STATISTICAL ANALYSIS PLAN

AMENDMENT 1

Study: MG0004

Product: Rozanolixizumab

A RANDOMIZED, OPEN-LABEL EXTENSION STUDY TO INVESTIGATE THE LONG-TERM SAFETY, TOLERABILITY, AND EFFICACY OF ROZANOLIXIZUMAB IN ADULT PATIENTS WITH GENERALIZED MYASTHENIA GRAVIS

Short Title:

A Phase 3 extension study to evaluate the safety, tolerability, and efficacy of rozanolixizumab in adult patients with generalized myasthenia gravis

Sponsor:

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Regulatory Agency Identifier Number(s):

Registry	**ID**
Eudra CT Number:	2019-000969-21
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Confidentiality Statement

Confidential

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VERSION HISTORY

SAP Version	Approval Date	Change	Rationale
1.0	18 Nov 2020	Not Applicable	Original version
Amendment 1	23 Sep 2021	See summary of changes in Section 14.1	Updated based on DEM2 and DEM3 comments

LIST OF ABBREVIATIONS

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
AUC	Area Under the Curve
BLQ	Below the Lower Limit of Quantification
BUN	Blood Urea Nitrogen
CI	Confidence Interval
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
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
eGFR	estimated Glomerular Filtration Rate
EOS	End of Study
EQ-5D-5L	5-Level European Quality of Life 5 Dimensions
ES	Enrolled Set
FDA	Food and Drug Administration
geoCV	Geometric Coefficient of Variation
GI	Gastrointestinal
HbA1c	Hemoglobin A1C
hCG	Human Chorionic Gonadotropin
HLGT	High Level Group Term
HLT	High Level Term
ICH	International Council for Harmonisation
IDMC	Independent Data Monitoring Committee
IEC	Independent Ethics Committee
IGRA	Interferon Gamma Release Assay
IMP	Investigational Medicinal Product
INR	International Normalized Ratio
IRB	Institutional Review Board
IVIg	Intravenous Infusion of Immunoglobulin G
LDH	Lactate Dehydrogenase
LLOQ	Lower Limit of Quantification

MA	Markedly Abnormal
MedDRA	Medical Dictionary for Regulatory Activities
MG	Myasthenia Gravis
MG-ADL	MG-Activities of Daily Living
MG-C	MG-Composite
MGII	MG Impairment Index
MGQoL15r	Revised 15-item MG Quality of Life
MRD	Minimum Required Dilution
NAb	Neutralizing Antibody
PDILI	Potential Drug-Induced Liver Injury
PEOT	Premature End of Treatment
PEX	Plasma Exchange
PK	Pharmacokinetic
PRO	Patient-Reported Outcome
PT	Preferred Term
PTT	Partial Prothrombin Time
QMG	Quantitative Myasthenia Gravis
RBC	Red Blood Cell
RLZ	Rozanolixizumab
RS	Randomized Set
SAP	Statistical Analysis Plan
sc	Subcutaneous
SD	Standard Deviation
SDR	Safety Data Review
SGPT	Serum Glutamic-Pyruvic Transaminase
SOC	System Organ Class
SS	Safety Set
TB	Tuberculosis
TEAEs	Treatment-Emergent Adverse Events
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 MG0004, including independent Data Monitoring Committee (IDMC) and final analyses. 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 2: 30 July 2020
- IDMC Charter v1.0: 31 March 2020

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 evaluate the long-term safety and tolerability of rozanolixizumab in study participants with generalized myasthenia gravis (MG)

2.1.2 Secondary objective

To evaluate the long-term efficacy of rozanolixizumab in study participants with generalized MG

2.1.3 Other objectives

- To assess the dose change in use of concomitant medications in study participants receiving rozanolixizumab
- To assess the plasma concentrations of rozanolixizumab administered by subcutaneous (sc) infusion
- To assess the pharmacodynamic effects of rozanolixizumab as measured by IgG levels, IgG subclasses and MG-specific autoantibodies levels
- To evaluate the incidence and emergence of anti-drug antibodies (ADAs) with respect to immunogenicity, pharmacokinetic (PK), and pharmacodynamics
- To assess the effect of rozanolixizumab on biomarkers including IgM, IgA, and IgE, serum and plasma complement levels, and serum cytokines
- To assess the effect of rozanolixizumab on tetanus IgG antibodies

2.2 Study endpoints

2.2.1 Safety endpoints

2.2.1.1 Primary safety endpoints

- Occurrence of treatment-emergent adverse events (TEAEs)
- Occurrence of TEAEs leading to permanent withdrawal of study medication

2.2.1.2 Other safety endpoints

- Occurrence of adverse events of special monitoring (AESMs)
- Vital sign values and changes from Baseline (systolic and diastolic blood pressure and pulse rate)
- 12-lead electrocardiogram (ECG) values and change from Baseline at each scheduled assessment
- Clinical laboratory findings (hematology, biochemistry, and urinalysis)

2.2.2 Efficacy endpoints

2.2.2.1 Secondary efficacy endpoints

- Change from Baseline in MG-Activities of Daily Living (MG-ADL) at each scheduled assessment during Treatment and Observation Periods
- Change from Baseline in MG-Composite (MG-C) score at each scheduled assessment during Treatment and Observation Periods
- Change from Baseline in Quantitative Myasthenia Gravis test (QMG) at each scheduled assessment during Treatment and Observation Periods
- Use of rescue medication (intravenous infusion of immunoglobulin G [IVIg] or plasma exchange [PEX]) (Y/N)

2.2.2.2 Other efficacy endpoints

- Change from Baseline in MG Impairment Index (MGII) total scores at each scheduled assessment during Treatment and Observation Periods
- Change from Baseline in MGII ocular subscores at each scheduled assessment during Treatment and Observation Periods
- Change from Baseline in MGII generalized domain subscores at each scheduled assessment during Treatment and Observation Periods
- Change from Baseline in the MG Symptoms Patient-Reported Outcome (PRO) 'Muscle Weakness Fatigability' score at each scheduled assessment during Treatment and Observation Periods
- Change from Baseline in the MG Symptoms PRO 'Physical Fatigue' score at each scheduled assessment during Treatment and Observation Periods
- Change from Baseline in the MG Symptoms PRO 'Bulbar symptoms' score at each scheduled assessment during Treatment and Observation Periods

- Change from Baseline in the MG Symptoms PRO 'Respiratory symptoms' score at each scheduled assessment during Treatment and Observation Periods
- Change from Baseline in the MG Symptoms PRO 'Ocular symptoms' score at each scheduled assessment during Treatment and Observation Periods
- Change from Baseline in revised 15-item MG Quality of Life (MG-QoL15r) questionnaire at each scheduled assessment during Treatment and Observation Periods
- Change from Baseline in 5-Level European Quality of Life 5 Dimensions (EQ-5D-5L) scores at each scheduled assessment during Treatment and Observation Periods

For study participants who require rescue treatment during the Observation Period of MG0003 or MGC0003 and subsequently enter MG0004, the following endpoints will be assessed:

- QMG responder rate (≥3.0 point improvement from Baseline) at each scheduled assessment during the first 6 weeks of the Treatment Period
- MG-C responder rate (≥5.0 point improvement from Baseline) at each scheduled assessment during the first 6 weeks of the Treatment Period
- MG-ADL responder rate (≥2.0 point improvement from Baseline) at each scheduled assessment during the first 6 weeks of the Treatment Period

2.2.3 Pharmacokinetic, and pharmacodynamic

2.2.3.1 Pharmacokinetic endpoints

- Plasma concentration of rozanolixizumab at each scheduled assessment during the Treatment and Observation Periods

2.2.3.2 Pharmacodynamic endpoints

- Change from Baseline in total IgG and IgG subclasses at each scheduled visit
- Change from Baseline in MG-specific autoantibodies at each scheduled visit

2.2.4 Anti-drug antibody endpoints

- ADAs at each scheduled assessment during the Treatment Period and Observation Periods

2.2.5 Immunological endpoints

- Change from Baseline in serum complement levels (C3 and C4) and plasma complement levels (C3a and C5a) at each scheduled assessment during Treatment Period
- Change from Baseline in serum cytokines at each scheduled assessment during Treatment and Observation Periods
- Change from Baseline in serum immunoglobulin concentrations (total IgA, IgE, and IgM) at each scheduled assessment during Treatment and Observation Periods
- Change from Baseline in anti-tetanus toxoid serum titers at each scheduled assessment during Treatment and Observation Period

2.2.6 Other endpoints

- Dose change in use of concomitant medications during Treatment and Observation Period (See Section 3.9)

- Change from Baseline in average daily dose (ADD) of concomitant medications (See Section 3.9)

2.3 Study design and conduct

This is a randomized, open-label Phase 3 extension study to evaluate the long-term safety, tolerability, and efficacy of rozanolixizumab (RLZ) in study participants with generalized MG.

Study participants will enter MG0004 from lead-in study MG0003. Study participants in MG0003 who complete the Observation Period or who require rescue medication during the Observation Period will be invited to be rerandomized in MG0004 (except for study participants who opt to receive IVIg or PEX as rescue medication). Study participants who receive IVIg or PEX as rescue therapy during the Observation Period of MG0003 will not be eligible to enroll in MG0004. Study participants who discontinue study medication in MG0003 for any reason other than requiring rescue medication will not be eligible for MG0004.

For any study participant who enrolls in MG0004, the final visit in MG0003 (Visit 14) will serve as the first visit in MG0004 (Visit 1). All activities should be completed at Visit 1 (±1 week). For criteria pertaining to laboratory measures, the last available value from MG0003 will be used for evaluation of study participant eligibility, as long as the measurement was taken within the last 4 weeks (not older than 32 days) prior to MG0004 Screening. Up to approximately 276 study participants will be enrolled into the lead-in study MG0003. All eligible study participants from MG0003 will be invited to participate in MG0004.

In MG0004, study participants will be randomized in a 1:1 ratio to receive 1 of 2 doses of rozanolixizumab (equivalent to approximately [redacted], respectively). Specifically, the following dose arms will be used in the study:

Dose arm 1: equivalent to approximately [redacted] rozanolixizumab

- Bodyweight <50kg: dose to be administered [redacted]
- Bodyweight ≥50kg and <70kg: dose to be administered [redacted]
- Bodyweight ≥70kg and <100kg: dose to be administered [redacted]
- Bodyweight ≥100kg: dose to be administered [redacted]

Dose arm 2: equivalent to approximately [redacted] rozanolixizumab

- Bodyweight <50kg: dose to be administered [redacted]
- Bodyweight ≥50kg and <70kg: dose to be administered [redacted]
- Bodyweight ≥70kg and <100kg: dose to be administered [redacted]
- Bodyweight ≥100kg: dose to be administered [redacted]

If one of the doses described above is determined to be discontinued after the interim analysis in MG0003, then that dose arm will be dropped from MG0004 as well, and study participants in the affected dose arm will be transferred to the continuing dose arm. If both dose arms are used in MG0004, study participants will be allowed to switch dose arms for tolerability and efficacy reasons at the discretion of the Investigator.

In MG0004, rozanolixizumab will be administered sc on a [redacted] basis over a 52-week Treatment Period. At the end of the 52-week Treatment Period in MG0004, study participants will participate in an 8-week Observation Period. The maximum study duration per study participant is 60 weeks.

This open-label extension (OLE) study will be replaced by MG0007, an OLE study with [redacted] based on MG worsening. Upon study site approval of MG0007, as well as fulfilment of regulatory requirements, study participants will have the opportunity to rollover directly into MG0007 and will no longer have the opportunity to rollover to MG0004. In the event a study participant has already started MG0004, a minimum treatment duration of 6 visits must be completed (if IMP treatment is withheld for low IgG, study participants missed dose(s) can be counted as part of the total 6 visits for completion of MG0004 and meet eligibility requirements for MG0007) and then the participant will discontinue MG0004 and have the opportunity to enter into MG0007. For study participants entering MG0007, he/she must complete the Premature End of Treatment (PEOT) Visit in MG0004 which will serve as the Screening Visit for MG0007 or as the End of Study (EOS) Visit for MG0004. If a study participant completes the Treatment Period and still in Observation Period of MG0004, he/she will then complete EOS Visit to serve as the Screening Visit for MG0007. Once the site is active for MG0007, no further participants will enroll in MG0004 and the study will be closed at the site once all eligible study participants have rolled over into MG0007.

A schematic of the study design is provided in Figure 2-1.

Figure 2-1: Study schematic

2.4 Determination of sample size

No formal sample size calculation can be performed. Up to approximately 240 study participants will be enrolled into the lead-in study MG0003. All eligible study participants from MG0003 will be invited to participate in MG0004 until study site approval of MG0007 as well as fulfilment of regulatory requirements.

3 DATA ANALYSIS CONSIDERATIONS

3.1 General presentation of summaries and analyses

Statistical analysis and generation of tables, figures, participant data listings, and statistical output 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 PK concentration data, summary statistics will include geometric mean, geometric coefficient of variation (geoCV), 95% confidence intervals (CIs) 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 time points

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 (see 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 MG0004 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 maximum duration of the study per participant will be approximately 60 weeks, consisting of the following 2 periods:

- Treatment Period: 52 weeks
- Observation Period: 8 weeks

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

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

- **Treatment Period** starts with the first day of IMP in MG0004 and ends after Week 52 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 if assessments from Treatment Period Week 52 are completed.
- **Observation Period** starts with one day after the end of the Treatment Period and ends after the final assessments at the End of Study (EOS) visit. Participants with assessment on any Observation Period day are considered to have started the Observation Period. Participants who complete the assessments at the EOS visit will be considered to have completed the

Observation Period. Participants who have a completed status in the study termination case report form (CRF) are considered to have completed the Treatment and Observation Period.

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

If not otherwise stated, Baseline values will be 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 in MG0004. Scheduled or unscheduled measurements can be used as the Baseline value.

Baseline values for serum or plasma complements and serum cytokines will be the Baseline values determined in MG0003.

Baseline for anti-drug antibody (ADA) for MG0004 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.

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 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 sign the informed consent.

3.5.2 Randomized Set

The Randomized Set (RS) will consist of all study participants who are randomized, using the treatment assigned instead of the actual treatment received.

3.5.3 Safety Set

The Safety Set (SS) will consist of all randomized study participants who received at least 1 dose of IMP in this study. Analysis of this set will be according to the treatment the study participants actually received in MG0004, and will be used for the efficacy, demographic, PK/PD and safety analyses. The treatment assignment using SS is described in Section 3.6.

3.6 Treatment assignment and treatment groups

For the analyses using SS by the first dose received, study participants will be grouped according to the dose levels of IMP participants first received [redacted] in this study (i.e. before any switching occurs) using the exposure data from CRF. For example, if study participants randomized to IMP [redacted] and first received IMP [redacted], then these study participants will be allocated to IMP [redacted]. If a study participant first received IMP [redacted] and then switched to [redacted], then the study participant will be allocated to [redacted].

For the analyses using SS by the most recent dose received, study participants will be grouped according to the most recent dose level of IMP participants received prior to each visit or the onset of events using the exposure data from CRF. For example, if a study participant first received IMP [redacted] and then switched to [redacted] prior to Visit 5, then the participant will be allocated to [redacted] at Visit 5.

For the efficacy analyses using SS by dose switch during the Treatment Period, study participants will be grouped into dose adjuster or dose non-adjuster. A study participant who receive different dose during the Treatment Period from the randomized dose level will be classified as a dose adjuster, otherwise dose non-adjuster. For example, if a study participant was randomized to and first received IMP [redacted] and then switched to [redacted], then the study participant will be allocated to dose adjuster.

For the analyses using RS, study participants will be grouped according to the dose levels of IMP to which study participants were randomized.

3.7 Center pooling strategy

The participants from lead-in study, MG0003, will be rolled over 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 or later of the Medical Dictionary for Regulatory Activities (MedDRA®).

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

3.9 Changes to protocol-defined analyses

- The following two exploratory endpoints will not be analyzed as they have been removed from the MG program as a whole and have been included in the protocol in error:
  - Change from Baseline in the MG Symptoms PRO multicomponent total score, at each scheduled assessment during Treatment and Observation Periods,
  - Change from Baseline in the enhanced MG Symptoms PRO total score, at each scheduled assessment during Treatment and Observation Periods.
- The increase or reduction in use of concomitant medications will be analyzed in the SAP, so objective is changed to "To assess the dose change in use of concomitant medications in study participants receiving rozanolixizumab" in the SAP.

- The dose change in use of concomitant medications in study participants receiving rozanolixizumab will be analyzed using number and percentage of participants with dose change of concomitant medications and change from Baseline in ADD in the study. There is no concentration data of concomitant medications in the study to generate area under the curve (AUC), so it is not included in the SAP.
- No study participants from MGC003 will rollover into MG0004. Thus, the maximum sample size of this study should be 240, not 276.

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, MGII and MG-QOL15r scores are described in Section 13.1, Section 13.2, Section 13.3, Section 13.4, Section 13.5, and Section 13.6, respectively.

For ordinal endpoints (e.g. EQ-5D-5L), the complete 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 dates is after last contact date, then assign last contact date as the stop date;
- If only the year is specified, then use December 31 of the known year. If an imputed stop dates is after last contact date, then assign last contact 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.

Table 4–1: Calculation rules for duration of AEs

Data availability	Onset date	Outcome date	Calculation 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 COVID-19 pandemic 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 pandemic on study data.

- Added an 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 pandemic;
- Included additional summary analyses based on the timing of COVID-19 impact (pre/during/post COVID-19 pandemic).

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 (e.g. repeated measurements during the Screening period);
- 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 Sections 8.4.2 for the rules applied to ECG triplicate measurements.

4.4 Interim analyses and data monitoring

There is no interim analysis planned for this study.

An independent Data Monitoring Committee (IDMC) will oversee the safety of the study by reviewing safety data at periodic data reviews.

The safety data of this study will also be pooled with other Rozanolixizumab studies and reviewed by the overarching DMC. The details of overarching DMC will be described in a separate document.

4.4.1 Timing for periodic data reviews

The safety data review (SDR) meetings will be held in collaboration with the MG0003 study team. The orientation SDR meeting of this study will be held at the first SDR meeting of MG0003 study.

First SDR meeting will be initiated when approximately 10 study patients have been randomized over 26 weeks and held at the second SDR meeting of MG0003 study. Ad-hoc meeting will be held based on the agreement of the IDMC.

4.4.2 Data required for periodic data reviews

All available data at the time of the data cut-off will be included at each SDR. The database will not be locked, but the data should be as clean as possible, and it is not required to have resolved all queries prior to each database snapshot. Study enrollment will not be halted during planned IDMC review of the safety and efficacy data.

Required safety data to be used to support the SDR will include the following:

- Adverse events
- ECGs
- Vital signs
- Medical and procedure history
- Prior and concomitant medications
- Demographics
- Safety labs (hematology, chemistry, urinalysis)
- Total IgG
- Pregnancy
- Columbia-Suicide Severity Rating Scale (C-SSRS)

These data will be summarized using descriptive statistics. Data will also be provided in listings.

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 study participants

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

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

- Age (18 to <65 years, ≥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 (MuSK+ or AChR+)

  Notes: Region captured from MG0003 CRF 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 Baseline (<median, ≥ median)
- MGFA disease class at Baseline
- Thymectomy at Baseline (yes, no)
- 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 participants in a particular category, otherwise it will not be performed.

5 STUDY POPULATION CHARACTERISTICS

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 summarized using the ES for overall. Additionally, the reasons for screen failures will be summarized by pre-, 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 summarized 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 randomized treatment and by each analysis set (RS and SS).
- **Disposition of analysis sets** will be summarized by treatment groups and analysis sets (RS and SS) using the RS.

- **Disposition and discontinuation reasons** using the RS and SS will contain the number and percentage of study participants by treatment group and RLZ total and also by pre-, during and post- the COVID-19 pandemic who:
    - Started Study,
    - Completed Study,
    - Discontinued Study with
        - Primary Reason for discontinuation, including transitioned to study MG0007 (primary reason for premature study termination as collected in the Study Termination Enrolled CRF).

    Note: The summary by pre-, during and post- the COVID-19 pandemic will be based on the start, completed and discontinuation date relative to the pandemic cut-off date will be presented in the same table. The discontinuation reason in each period will also be summarized. Discontinuation due to COVID-19 pandemic will be listed as sub-category under "Other" reason.
- **Discontinuation due to AEs** using the RS and SS will summarize the total number of study participants who discontinued the study due to AEs by treatment group 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 pandemic** using the RS will summarize number and percentage of participants in each impact category by visit.

Listings of study participant disposition, study discontinuation and study participants who did not meet study eligibility criteria will be provided.

5.2 Important Protocol deviations

A summary of number and percentage of participants with an important protocol deviation by relationship to COVID-19 pandemic and treatment group will be provided for the RS. Additionally, the summary will be repeated by pre-, 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 RS.

6 DEMOGRAPHICS AND OTHER BASELINE CHARACTERISTICS

6.1 Demographics

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

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)
- BMI (kg/m^2), to be calculated as: BMI = Weight (kg) / (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
- Needed rescue therapies in the observation period of MG0003 and entered MG0004

  Note: Height captured at screening visit from MG0003 CRF will be summarized and used in BMI calculation. Other variables listed here are captured from MG0004 CRF.

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

6.2 Other Baseline characteristics

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

- Baseline MuSK antibody status (positive, negative)
- 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

6.3 Medical history and concomitant diseases

Any medical conditions that were not reported in MG0003 will be captured on CRF of this study and listed using the RS. Besides, procedure history will be provided in separate by-participant listings using the RS.

6.4 Prior and concomitant medications

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

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 RS.

Medications classified as prior or concomitant will be listed using the RS. A by-participant listing of participants taking steroids, immunosuppressants and AChE Inhibitors will be listed, including ADD at Baseline, ADD at last study visit and change from Baseline in ADD (See Section 11.1). A by-participant listing of concomitant procedures will also be listed using the RS. 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 IMP in MG0004.
- **Concomitant** medications will include any medications that have been taken at least once after the first administration of IMP during the Treatment and/or Observation Period of MG0004.

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 concomitant 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 and 7 days after the last dose of IMP.
- **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 EOS visit.

Thus, a medication taken from the time of the first drug administration in the Treatment Period to the end of the study will be assigned to the Treatment Period and the Observation Period.

7 MEASUREMENTS OF TREATMENT COMPLIANCE

Not applicable. The summaries of infusions will be detailed in Section 8.1.

8 SAFETY ANALYSES

All safety analyses will be presented using the SS. Listings will be presented by treatment group and participant; tabulations will be presented by treatment group. Unless otherwise specified, safety analyses will be presented by the most recent dose the study participants received in MG0004 as described in Section 3.6.

8.1 Extent of exposure

The following descriptive summaries will be generated using the SS by first dose received:

a) Study IMP duration (weeks) by first dose received, calculated as follow:

$$Study\ IMP\ duration\ (weeks) = \frac{Date\ of\ last\ dose - Date\ of\ first\ dose + 1}{7}$$

b) Cumulative study IMP Duration using > 0 weeks, ≥ 6 weeks, ≥ 12 weeks, ≥ 18 weeks, ≥ 24 weeks, ≥ 30 weeks, ≥ 36 weeks, ≥ 42 weeks and ≥ 48 weeks and 52 weeks;

c) Number of Infusions Received as continuous and using the following categorical values: 1-6, 7-12, 13-18, 19-24, 25-30, 31-36, 37-42, 43-48, and 49-52.

The number of participants with dose change at each visit will be summarized using the SS by the most recent dose received.

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 as described in 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 (i.e., all Grade 1 AEs as per CTCAE criteria will be included in the 'mild' category together with those AEs classified as mild as per the standard intensity classification). 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 (i.e. an AE with Grade 1 and moderate as intensity classification will be classified into moderate).

A TEAE is defined as an AE starting on or after the time of first administration of IMP in MG0004 or any unresolved event already present before the first administration of IMP in MG0004 that worsens in intensity following exposure to IMP in MG0004, up to and including 8 weeks (56 days) after the end of the Treatment Period or 8 weeks after the last of IMP in study participants who discontinue the study or IMP.

A persistent AE is defined as an unresolved AE that extends continuously from MG0003 to MG0004 and does not worsen in intensity following exposure to IMP in MG0004. Persistent AEs will be recorded in MG0004 database and as other non-TEAEs will be listed only.

Where dates are missing or partially missing, AEs will be assumed to be treatment-emergent unless evidence exists that does not allow the AE to be treatment-emergent. Handling of missing dates for classification of AEs as TEAEs is described in Section 4.2.2.

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

- **Treatment Period:** a TEAE will be assigned to the Treatment Period if the start date of the event is on or after the date of the first administration of MG0004 IMP on Day 1, up to 7 days after the last dose of IMP;
- **Observation Period:** a TEAE will be assigned to the Observation Period if the start date of the event is greater than the day after Treatment Period until 8 weeks following the final dose; events starting later than 8 weeks following the final dose of IMP are not considered TEAEs.

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.

8.2.2 Adverse events summaries

TEAEs will be summarized by the most recent dose level prior to onset of TEAEs and RLZ total, including the number and percentage of study participants and frequency. Additional details are described below:

1. Overview of TEAEs 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).

2. Incidence of TEAEs will be summarized 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 will be summarized by decreasing frequency of PT.

AESMs include severe headache, severe GI disorders (i.e., abdominal pain, diarrhea, vomiting), and opportunistic infection.

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 AEs, study participant discontinuation from study due to AEs, AEs leading to death, AESIs, AESMs will be presented by treatment group and participant. Persistent AEs and TEAE will be flagged in the listings. Most recent dose will be presented in listing even when the AE start date is partial.

8.2.3 Adverse events of focus

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

- Headaches
- Gastrointestinal disturbances
- Hypersensitivity reactions
- Anaphylactic reactions
- Injection site reaction
- Infusion 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 by SOC, HLT, and PT:

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

2. Additionally, the summaries for the AEOF headache and gastrointestinal disturbances in Treatment Period by intensity will be presented separately by most recent dose level and RLZ total.

3. Graphs for AEOF headache in Treatment Period by time of onset (relative to infusion), severity, causality and duration for each study participant will also be provided.

A by-subject listing of all AEOF by category (as listed above) will be provided by treatment group 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 13.8.

8.3 Clinical safety laboratory assessments

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	Blood Urea Nitrogen (BUN)	Potassium	Aspartate Aminotransferase (AST) / Serum Glutamic-Oxaloacetic Transaminase (SGOT)	Total and direct bilirubin
	Estimated Glomerular Filtration Rate (eGFR)[a]	Sodium	Alanine Aminotransferase (ALT) / Serum Glutamic-Pyruvic Transaminase (SGPT)	Total Protein
	Glucose (fasting)	Calcium	Alkaline phosphatase (ALP)	Creatinine
	Lactate dehydrogenase (LDH)	C-reactive protein	Albumin	
Routine Urinalysis	• Specific gravity • Albumin, albumin/creatinine, creatinine • pH, glucose, protein, ketones, bilirubin, urobilinogen, nitrite, leukocyte esterase, hemoglobin by dipstick • Microscopic examination (if blood or protein is abnormal)			
Other Screening Tests	• Urine human chorionic gonadotropin (hCG) pregnancy test (as needed for women of childbearing potential)[b] • Serology testing for HIV, hepatitis B, and hepatitis C • Partial Prothrombin Time (PTT), and International Normalized Ratio (INR), and Hemoglobin A1C (HbA1c) tests			
NOTES: All study-required laboratory assessments will be performed by a central laboratory. The results of each test must be entered into the CRF.				

Laboratory Assessments	Parameters
[a] eGFR is calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula which is eGFR = 141 * min(Scr/κ,1)α * max(Scr/κ, 1)$^{-1.209}$ * 0.993^{Age} * 1.018 [if female] * 1.159 [if black]; where Scr is serum creatinine (mg/dL), κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1. If race is not captured, participant will be assumed not Black in the calculation. [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 by most recent dose received and RLZ total at each scheduled visit.

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.

The number and percentage of participants who meet each of the markedly abnormal (MA) criteria outlined in Section 13.7 will be summarized by most recent dose received 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) by most recent dose received.

All central or local 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. 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 will be summarized by treatment group 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 has one value unknown, then he/she should not be considered for meeting the above criteria.

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

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 will be summarized by vital signs variable (pulse rate, systolic and diastolic blood pressure, and temperature), scheduled visit, most recent dose received and RLZ total.

The number and percentage of participants who meet each of the MA criteria outlined in Section 13.7 will be summarized by most recent dose received and RLZ total at any visit (including unscheduled visit).

Additionally, the vital signs variables that are categorized as normal or MA based on the MA criteria will be presented in shift tables from Baseline to any post-Baseline visit (including unscheduled visit) by most recent dose received.

A by-participant listing of all vital sign measurements and change from Baseline will be presented by treatment group 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 by most recent dose received 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 will be provided in a shift table from Baseline to worst post-Baseline interpretation during the study.

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 participants who meet each of the MA criteria outlined in Section 13.7 will be summarized by most recent dose received 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 will be listed.

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]

- [redacted]
- [redacted]
- [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 "Has subject engaged in Non-Suicidal Self-Injurious Behavior?" in questionnaire.

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

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 will be performed based on the SS by first dose received as described in Section 3.6, unless specified otherwise. No statistical testing will be performed for efficacy analyses.

9.1 Analysis of the secondary efficacy endpoints

9.1.1 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 with associated change from Baseline will be summarized by first dose received and scheduled visit 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 (e.g. visit performed by video call) due to COVID-19 pandemic.

The subgroup summaries will also be performed as specified in Section 4.9.

The MG-ADL total score (excluding ocular items) with associated change from Baseline will be summarized by first dose received and scheduled visit using descriptive statistics.

By-participant listings of MG-ADL values will be provided.

9.1.2 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 total scores and total score (excluding ocular items) with associated change from Baseline will be summarized by first dose received and scheduled visit using descriptive statistics.

The subgroup summaries (by MuSK+ or AChR+ only) will also be performed as specified in Section 4.9.

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

9.1.3 QMG scale

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 first dose received and scheduled visit using descriptive statistics.

The subgroup summaries (by MuSK+ or AChR+ only) will also be performed as specified in Section 4.9.

By-participant listings of QMG scores will be provided.

9.1.4 Use of rescue medication (IVIg, PEX) due to worsening

The use of rescue therapy will be identified as a 'yes' response to the "Rescue Medication?" question on the Prior and Concomitant Medications CRF and the start date of the rescue therapy is on or after Baseline.

The number of participants in each treatment group with the use of rescue therapy (IVIg, PEX) during the Treatment Period due to worsening will be summarized by first dose received.

9.2 Analysis of other efficacy endpoints

9.2.1 MGII

The complete list of MGII items and scores are provided in Table 13-8. The total score and sub-scores will be calculated according to the rules set down in Section 13.5.

The MGII total score and sub-scores (Ocular and a Generalized domain) with associated change from Baseline values will be summarized separately by first dose received and each scheduled visit.

A by-participant listing of MGII scores will be provided.

9.2.2 MG Symptoms PRO

The MG Symptoms PRO scale scores (physical fatigue, muscle weakness fatigability, bulbar symptoms) will be calculated according to the rules set down in Section 13.4. The scale scores with associated change from Baseline values will be summarized by first dose received and each scheduled visit.

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

9.2.3 MG-QOL15r

The MG-QOL15r total score is calculated by summing all the individual items. See Section 13.6 for scoring details.

The MGQOL15r total score and change from Baseline values will be summarized by first dose received and each scheduled visit.

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

9.2.4 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 first dose received. The observed values of EQ VAS scores and change from Baseline will be summarized by first dose received and each scheduled visit. 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.

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

Participants will be classified as responders at a scheduled visit if the MG-ADL total score is at least a 2-point improvement (decrease) from Baseline. Missing data will be imputed using NRI per Section 4.2.1.

The number and percentage of observed responders will be summarized by first dose received and scheduled visit for participants who require rescue treatment during the Observation Period of MG0003 and subsequently enter MG0004 only.

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

Participants will be classified as responders at a scheduled visit if the QMG total score is at least a 3-point improvement (decrease) from Baseline. Missing data will be imputed using NRI per Section 4.2.1.

The number and percentage of observed responders will be summarized by first dose received and scheduled visit for participants who require rescue treatment during the Observation Period of MG0003 and subsequently enter MG0004 only.

9.2.7 MG-C responder rate (≥5.0 points improvement from Baseline)

Participants will be classified as responders at a scheduled visit if the MG-C total score is at least a 5-point improvement (decrease) from Baseline. Missing data will be imputed using NRI per Section 4.2.1.

The number and percentage of observed responders will be summarized by first dose received and scheduled visit for participants who require rescue treatment during the Observation Period of MG0003 and subsequently enter MG0004 only.

9.2.8 Minimum symptom expression

Minimum Symptom Expression (MSE) is designed to assess how many participants become free or virtually free of MG symptoms as measured by achieving an MG-ADL total score of 0 or 1 on therapy (Vissing et al. 2020). The total score will be calculated according to the rules set down in Section 13.3.

The number and percentage of participants achieving MSE at scheduled visit will be summarized by first dose received.

10 PHARMACOKINETICS AND PHARMACODYNAMICS

All PK and PD analyses described in this section will be performed by first dose received on the SS, as described in Section 3.6, unless specified otherwise.

10.1 Pharmacokinetics

Individual plasma concentrations of rozanolixizumab will be summarized by most recent dose received 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 first dose received for the SS and will include the actual sampling time in days relative to the previous dose, most recent 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 first dose received and time point for observed values, change from Baseline, and percentage change from Baseline.

The maximum change from Baseline in total serum IgG (absolute and percentage change) will be reported in the listing and summarized by first dose received. In the event that a change from Baseline in total serum IgG is not observed in a given participant, the maximum change will be reported as the smallest increase from Baseline.

Mean and mean percentage change from Baseline values in total serum IgG will be plotted over time by first dose received with dose groups overlaid on the same plot.

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

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, and MG-ADL change from Baseline, as specified in Section 10.3.2.

10.2.2 MG-specific autoantibodies

MG-specific autoantibodies (anti-MuSK/anti-AChR) will be summarized by first dose received and RLZ total at scheduled visits for observed values, absolute and percentage changes from Baseline. The maximum change from Baseline in MG-specific autoantibodies (absolute and percentage change) will be reported in the listing and summarized for each treatment.

MG-specific autoantibodies will also be summarized at scheduled visit by the participants who are anti-MuSK or anti-AChR autoantibody-positive at the Baseline visit.

Mean absolute and mean percentage change from Baseline values in MG-Specific autoantibodies will be plotted over time by treatment group and RLZ total. Additionally, mean percentage change from Baseline in anti-MuSK, total IgG, MG-ADL, QMG, and MG-C will be plotted by first dose received. The same plot will be repeated for percentage change from Baseline values in anti-AChR.

MG-specific autoantibodies will be listed, together with total IgG, MG-ADL, QMG, MG-C change from Baseline.

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

For the immunogenicity assessment, two types of anti-drug antibody (ADA) assays will be performed, a binding anti-drug antibody assay and a neutralizing antibody assay.

For the binding assay, 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 the binding ADA assay will be tested in the neutralizing assay, which produces a positive or negative result.

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**.

Note: if a participant has no baseline ADA, then she/he can't be treated as "Inconclusive".

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 ADA should be the last measurement prior to receiving the very first rozanolixizumab (RLZ) infusion in either MG0004 or the feeder study MG0003. Specifically, baseline for ADA is defined as:

- MG0003 ADA baseline if participants randomized to RLZ groups in MG0003 (note: MG0003 post-baseline ADA samples will not be considered for the ADA participant status in MG0004);
- MG0004 ADA baseline if participants randomized to placebo in MG0003.

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 of the scheduled sampling points (ie Week 5, 9, 21, 33, 45, 52 and 60) and EOS visit, unless specified otherwise.

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 i.e. 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 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, i.e. 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.

[1] The fold difference increase from baseline value, i.e. 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 participants with ADA (positive, negative, inconclusive, missing) and NAb (positive, negative, missing) sample status at the time of each visit will be summarized by first dose received and RLZ total. Denominator is the number of study participants having a non-missing result at that visit.
- Number and percentage of participants in each of the individual and combined ADA participant status categories presented in Table 10-1 will be summarized by first dose received and RLZ total at each scheduled visit and EOS visit. The table will be repeated by prior treatment in MG0003 (RLZ total or placebo) up to Week 9.

- Total prevalence of pre-existing ADA and NAb, defined as number and percentage of participants having an ADA 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 in MG0003 (RLZ or placebo). The same will be repeated for NAb.
- 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. The table will be repeated by prior treatment in MG0003 (RLZ or placebo).
- Summary table of mean maximum percentage CFB in total IgG and mean CFB in MG-ADL, summarized by ADA participant categories 1, 2, 9, 10, 11 and 12 for the corresponding time period of interest and by treatment group and RLZ total [redacted].
- Overall summary table of TEAEs at Week 9 and EOS summarized by ADA participant categories 1, 2, 7 and 8 for the corresponding time period of interest.
- Summary of incidence of TEAE at Week 9 and EOS by ADA participant category 1, 2, 7 and 8 for the corresponding time period of interest.
- Summary table of AEOF hypersensitivity reactions, anaphylactic reactions and infusion reactions at Week 9 and EOS by ADA participant category 1, 2, 7 and 8 for the corresponding time period of interest.

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), and individual ADA participant category (3, 4, 5, 6) up to EOS. The dosing will be represented in the x-axis with bars/arrows at the time of dose.
- Spaghetti plots of individual time course of ADA titer for ADA positive participants in categories 9, 10, 11 and 12 (determined through EOS), whereby all categories are overlaid on the same plot and visualized using different symbols and colors. The ADA titer results will be presented on a log-scale. Dosing time points should be indicated below the x-axis. The same plot will be repeated for NAb titer for NAb positive participants in categories 9 and 11.
- A box-and-whisker plot of maximum postdose ADA titer (on log-scale) through Week 5, Week 9, Week 52 and EOS versus ADA participant category for categories 9, 10, 11 and 12 (determined for the corresponding time period of interest). 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 timepoint of interest (Week 5, 9, 52 and EOS). Separate plots for each treatment group and RLZ total [redacted].

- Spaghetti plots of individual time course of percentage CFB for total IgG, for each of the ADA participant categories 1, 2, 9, 10, 11 and 12 and time period of interest (Baseline up to Week 5, Week 9, and EOS) whereby the ADA participant categories are multipaneled. Separate plots for each treatment group and RLZ total [redacted]. 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 (Week 5, 9, 21, 33, 45, 52, and 60). 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 (Week 5, 9, 21, 33, 45, 52, and 60). The same plot will be repeated for NAb titer.

Listing:

- By-subject listing by 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).

10.4 Immunology

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

10.4.1 Serum complement levels and plasma complement levels

Serum (C3 and C4) and plasma (C3a and C5a) complement variables will be listed by treatment group, visit and time point including changes from Baseline. Descriptive summaries will be presented for both absolute values and changes from Baseline for participants who experience a severe headache, infusion reaction or hypersensitivity reaction. The Baseline values are defined as Section 3.3.

Measurements BLQ will be imputed with half of the LLOQ for the purpose of calculating change from Baseline. Measurements above the limit of quantification (ALQ), if applicable, will be imputed to the upper limit of quantification.

Serum and plasma complement results will be listed.

10.4.2 Cytokines

Cytokines will be summarized by treatment group, visit and time point for both absolute values and changes from Baseline for participants experiencing with severe headache, infusion reactions or hypersensitivity reaction. The Baseline values are defined as Section 3.3.

Measurements BLQ will be imputed with half of the LLOQ for the purpose of calculating change from Baseline. Measurements ALQ, if applicable, will be imputed to the upper limit of quantification.

Cytokines results will be listed.

10.4.3 Serum immunoglobulin concentrations

Immunoglobulins (IgE, IgA and IgM) will be summarized by treatment group and visit for absolute values, change from Baseline, and percentage change from Baseline.

Measurements BLQ will be imputed with half of the LLOQ for the purpose of calculating change from Baseline. Measurements ALQ, if applicable, will be imputed to the upper limit of quantification.

Immunoglobulins (IgE, IgA, and IgM) will be listed.

10.4.4 Anti-tetanus toxoid serum titers

Anti-tetanus toxoid serum titers will be summarized by treatment group and visit for both absolute values, change from Baseline, and percentage change from Baseline. Same summary will be repeated excluding all participants with undetectable baseline titers.

The mean change from Baseline in anti-tetanus toxoid serum titers versus time at each scheduled timepoint will be plotted by treatment group excluding all participants with undetectable baseline titers. Mean change from Baseline in IgG values will be overlaid on the same plot.

Measurements BLQ will be imputed with half of the LLOQ for the purpose of calculating change from Baseline. Measurements ALQ, if applicable, will be imputed to the upper limit of quantification.

Anti-tetanus toxoid serum titers will be listed.

11 OTHER ANALYSES

11.1 Dose change in use of concomitant medications over time

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

- The number and percentage of participants with dose change in use of steroids (ATC3 code: [redacted]), immunosuppressants (ATC3 code: [redacted]) or AChE Inhibitor (ATC3 code: [redacted]) during the study;
- Average daily dose (ADD) by PT of medications at Baseline and last study visit (i.e. PEOT/EOS visit);

  Note: ADD will be calculated for each PT according to the dose and dose frequency on Prior and Concomitant Medications CRF (e.g. 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 MG0004. ADD at last study visit is calculated using the dose taken at EOS/PEOT visit. In the case last dose is stopped before EOS/PEOT visit, ADD at last study visit will be counted as zero.
- 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 participants with dose change of steroids, including MG-ADL total score at Baseline and last study visit (EOS/PEOT 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 Specific analyses for Pharmaceuticals and Medical Devices Agency (PMDA)

The following endpoints will be summarized for participants in Japan only:

- Study participant characteristics, including important PDs (as specified in Section 5)
- Demographics and other baseline characteristics, including medical history, prior and concomitant medications (as specified in Section 6)
- Study IMP duration and number of infusions (as specified in Section 8.1)
- Use of rescue medication (IVIg, PEX) due to worsening (as specified in Section 9.1.4)
- MG-ADL total score and change from Baseline (as specified in Section 9.1.1)
- TEAE Summaries (as specified in Section 8.2.2)
  - 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
    - Any TEAEs
    - Any TEAEs by maximum intensity (mild, moderate and severe)
    - Any TEAEs by relationship
    - Serious TEAE
    - Participant discontinuation due to TEAEs
    - Permanent withdrawal of IMP due to TEAEs
- ADA summaries (as specified in Section 10.3.2):
  - Number and percentage of participants with positive, negative, missing or inconclusive sample ADA status at the time of each visit and RLZ total will be summarized by treatment group and RLZ total.
  - Number and percentage of participants in each of the ADA classifications presented in Table 10-1 will be summarized by treatment group and RLZ total.

11.3 Headache questionnaire

The results of the headache questionnaire will be listed for each study participant using ES. No summary tabulations will be provided for these assessments.

11.4 Myasthenia Gravis Foundation of America (MGFA) by Visit

The results of MGFA by visit will be listed for each study participant using RS. No summary tabulations will be provided for these assessments.

12 REFERENCES

Myasthenia Gravis Symptoms PRO Instrument Scoring Manual. Modus Outcomes, 2019

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Nehring, S.M.; Goyal, A.; Patel, B.C. C Reactive Protein (CRP) (2020). StatPearls Publishing, web link: https://www.ncbi.nlm.nih.gov/books/NBK441843/.

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Shankar G, Arkin S, Cocea L, et al. Assessment and reporting of the clinical immunogenicity of therapeutic proteins and peptides-harmonized terminology and tactical recommendations. AAPS J. 2014 Jul;16(4):658-73.Vissing, J., Jacob, S., Fujita, K. P., O'Brien, F., & Howard, J. F. (2020). 'Minimal symptom expression'in patients with acetylcholine receptor antibody-positive refractory generalized myasthenia gravis treated with eculizumab. Journal of neurology, 1-11.

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.

[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

Item	None	Mild	Moderate	Severe
Grade	0	1	2	3
[redacted]				

Item	None	Mild	Moderate	Severe
Grade	0	1	2	3
[redacted]				

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.

[redacted] 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.

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

Item	Result/Grade	Result/Grade	Result/Grade	Result/Grade
[redacted]				

[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. The total score is obtained by summing the responses to each individual item. Thus, the score ranges from 0 to 24.

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 dated 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, Table 13-5, and Table 13-6.

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, i.e. 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 13-7.

Table 13-4: MG Symptoms: Ocular, Bulbar, and Respiratory Symptoms Rescoring

[redacted]

Table 13-4: MG Symptoms: Ocular, Bulbar, and Respiratory Symptoms Rescoring

[redacted]

Table 13-5: MG Symptoms: Physical Fatigue Rescoring

[redacted]

[redacted]

Table 13-6: MG Symptoms: Muscle Weakness Fatigability

[redacted]

[redacted]

Table 13-7: Description of the MG Symptoms PRO Scale Scores

[redacted]

13.5 Myasthenia Gravis Impairment Index

The MG-II is provided in Table 13-8. The MGII can be summarized as a total score and also as 2 sub-scores reflecting an Ocular and a Generalized domain.

The total score is the raw sum of all the items, including the clinical examination and the patient-reported questionnaire.

The ocular score is calculated by summing 8 items reflecting ocular impairments. These items are: patient questionnaire items 1 to 6 and examination items 1 and 2.

The generalized score is calculated by adding items 7 to 22 from the patient questionnaire and items 3 to 6 from the examination.

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

- In the case where at least 7 of the 8 items from the Ocular subscale are answered, the Ocular subscale score will be generated after imputing the missing response by the average of non-missing responses, by adding all item scores. If there are 2 or more missing data out of the 8 Ocular subscale items, then the Ocular subscale score will be missing.
- In the case where at least 18 of the 20 items from the Generalized subscale are answered, the Generalized subscale score will be generated after imputing the missing response(s) by the average of non-missing responses, by adding all item scores. If there are 3 or more missing data out of the 20 Generalized subscale items, then the Generalized subscale score will be missing.
- In the case where both the Ocular and the Generalized subscale scores are non-missing, then the Total score will be calculated as the sum of the Ocular and the Generalized subscale scores. If one of the two subscale scores are missing, then the Total score will be missing.

Table 13-8: MG Impairment Index

[redacted]

Table 13-8: MG Impairment Index

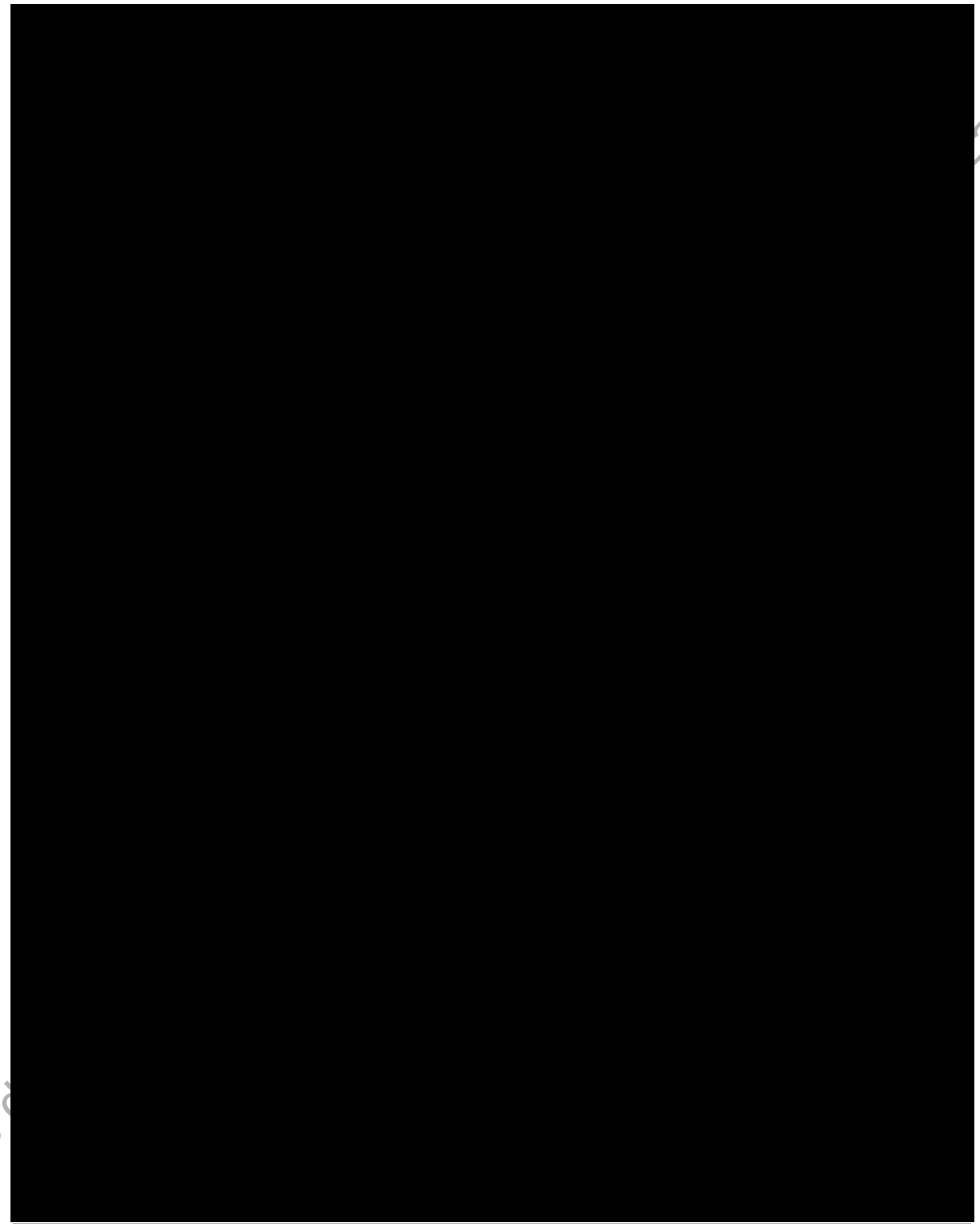


Table 13-8: MG Impairment Index

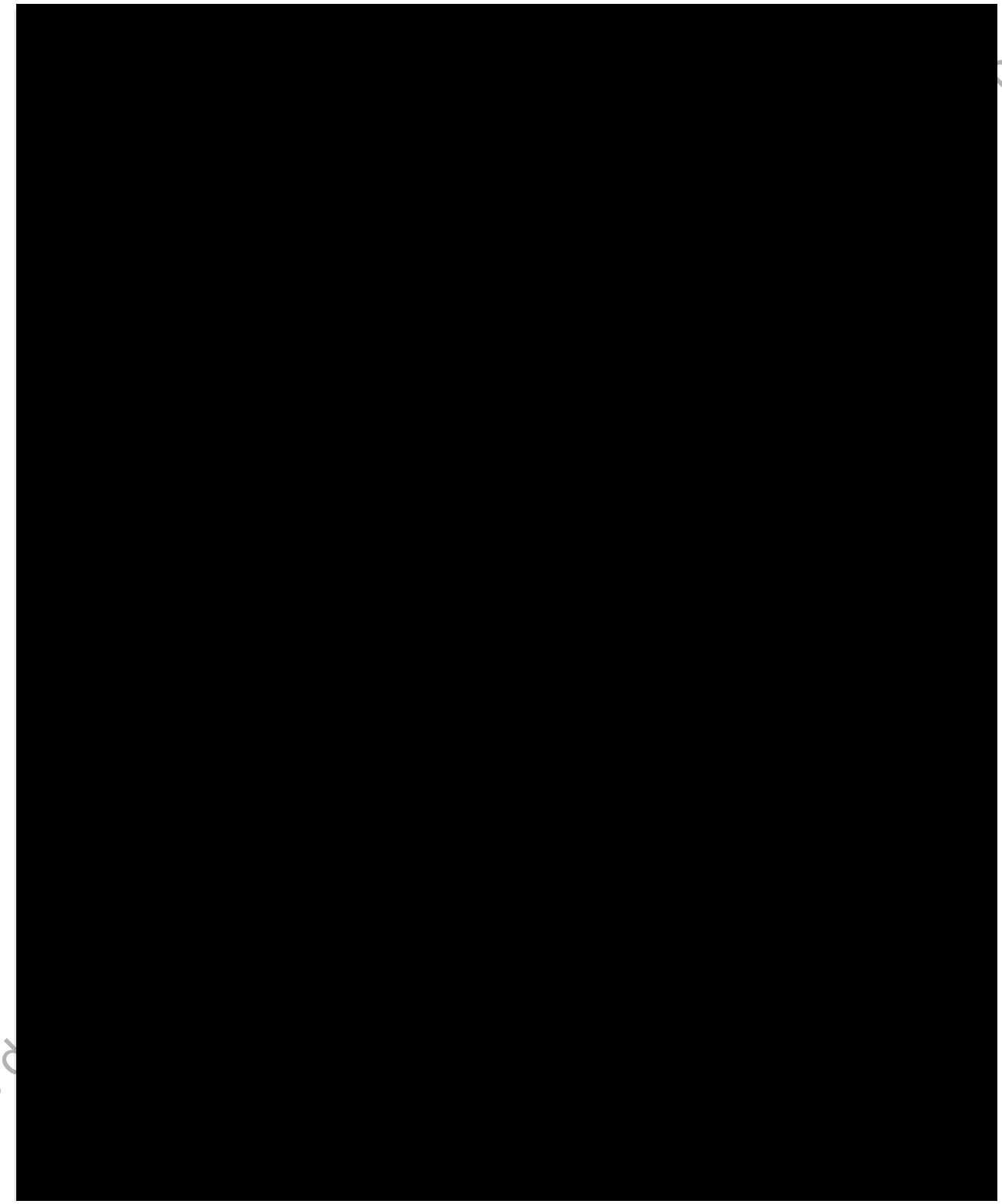


Table 13-8: MG Impairment Index

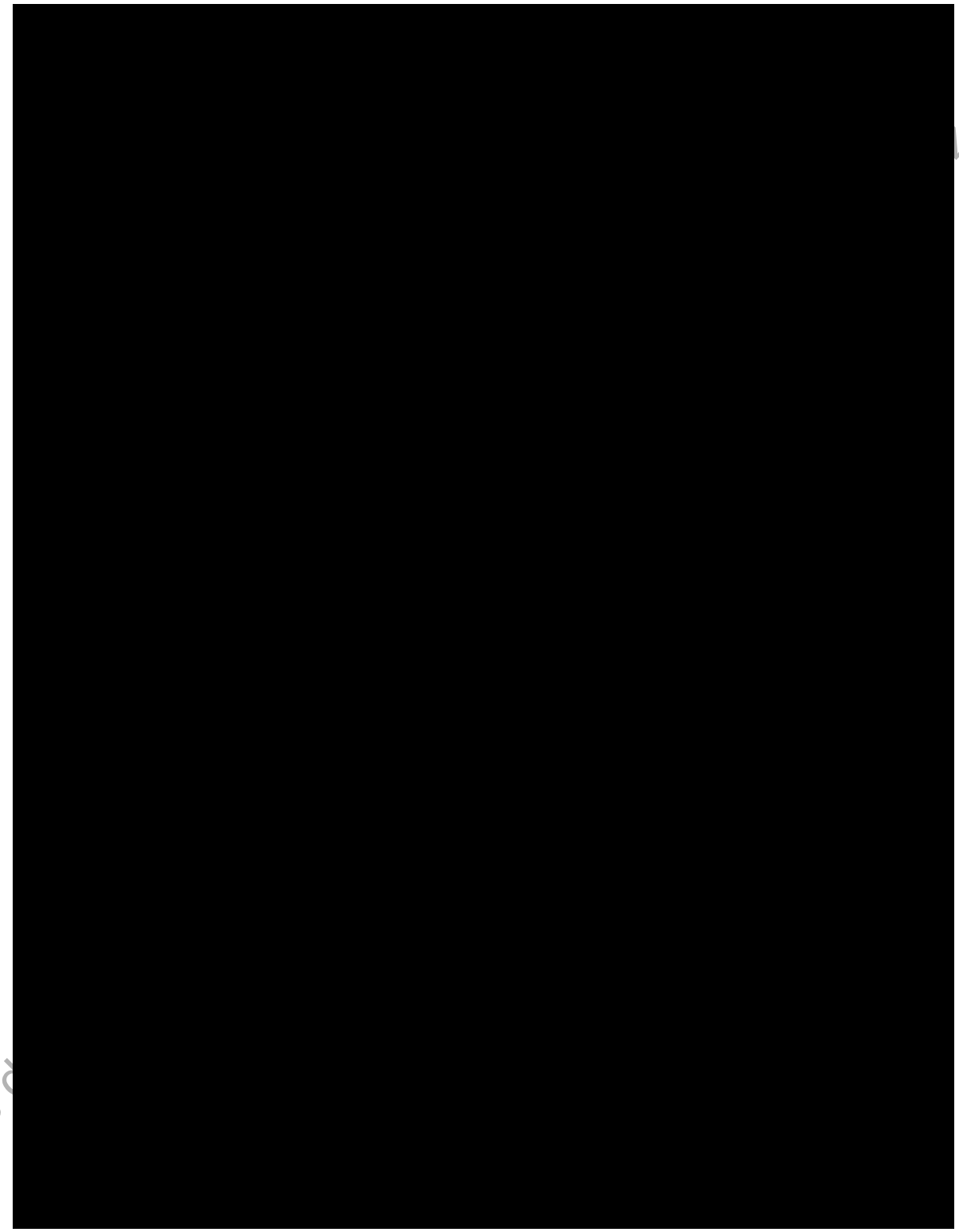
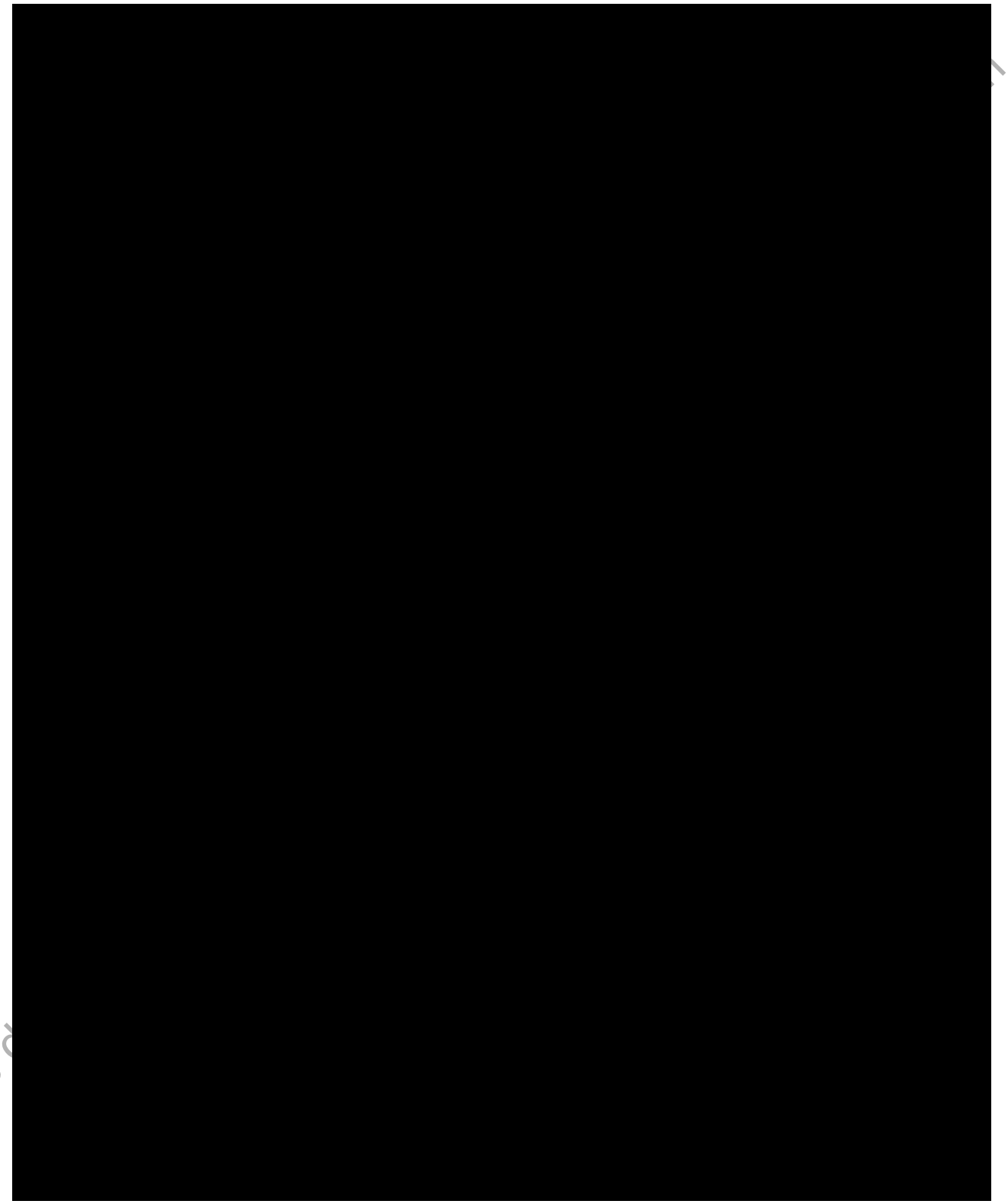


Table 13-8: MG Impairment Index



13.6 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 (i.e. 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% (i.e. 5 items or more) are missing, the total score will not be generated.

Table 13-9: 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_eng-USorl.doc

13.7 Markedly abnormal laboratory and diagnostic 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 13-10: 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 13-11: 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
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	>10 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: <2.5 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
Total Cholesterol	mg/dL	mmol/L	>400 /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] * 1.159 [if black]; where Scr is serum creatinine (mg/dL), κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1. For derivation from values in standard units (umol/L) the κ values are 61.88 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/.

[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 13-12: 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)

Parameter	Abnormality Criteria
Body Weight	≥ 10% decrease from Baseline ≥ 10% increase from Baseline

Table 13-13: 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

13.8 AEs of focus for Rozanolixizumab program

The AEOF selection criteria is specified in the Rozanolixizumab 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 Rozanolixizumab for MG studies:

No	Event (also included in Title of TFL output)	Selection criteria
1	Headache (Note: also included in AESM if severe)	TEAE with HLGT='Headaches'
2	Gastrointestinal disturbances (Note: also included in AESM if severe)	TEAE with HLT='Gastrointestinal and abdominal pains (excl oral and throat)' or HLT='Gastrointestinal signs and symptoms NEC' or HLT='Nausea and vomiting symptoms' or HLT='Diarrhoea (excl infective)' or HLT='Gastritis (excl infective)'
3	Hypersensitivity reactions	SMQ='Hypersensitivity'
4	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 any 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.
5	Injection site reactions	TEAE with HLT='Injection site reactions' or HLT='Infusion site reactions' or HLT='Administration site reactions NEC'
6	Infusion Reactions	Infusion reaction marked on AE CRF page (based on the assessment by the Investigator)
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)	Opportunistic infections (including tuberculosis) will be summarized in a stand-alone table using UCB-defined search criteria. Opportunistic infections are identified in two steps using the attached spreadsheet for MedDRA v24.0 in UCB Rozimab Safety AEs of Focus document: Step 1: Refer to column B of the spreadsheet which identifies the Preferred Terms (PTs) to be classified as opportunistic infections using either a single 'x' or a double 'xx'.

		• TEAEs which code to a PT flagged with a single 'x' need to also be serious in order to be considered an opportunistic infection. • All TEAEs which code to a PT flagged with a double 'xx' are considered to be an opportunistic infection, regardless of seriousness. All serious TEAEs in the study database which code to a PT flagged with a single 'x' and all TEAEs in the study database which code to a PT flagged with a double 'xx' will be summarized as an opportunistic infection in the stand-alone table. [CQ97NAM= 'Opportunistic Infection - Automatic'] Step 2: Refer to column C of the spreadsheet which identifies the PTs that need to be evaluated on a case-by-case basis by the study physician and safety physician in order to determine whether it is a true opportunistic infection or not. The process for physician review is as follows: 1. Study programming team creates a spreadsheet which lists all of the subjects with a TEAE present in the database which codes to a PT identified as case-by-case. [CQ98NAM= Opportunistic Infection - Manual Review Candidate] Information from the AE dataset to be included in the spreadsheet: Subject ID, AE verbatim term, System Organ Class (SOC), High Level Term (HLT), Lower Level Term (LLT), PT, AE start date, AE end date, seriousness, severity, relationship to study medication, action taken. Additionally, a column will be included where the study physician/safety physician can document their decision on the case. 2. Study physician/safety physician (SPs) reviews the cases in the spreadsheet separately and reconciles final decision, and indicates in the additional column which AEs are confirmed to be opportunistic infections via a single 'x'. 3. Study programming team incorporates these decisions into the AE dataset by merging the SPs decisions for individual subjects / PTs and flagging both the automatic and the confirmed opportunistic infections as such in the dataset. [CQ99NAM= 'Opportunistic Infection – Adjudicated']

		The SPs reviews the context of all of a subject's data (AEs and possibly other) and concludes individually. Indicators of relevant cases may be e.g. repetitive occurrences, conjunction of other events or findings considered relevant. All subjects with a case-by-case PT reported that has been confirmed by the SPs to be an OI will be summarized as such in the stand-alone table, along with all of the events identified in Step 1 of this process. [CQ99NAM= 'Opportunistic Infection – Adjudicated'] The timing and frequency of Step 2 should be outlined and agreed to by the study team at the beginning of the study. It is suggested that this process be executed multiple times throughout the course of the study, more frequently in the weeks leading up to database lock, and one final time immediately prior to database lock. Following the initial physician review of case-by-case events, subsequent reviews will be based on the cumulative set of case-by-case events present in the database at each time point of spreadsheet creation. Physician decisions from previous runs should be retained in each subsequent run. The final run of the spreadsheet, with all SP decisions on the full set of case-by-case events, will be archived at the conclusion of the study analysis prepared for agency submission.
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'
11	Drug related hepatic disorders	TEAEs in SMQ='Drug related hepatic disorders - comprehensive 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:

- Adverse event summaries to be consistent with MG0003
- Update definitions of ADA participant categories, and update related analyses
- Minor cosmetic changes

Modifications and changes

Section # and Name	Description of Change	Brief Rationale
General	Added RLZ total to summary tables	To be consistent with MG0003
General	Minor administrative, formatting, and typographical changes have been made.	Updated to provide clarity and be consistent with remainder of SAP.
3.3 Definition of Baseline values	Modified general definition of Baseline values and added Baseline definition for anti-drug antibody.	To consider actual assessment time and add more accurate definition for ADA considering MG0003 treatment effect
3.8 Coding dictionaries	Updated MedDRA and WHODD version	Newer versions were released
4.9 Examination of subgroups	The stratification factors MuSK(+/-) and AChR(+/-) in the subgroup analysis were changed to be based on the values from MG-specific autoantibody assessment taken at Baseline in MG0003.	To be consistent with MG0003
5.1 Subject disposition	Added a table to summarize the number of participants at each visit by treatment group.	Based on DEM3 comment to understand the pattern of dropouts
6.1 Demographics	Age was changed to be the age at the time of MG0003 entry.	To compare age population across MG studies
6.1 Demographics	Added race, ethnicity group and needed rescue therapies in the observation period of MG0003 and entered MG0004	To be consistent with MG0003 and MG0007

6.2 Other Baseline characteristics	Defined MG-ADL cutoff as 5	The cutoff was determined in MG0003
6.4 Prior and concomitant medications	Added definitions of rescue medications	To provide clear definitions of rescue medications in programming
8.2 Adverse events	Reorganized adverse event summaries	To be consistent with MG0003
8.3.1 Potential drug-induced liver injury	Modified PDILI criteria and added new summaries	To be consistent with PSAP
8.4.2 Electrocardiograms	Removed QTcB	QTcB is not of interest
8.4.3.2 Suicidal risk monitoring	Suicidal risk monitoring summary analysis was removed	Listing is enough to provide all information
9.1.1 MG-ADL score	Added COVID-19 free analysis for MG-ADL summary. Added MG-ADL (excluding ocular items) summary.	To evaluate impact of COVID-19 pandemic. To be consistent with MG0003.
9.1.2 MG-C score	Added by MuSK+ or AChR+ summary of MG-C score	Missing from last version
9.1.3 QMG scale	Changed subgroup analysis by MuSK+ or AChR+ only	Other subgroups are not needed
9.2.5 MG-ADL responder rate (≥2.0 points improvement from Baseline)	Removed summary for imputed values and changed the summary for all visits instead of first 6 weeks	NRI imputation is not applicable to MG0004.
9.2.6 QMG responder rate (≥3.0 points improvement from Baseline)	Removed summary for imputed values and changed the summary for all visits instead of first 6 weeks	NRI imputation is not applicable to MG0004.
9.2.7 MG-C responder rate (≥5.0 points improvement from Baseline)	Removed summary for imputed values and changed the summary for all visits instead of first 6 weeks	NRI imputation is not applicable to MG0004.
10 PHARMACOKINETICS AND PHARMACODYNAMICS	Updated ADA participant categories and related summary analysis	To be consistent with MG0003

11.2 Specific analyses for Pharmaceuticals and Medical Devices Agency (PMDA)	Updated AE summaries based on changes in Section 8.2	To be consistent with AE summaries on all participants
11.3 Headache questionnaire	Added text in SAP for headache listing in shells	To be consistent with shells
11.4 Myasthenia Gravis Foundation of America (MGFA) by Visit	Added MGFA listing to SAP	To include MGFA data
13.7 Markedly abnormal laboratory and diagnostic criteria for Rozanolixizumab program	Added corrected calcium algorithm and updated the marked abnormality criteria for corrected calcium and eGFR formula parameters.	For clarity
13.8 AEs of focus for Rozanolixizumab program	Updated definitions of AEOF	To be consistent across MG studies

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.