section # and Name	Description of Change	Brief Rationale
4.4 Interim analyses and data monitoring	Updated descriptions of two interim cuts	For clarity
4.9.3 Manual Push Analysis	Added manual push analysis for participants who used manual push	To understand the impact of manual push
8.1 Extent of exposure	Updated the summary for extent exposure	To address DEM3 comment
8.2.2 Adverse events summaries	Added text to clarify the treatment groups used in the summary; The AESM definition was updated; Added manual push listing for TEAE; Added summary tables for non-TEAE	For clarity and to match with rozanolixizumab program SAP; To understand the impact of manual push
8.3 Clinical laboratory evaluations	Table 8-1 was updated.	To match with protocol amendment 3
8.3.1 Potential drug-induced liver injury	Updated pDILI definition	To be consistent with rozanolixizumab program SAP
9.6 Time to first MG-ADL response	[redacted]	To address DEM3 comment
9.11 Time between consecutive treatment cycles	Updated the summary and survival analysis for time between consecutive treatment cycles	To address DEM3 comment
10.2.1 Total serum IgG and IgG subclasses	Added total IgG manual push listing for participants who used manual push and included the IgG data after 8 weeks of using rescue therapy; Added a subject plot for MG-ADL, QMG, and IgG over time for participants with weight below 50kg	To understand the impact of manual push and to include more valid data into summary
10.2.2 MG-specific autoantibodies	Mean percentage change from Baseline of total IgG in autoantibodies plot was updated to median percentage change from Baseline of total IgG; Added anti-AChR v1 (determined with reagent 1) and anti-AChR v2 (determined with reagent 2) into the summary.	More appropriate statistic to summarize this measure and to reflect the change of anti-AChR sample analysis method
10.4.2 Serum cytokines	Removed changes from baseline for serum cytokines listing	As it is not required in the protocol amendment 3
11.3 Time to first rescue therapy	Removed censoring at the start date of the TEAE leading to withdrawal and updated survival analysis summary for time to first rescue therapy	For consistency with MG0003 and to address DEM3 comment
11.4 Healthcare resource utilization, including hospitalization	Updated calculation and imputation rule for hospitalization; Added a listing for Health Care Provider Consultations Not Foreseen by the Protocol CRF	To address DEM3 comment
11.5 [redacted]	Removed table and figure for [redacted]	Data not suitable for summary table and figure

Section # and Name	Description of Change	Brief Rationale
12 REFERENCES	Added source for COVID-19 end date	For clarity
13.2 Myasthenia Gravis-Composite scale	Added imputation rule for missing baseline total MG-C score	For clarity
13.6 Markedly abnormal criteria for Rozanolixizumab program	Updated the marked abnormality criteria for creatinine, CRP, potassium; Race factor was removed from eGFR formula	To match with rozanolixizumab program SAP
13.7 AEs of focus for Rozanolixizumab program	Aseptic meningitis was added as AEOF.	To match with rozanolixizumab program SAP

STATISTICAL ANALYSIS PLAN SIGNATURE PAGE

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

Approval Signatures

Name: mg0007-sap-amend-2

Version: 3.0

Document Number: CLIN-000226134

Title: MG0007 - Statistical Analysis Plan Amendment 2

Approved Date: 01 Mar 2024

Document Approvals	
Approval Verdict: Approved	Name: [redacted] Capacity: Clinical Date of Signature: 01-Mar-2024 15:08:32 GMT+0000
Approval Verdict: Approved	Name: [redacted] Capacity: Subject Matter Expert Date of Signature: 01-Mar-2024 16:27:22 GMT+0000