STATISTICAL ANALYSIS PLAN

A Randomized, Double-Blinded, Placebo-Controlled, Phase 3, Parallel-Group Design Study Evaluating the Efficacy and Safety of Efgartigimod IV in Adult Participants With Acetylcholine Receptor Binding Antibody Seronegative Generalized Myasthenia Gravis

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Ab	antibody
AChE	acetylcholinesterase
AChR	acetylcholine receptor
ADA	anti-drug antibodies
ADaM	analysis data model
ADY	ADaM variable to indicate relative day in the study
AE	adverse event
AESI	adverse events of special interest
ALP	alkaline phosphatase
ALT	alanine transaminase
AQL	above the upper quantification limit
AST	aspartate transaminase
ATC	anatomical therapeutic chemical
AUEC	area under the effect curve
AWADY	ADaM variable to indicate relative day for windowing
BQL	below the lower quantification limit
BUN	blood urea nitrogen
BMI	body mass index
bpm	beats per minute
CEE	Central and Eastern Europe
CFB	change from baseline
CI	confidence interval
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CMH	Cochran-Mantel-Haenszel
CRP	c-reactive protein
CTCAE	Common Terminology Criteria for Adverse Events
CTP	clinical trial protocol
CV%	coefficient of variation
Cn	cycle n
DBP	diastolic blood pressure
ECG	electrocardiogram
eCRF	Electronic case report form

EDC	electronic data capture
EEA	European economic area
EFG	Efgartigimod
EFTA	European Free Trade Association
eGFR	estimated glomerular filtration rate
ENR	Enrolled analysis set consists of all participants who provided informed consent
EoS	end of study
EQ-5D-5L	EuroQoL 5 Dimensions 5 Levels
ER	emergency room
EU	European Union
FU	follow-up
FWER	family-wise error rate
GGT	gamma-glutamyl transferase
GM	geometric mean
gMG	generalized myasthenia gravis
HbA1c	glycosylated hemoglobin
hCG	human chorionic gonadotropin
HR	heart rate
ICE	intercurrent event
ICF	informed consent form
ICH	International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
ICU	intensive care unit
ID	identification
IDMC	independent data monitoring committee
IgG	immunoglobulin gamma
IMP	investigational medicinal product
INF	infinity
IP	intertreatment period
IRR	infusion-related reaction
ITT	intent-to-treat analysis set consists of all randomized participants
IV	intravenous(ly)

LATAM	Latin America
LDL	low-density lipoprotein
LRP4	low-density lipoprotein receptor-related protein 4
LS	least square
MEA	Middle East and Africa
MCH	mean corpuscular hemoglobin
MCV	mean corpuscular volume
MedDRA	Medical Dictionary for Regulatory Activities
MG	myasthenia gravis
MG-ADL	myasthenia gravis activities of daily living
MGFA	Myasthenia Gravis Foundation of America
MGC	Myasthenia Gravis Composite
MG-QoL15r	15-item Quality of life scale for Myasthenia Gravis [revised version]
[redacted]	[redacted]
MMRM	mixed models for repeated measures
MSE	minimal symptom expression
MuSK	muscle-specific kinase
MuSK-Ab	anti-MuSK antibody(ies)
NAb	neutralizing antibody
NA	not applicable
NCI	National Cancer Institute
Neuro-QoL Short Form-Fatigue	Neurology Quality of Life Short Form for Fatigue
NSID	non-steroidal immunosuppressive drug
PAS	participant analysis set
PBO	placebo
PD	pharmacodynamic(s)
PE	physical examination
PGI-C	Patient Global Impression of Change
PGI-S	Patient Global Impression of Severity
PHQ-9	Patient Health Questionnaire item 9
PK	pharmacokinetic(s)
PRO	patient-reported items

PT	preferred term
PYFU	patient years of follow-up
QMG	quantitative myasthenia gravis
QoL	quality of life
QTc	corrected QT interval
QTcF	Fridericia's corrected QT interval
Qn	quartile n
RBC	red blood cell
SAE	serious adverse event
SAF	safety analysis set
SAP	statistical analysis plan
SBP	systolic blood pressure
SD	standard deviation
SDTM	study data tabulation model
SE	standard error
SGS CR	SGS Clinical Research
SoA	schedule of activities
SOC	system organ class
SOP	standard operating procedure
SMQ	Standardized MedDRA Queries
STAT	statistics
TEAE	treatment-emergent adverse event
TLF	tables, listings, and figures
TP	treatment period
TSQM-9	Treatment Satisfaction Questionnaire for Medication-9 items
UK	United Kingdom
VAS	visual analogue scale
VS	vital signs
V1	visit 1
WHO	World Health Organization
WI	work instruction

DEFINITION OF TERMS

AChR-Ab seronegative participants	AChR-Ab seronegative participants refers to participants in whom the anti-AChR-Ab cannot be detected per the actual lab results.
bias	The systematic tendency of any factors associated with the design, conduct, analysis, and evaluation of the results of a clinical study to make the estimate of a treatment effect deviate from its true value. Bias introduced through deviations in conduct is referred to as 'operational' bias. The other sources of bias listed above are referred to as 'statistical'.
covariate	Numerical explanatory variable
CRF	A printed, optical, or electronic document designed to record protocol required information to be reported to the sponsor for each study participant.
display	Analysis table, listing, or figure
estimand	A precise description of the treatment effect reflecting the clinical question posed by the study objective. It summarizes at a population-level what the outcomes would be in the same participants under different treatment conditions being compared.
estimate	A numerical value computed by an estimator.
estimator	A method of analysis to compute an estimate of the estimand using clinical study data.
factor	Categorical explanatory variable
functional test	Assessment by the investigator consisting of physical tests only. In ARGX-113-2308, functional tests are limited to QMG.

intercurrent events	Events occurring after treatment initiation that affects either the interpretation or the existence of the measurements associated with the clinical question of interest.
intercurrent event strategy	Strategy for addressing intercurrent events when defining the clinical question of interest. Composite variable strategy: an intercurrent event is considered in itself to be informative about the participant's outcome and is therefore incorporated into the definition of the variable. Hypothetical strategy: a scenario is envisaged in which the intercurrent event would not occur: the value of the variable to reflect the clinical question of interest is the value which the variable would have taken in the hypothetical scenario defined. Treatment policy strategy: the occurrence of the intercurrent event is considered irrelevant in defining the treatment effect of interest: the value for the variable of interest is used regardless of whether or not the intercurrent event occurs. While on treatment strategy: response to treatment prior to the occurrence of the intercurrent event is of interest, only values recorded up to that point are used.
IMP	Pharmaceutical form of an active ingredient or placebo, being tested or used as a reference in a clinical study.
missing data	Data that would be meaningful for the analysis of a given estimand but were not collected. They should be distinguished from data that do not exist or data that are not considered meaningful because of an intercurrent event.
principal stratification	Classification of participants according to the potential occurrence of an intercurrent event on all treatments.
principal stratum	Any of the strata (or combination of strata) defined by principal stratification.
significant digit	All digits of a number used to express it to the required degree of accuracy, starting from the first non-zero digit.
standardized unit	unit populating --STRESU in the clinical database

supplementary analysis	A general description for analyses that are conducted in addition to the main and sensitivity analysis with the intent to provide additional insights into the understanding of the treatment effect.
treatment-emergent abnormality / toxicity	Any postbaseline abnormality/toxicity which was not present at baseline or which worsened following baseline (eg, hemoglobin normal or grade 1 at baseline and grade 2 postbaseline; glucose low at baseline and high postbaseline; QTcF]450; 480] ms at baseline and >500 ms postbaseline). If baseline is missing any postbaseline abnormality/toxicity will be considered treatment-emergent.

1. INTRODUCTION

This version of the SAP describes the statistical analyses to be performed for the IDMC and primary analysis of study ARGX-113-2308 (BE-80-2400025). It is based on the most recent version of the protocol, version 3.0 of 23 September 2024. Table, figure, and listing specifications are contained in a separate document.

This version of the SAP describes the PK, PD, immunogenicity, general characteristics, and safety portions of the statistical analysis. It specifies the analysis displays to be presented and elaborates on the methods and procedures described in the statistical methods section of the protocol.

The statistical analysis will process and present the results following the ICH standards, in particular the ICH-E3, ICH-E6, and ICH-E9 guidelines[1-4].

1.1 STUDY OBJECTIVES AND ENDPOINTS

Table 1: Objectives and endpoints

Objectives	Endpoints
Primary	
• To determine the efficacy of efgartigimod IV compared to placebo in participants with AChR-Ab seronegative gMG in part A	• MG-ADL total score change from baseline to day 29 in part A
Key Secondary endpoints (Hierarchical testing)	
• To determine the efficacy of efgartigimod IV compared to placebo in participants with AChR-Ab seronegative gMG in part A	• QMG total score change from baseline to day 29 in part A • Proportion of participants who are both MG-ADL and QMG responders in part A
• To determine the efficacy of efgartigimod IV compared to placebo in part A in the following subgroups of AChR-Ab seronegative gMG[a]: ○ MuSK-Ab seropositve participants ○ the triple seronegative participants	• In the subgroups of MuSK-Ab seropositive and triple seronegative participants respectively: MG-ADL total score change from baseline to day 29 in part A

Secondary (Non-Hierarchical testing)	
• To determine the efficacy of efgartigimod IV compared to placebo, and the long-term efficacy of efgartigimod IV in participants with AChR-Ab seronegative gMG	• Proportion of participants with MSE (defined as an MG-ADL total score of 0 or 1) • Proportion of participants who are MG-ADL responders in part A • Proportion of participants who are QMG responders in part A • Proportion of participants who are early MG-ADL responders in part A • MG-ADL total score actual value and change from baseline over time in part A and part A+B • QMG total score actual value and change from baseline over time in part A and part A+B • MG-QoL15r score change from baseline to day 29 in part A • MG-QoL15r actual values and change from baseline over time in part A and part A+B • EQ-5D-5L VAS actual value and change from baseline over time in part A and part A+B
• To assess the safety and tolerability of efgartigimod IV compared to placebo and the long-term safety and tolerability of efgartigimod IV in participants with AChR-Ab seronegative gMG	• Incidence and severity of AEs and SAEs in part A and part A+B • Clinically relevant changes in laboratory parameters, ECGs, and vital signs in part A and part A+B
• To assess the PD effect of efgartigimod IV in participants with AChR-Ab seronegative gMG	• Total IgG actual values and percent changes from baseline over time in part A and part A+B
Exploratory	
• To determine the efficacy of efgartigimod IV compared to placebo and the long-term efficacy of efgartigimod IV in participants with AChR-Ab seronegative gMG	• AUEC of change from baseline in the MG-ADL total score from day 1 through end of part A • AUEC of change from baseline in QMG from day 1 through end of part A • MGC actual value and change from baseline over time in part A and part A+B • Neuro-QoL Short Form-Fatigue T-score actual value and change from baseline over time in part A and part A+B • [redacted] • Proportion of participants in each category of PGI-C and PGI-S in part A and part A+B
• To assess the PK of efgartigimod IV compared to placebo in participants with AChR-Ab seronegative gMG in part A	• Efgartigimod serum concentrations over time in part A
• To assess the [redacted]	• [redacted]

• To assess the immunogenicity of efgartigimod IV in participants with AChR-Ab seronegative gMG	• Incidence and prevalence of ADAs against efgartigimod over time in part A+B • Incidence and prevalence of NAb against efgartigimod over time in part A+B
• To assess participant satisfaction with efgartigimod IV treatment in participants with AChR-Ab seronegative gMG	• TSQM-9 domain scores in part A+B

[a] Addition to the ARGX-113-2308 CTP, documented in section 6.1

1.2 STUDY DESIGN

This phase 3, multicenter study in adult participants with AChR-Ab seronegative gMG consists of 2 parts: part A is a randomized, double-blinded, placebo-controlled, parallel-group design to evaluate the efficacy and safety of efgartigimod IV, and part B is open-label to enable the collection of additional long-term efficacy, safety, and tolerability data.

Study periods include the following:

- Screening: up to 5 weeks (refer to CTP Section 8.1.1.2)
- Part A (8 weeks total)
  - Composed of a single TP and IP, grouped as a single cycle
  - TP: 3 weeks of once weekly IMP infusions (4 total)
  - IP: 5 weeks follow-up
- Part B (up to 2 years)
  - Composed of TPs and IPs grouped in cycles (Cn=TPn+IPn)
  - C1 and C2: 3-week TP and 4-week IP
  - C3 onward: 3-week TP (once-weekly efgartigimod, 4 in total) and an IP of indeterminant length based on participant clinical status; the IP can be no shorter than 7 days

An MG diagnostic adjudication committee (CTP Section 10.1.6.2) will confirm participant AChR-Ab seronegative gMG diagnosis before randomization. At part A V1 (baseline), approximately 110 participants whose eligibility was confirmed will be stratified by MuSK-Ab status and randomized in a 1:1 ratio to receive either efgartigimod IV 10 mg/kg or placebo.

In part A, IMP will be administered concomitantly with a stable dose of the participant's current gMG therapy. Participants must maintain a stable regimen of concurrent gMG medications throughout part A until the start of C3 in part B. More details are provided in CTP Section 6.9. From part B C3 TP onward, changes to concomitant gMG treatment are permitted.

Although part B is open-label, participants and investigators will remain blinded to treatment assignment throughout the first 2 cycles in part B to ensure part A data are uncompromised for the interim analysis (CTP Section 9.4).

Participants whose dose was interrupted (1 missing dose) in part A can continue in part B if part A was completed. Participants who are missing more than 1 dose of IMP or receive rescue therapy in part A will not be permitted to transition to part B.

Information on participant discontinuation from IMP and withdrawal from study is provided in CTP Section 7.

All participants in part B will receive open-label efgartigimod IV. During part B from C3 onward, TPs can be initiated earlier at the discretion of the investigator.

Part B will remain open in all countries for a maximum of 2 years following completion of part A. Part B may end earlier than 2 years in countries where efgartigimod becomes available for AChR-Ab seronegative gMG commercially or through a continued access program, whichever comes first.

The schedule of assessments is in appendix 9.5.

1.3 STATISTICAL HYPOTHESES

The statistical hypothesis is derived from the primary study objective as stated in CTP Section 3.

The primary endpoint in this study is the change from baseline in MG-ADL total score at day 29 (week 4). The primary hypothesis tested in the study is the following:

$$H_0: \delta = \Delta\mu_{EFG} - \Delta\mu_{PBO} = 0$$

$$H_1: \delta = \Delta\mu_{EFG} - \Delta\mu_{PBO} \neq 0$$

$\Delta\mu_{EFG}$ is the mean change from baseline in MG-ADL total score at day 29 (week 4) in the efgartigimod IV arm and $\Delta\mu_{PBO}$ is the mean change from baseline in MG-ADL total score at day 29 (week 4) in the placebo arm.

- Null hypothesis: no difference between efgartigimod IV and placebo in mean change from baseline in MG-ADL total scores at day 29 (week 4)
- Alternative hypothesis: difference between efgartigimod IV and placebo in mean change from baseline in MG-ADL total scores at day 29 (week 4)

The null and alternative hypotheses corresponding to the secondary estimands (hierarchical testing, see Section 1.3.1) are as follows:

- Secondary objective [1]:
  - Null hypothesis: no difference between efgartigimod IV and placebo in mean change from baseline in QMG total scores at day 29 (week 4)
  - Alternative hypothesis: difference between efgartigimod IV and placebo in mean change from baseline in QMG total scores at day 29 (week 4)
- Secondary objective [2]:
  - Null hypothesis: no difference between efgartigimod IV and placebo in achieving both MG-ADL and QMG responder status
  - Alternative hypothesis: difference between efgartigimod IV and placebo in achieving both MG-ADL and QMG responder status
- Secondary objective [3 and 4]: the null hypothesis and the alternative hypothesis of the primary endpoint will be tested, restricted to the following subgroups:
  - MuSK-Ab seropositve participants
  - the triple seronegative participants

1.3.1 Multiplicity adjustment

Given the cumulative efficacy data of efgartigimod in AChR-Ab seronegative patients with gMG and the fact that the study includes a rare subset of an already rare disease, a closed testing procedure that controls the family-wise error rate in the strong sense at the overall 10% level will be applied.

The statistical comparisons for the primary efficacy endpoint and the key secondary endpoints will be conducted in the following hierarchical order:

1) MG-ADL total score change from baseline to day 29 in part A
2) QMG total score change from baseline to day 29 in part A
3) Proportion of participants who are both MG-ADL and QMG responders in part A
4) MG-ADL total score change from baseline to day 29 in part A for the MuSK-Ab seropositve participants
5) MG-ADL total score change from baseline to day 29 in part A for the triple seronegative participants

This means the statistical hypotheses are tested in the prespecified order at the same significance level of α=10% using 2-sided tests if all preceding hypotheses are rejected. Once a hypothesis is not rejected, subsequent hypotheses cannot be formally tested and therefore cannot be rejected.

1.4 EXPECTED SAMPLE SIZE

Approximately 110 adult participants who meet the study eligibility criteria will be stratified by MuSK-Ab status and randomized within each stratum in a 1:1 ratio to receive efgartigimod IV or placebo.

Assuming an SD of [redacted] in the efgartigimod IV arm of part A and [redacted] in the placebo arm based on ARGX-113-1704 study results in the AChR-Ab seronegative population, a total of [redacted] participants ([redacted] in each arm) provides [redacted]% power to detect a difference in change from baseline of [redacted] in MG-ADL total score at week 4 in the efgartigimod IV arm compared to the placebo arm. The sample size calculation was performed with a 2-sample t-test with a 2-sided Type I error rate of [redacted] using Cytel East (Cytel, Cambridge, MA, United States).

Accounting for [redacted]% attrition, approximately 110 participants will be recruited in the study.

1.5 RANDOMIZATION AND BLINDING

In part A, at V1 and once eligibility has been confirmed, participants will be stratified by MuSK-Ab status and randomized in 1:1 ratio to receive placebo or efgartigimod IV. In part B, all participants will receive efgartigimod IV.

Part A is double-blinded. Part B is open-label.

At the time of primary analysis (refer to Section 1.6), sponsor unblinding will occur. The study's final unblinding will occur when all participants have completed the study and the complete database is locked.

1.6 INTERIM ANALYSIS

The primary analysis will be conducted when all participants complete part A of the study. This analysis will be the final analysis for part A.

After the primary analysis, additional analyses could be performed to support questions for authorities and/or submissions.

The outputs to be generated for the primary analysis are mentioned in section 8.

1.7 IDMC ANALYSIS

The IDMC will review and evaluate study data periodically for participant safety, study conduct and progress, and provide recommendations to the sponsor regarding the continuation, modification, or termination of the study.

The IDMC analysis is a subset of the main analysis and will follow the same conventions as described in this SAP. The outputs to be generated for the IDMC are flagged in section 8.

Details on the composition, objectives, role & responsibilities of the IDMC, as well as the timing & frequency of the IDMC meetings, can be found in the latest version of the IDMC Charter.

1.8 SOFTWARE

SAS version 9.4 or later (SAS Institute Inc., Cary, NC, USA) will be used for programming.

1.9 VALIDATION MODEL

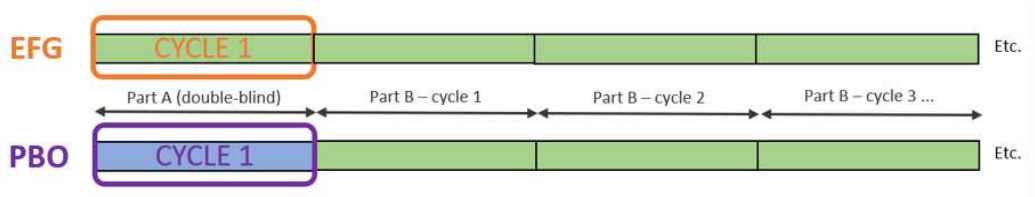
SGS STAT SOPs and WIs effective at the project start will be followed throughout the project, provided the applicable regulatory requirements are still met.

ADaM datasets, analysis tables, and listings will be validated according to model B (review by an independent person), except the following: ADSL and primary and key secondary endpoint (ADaM and TLFs). These datasets will follow validation model C (review by an independent person and independent programming of the parameters indicated in this SAP). See SOP.STAT.020.

2. GENERAL METHODOLOGY

2.1 PART A AND PART A+B ANALYSIS

2.1.1 Part A Analysis



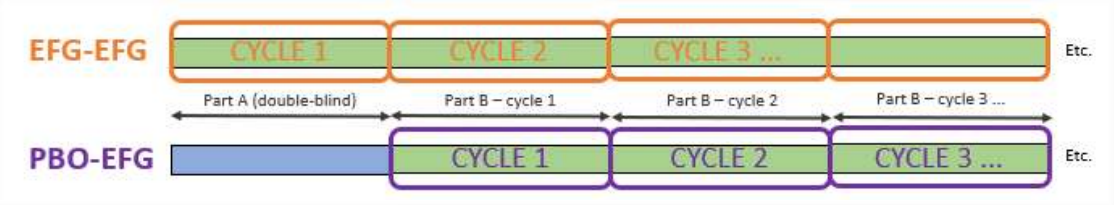
Only data under part A will be considered for the part A analysis, comparing efgartigimod IV with placebo.

Following treatment arms will be used:

- Efgartigimod IV: participants from the EFG IV arm in part A
- Placebo: participants from the PBO arm in part A

Part A analyses will not be repeated once all participants have completed part A and the primary analysis has taken place.

2.1.2 Part A+B Analysis



Only data under efgartigimod will be considered for the part A+B analysis, assessing the long-term effect of efgartigimod IV. As a result, part A data of participants in the placebo arm are not included in the part A+B analysis, except for the derivation of the pooled baseline if no predose value in part B is available.

Cycle 1 will consist of part A data of participants from the efgartigimod IV arm and part B Cycle 1 data of participants in the placebo arm; Cycle 2 will consist of part B Cycle 1 data of participants in the efgartigimod IV arm, and part B Cycle 2 data of participants in the placebo arm; etc.

No separate analysis for part B only will be done.

Following treatment arms will be used:

- EFG IV-EFG IV: participants in the efgartigimod IV arm who received efgartigimod in part A. Data related to part A and part B will be considered for this arm
- PBO-EFG IV: participants in the placebo arm who received efgartigimod IV in part B. Only data related to part B will be considered for this arm.
- TOTAL EFG IV: participants in the EFG IV-EFG IV and PBO-EFG IV arm

See sections 2.3.1 (Analysis phases and periods; Table 2) and 2.3.4 (Analysis visits; Table 4) for more details.

2.2 ANALYSIS SETS

2.2.1 Analysis sets

The following participant analysis sets (PAS) will be used:

enrolled analysis set:	all participants who *provided informed consent*
intent-to-treat analysis set:	all *randomized* participants
safety analysis set (part A):	all participants who *received at least one dose of IMP or a part of a dose* in part A
safety analysis set (part A+B):	all participants who *received at least one dose of efgartigimod IV or a part of a dose* in part A or B
pharmacokinetics analysis set:	all participants in the SAF analysis set (part A) for whom at least one postdose serum PK concentration is available in part A, excluding placebo participants

Notes:

- Provided informed consent is defined as having a complete informed consent signature date in the database.
- Randomized is defined as having a complete randomization date in the database or any information to confirm randomization.
- Received at least one dose of IMP/efgartigimod is defined as having an exposure date or any information confirming exposure to IMP/efgartigimod present in the database.

All outputs will be performed using the PAS as indicated in section 8.

2.2.2 As planned versus as actual analysis

When using the ITT analysis set, participants will be classified according to their planned treatment arm. For analyses performed on the safety or PK analysis set, the actual treatment arm will be considered. The actual treatment arm will be the same as the planned treatment arm unless the participant received IMP other than the planned one for the whole study.

For IDMC analyses performed before database lock, misallocation(s), if any, might not yet have been identified and entered in the clinical database, and therefore, these IDMC analyses will be done on the planned treatment.

Wherever the stratification factors will be used for subsetting, the actual values (ie, based on actual values recorded at screening) of these will be used, rather than the values coming from the randomization. For the primary endpoint analysis, the impact of using the stratification factors as randomized will be assessed as a sensitivity analysis (see Section 4.1.3.1).

2.3 PHASES, PERIODS AND TIME POINTS

2.3.1 Analysis phases and periods

All events and assessments will be allocated to phases, periods and subperiods as detailed in Table 2.

Table 2: Analysis phase, period, and subperiod definition

Phase	Period	Subperiod EFG-EFG / PBO-EFG[a]	Start	End
Screening			Date of signing the informed consent form (ICF), with 00:00 added as time part.	First IMP administration date/time – 1 minute
Treatment + Follow-up	Double-Blind Period	Cycle 1 / -	First IMP administration date(time)	First efgartigimod administration date(time) in part B – 1 minute or, if no part B, date of last contact[b] with 23:59 added as time part
	Open-Label Period	Cycle 2 / Cycle 1	First efgartigimod administration date(time) in part B	First efgartigimod administration date(time) in next cycle – 1 minute or, if the last cycle, date of last contact[b] with 23:59 added as time part
		Cycle n[c]	First efgartigimod administration date(time) in cycle n	First efgartigimod administration date(time) in cycle (n + 1) – 1 minute or, if the last cycle, date of last contact[b] with 23:59 added as time part

[a] Subperiod is only relevant in the part A+B analysis and is defined depending on the treatment arm during the double-blind period, see also section 2.1.2.
[b] date of last contact or data cutoff date for ongoing participants at the time of an interim/IDMC analysis
[c] n = n^{th} cycle of the participant (from 3 onward for EFG-EFG or from 2 onward for PBO-EFG participants)

AEs and concomitant medications will be allocated to phases, periods, and subperiods as described in sections 5.1.2 and 3.5.2 respectively. All other assessments will be allocated to phases, periods, and subperiods based on the assessment date/time.

In case of (partially) missing date/time fields disabling allocation or date(time) equal to dosing date(time), information from visit label and protocol SoA will be used to allocate to the correct phase, periods, and subperiods. If this is not possible, assessments will be allocated to the first possible (sub)period unless the available parts of the assessments start or stop date/time provide evidence the assessments did not occur during that (sub)period.

2.3.2 Baseline and change from baseline

The study baseline value (ie, the baseline in the part A analysis) is defined as the last available nonmissing value before the first administration of IMP.

For the part A+B analysis, two baselines are defined:

- The pooled baseline value is defined as the last available nonmissing value before the first efgartigimod administration. For participants in the efgartigimod IV arm, this aligns with the study baseline. For participants in the placebo arm, this aligns with the last available nonmissing value before the first efgartigimod administration in part B.
- The cycle n baseline value is defined as the last available nonmissing value before the first efgartigimod administration in cycle n.

For immunogenicity, cycle baseline from cycle 2 on is defined as the last available nonmissing value in the previous cycle.

Assessments performed on the same day as the first IMP/efgartigimod administration but without time information collected or with time information exactly equal to the time of first IMP/efgartigimod administration and which are planned predose will be considered as predose. In case the participant never received IMP/efgartigimod, the date(time) of randomization will be used instead of first IMP/efgartigimod administration date(time) to derive the baseline value. Questionnaires and functional tests given on the day of the first administration of IMP/efgartigimod (pre- or postadministration) are considered in the baseline selection.

Change from baseline is defined as:

Change from (study/pooled/cycle n) baseline at time point t = value at time point t – respective baseline value.

Percentage change from (study/pooled/cycle n) baseline at time point t is defined as follows:

- When baseline value is not zero: 100*((value at time point t – respective baseline value) / respective baseline value)
- When baseline value is zero: not calculated

2.3.3 Relative day

The relative day in the study is calculated as follows:

- ADY = assessment date – first IMP administration date, if assessment date is before the first IMP administration date
- ADY = assessment date – first IMP administration date +1, if assessment date is on or after the first IMP administration date

The relative day for windowing is calculated as follows for analyses by analysis visits by cycle (Table 4):

- AWADY = assessment date – first efgartigimod administration date in the cycle, if assessment date is before the first efgartigimod administration date in the cycle
- AWADY = assessment date – first efgartigimod administration date in the cycle + 1, if assessment date is on or after the first efgartigimod administration date in the cycle

2.3.4 Analysis visits

All assessments, including unscheduled assessments, will be allocated to analysis visit windows. Tables and listings will present the analysis visit as defined below, not the eCRF visits. Allocations of assessments will be performed using ADY / AWADY (see section 2.3.3) according to below tables:

Table 3: Analysis visits for the part A analysis

Analysis visit	Target ADY	Lower limit ADY	Upper limit ADY
Baseline	1	-INF	1[a]
Week 1	8	1[a]	11
Week 2	15	12	18
Week 3	22	19	25
Week 4	29	26	32
Week 5	36	33	39
Week 6	43	40	46
Week 7	50	47	53
Week 8	57	54	end of part A

[a] An assessment on day 1 before the first administration of IMP will be allocated to baseline (refer to Section 2.3.2). Otherwise, the assessment will be allocated to week 1.
Questionnaires and functional tests given on the day of the first administration of IMP (pre- or postadministration) are allocated to baseline

Table 4: Analysis visits by cycle for the part A+B analysis

Analysis visit	Target AWADY	Lower limit AWADY	Upper limit AWADY[c]
Baseline	1	-INF	1[a]
Week 1	8	1[a]	11
Week 2	15	12	18
Week 3	22	19	25
Week 4	29	26	39
Week 7	50	40	60
Week 7 + x[b]*3	50 + x*21	40 + x*21	60 + x*21
Around 1 year after study entry[d]	366	183	[INF]

[a] An assessment on day 1 before the first administration of efgartigimod will be allocated to baseline (refer to Section 2.3.2). Otherwise, the assessment will be allocated to week 1.
Questionnaires and functional tests given on the day of the first administration of efgartigimod (pre- or postadministration) are allocated to baseline

[b] x ranges from 1 till the number of intertreatment period visits - 1.
[c] The upper limit AWADY of the last analysis visit within the cycle is the end of the cycle (see section 2.3.1).
[d] Analysis windows only apply to TSQM-9 and are based on ADY instead of AWADY

Per parameter and analysis window, the value closest to the target AWADY / ADY will be used in analysis tables and figures. If more than one value is located at the same distance from the target, then the latest in time will be selected. The value latest in time will be identified using, in order of preference, the assessment time, the visit label or the group identifier (if applicable). Missing values are removed before the selection is made. For efficacy assessment where ICEs are defined, the selection of closest to target occurs after having applied the ICE strategy.

Baseline is defined in section 2.3.2.

The exception to this rule is immunogenicity where the selection is done on a sample basis to keep the ADA and NAb results together. Per sample and analysis visit (including pooled baseline and cycle n baseline), the value closest to the target day will be used in the analysis displays. If more than one value is located at the same distance from the target, then the latest in time will be selected. The value latest in time will be identified using, in order of preference, the assessment date(time), the visit label, or group identifier (if applicable). If multiple immunogenicity assessments fall into the same visit window (including pooled baseline and cycle 1 baseline) and the selection process results in an unevaluable ADA status, then the selection process should be repeated without that one ADA result (leading to unevaluable status) as an evaluable status is preferred over an unevaluable ADA status. This means that missing values resulting in an unevaluable ADA status are not removed but given the lowest priority when the selection is made.

(Partially) missing safety, immunogenicity, and PD assessment dates disabling allocation to analysis visits will imputed with the visit date. (Partially) missing PK assessment dates will not be imputed and thus these assessments will not be considered in the per timepoint analysis.

2.3.5 Worst-case

A worst-case analysis visit will be created for part A analysis and for part A+B analysis (overall) for parameters with defined abnormalities and/or toxicity grades (eg, labs, vital signs, ECGs) and for suicidality to summarize values considered as the worst-case. For abnormalities, the worst-case is derived per parameter and if both the lowest and highest values are considered abnormal, a participant can have two worst-case analysis visits for the same parameter. For toxicity grades, the worst-case is the value associated with the highest toxicity grade and is derived per parameter and toxicity direction (hypo/hyper).

All nonmissing postbaseline values, including unscheduled assessments and assessments not selected for the analysis visit, will be considered when deriving the worst-case analysis visit.

2.3.6 Best response

A best response analysis visit (ie, minimum postbaseline value and maximum drop from baseline) will be created for part A and by cycle for part A+B for MG-ADL and QMG scores to summarize values considered as the best response.

All non-missing postbaseline values (within part A or within cycle for part A+B), including unscheduled assessments and assessments not selected for the analysis visit, will be considered when deriving the best response analysis visit.

2.4 IMPUTATION AND ROUNDING RULES

2.4.1 Missing values

For imputation on missing values related to efficacy, see appropriate section of the applicable efficacy endpoint.

2.4.2 Values below or above a threshold

Safety and total IgG non-numeric values expressed as BQL or AQL will be imputed by the value of the quantification limit itself. For participants with an imputed baseline total IgG value, the total IgG will be excluded from the statistical analysis involving change and percent change from baseline. Anti-MusK antibodies BLQ will not be imputed.

PK concentrations below the detection limit will be flagged as BQL in the listings. For descriptive statistics by scheduled timepoint, BQL values will be set to zero.

For ADA against efgartigimod, positive ADA samples reported as 'negative titer' will be imputed by 1.

Listings will always present the original value.

2.4.3 Rounding

Variables will be rounded to the appropriate number of decimals at display level:

- Time since diagnosis, BMI, compliance, and Neuro-QoL Fatigue T-score will be rounded to 1 decimal.
- AUEC, TSQM-9 domain scores, [redacted] and MG-QoL15r total score will be rounded to the integer.
- eGFR will be rounded to 2 decimals.
- Safety laboratory results will be rounded to a maximum of 3 decimal.

2.4.4 Outliers

There will be no outlier detection. All measured values will be included in the analyses.

2.5 PRESENTATION OF RESULTS

To support the marketing authorization application in China, all descriptive outputs in this SAP will be repeated for the Chinese population (mainland Chinese is defined as any participant enrolled by an investigational site located in mainland China and with a race "Chinese"), and for the East Asian population (East Asian is defined as any participant enrolled by an investigational site located in East Asia [as defined in section 3.3.2], and with a race "Asian").

These additional descriptive outputs will not be included for the IDMC or in the submissions to other health authorities.

2.5.1 Calculation of descriptive statistics and percentages

For continuous variables, full descriptive statistics will only be presented if there are at least 2 nonmissing observations. Alternatively, only the number of nonmissing data points and mean are shown.

Descriptive statistics for continuous variables, except for PD and PK (described below), will include the number of nonmissing data points, the arithmetic mean, the SD, the median, minimum, Q1, Q3, and maximum. For efficacy measures, the SE, 90% CI and 95% CI on the mean (based on t distribution, without continuity correction) will be provided in addition.

Descriptive statistics for PD parameters will include the number of nonmissing data points, the arithmetic mean, the SD, the SE, the 95% CI, the median, minimum, Q1, Q3, and maximum. Descriptive statistics of total IgG levels will be presented in µg/mL.

Descriptive statistics for PK serum concentrations will include the number of observed values, arithmetic mean, SD, median, minimum and maximum, CV%, GM and geometric CV%.

Descriptive statistics for immunogenicity titer values will include the number of observed values, arithmetic mean, SE, 95% CI, median, Q1, Q3, minimum, maximum, GM, and geometric CV%.

Mean, 90% CI, 95% CI, Q1, Q3 and median and GM will be presented with one more decimal place than the measured values. SE and SD will be presented with two more decimal places than the measured values. Minimum and maximum will be presented with the same number of decimal places as the measured values. CV% and geometric CV% will be presented with one decimal place.

P-values will be presented with four decimal places, ratios with three decimal places, and test statistics with two decimal places.

Descriptive statistics for PK concentrations will be presented with 3 significant digits in µg/mL, except values ≥1000 which will be presented without the decimals and rounded to the nearest integer. If at least one BQL value is reported at a specific time point, the GM and geometric CV% for that time point will not be calculated. In addition, if more than half of the values per time point are BQL, the arithmetic mean will be reported as BQL and SD, CV%, GM, and geometric CV% will not be calculated. Serum concentrations will be listed as received by the bioanalytical laboratory.

For event-type safety data, the number and percentage of participants with an event will be shown. The denominator will be all participants in the PAS per treatment arm and cycle. All cycles will be shown, even if no events were reported.

For frequency tabulations and cross-tabulations, the denominator will be the number of participants in the PAS per treatment arm with nonmissing values. For tables where results are shown by analysis visit, the denominator will be the number of participants in the PAS per treatment arm and analysis visit with nonmissing values. For cross-tabulations of postbaseline results versus baseline results, a ‘missing’ category will be shown for baseline results, if applicable, and included in the calculations of percentages.

Percentages will be presented with one decimal place.

2.5.2 Presentation of treatments

The following treatment arm labels will be used in the outputs for the part A analysis:

- Efgartigimod IV
- Placebo

The following treatment arm labels will be used in the outputs for the part A+B analysis:

- EFG IV-EFG IV
- PBO-EFG IV
- TOTAL EFG IV

2.5.3 Ordering in tables, listings, and figures

Separate output will be created for part A and part A+B analysis. Table numbering will contain the 'A' or 'AB' suffix, respectively; the table title will contain 'PART A' or 'PART A+B', respectively.

In the outputs, treatment arms will be presented in the order as mentioned in Section 2.5.2. For general characteristics in the part A analysis, a total column will be added as the last column. For outputs by antibody status (ie, MuSK-Ab and anti- LRP4 status), the MuSK-Ab seropositive participants will be shown first, then the anti-LRP4 seropositive participants who are MuSK-Ab seronegative, and then the triple seronegative participants. Anti-LRP4 seropositive participants will only be presented when data is available for at least 4 participants in that PAS (overall). The MuSK-Ab and anti-LRP4 status will be defined based on the actual lab results at screening, unless otherwise specified (see Section 2.2.2).

Summary tables related to part A analysis will be presented by treatment arm and analysis visit, while summary tables related to part A+B analysis will be presented by treatment arm, cycle and analysis visit.

In tables showing several parameters, each parameter will begin on a new page and parameters will be sorted alphabetically, within the parameter category if applicable. In tables by analysis visit, only analysis visits for which there is data available for at least 10 participants in that PAS (overall) will be included and worst-case will be shown last, if present.

In listings for general characteristics, results will be ordered by treatment arm and participant identifier, unless specified otherwise. All other listings will be ordered by treatment arm, participant identifier, analysis visit, and time point, unless specified otherwise.

2.5.4 Cohorts

In the part A+B analysis, adverse event analyses will be performed on all participants included in the safety analysis set (part A+B) over the whole observation period, and also by cycle. Due to the difference in length of the observational periods, the number of participants will be different across cycles. The number of participants in the first cycle will be higher than the number of participants in the second cycle, and so forth. To account for this attrition, cohorts of participants who participate in at least 2

cycles, who participate in at least 3 cycles, etc will be created. The analyses performed on the safety analysis set using all available data will be repeated for each of these cohorts to evaluate safety over cycles within similar cohorts. A cohort will need to consist of at least 10 participants (overall) to be shown in the results.

In tables by cycle, analyses will first be performed on the cohort of all participants in a cycle and will then be repeated (as applicable) for each of these cohorts per cycle and for any cycle:

- Cohort of all participants in a cycle
  - Cycle 1
  - Cycle 2
  - Cycle 3
  - Etc.
  - Any cycle
- Cohort of participants with at least 2 cycles
  - Cycle 1
  - Cycle 2
  - Any cycle (ie, cycle 1 or cycle 2)
- Etc.

3. GENERAL CHARACTERISTICS ANALYSES

3.1 PARTICIPANT DISPOSITION

The following participant data will be tabulated:

- The number of participants in each PAS and the number and percentage of screen failures (including reasons for screen failures) and of participants randomized but not treated
- The number and percentage of participants by country and site
- The number and percentage of participants who completed or discontinued the study as documented on the study termination page and the number and percentage of participants for each study discontinuation reason (overall and by cycle) and the number of participants continued to part B (part A analysis) or ongoing participants (part A+B analysis).
- The number and percentage of participants who completed or discontinued the treatment as documented on the treatment termination page and the number and percentage of participants for each treatment discontinuation reason (overall and by cycle) and the number of ongoing participants (if applicable).

For part A+B analysis, study and treatment discontinuation will be presented by cycle and overall. Additionally, the following participant data will be tabulated for part A+B analysis:

- Descriptive statistics of the study and analysis phase duration (see section 2.3.1). Study duration is calculated as date of study termination (or data cutoff date for ongoing participants) – date of informed consent + 1 day.
- Descriptive statistics of the cycle (subperiod) duration (see section 2.3.1), calculated as cycle end date - cycle start date + 1 day. This table will consider completed cycles only (ie, last cycle is not accounted for in ongoing participants).
- Frequency tabulation of the treatment and follow-up duration per 6-monthly period, showing the number and percentage in each category and additionally cumulative number and percentages. Categories are defined as follows: <6 months (< 168 days); 6 to <12 months (168 - 350 days); 12 to <18 months (351 - 532 days); 18 to <24 months (533 - 715 days); 24 to <30 months (716 - 897 days); 30 to <36 months (898 - 1080 days); 36 to <42 months (1081 - 1263 days); 42 to <48 months (1264 - 1445 days).

All information collected concerning allocation, study and treatment discontinuation will be listed.

3.2 PROTOCOL DEVIATIONS AND ELIGIBILITY

Protocol deviations will be allocated to the study part during which it occurred based on the deviation start date (see also section 2.3.1).

The number and percentage of participants with protocol deviations will be summarized separately for part A and for part A+B, by important/non-important deviations, and by class of deviation using the ITT analysis set.

All information concerning important and nonimportant protocol deviations, violations on eligibility criteria, and participants not treated will be listed.

3.3 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

3.3.1 Available data

The following parameters will be available:

- Demographics: sex at study start, women of childbearing potential, age at informed consent, race (with subcategories), ethnicity, height at screening, body weight at baseline, year of birth, date of signing ICF
- Baseline disease characteristics: date of diagnosis, MGFA Classification at screening and at diagnosis, thymectomy (as reported on the medical history or procedures form), MuSK-Ab value, anti-LRP4 status, MG-ADL total score at screening and at baseline, and QMG total score, MG-QoL15r total score and EQ-5D-5L VAS score at baseline.

3.3.2 Derivation rules

For below derived parameters, whenever 'baseline' is mentioned, it should be read as study baseline for the part A analysis and pooled baseline for the part A+B analysis:

- BMI at baseline (kg/m²) = (body weight at baseline (kg)) / (height at screening (m))²

  Note: The BMI will be recalculated and rounded as detailed in section 2.4.3, only when not available in the database.
- Weight at baseline category:
  - <50 kg
  - 50 - <75 kg
  - 75 - <120 kg
  - ≥120 kg
- BMI at baseline category:
  - Underweight: <18.5 kg/m²
  - Normal weight: 18.5 - <25 kg/m²
  - Overweight: 25 - <30 kg/m²
  - Obese: ≥30 kg/m²
- Age category:
  - 18 - <65 years
  - ≥65 years
- Race category:
  - Asian
  - Black or African American
  - White
  - Other: combining all remaining categories

- Region:
  - East Asia: China, Japan, Mongolia, North Korea, South Korea, Taiwan
  - Europe: EU and EEA countries, EFTA countries (Norway, Iceland, Liechtenstein and Switzerland) and UK
  - Latin America (LATAM): Mexico, Argentina, Chile
  - Middle East and Africa (MEA): Israel, Jordan, Tunisia, Turkey, South Africa
  - non-EU Central and Eastern Europe (non-EU CEE): Russia, Georgia, Serbia, Ukraine
  - North America: United States, Canada
  - Rest of world: any countries not mentioned above

    Note: due to low number of participants in following regions they will be merged with the rest of world region: LATAM, MEA and non-EU CEE for this study
- Time since diagnosis (years): (date of ICF – date of initial diagnosis)/365.25

  Note: Partially missing dates will be imputed as follows:
  - Missing day of diagnosis will be imputed with 1
  - Missing day and month of diagnosis will be imputed with 1JAN

  Note: Results will be rounded as detailed in section 2.4.3
- MG-ADL total score at baseline category:
  - 0-4
  - 5-7
  - 8-9
  - ≥10
- QMG total score at baseline category:
  - 0-9
  - 10-16
  - >16
- MuSK-Ab status:
  - Positive: value ≥ 0.4 U/mL (Chinese lab) or value > 0.02 nmol/L (non-Chinese lab)
  - Negative: value < 0.4 U/mL (Chinese lab) or value ≤ 0.02 nmol/L (non-Chinese lab)
- Antibody status:
  - MuSK-Ab seropositive: MuSK-Ab seropositive (and LRP4-Ab either seropositive or seronegative)
  - LRP4-Ab seropositive: LRP4-Ab seropositive and MuSK-Ab seronegative
  - Triple seronegative: MuSK-Ab seronegative and LRP4-Ab seronegative (and AChR-Ab seronegative, per study inclusion criteria)

3.3.3 Presentation of results

Demographics will be summarized overall and by antibody status using descriptive statistics for age, height, body weight, and BMI. Frequency tabulations will be provided for age category, sex, weight category, BMI category, race category, ethnicity, and region. Additionally, the number of participants being considered a Chinese participant will be summarized. For weight and BMI (including categories) at baseline, the study baseline will be shown in part A and the pooled baseline in the part A+B analysis.

Baseline disease characteristics will be presented overall and by antibody status using descriptive statistics for time since diagnosis, MG-ADL total score (at screening and at baseline), QMG total score, MG-QoL15r total score and EQ-5D-5L VAS score at baseline; and frequency tabulations for MGFA Classification (at screening and at diagnosis), thymectomy, MuSK-Ab status, Anti-LRP4 status, antibody status, and MG-ADL and QMG total score categories (at baseline). For questionnaire scores at baseline, the study baseline will be shown in part A and the pooled baseline in the part A+B analysis.

All demographic data and baseline disease characteristics will be listed.

3.4 MEDICAL HISTORY AND CONCOMITANT DISEASES

3.4.1 Available data

Medical history and concomitant diseases findings are coded according to MedDRA into SOC and PT using version 28.0. For each finding, a start and stop date or ongoing flag is collected.

3.4.2 Derivation rules

Findings will be categorized as follows:

- Medical history finding: not ongoing at screening, ended before date of signing IC (end date prior to IC date or MHENRTPT = BEFORE)
- Concomitant disease finding: still ongoing at screening (no end date prior to IC date or MHENRTPT = ONGOING)

3.4.3 Presentation of results

Medical history and concomitant diseases will be tabulated in a separate output showing:

- The number and percentage of participants with findings
- The number and percentage of participants with findings by SOC and PT

All medical history and concomitant diseases data will be listed. A separate listing will be created for hospitalizations, including information of ER visits, and ICU admissions.

3.5 PRIOR AND CONCOMITANT THERAPY

3.5.1 Available data

All therapies are coded using the March 2025 version of the WHO-DRUG. ATC selection is performed. ATC coding up to level 4 is available in the clinical database. For each therapy, a start date or prior flag and stop date or ongoing flag are collected.

3.5.2 Derivation rules

Based on their start and stop dates, therapies will be allocated to one or both of the following categories with respect to the first IMP (for part A) or efgartigimod (for part A+B) dose date:

- Prior therapy: the therapy started before the first dose
- Concomitant: the therapy was taken on or after the first dose

Based on their start and stop date, therapies will be allocated to each analysis phase, period, and subperiod during which they were administered (see Section 2.3.1).

A medication that started before the first dose and continued during the study will be classified as both prior and concomitant. Therapies with (partially) missing dates will be allocated to both categories and each analysis phase, period, and subperiod unless the available parts of the therapy start or stop date or prior and ongoing flags provide evidence not to do so.

Additionally, MG-specific therapies (see Appendix 9.3) that started before the first dose (ie, prior MG therapies) will be allocated to one of the following categories:

- MG therapy stopped prior to ICF.
- Baseline MG therapy: MG therapy stopped on or after ICF.

Rescue medication will be identified based on the CMRTIND or PRRTIND flag.

3.5.3 Presentation of results

Prior and concomitant therapies will be tabulated (separately) by ATC class (level 1 and 3) and generic term. The table for prior therapies will exclude MG therapies. The table for concomitant therapies will include MG therapies.

Separate tables will be created for prior MG therapies and for baseline MG therapies. These tables will also show the number of participants with at least 1, 2, 3 etc. For baseline MG therapies, the number of participants per medication class (ie, steroids, NSIDs, and AChE inhibitors; see appendix 9.3) and the combination of classes will also be shown. MG therapies tables will be repeated by antibody status.

All prior and concomitant therapies data will be listed with detailed information about ATC classes. A separate listing will be created of participants receiving rescue medications.

Prior and concomitant procedures will be listed.

3.6 EXPOSURE TO IMP AND TREATMENT COMPLIANCE

3.6.1 Available data

For each IMP administration, the start and end date(times) and the volumes will be recorded.

3.6.2 Derivation rules

The following parameters will be derived:

- Total number of administrations: sum of all administrations of IMP (overall and by cycle, where applicable).
- The actual efgartigimod dose in mg/kg will be calculated as [(actual volume extracted from vials mL* 20 (mg/mL)) / (actual volume extracted from vials (mL)+ actual volume of NaCl solution added to IV bag (mL))]*[actual volume infused (mL)/last available participant weight (kg) before or at day of dosing]

  Note: For placebo kits, the actual dose will not be derived but will be considered 0 mg/kg.
- Any dose of efgartigimod IV that is 10% more than the planned dosage amount within a single infusion will be considered an overdose.
- Actual efgartigimod dose category:
  - <9 mg/kg (underdose)
  - 9-11 mg/kg
  - >11 mg/kg (overdose)
- Compliance (%) per treatment cycle = 100*(number of doses received / number of doses expected). For completed cycles, the expected number of doses is 4; for the last cycle of ongoing or discontinued participants, the number of expected doses is based on the number of treatment visits expected to have been performed up until the last performed visit.
- Compliance category:
  - <80%
  - 80-100%
  - >100%

3.6.3 Presentation of results

Exposure information will be presented using descriptive statistics for total number of administrations (overall), and compliance (by cycle) and frequency tabulations for the total number of administrations (by cycle), the actual efgartigimod dose category (by cycle and infusion), and the compliance category (by cycle).

All exposure data will be listed. Participants with an overdose of IMP will be listed.

4. EFFICACY, PHARMACOKINETIC, PHARMACODYNAMIC, AND IMMUNOGENICITY ANALYSES

4.1 EFFICACY AND QOL

4.1.1 Available data

Efficacy will be assessed using the MG-ADL, QMG, MGC, and [redacted]. A questionnaire with an assessment time of 00:00 means the time was unknown and the assessment time should therefor be considered as missing.

The MG-ADL scale is an 8-item instrument used to assess MG symptoms and their effects on daily activities. Each item is graded on 4-point symptom severity scale (0=normal to 3=most severe), with the total score ranging from 0 to 24 (CTP Section 8.2.1).

The QMG scale includes 13 items that measure endurance or fatigability and accounts for fluctuations in disease state. Each item is scored on a 4-point severity scale (0=no symptoms to 3=severe symptoms), with the total score ranging from 0 to 39 (CTP Section 8.2.2).

The MGC scale is a composite of 10 items measuring clinical status of participants with MG. Each item is graded on a 4-point symptom severity scale with higher scores indicating more severe symptoms. The total MGC score ranges from 0 (no symptoms) to 50 (maximum severity) (CTP Section 8.2.3).

[redacted]

Quality of life will be assessed by means of following questionnaires:

- MG-QoL15r (CTP Section 8.2.5)
- Neuro-QoL Short Form – Fatigue (CTP Section 8.2.6)
- PGI-S (CTP Section 8.2.7)
- PGI-C (CTP Section 8.2.7)
- EQ-5D-5L (CTP Section 8.2.8)

Participant satisfaction with efgartigimod will be assessed using TSQM-9 (CTP Section 8.2.9).

4.1.2 Derivation rules

For all references to weeks, analysis visits are considered as described in section 2.3.4 unless specified otherwise. If multiple assessments fall within the same analysis window, only the assessment closest to the target date based on the total score will be considered unless specified otherwise, other assessments within this window will only be listed and not considered in the below analyses.

4.1.2.1 PRIMARY ENDPOINT

The primary clinical question of interest is the following:

What is the difference in MG-ADL total score change from baseline to day 29 in part A in AChR-Ab seronegative participants with gMG administered efgartigimod IV vs placebo?

The following attributes describe the estimand:

1) Treatment condition: IMP (efgartigimod IV vs placebo)
2) Population: adults with AChR-Ab seronegative gMG
3) Variable (or endpoint): change from baseline at day 29 (week 4 analysis visit) in the MG-ADL total score in part A
4) ICEs:

ICE	Approach for dealing with the ICE
Initiating rescue therapy before week 4 analysis visit[a]	Treatment policy strategy: The occurrence of the ICE is considered irrelevant, and all data are taken as collected.
Discontinuing IMP for any reason	Treatment policy strategy: The occurrence of the ICE is considered irrelevant, and all data are taken as collected.

[a] 'The initiation of rescue therapy before week 4 analysis visit' is identified as ICE if the start date of the first intake of rescue therapy falls before the end of the week 4 analysis visit upper boundary

5) Population-level summary: the difference in mean changes between treatment conditions

A supplementary estimand, using a different ICE strategy, is defined:

ICE	Approach for dealing with the ICE
Initiating rescue therapy before week 4 analysis visit[a]	Hypothetical strategy: Data after the deviation are censored and imputed under the hypothetical condition in which rescue therapy was not administered[b]
Discontinuing IMP for any reason	Treatment policy strategy: The occurrence of the ICE is considered irrelevant, and all data are taken as collected.

[a] 'The initiation of rescue therapy before week 4 analysis visit' is identified as ICE if the start date of the first intake of rescue therapy falls before the end of the week 4 analysis visit upper boundary

[b] Per maximum likelihood method underlying MMRM

4.1.2.2 KEY SECONDARY ENDPOINTS (HIERARCHICAL TESTING)

The key secondary clinical questions of interest are the following:

1) What is the difference in QMG total score change from baseline to day 29 in part A in participants administered efgartigimod IV vs placebo?
2) What is the difference in proportion of participants who are both MG-ADL and QMG-responders in part A in participants administered efgartigimod IV vs placebo?
3) What is the difference in MG-ADL total score change from baseline to day 29 in part A in MuSK-Ab seropostive participants with gMG administered efgartigimod IV vs placebo?
4) What is the difference in MG-ADL total score change from baseline to day 29 in part A in triple seronegative participants with gMG administered efgartigimod IV vs placebo?

For the first key secondary endpoint, the attributes describing the estimands are similar to the primary endpoint (see Section 4.1.2.1).

For the second key secondary endpoint, the attributes describing the estimands are similar to the primary endpoint, with the exception of the ICEs and their strategies. These are defined as follows:

ICE	Approach for dealing with the ICE
Initiating rescue therapy	Composite strategy: Participant will be classified as a failure (nonresponder) if responder status was not achieved before the ICE.
Discontinuing IMP for any reason	Treatment policy strategy: The occurrence of the ICE is considered irrelevant, and all data are taken as collected.

A supplementary estimand, using a different ICE strategy, is defined:

ICE	Approach for dealing with the ICE
Initiating rescue therapy	Treatment policy strategy: Participants will be classified as a (non)responder using all data as collected, considering the occurrence of the ICE as irrelevant.
Discontinuing IMP for any reason	Treatment policy strategy: The occurrence of the ICE is considered irrelevant, and all data are taken as collected.

For the third and fourth key secondary endpoint, the attributes describing the estimands are similar to the primary endpoint (see Section 4.1.2.1, no supplementary estimands will be derived).

The MG-ADL and QMG total score will be used as collected; no recalculation will be performed.

A participant is considered an **MG-ADL responder** if there is a ≥2-point reduction in MG-ADL total score compared to baseline that is maintained for at least the next 4 consecutive weeks (ie, at least 5 consecutive measurements in a period of 4 weeks, handling intermittent missing assessments see Table 5) (see section 2.3.4) with the first reduction occurring no later than 1 week after the last IMP administration in part A.

A participant is considered a **QMG responder** if there is a ≥3-point reduction in the QMG total score compared to baseline that is maintained for at least the next 4 consecutive weeks (ie, at least 5 consecutive measurements in a period of 4 weeks, handling intermittent missing assessments see Table 5) (see section 2.3.4) with the first reduction occurring no later than 1 week after the last IMP administration in part A.

The following rules are intended for the handling of missing values (after handling of ICEs) in the derivation of the MG-ADL or QMG responder status:

- *Intermittent* missing data at only 1 of 4 postonset (O) consecutive analysis windows: if the missing data follows one of the following score patterns: OmXXX, OXmXX, OXXmX or OXXXmX, then the participant will be considered as having achieved a response (see Table 5). If no such pattern is present, the participant will be considered as not having achieved a response
- Intermittent missing data following onset of response at 2 or more of 4 consecutive postonset analysis windows: the participant will be considered as not having achieved a sustained response

Table 5: Handling of intermittent missing data for MG-ADL or QMG response

Reason for missing data	Score change pattern[a]	Interpretation (binary response)
Missing data at 1 visit after onset of response	OmXXX, OXmXX, OXXmX, OXXXmX	Responder
	mOXXX, OXXXmY	Nonresponder
Missing data at 2 or more of 4 consecutive postonset analysis visits	NA	Nonresponder
Missing data not covered by above scenarios	NA	Nonresponder

m = missing value;
X = decrease of at least 2 points on the MG-ADL total score/decrease of at least 3 points on the QMG total score;
Y = increase or decrease of less than 2 points in MG-ADL total score/increase or decrease of less than 3 points in QMG total score;
O = onset of decrease of at least 2 points on the MG-ADL total score/onset of decrease of at least 3 points on the QMG total score;
[a] A sequence of nonresponse will be overruled if a participant also fulfils the criteria of being a responder with onset at any time at or before 1 week after the last IMP administration.

A participant is considered an **MG-ADL and QMG responder** if the participant is both an MG-ADL responder and a QMG responder. This response is further referred to as "MG-ADL/QMG responder" in tables and listings.

4.1.2.3 SECONDARY ENDPOINTS (NONHIERARCHICAL TESTING)

For these secondary efficacy endpoints no estimands are defined. They will be derived as follows:

- Proportion of MG-ADL and/or QMG responders in part A (see section 4.1.2.2). Characterization of MG-ADL and/or QMG responders to be derived:

- Onset (first drop in the sequence of at least 4 week/5 assessments)
- Magnitude of response (maximum drop from baseline within the duration of response - see note)
- Minimum post-baseline value (within the duration of response - see note)
- Percentage of early responders (onset of response no later than 2 weeks after the first administration of IMP)

Note: response starts with the first drop in the sequence of at least 4 week/5 assessments and ends with the first drop <2/<3 after the onset

- MG-ADL total score actual value and change from baseline over time in part A and part A+B will be analyzed descriptively and categorically.

  Categories to be used for actual values: 0, 1, 2, 3, 4, 5-7, 8-9, 10-12, 13-16, 17-20 and 21-24.

  Categories to be used for changes from baseline: >0, 0, -1, -2, -3, -4, -5, -6, -7, -8, -9, -10, <-10.

  Of note, MSE is defined as an MG-ADL total score of 0 or 1.
- QMG total score actual value and change from baseline over time in part A and part A+B will be analyzed descriptively and categorically.

  Categories to be used for actual values: 0, 1, 2, 3, 4, 5-7, 8-9, 10-12, 13-16, 17-20, 21-24, and ≥25.

  Categories to be used for changes from baseline: >0, 0, -1, -2, -3, -4, -5, -6, -7, -8, -9, -10, <-10.
- MG-QoL15r total score actual values and change from baseline over time in part A and part A+B
- EQ-5D-5L VAS actual value and change from baseline over time in part A and part A+B

4.1.2.4 EXPLORATORY ENDPOINTS

The following exploratory efficacy endpoints will be derived:

- AUEC of change from baseline in MG-ADL total score for the following intervals (see derivation details below):
  - Day 1 through Day 8 (Baseline - Week1)
  - Day 8 through Day 15 (Week 1 - Week 2)
  - Day 15 through Day 22 (Week 2 - Week 3)
  - Day 22 through Day 29 (Week 3 - Week 4)
  - Day 1 through Day 29 (Baseline - Week 4)
  - Day 1 through the end of part A (Baseline - Week 8)

- AUEC of change from baseline in QMG total score for the same intervals as above (see derivation details below).
- MGC total score actual value and change from baseline over time in part A and part A+B
- Neuro-QoL Short Form - Fatigue T-score actual value and change from baseline over time in part A and part A+B

  Character results for the individual Neuro-QoL questions will be mapped to their numerical equivalent: never (1), rarely (2), sometimes (3), often (4), always (5). The total raw score can be calculated as follows in case at least 50% of the items were answered: 8*(sum of all answers/number of items answered). The corresponding T-score can be derived using the table in appendix 9.1.
- [redacted]
- Proportion of participants in each change category in EQ-5D-5L (per domain) at each postbaseline analysis visit:
  - Worsened: postbaseline score is higher than baseline score
  - No change: postbaseline score is equal to baseline score
  - Improved: postbaseline score is lower than baseline score

  Note: The lowest score is 1 'no problem' and the highest is 5 'unable/severe'.
- Proportion of participants in each category of PGI-S and PGI-C in part A and part A+B
- Proportion of participants in each change category in PGI-S at each postbaseline analysis visit:
  - Worsened: postbaseline score is higher than baseline score
  - No change: postbaseline score is equal to baseline score
  - Improved: postbaseline score is lower than baseline score

  Note: The lowest score is 1 'none' and the highest is 5 'very severe'.

- TSQM-9 domain scores in part A+B
  The TSQM-9 is a 9-item questionnaire that measures a participant's satisfaction with their treatment. Participant satisfaction is assessed across 3 categories:
  - Global satisfaction:
    - No missing items: ([Sum(Item 7 to Item 9) – 3] / 14) * 100
    - Item 7 or 8 missing: ([(Sum(the two completed items)) – 2] / 10) * 100
    - Item 9 missing: ([(Sum(Item7 and Item8)) – 2] / 8) * 100
  - Effectiveness,
    - No missing items: ([Sum(Item 1 to Item 3) – 3] / 18) * 100
    - 1 missing item: ([(Sum(the two completed items)) – 2] / 12) * 100
  - Convenience
    - No missing items: ([Sum(Item 4 to Item 6) – 3] / 18) * 100
    - 1 missing item: ([(Sum(the two completed items)) – 2] / 12) * 100

  Domain scores will be rounded as detailed in section 2.4.3

AUEC will be calculated using the linear trapezoidal rule, by summing all individual trapezoids, which will be calculated as follows:

$AUEC_{ti\text{-}ti+1} = 1/2*(CFB_i + CFB_{i+1})*(t_{i+1} – t_i)$.

Where:

- CFB_i is the change from baseline at time point t_i (in days). The change from baseline on day 1 (baseline) is 0.
- Only analysis visits as used in descriptive statistics tables (ie, with ADY closest to target ADY) will be considered.
- AUEC will be calculated in days, using actual dates of assessments.
- AUEC will be rounded as detailed in section 2.4.3.

In case the start or end visit of the interval is missing, the AUEC will not be derived.

In case 2 or more consecutive visits are missing within the AUEC interval (ie, in between the start and end visit of the AUEC interval), the AUEC will not be derived.

4.1.3 Presentation of results and statistical analysis

All efficacy and quality of life analyses for part A will be done using the ITT analysis set. For part A+B, the safety analysis set (part A+B) will be used.

All statistical comparisons will be made using two-sided tests at the 0.10 significance level unless specifically stated otherwise.

All efficacy, TSQM-9 and quality of life data will be listed.

4.1.3.1 PRIMARY ENDPOINT

An MMRM approach will be used to model the primary endpoint (change from baseline in the MG-ADL total score at week 1 through week 4 in part A) while assuming an unstructured variance-covariance structure for the repeated measures from a participant. The model will include the baseline MG-ADL total score as a covariate, the analysis visit, treatment arm, and MuSK-Ab status (as defined in 3.3.2)

as factors, and the interaction term between the treatment arm and the analysis visit. LS means and SE with 90% 2-sided CI for placebo and efgartigimod IV will be reported, along with the difference in LS means of efgartigimod IV vs placebo (with SE), 90% 2-sided CI, and 2-sided p-value. The Kenward-Roger approach will be used to estimate the denominator degrees of freedom.

If the default Newton–Raphson algorithm used by SAS PROC MIXED fails to converge, the following steps will be taken to avoid lack of convergence while maintaining an unstructured covariance:

1) The Fisher scoring algorithm (via the SCORING=5 option of the PROC MIXED statement) will be used to obtain the initial values of covariance parameters.
2) If the above fails, the no-diagonal factor analytic structure will be used, which effectively performs the Cholesky decomposition via the TYPE=FA0(V) option of the REPEATED statement, where V is the total number of distinct visits in the response vector (counting only rows where all model components are nonmissing).
3) If all of the above fail, the variance-and-correlations parameterization will be attempted using TYPE=UNR.

In the rare case where all of the above steps fail, the following covariance structures will be tested for convergence (in order): ANTE(1), TOEPH, ARH(1), CSH, TOEP, AR(1), and CS. However, if one of these simpler covariance structures is used, this needs to be implemented in combination with sandwich variance estimator (EMPIRICAL option).

After handling ICEs as described, all randomized participants with a baseline MG-ADL total score and ≥1 postbaseline MG-ADL total score at or before week 4 will be included in the MMRM. Supplementary analysis will be done using an alternative estimand approach for handling ICEs (see Section 4.1.2.1).

A sensitivity analysis on the primary endpoint will be performed to account for missing data. All missing MG-ADL assessments after handling ICEs will be imputed using a jump-to-refence imputation strategy: missing values of a participant will be imputed using the estimated marginal mean of the study's reference arm at the corresponding participant's missing visits.

The imputation strategy will be implemented adopting the MI procedure as described by Carpenter et al.[10]:

1) Using a Bayesian approach based on MCMC sampling, posterior parameter estimates will be drawn from a MMRM model.
2) Imputed datasets will be generated using the draws from the previous step.

   The J2R method was implemented as follows:

   For participants in the placebo arm all missing values will be imputed under the Missing At Random (MAR) assumption.

   For participants in the active treatment arm, imputed values will be adjusted by removing the estimated treatment effect at each visit (from the corresponding posterior sample), thereby assuming participants would behave like those in the placebo group.

   A statistical analysis will be run on each imputed dataset.

3) Results will be pooled based on Rubin's rules to obtain an overall estimation of the treatment effect.

Multiplicity adjustment will be applied as described in Section 1.3.1.

The main analysis of the primary endpoint will be repeated using MuSK-Ab status as randomized, as well as by antibody status (third and fourth key secondary endpoints). The table will also be repeated for the following subgroup variables: age category, region, sex, race, baseline MG-ADL total score category (see 3.3.2), and MusK-Ab status (as defined in 3.3.2). For subgroup analyses, the studied subgroup and all interactions with visit and treatment will be added to the model. For the model "by Antibody status" only, the MuSK-Ab status should be removed from the list of covariates.The LS mean difference will be calculated using observed margins of baseline covariates (including the studied subgroup) in the population at baseline. Based on this model, the estimates of the endpoint at week 4 (with 90% CI) for each subgroup in each treatment group, and the treament difference estimates with the 90% CI in each subgroup will be displayed. Categories of a subgroup with less than 10 participants in the category will not be tabulated (but still included in the model). Additionally, in the event of a potential unblinding during the study, a sensitivity analysis on the overall AChR-Ab seronegative population will be performed removing any participants affected by such event as identified in the database..

4.1.3.2 KEY SECONDARY ENDPOINTS (HIERARCHICAL TESTING)

The first key secondary endpoint will be analyzed in a similar fashion as the primary endpoint.

The proportion of MG-ADL/QMG responders in efgartigimod IV and placebo arms in part A will be compared using a stratified CMH test with the stratification factor MuSK-Ab status (as defined in 3.3.2); a strata-adjusted difference in proportions with its 90% CI and 2-sided p-value and an adjusted common OR with its 90% confidence interval will be provided. For the difference in proportions, stratified confidence limits will be obtained using the Klingenberg approach that uses Mantel-Haenszel weights to combine the stratum components.

Supplementary analysis will be done using an alternative estimand approach for handling ICEs (see Section 4.1.2.2).

Multiplicity adjustment will be applied as described in Section 1.3.1.

The main analysis of the first and second key secondary endpoints will be repeated by antibody status (excluding anti-LRP4 seropositive participants from the CMH; with nominal p-values).

4.1.3.3 SECONDARY (NON-HIERARCHICAL TESTING) AND EXPLORATORY ENDPOINTS

The MG-QoL15r total score change from baseline at day 29 in part A will be analyzed in a similar fashion to the main analysis of the primary endpoint (with nominal p-values).

Actual values and changes from baseline (study baseline for part A, pooled and cycle baseline for part A+B) for the continuous variables will be summarized descriptively by analysis visit for part A and by analysis visit and cycle for part A+B. For MG-ADL and QMG total scores, the best response (see section 2.3.6) will also be shown.

The tables for part A will include 90% confidence limits for the difference in change between the two treatment arms based on a 2-sample t-test (using Satterthwaite's approximation). For MG-ADL and QMG total scores, descriptive statistics will be repeated by antibody status.

For TSQM-9, only actual values of the domain scores will be summarized descriptively.

Frequency tabulations for the categorical variables in part A and part A+B will include cumulative percentages (except for binary variables and PGI-C). Frequency tabulations for the MG-ADL and QMG categories will also show the best response (see section 2.3.6) and repeated by antibody status. Frequency tabulations of (early) MG-ADL and QMG responders will be tabulated overall and by antibody status. Tables by antibody status will include an Agresti-Min CI for the difference. Overall tables will include either an Agresti-Min CI (in case of <30 participants in one of the treatment arms) or a Newcombe CI (in case of ≥30 participants in each treatment arm) for the difference. The proportion of MG-ADL and/or QMG responders in part A will also be compared using a stratified CMH test, in a similar fashion to the main analysis of the second key secondary endpoint (MG-ADL/QMG response) (with nominal p-values).

For MG-ADL, QMG and MG-ADL/QMG responders, a table showing the characterization of responders will be prepared: number of responders, onset of response (frequency in weeks), magnitude of response (descriptive statistics and frequency), minimum post-baseline value (descriptive statistics and frequency) and early responder (yes/no, frequency).

For Part A analysis only, EQ-5D-5L and PGI-S results will also be presented as cross-tabulations of the result at each postbaseline analysis visit versus the study baseline result. Finally, frequency tabulations of the EQ-5D-5L and PGI-S change categories at each postbaseline analysis visit will be created. For EQ-5D-5L, these tables will be created by domain.

4.2 PHARMACOKINETICS

4.2.1 Available data

Blood samples will be collected for the determination of efgartigimod concentration at the time points indicated in the schedule of assessments (see section 9.5).

Time windows for PK samples are specified as follows:

- Dosing days:
  - predose PK sample: within 2 hours before the start of the infusion
  - postdose PK sample: within 1 hour after the end of the infusion
- Non-dosing days: +/- 2 days

4.2.2 Derivation rules

The following PK samples will be excluded from the descriptive statistics:

- When a predose sample is taken after IMP administration.
- When the IMP administration before the scheduled PK sample is missed (not applicable for the participant's first efgartigimod administration):
  - When visit (X-1) IMP administration is missed, visit X **predose** PK sample will be excluded.
- When PK samples are taken outside the visit windows (not applicable for the sample taken prior to the participant's first efgartigimod administration).

4.2.3 Presentation of results

Concentration data will be summarized using descriptive statistics at each analysis visit by cycle and scheduled time point (if applicable), overall and by antibody status.

Individual concentration data and actual blood sampling times from start of infusion for PK assessments will be listed. Samples excluded from the summaries will be flagged in the listings and the reason for exclusion will be added.

4.3 PHARMACODYNAMICS

4.3.1 Available data

The following PD parameters will be measured:

- Total IgG
- [redacted]

4.3.2 Derivation rules

Percent changes (compared to study, pooled or cycle baseline, where applicable) at each visit (by cycle, where applicable) will be derived for total IgG level only.

BQL or AQL values will be handled as described in section 2.4.2.

4.3.3 Derivation rules

Summary statistics will be provided for total IgG only in terms of actual values and percent changes from study/pooled/cycle baseline for each analysis visit. Total IgG tables will be provided by antibody status and overall, excluding values per cycle after rescue therapy during that cycle from the descriptive analyses. For the IDMC analysis, summary statistics in terms of actual values in total IgG will be provided, including all values.

All actual values and percent change from baseline in total IgG and actual values in MuSK-Ab level values will be listed.

4.4 IMMUNOGENICITY

4.4.1 Available data

ADA to efgartigimod is measured per schedule of assessment (see section 9.5). Samples in part A will not be analyzed for the placebo arm.

Immunogenicity samples are analyzed in a 3-tiered approach:

- All samples are evaluated in the ADA screening assay and are scored ADA screening positive or negative
- If a sample scored positive in the ADA screening assay, it is further evaluated in the confirmatory assay and is scored confirmed positive (positive immuno-depletion) or confirmed negative (negative immuno-depletion)
- If a sample is scored as confirmed positive, the samples are further characterized in the ADA titration assay (to determine titer) and are also further analyzed in the NAb assay to confirm neutralizing activity (positive or negative). For NAb against efgartigimod, a screening assay is performed and the results are reported as negative or positive.

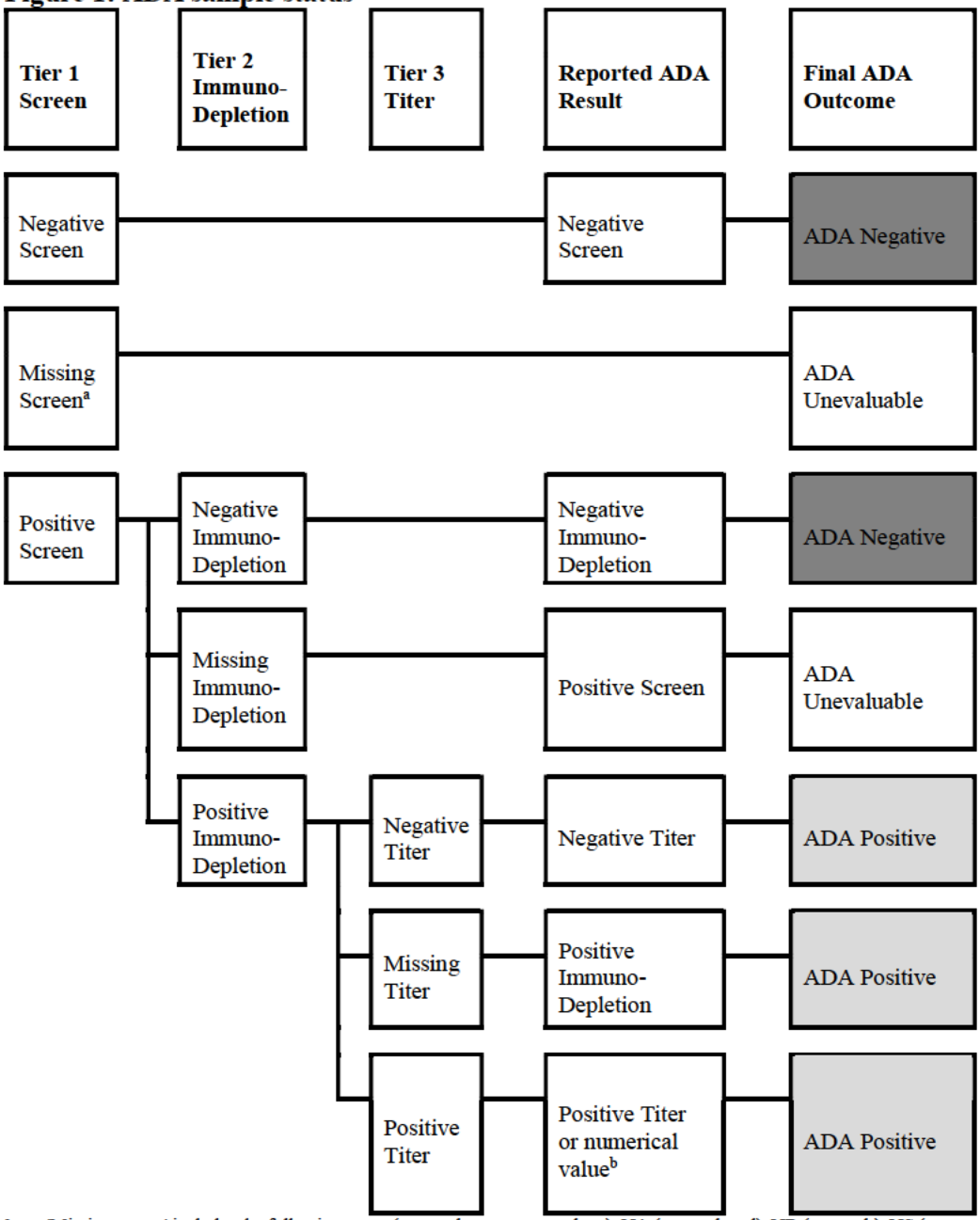
If a sample could not be analyzed or is reported as 'positive screen', the ADA sample status is ADA unevaluable.

If available, a titer result will be reported for the ADA confirmed positive samples. However, a titer result is not always available:

- In case the ADA confirmed positive sample could not be run in the titration assay (eg, due to insufficient sample volume/quality to perform the titer analysis), the result will be described as 'positive immuno-depletion' and the sample should be considered ADA positive.
- If a sample is negative in the titration assay, it will be reported as 'negative titer' but it should be considered ADA positive since it was confirmed positive in the second tier.

An overview of this 3-tiered approach and all possible ADA sample results that will be reported by the laboratory is given in Figure 1. From these reported ADA sample results a final ADA sample status needs to be derived during the statistical analysis, as presented in the final column ('Final ADA Outcome'):

Figure 1: ADA sample status



[a] 'Missing screen' includes the following terms (reported as reason not done): NA (not analyzed), NR (no result), NS (no sample), and SL (sample lost). More details can be found in the IS data transfer agreement from the specialty labs to SGS SD office.

[b] 'Positive titer' is reported in case it was not possible to retrieve a numerical value.

4.4.2 Derivation rules

The participant classifications described in the sections below will be derived by cycle and overall for part A+B.

4.4.2.1 PARTICIPANT CLASSIFICATION FOR ADA AGAINST EFGARTIGIMOD

Table 6 below gives an overview of how the ADA participant classification will be derived, starting from the participant pooled baseline ADA sample status. See also section 4.4.1:

Table 6: Participant classification for ADA against efgartigimod

Participant ADA classification	**Highest[a] post baseline[e] sample status**				
	ADA negative	**ADA positive (missing titer[b])**	**ADA positive (negative titer[c] or numerical titer)**		**ADA unevaluable**
Baseline ADA sample status					
ADA negative	ADA negative	Treatment-induced ADA	Treatment-induced ADA		*ADA unevaluable*
ADA positive (missing titer[b])	Treatment-unaffected ADA	*ADA unevaluable*	*ADA unevaluable*		*ADA unevaluable*
ADA positive (negative titer[c] or numerical titer)	Treatment-unaffected ADA	*ADA unevaluable*	**titer < 4x baseline titer:** Treatment-unaffected ADA	**titer ≥ 4x baseline titer:** Treatment-boosted ADA[d]	*ADA unevaluable*
ADA unevaluable	*ADA unevaluable*	*ADA unevaluable*	*ADA unevaluable*		*ADA unevaluable*

ADA = antidrug antibodies

[a] Highest sample status, with order: (from low to high): ADA unevaluable, ADA negative, ADA positive (positive immuno-depletion or positive titer), ADA positive with titer <1 (negative titer), ADA positive with titer ≥1 (numerical value selecting the sample with highest titer);

[b] Samples with missing titer will have a reported ADA result of 'positive immuno-depletion' or 'positive titer';

[c] Results reported as 'negative titer' or '<1' will be set to value of 1;

[d] A 4-fold difference in titer values is considered significant in case a 2-fold serial dilution is applied (= two times the dilution factor)[5].

[e] Within the cycle in part A+B /within part A+B

The following definitions will be used in the summary tables:

- ADA evaluable participant = participant classified as any of following categories: ADA negative, treatment-unaffected ADA, treatment-induced ADA, treatment-boosted ADA. The first two categories are classified as 'ADA negative', and the latter two as 'ADA positive'.
- ADA unevaluable participant = participant classified as ADA unevaluable or with missing baseline ADA sample or without postbaseline ADA samples (in case no ADA data are available at all, the participant cannot be classified)
- ADA incidence = percentage of participants with treatment-induced or treatment-boosted ADA (denominator: number of evaluable participants)
- ADA prevalence = percentage of participants with treatment-unaffected ADA, treatment-induced ADA or treatment-boosted ADA (denominator: number of evaluable participants)

4.4.2.2 *PARTICIPANT CLASSIFICATION FOR NAB AGAINST EFGARTIGIMOD*

All ADA confirmed positive samples will also be evaluated in the NAb assay. All samples that were not analyzed in the NAb assay (ie, the ADA negatives) are per default NAb negative. Additionally, if a NAb sample is not reported for ADA confirmed positive samples, the NAb sample status is NAb unevaluable.

All samples evaluated in the NAb assay will be scored as NAb positive, NAb negative, or NAb unevaluable by the laboratory. Based on these results, the participants will be categorized according to their pooled baseline and postbaseline sample status as detailed in Table 7.

Table 7: Participant classification for NAb against efgartigimod

Participant NAb classification	Highest[a] post baseline[b] NAb sample status		
	NAb negative	**NAb positive**	**NAb unevaluable**
Baseline NAb sample status			
NAb negative	baseline neg – postbaseline neg	baseline neg – postbaseline pos	*NAb unevaluable*
NAb positive	baseline pos – postbaseline neg	baseline pos – postbaseline pos	*NAb unevaluable*
NAb unevaluable	*NAb unevaluable*	*NAb unevaluable*	*NAb unevaluable*

NAb = neutralizing antibody; neg = negative; pos = positive
[a] Highest sample status in order: (from low to high): NAb unevaluable, NAb negative, NAb positive.
[b] Within the cycle in part A+B /within part A+B

The following definitions will be used in the summary tables:

- NAb unevaluable participant = participant classified as NAb unevaluable or with missing baseline NAb sample or without postbaseline NAb samples (in case no NAb data are available at all, the participant cannot be classified)
- NAb incidence = percentage of participant with participant classification 'baseline neg – postbaseline pos' or 'baseline pos – postbaseline pos' (denominator: number of evaluable participants)
- NAb prevalence = percentage of participant with participant classification 'baseline neg – postbaseline pos', 'baseline pos – postbaseline pos' or 'baseline pos – postbaseline neg' (denominator: number of evaluable participants)

4.4.3 *Presentation of results*

The safety analysis set (part A+B) will be used for the immunogenicity evaluation. Analysis will be performed for ADA against efgartigimod.

Frequency tabulations (number and percentages) will be provided with ADA negative/positive/unevaluable samples per analysis visit and by ADA participant classification.

Frequency tabulations (number and percentages) for ADA against efgartigimod will be provided by cycle and overall for:

- ADA evaluable and unevaluable participants
- ADA pooled baseline sample status
- ADA participant classification
- incidence and prevalence of ADA

For details on the definitions, see the above section 4.4.2.1.

The above frequency tabulations will be repeated for NAb assay using the definitions as defined in section 4.4.2.2.

In addition, a frequency tabulation (number and percentages) will be provided for Nab against efgartigimod positive participants within efgartigimod overall ADA participants classification (treatment-unaffected ADA, treatment-induced ADA, treatment-boosted ADA, ADA negative and ADA unevaluable).

Correlation tables by cycle ADA against efgartigimod and cycle NAb against efgartigimod participant classification will be provided for the following parameters:

- Actual values and changes from baseline in MG-ADL total score over time
- Drug concentration over time
- Actual values and percent change from baseline in total IgG over time
- TEAEs by MedDRA SOC and PT
- Serious TEAEs by MedDRA SOC and PT
- IRRs

Correlation tables by cycle NAb against efgartigimod participant classification only need to be provided as soon as there are at least 5 participants in the sum of baseline negative – postbaseline positive and baseline positive – postbaseline positive NAb positive categories in (one of) the treatment arms. Correlation tables will be provided for the efgartigimod-efgartigimod arm (first cycle only) and the total arm (all cycles) by cycle (and overall, where applicable).

ADA against efgartigimod titer values will be summarized by means of descriptive statistics by overall ADA participant classification by analysis visit and cycle.

All available data on ADA and NAb against efgartigimod will be listed, while also showing the sample status and participant classification.

5. SAFETY ANALYSES

5.1 ADVERSE EVENTS

5.1.1 Available data

AEs are coded according to MedDRA into SOC and PT using version 28.0. AEs were graded using the NCI CTCAE v5.07. For each AE, start and stop date(time)s are collected as well as severity, a seriousness flag, treatment-relatedness, relatedness to procedures, action taken towards the IMP and outcome.

5.1.2 Derivation rules

TEAE are defined as AEs with onset on or after the first administration of IMP/efgartigimod for the part A/part A+B analysis, respectively.

AEs will be considered treatment-emergent based on their start date(time). If the AE start date(time) is incomplete or missing, the AE will be considered treatment-emergent unless the available part of the AE start or stop date(time) provide evidence not to do so. For the part A+B analysis, the AE will also be allocated to the first cycle that is possible based on the available part of the AE start and stop date(time). Cycles are defined in section 2.3.1. No imputation of missing/incomplete dates will be done.

A death case is defined as an AE with outcome ‘fatal’.

An AE for which the study drug was discontinued is defined as an AE with action taken ‘drug withdrawn’.

If treatment-relationship is missing it is considered treatment related.

IRRs are defined as all AEs with a MedDRA PT that is listed in either:

- MedDRA Hypersensitivity SMQ broad selection
- MedDRA Anaphylactic reaction SMQ broad selection
- MedDRA Extravasation events (injections, infusions and implants) SMQ broad selection, excluding implants

AND occurs within 48 hours of an infusion, or within 2 days if the AE start time is not available. If the AE start date is incomplete, the AE will be considered as an IRR, unless the available parts of the AE start date provide evidence it did not occur within 48 hours of an infusion.

Within the efgartigimod program, infections are considered AESIs and are defined as events with a PT that falls under the MedDRA SOC ‘Infections and infestations’.

AE onset, day since last administration, and duration will be calculated as follows when start and stop dates are fully known:

- AE onset day (vs first administration) =
    - AE start date ≥ date of first administration: AE start date – date of first IMP/efgartigimod administration + 1 day
    - AE start date < date of first administration: AE start date – date of first IMP/efgartigimod administration

- AE onset day (vs start of cycle) = AE start date - cycle start date + 1 day
- Day since last administration: AE start date - date of last IMP before AE start date
- AE duration (days) =
  - AE end date – AE start date + 1 day
  - End of study date – AE start date + 1 day (when the AE start date is fully known but the AE is not resolved at the end of the study)

    In this case, the duration will be presented as ">x days" in listings. For ongoing participants (interim and IDMC analysis) who have an ongoing AE, the same approach will be taken using the clinical data cutoff date (interim analysis) or database snapshot date (IDMC analysis).

If start and stop date are not fully known, then AE onset, day since last administration and duration will be missing, as appropriate.

Event rates per 100 PYFU is defined as 100 * the number of events divided by the sum of follow-up time during which an event is considered treatment-emergent of all participants per treatment arm expressed in years (ie, divided by 365.25).

5.1.3 Presentation of results

Summary tables will present TEAEs only. However, all AEs reported during the study will be listed. Summary tables by SOC and PT will be sorted alphabetically. Part A+B tables will be presented by cycle and overall.

An overview table overall (and by cohort and cycle within the cohort, where applicable) will show the number and percentage of participants with at least one event, the number of events and the event rates per 100 PYFU for the following:

- TEAEs
- Serious TEAEs
- Grade ≥ 3 TEAEs
- Fatal TEAEs
- Treatment-related TEAEs according to PI
- Procedure-related TEAEs according to PI
- Serious treatment-related TEAEs according to PI
- TEAEs leading to IMP discontinuation
- TEAEs leading to IMP interruption
- TEAEs of special interest
- IRRs

For the part A analysis, the overview table will also include a 95% Agresti-Min CI (if <30 participants in each group - eg, for IDMC analyses) or the 95% Newcombe CI (if >=30 participants in each group) for the difference in AE rate between efgartigimod and placebo.

For the part A+B analysis the overview table will also include a 95% Clopper-Pearson CI for the percentage of participants with events.

Summary tables by MedDRA SOC and PT will include the number and percentage of participants with at least one event and the number of events (except for tables by worst toxicity). Each AE record in the clinical database is considered as a distinct adverse event and is counted as such.

These tables will be provided for:

- TEAEs (by cohort and cycle within the cohort, where applicable)
- Serious TEAEs (by cohort and cycle within the cohort, where applicable)
- Nonserious TEAEs
- Grade ≥ 3 TEAEs (by cohort and cycle within the cohort, where applicable)
- TEAEs by worst toxicity
- Treatment-related TEAEs
- Procedure-related TEAEs
- Serious treatment-related TEAEs
- TEAEs leading to IMP discontinuation (by cohort and cycle within the cohort, where applicable)
- TEAEs leading to IMP interruption
- TEAEs of special interest (by cohort and cycle within the cohort, where applicable)
- Grade ≥ 3 TEAEs of special interest
- IRRs
- serious IRRs

Note: only show 'all participants in a cycle' cohort for IDMC analyses.

All AEs, including pre-treatment events will be listed. Separate listings will be prepared for serious AEs, fatal AEs, AEs leading to IMP discontinuation or interruption, AESIs and IRR. A listing showing all coding information will be prepared as well.

5.2 CLINICAL LABORATORY EVALUATION

5.2.1 Available data

Per protocol, the following safety laboratory parameters are expected:

- Biochemistry: creatinine, BUN, ALT, AST, total and direct bilirubin, GGT, CRP, ALP, albumin, potassium, sodium, calcium, glucose (nonfasting)
- Hematology: platelet count, RBC count, hemoglobin, hematocrit, RBC indices (MCV, MCH, %reticulocytes), white blood cell count with differential (% and absolute numbers of neutrophils, lymphocytes, monocytes, eosinophils, basophils)
- Urinalysis:
    - Continuous: specific gravity, pH
    - Categorical: glucose, protein, blood, ketones, bilirubin, urobilinogen, nitrite, leukocyte esterase by dipstick, highly sensitive serum hCG pregnancy test at screening and urine test at other time points (for female participants of childbearing potential), microscopic evaluation

For each laboratory record, laboratory test, test result in standardized unit, sample date(time) and clinical significance as assessed by the investigator are collected. Normal ranges are available as provided by the laboratory.

5.2.2 Derivation rules

The following parameters will be derived if not available in the clinical database:

- eGFR (CKD-EPI[6]) (mL/min/1.73m²) = 141 * minimum(creatinine (µmol/L)/(88.4*K); 1)$^{\alpha}$ * maximum(creatinine (µmol/L)/(88.4*K); 1)$^{-1.209}$ * 0.993$^{age\ (years)}$ * [1.018 if female] * [1.159 if race = black]

  where K = 0.7 if female and K = 0.9 if male; α = -0.329 if female and α = -0.411 if male; age = age at IC

The following abnormality categories will be defined for parameters with no toxicity grade available:

- Low: value < lower limit of normal range
- Normal: lower limit of normal range ≤ value ≤ upper limit of normal range
- High: value > upper limit of normal range

Notes:

- Classification will be performed in standardized units, using nonimputed values and limits.
- For the worst-case analysis visit, as defined in section 2.3.5, an additional category low + high is defined if there are both low and high postbaseline values
- All results will be used, both from fasted and nonfasted samples.
- Abnormalities will not be derived for categorical results.

Toxicity grades will be computed according to the NCI CTCAE toxicity grading list (version 5.0)[7]. The implementation of these toxicity grades for analysis is presented in appendix 9.4. Only the parameters described in appendix 9.4 will be computed, according to the declared limits for each grade.

5.2.3 Presentation of results

All tables will only show analysis visits and parameters as expected per SoA.

Only continuous laboratory parameters expected per protocol will be tabulated. The statistical analysis will present results in standardized units, except for eGFR, which will be reported in mL/min/1.73m^2.

Continuous laboratory parameters will be summarized using descriptive statistics at each analysis visit (by cycle, where applicable). Actual values and changes from baseline (study baseline for part A and pooled baseline for part A+B) will be shown in the same table. Categorical parameters will be listed only.

Laboratory abnormalities will be presented as cross-tabulations of the abnormality at each postbaseline analysis visit and at the worst-case analysis visit versus the baseline (study baseline for part A and pooled baseline for part A+B) abnormality. The number of participants with treatment-emergent abnormalities will also be shown (see Definition of terms). Parameters for which toxicity grades are defined will not be included in the abnormalities tables. The denominator for the percentage is the total

number of participants with nonmissing data for the parameter, treatment arm, and analysis visit in the PAS.

Laboratory toxicity grades will be presented as cross-tabulations of the toxicity at each postbaseline analysis visit and at the worst-case analysis visit versus the baseline toxicity (study baseline for part A and pooled baseline for part A+B). Numbers and cumulative numbers over decreasing toxicity grading of participants with treatment-emergent toxicities will also be shown. The denominator for the percentage is the total number of participants with nonmissing data for the parameter, treatment arm, and analysis visit in the PAS. Parameters with toxicity grades defined in both directions (hypo and hyper) will be shown by direction.

All laboratory data will be listed, including screening tests and laboratory tests not foreseen per protocol, but only for participants with any postbaseline abnormality or toxicity grade ≥1. For the IDMC analysis, laboratory data will only be listed for participants with any postbaseline toxicity grade ≥3. An additional listing will be created, selecting participants with all of following three criteria (Hy's law) met in a same assessment: 1) ALT or AST >3*ULN 2) total bilirubin ≥2*ULN 3) ALP <2*ULN[9]. In this listing, the following parameters will be shown: ALT, AST, ALP, GGT, and total bilirubin.

For the IDMC analyses only, boxplots (including mean value) of actual values by analysis visit and cycle will be prepared for the following subset of lab parameters: leukocyte count, lymphocyte count, albumin, eGFR, ALT, AST, and bilirubin.

5.3 VITAL SIGNS

5.3.1 Available data

The following vital signs parameters are collected: SBP and DBP in semisupine position, pulse rate, body temperature and weight.

For each vital sign record, parameter name, test result and unit, assessment date(time), and clinical significance as assessed by the investigator are collected.

5.3.2 Derivation rules

Abnormalities are defined in Table 8 below.

Table 8: Criteria to define vital signs abnormalities

	Pulse rate (bpm)	SBP (mmHg)	DBP (mmHg)	Temperature (°C)
Low	<50	<90	<45	<35.8
Normal	50-100	90-140	45-90	35.8-37.5
High	>100	>140	>90	>37.5

Note: For the worst-case analysis visit, as defined in section 2.3.5, an additional category low + high is defined if there are both low and high postbaseline values.

5.3.3 Presentation of results

All tables will only show analysis visits and parameters as expected per SoA.

Vital signs parameters will be summarized using descriptive statistics at each analysis visit (by cycle, where applicable). Actual values and changes from baseline (study

baseline for part A and pooled baseline for part A+B) will be shown in the same table.

Abnormalities will be presented as cross-tabulations of the abnormality at each postbaseline analysis visit and at the worst-case analysis visit versus the baseline abnormality (study baseline for part A and pooled baseline for part A+B). The number of participants with treatment-emergent abnormalities will also be shown. The denominator for the percentage is the total number of participants with nonmissing data for the parameter, treatment arm, and analysis visit in the PAS.

All vital signs data will be listed, but only for participants with any postbaseline abnormality.

5.4 ELECTROCARDIOGRAMS

5.4.1 Available data

The following ECG parameters will be collected: heart rate, QRS interval, PR interval, QT interval, and QTcF.

For each ECG record, parameter name, test result and unit, assessment date(time), and clinical significance as assessed by the investigator are collected.

5.4.2 Derivation rules

Abnormalities for HR, QRS, and PR interval are defined in Table 9 below.

Table 9: ECG normal ranges

	Heart rate (bpm)	PR (ms)	QRS (ms)
Low	<50	<120	-
Normal	50-100	120-220	0-120
High	>100	>220	>120

Note: For the worst-case analysis visit, as defined in section 2.3.5, an additional category low + high is defined if there are both low and high postbaseline values.

For QTcF interval (ms), the following categories are defined[8]:

- Actual values:
  - ≤ 450 (normal)
  -]450; 480]
  -]480; 500]
  - > 500
- Changes:
  - ≤ 30 (normal)
  -]30; 60]
  - > 60

Note: The worst-case, as defined in section 2.3.5, is the highest postbaseline value and associated change.

5.4.3 Presentation of results

All tables will only show analysis visits and parameters as expected per SoA. Uncorrected QT interval will only be listed.

Continuous ECG parameters will be summarized using descriptive statistics at each analysis visit (by cycle, where applicable). Actual values and changes from baseline (study baseline for part A and pooled baseline for part A+B) will be shown in the same table.

Abnormalities of the actual values will be presented as cross-tabulations of the abnormality at each postbaseline analysis visit and at the worst-case analysis visit versus the baseline abnormality (study baseline for part A and pooled baseline for part A+B). Numbers and cumulative numbers from worst to best (normal) category (QTc only) of participants with treatment-emergent abnormalities will also be shown. The denominator for the percentage is the total number of participants with nonmissing data for the parameter, treatment arm, and analysis visit in the PAS.

Abnormalities of the QTc changes will be presented as tabulations of the change abnormality at each postbaseline analysis visit and at the worst-case analysis visit. Cumulative numbers of participants with change abnormalities will also be shown. The denominator for the percentage is the total number of participants with nonmissing data for the parameter, treatment arm, and analysis visit in the PAS.

All ECG data will be listed, but only for participants with any postbaseline abnormality or change.

5.5 SUICIDALITY ASSESSMENT

5.5.1 Available data

This suicidality assessment will be conducted by asking the following question, derived from the PHQ-9: "Over the last 2 weeks, how often have you been bothered by thoughts that you would be better off dead, or of hurting yourself in some way?" (Simon, Rutter et al. 2013). Possible outcomes: Not at all (0), Several days (1), More than half the days (2), Nearly every day (3).

5.5.2 Presentation of results

All tables will only show analysis visits and parameters as expected per SoA.

Suicidality assessment results will be presented using a frequency tabulation by analysis visit (by cycle, where applicable) and at the worst-case (across all cycles, where applicable). The denominator for the percentage is the total number of participants with nonmissing data per treatment and per analysis visit in the participant safety analysis set.

All suicidality assessment data will be listed, but only for participants with any postbaseline category ≥ 1.

6. VERSION HISTORY

This SAP for study ARGX-113-2308 is based on the protocol version 3.0, dated 23 SEP 2024.

6.1 CHANGES NOT COVERED BY PROTOCOL AMENDMENTS BEFORE DATABASE LOCK

In Section 1.1, determination of the efficacy of efgartigimod IV compared to placebo in two subgroups (MuSK-Ab seropositve and triple seronegative) of the overall AChR-Ab seronegative gMG population has been added to the key secondary endpoints. Therefore section 1.3 has been updated to include the corresponding hypotheses and in Section 1.3.1: MG-ADL total score change from baseline to day 29 in part A for the MuSK-Ab seropositve and triple seronegative subgroups have been added to the hierarchical testing strategy. Also section 4.1.2.2 has been updated to add analyses strategies to be used for the additional key secondary endpoints. This will allow to determine the efficacy of efgartigimod in these subgroups in a FWER controlled way.

Section 4.1.2.1:

1) MuSK-Ab status was added as factors in the MMRM models.
2) An extra sensitivity analysis dealing with missing data was added for the primary endpoint.

6.2 CHANGES NOT COVERED BY PROTOCOL AMENDMENTS AFTER DATABASE LOCK

NA

6.3 CHANGES TO THE FINAL STATISTICAL ANALYSIS PLAN

The following updates were done on sponsor's request to final version 2.0:

Section	Section title	Change description
1.1 1.3 1.3.1 4.1.2.2	Study objectives and endpoints Statistical hypotheses Multiplicity adjustment Key secondary endpoints (hierarchical testing)	A third and fourth key secondary endpoint were added.
2.1 2.5.2	Part A and part A+B analysis Presentation of treatments	Treatment arm labels were updated.
2.3.1	Analysis phases and periods	Last contact date is used to end the last (sub)period/phase iso date of study termination.
2.3.2	Baseline and change from baseline	Definition of cycle baseline for immunogenicity was modified to only consider values in the previous cycle.
2.3.4	Analysis visits	Priority rule for ICE handling and analysis visit selection was added. Added clarifications for the selection of analysis visits for immunogenicity.
2.3.5	Worst-case	Worst-case for suicidality added.

Section	Section title	Change description
2.4.2	Values below or above a threshold	No imputations to be done for anti-MusK antibodies.
2.4.3	Rounding	Rounding rules added.
2.5.1	Calculation of descriptive statistics and percentages	90% CI added to descriptive outputs.
3.1	Participant disposition	The number of participants continued to part B was added to the disposition table.
3.2	Protocol deviations and eligibility	Protocol deviations are allocated to analysis periods and reported separately for part A and A+B.
3.3.2 3.3.3	Demographic and other baseline disease characteristics - Derivation rules Presentation of results	Baseline variables in demographics and baseline disease characteristic tables are study baseline in part A and pooled baseline in part A+B tables.
3.3.2	Demographic and other baseline disease characteristics - Derivation rules	Derivations added for QMG total score category, MuSK-Ab status, and antibody status.
3.4 5.1	Medical history and concomitant diseases Adverse events	MedDRA version updated.
3.5.1	Prior and concomitant therapy - available data	WHO-DRUG verion updated.
3.5.2	Prior and concomitant therapy - derivation rules	Definition of prior and concomitant updated to differentiate between part A and part A+B analysis.
3.5.3	Prior and concomitant therapy - presentation of results	Table by antibody status added.
3.6.2	Exposure to IMP and treatment compliance - derivation rules	Compliance definition adjusted.
3.6.3	Exposure to IMP and treatment compliance - presentation of results	Clarified which parameters are to be shown overall and which by cycle.
4.1.1	Efficacy and QOL - available data	Questionnaire time reported as 00:00 is to be considered as missing.
4.1.2	Efficacy and QOL - derivation rules	Analysis visits are used in derivations unless specified otherwise. ICE of rescue therapy was further defined. Further details were added to MG-ADL responder and QMG responder definitions. Derivation rules were added for [redacted], TSQM-9 domain scores, and change category of EQ-5D-5L and PGI-S.
4.1.3	Efficacy and QOL - presentation of results	Statistical comparisons are done at the 0.10 significance level. A sensitivity analysis was added on the primary endpoint to account for missing data. Subgroup analyses were added for the primary endpoint. Cross-tabulations and tables of change categories were added for EQ-5D-5L and PGI-S.

Section	Section title	Change description
4.3	Pharmacodynamics	[redacted]
4.4	Immunogenicity	Incidence and Prevalence table for ADA against efgartigimod by MG baseline therapy was removed.
5.1.3	Adverse events - presentation of results	Event rates were added to the A+B tables by MedDRA SOC and PT.
5.2.3	Clinical laboratory evaluation - presentation of results	A listing on Hy's law was added.
7	References	References were added.
8	List of tables and listings	List was updated per above listed updates to the analysis.
9.2	SAS code	Code was aligned with the updates in the efficacy analysis.
9.3	MG therapies and procedures	List was updated per sponsor input.
9.4	Toxicity grades	Reference to rules on handling of local lab values was removed as this is not applicable in this study.

7. REFERENCES

1 ICH-E3 Structure and Content of Clinical Study Reports - Step 4: 30 November 1995.

2 ICH E6 (R2) Guideline for Good Clinical Practice - Step 5, December 2016.

3 ICH E9 Statistical Principles for Clinical Trials – Step 5 – Note for Guidance on Statistical Principles for Clinical Trials (CPMP/ICH/363/96), September 1998.

4 ICH E9 (R1) Statistical Principles for Clinical Trials, Addendum on Estimands and Sensitivity Analysis in Clinical Trials – Step 5 – November 2019.

5 G. Shankar, S. Arkin, L. Cocea, V. Devanarayan, S. Kirshner, A. Kromminga, V. Quarmby, S. Richards, C. K. Schneider, M. Subramanyam, S. Swanson, D. Verthelyi, and S. Yim (2014). "Assessment and Reporting of the Clinical Immunogenicity of Therapeutic Proteins and Peptides— Harmonized Terminology and Tactical Recommendations" AAPS J 16(4): 658-673.

6 A new equation to estimate glomerular filtration rate. Levey AS, Stevens LA, Schmid CH et al. Ann Intern Med 2009 150:604–12.

7 National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0, November 2017.

8 Die Systolendauer im Elektrokardiogramm bei normalen Menschen und bei Herzkranken. Fridericia LS Acta Med Scand 1920 15:469–485.

9 Guidance for Industry Drug-Induced Liver Injury: Premarketing Clinical Evaluation. FDA CDER and CBER, July 2009

10 Carpenter JR, Roger JH, Kenward MG. Analysis of longitudinal trials with protocol deviation: a framework for relevant, accessible assumptions, and inference via multiple imputation. J Biopharm Stat. 2013; 23(6):1352–1371.

8. LIST OF TABLES AND LISTINGS

8.1 TABLES

Separate outputs will be created for part A and part A+B analysis. Table numbering will contain the suffix 'A' or 'AB', respectively; the table title will contain 'PART A' or 'PART A+B', respectively.

Table number	Title	PAS	PA	Topline	FA	IDMC	Mock ID
14.1 DEMOGRAPHIC DATA							
GENERAL CHARACTERISTICS (14.1.X)							
14.1.1	Participant Analysis Sets	ENR	All	X	All		DST01
14.1.2	Participant Disposition by Country and Site	SAF	A		A+B		DST02
14.1.3	Participant Disposition by Analysis Visits	SAF	A+B	X	A+B		
14.1.4	Study and Cycle Duration	SAF	A+B	X	A+B		DST05
14.1.5	Treatment and Follow-up Duration in 6-Monthly Periods	SAF	A+B		A+B		DST06
14.1.6	Treatment Discontinuation	SAF	A/A+B	X	A+B	A/A+B	DST03
14.1.7	Study Discontinuation	SAF	A/A+B	X	A+B		DST04
14.1.8	Protocol Deviations	ITT/SAF	A		A+B		DVT01
14.1.9	Demographic Data	ITT/SAF	A/A+B	X	A+B	A/A+B	DMT01
14.1.10	Demographic Data by Antibody Status	ITT	A	X			DMT01
14.1.11	Baseline Disease Characteristics	ITT/SAF	A/A+B	X	A+B	A/A+B	DMT01
14.1.12	Baseline Disease Characteristics by Antibody Status	ITT	A	X			DMT01
14.1.13	Medical History	SAF	A				MHT01
14.1.14	Concomitant Diseases	SAF	A/A+B		A+B		MHT01

Table number	Title	PAS	PA	Topline	FA	IDMC	Mock ID
14.1.15	Prior Therapies by ATC Class (Level 1 and 3) and Generic Term	SAF	A		A+B		CMT01
14.1.16	Concomitant Therapies by ATC Class (Level 1 and 3) and Generic Term	SAF	A/A+B		A+B		CMT01
14.1.17	Prior MG Therapies by Generic Term	SAF	A	X	A+B		CMT02
14.1.18	Prior MG Therapies by Generic Term by Antibody Status	SAF	A	X			CMT02
14.1.19	Baseline MG Therapies by Generic Term	SAF	A	X	A+B		CMT02
14.1.20	Baseline MG Therapies by Generic Term by Antibody Status	SAF	A				CMT02
14.1.21	Classes of Baseline MG Therapies	SAF	A	X	A+B		CMT03
14.1.22	Classes of Baseline MG Therapies by Antibody Status	SAF	A				CMT03
14.1.23	IMP Administration	SAF	A/A+B	X	A+B		EXT01
14.2 EFFICACY DATA							
EFFICACY (14.2.1.X)							
14.2.1.1	Overview of Efficacy Endpoints Hierarchical Testing	ITT	A	X			EFT01
14.2.1.2	Frequency Tabulation of Intercurrent Events	ITT	A	X			EFT02
14.2.1.3.1	MG-ADL: Mixed Model for Repeated Measurements in MG-ADL Total Score – Treatment Policy Strategy	ITT	A	X			EFT06
14.2.1.3.2	MG-ADL: Mixed Model for Repeated Measurements in MG-ADL Total Score - Treatment Policy Strategy Using Stratification Factors as Randomized	ITT	A	X			EFT06
14.2.1.3.3	MG-ADL: Mixed Model for Repeated Measurements in MG-ADL Total Score – Treatment Policy Strategy by Subgroup	ITT	A	X			EFT06
14.2.1.3.4	MG-ADL: Mixed Model for Repeated Measurements in MG-ADL Total Score – Hypothetical Strategy	ITT	A	X			EFT06

Table number	Title	PAS	PA	Topline	FA	IDMC	Mock ID
14.2.1.3.5	MG-ADL: Mixed Model for Repeated Measurements in MG-ADL Total Score – Treatment Policy Strategy (Sensitivity Analysis)	ITT	A				EFT06
14.2.1.3.6	MG-ADL: Descriptive Statistics of Actual Values and Changes from Baseline in MG-ADL Total Score by Analysis Visit and Cycle	ITT/SAF	A/A+B	X	A+B		EFT03a
14.2.1.3.7	MG-ADL: Descriptive Statistics of Actual Values and Changes from Baseline in MG-ADL Total Score by Analysis Visit by Antibody Status	ITT	A	X			EFT03b
14.2.1.3.8	MG-ADL: Frequency Tabulation of Actual Values in MG-ADL Total Score by Analysis Visit and Cycle	ITT/SAF	A/A+B	X	A+B		EFT07d
14.2.1.3.9	MG-ADL: Frequency Tabulation of Actual Values in MG-ADL Total Score by Analysis Visit by Antibody Status	ITT	A	X			EFT07e
14.2.1.3.10	MG-ADL: Frequency Tabulation of Changes from Baseline in MG-ADL Total Score by Analysis Visit and Cycle	ITT/SAF	A		A+B		EFT07d
14.2.1.3.11	MG-ADL: Frequency Tabulation of Changes from Baseline in MG-ADL Total Score by Analysis Visit and Cycle by Antibody Status	ITT	A				EFT07e
14.2.1.3.12	MG-ADL: Stratified Cochran-Mantel-Haenszel in MG-ADL Responder – Composite Variable Strategy	ITT	A				EFT08
14.2.1.3.13	MG-ADL: Frequency tabulation of MG-ADL Responders by Antibody Status and Overall	ITT	A	X			EFT07a
14.2.1.3.14	MG-ADL: Frequency tabulation of Early MG-ADL Responders by Antibody Status and Overall	ITT	A				EFT07a
14.2.1.3.15	MG-ADL: Characterization of MG-ADL Responders by Antibody Status and Overall	ITT	A				DMT01
14.2.1.3.16	MG-ADL: AUEC of Change from Baseline in MG-ADL Total Score per Dosing Interval and Over Part A	ITT	A				EFT03a

Table number	Title	PAS	PA	Topline	FA	IDMC	Mock ID
14.2.1.3.17	MG-ADL: Mixed Model for Repeated Measurements in MG-ADL Total Score – Multiple Imputation (Sensitivity Analysis)	ITT	A				EFT06
14.2.1.4.1	QMG: Mixed Model for Repeated Measurements in QMG Total Score – Treatment Policy Strategy	ITT	A	X			EFT06
14.2.1.4.2	QMG: Mixed Model for Repeated Measurements in QMG Total Score - Treatment Policy Strategy by Antibody Status	ITT	A	X			EFT06
14.2.1.4.3	QMG: Mixed Model for Repeated Measurements in QMG Total Score – Hypothetical Strategy	ITT	A	X			EFT06
14.2.1.4.4	QMG: Descriptive Statistics of Actual Values and Changes from Baseline in QMG Total Score by Analysis Visit and Cycle	ITT/SAF	A/A+B	X	A+B		EFT03a
14.2.1.4.5	QMG: Descriptive Statistics of Actual Values and Changes from Baseline in QMG Total Score by Analysis Visit and Cycle by Antibody Status	ITT	A	X			EFT03b
14.2.1.4.6	QMG: Frequency Tabulation of Actual Values in QMG Total Score by Analysis Visit and Cycle	ITT/SAF	A		A+B		EFT07d
14.2.1.4.7	QMG: Frequency Tabulation of Actual Values in QMG Total Score by Analysis Visit and Cycle by Antibody Status	ITT	A				EFT07e
14.2.1.4.8	QMG: Frequency Tabulation of Changes from Baseline in QMG Total Score by Analysis Visit and Cycle	ITT/SAF	A		A+B		EFT07d
14.2.1.4.9	QMG: Frequency Tabulation of Changes from Baseline in QMG Total Score by Analysis Visit and Cycle by Antibody Status	ITT	A				EFT07e
14.2.1.4.10	QMG: Stratified Cochran-Mantel-Haenszel in QMG Responder – Composite Variable Strategy	ITT	A				EFT08
14.2.1.4.11	QMG: Frequency tabulation of QMG responders by Antibody Status and Overall	ITT	A	X			EFT07a
14.2.1.4.12	QMG: Characterization of QMG Responders by Antibody Status and Overall	ITT	A				DMT01

Table number	Title	PAS	PA	Topline	FA	IDMC	Mock ID
14.2.1.4.13	QMG: AUEC of Change from Baseline in QMG Total Score per Dosing Interval and Over Part A	ITT	A				EFT03a
14.2.1.5.1	MG-ADL/QMG: Stratified Cochran-Mantel-Haenszel in MG-ADL/QMG Responder – Composite Variable Strategy	ITT	A	X			EFT08
14.2.1.5.2	MG-ADL/QMG: Stratified Cochran-Mantel-Haenszel in MG-ADL/QMG Responder – Treatment Policy Strategy	ITT	A	X			EFT08
14.2.1.5.3	MG-ADL/QMG: Stratified Cochran-Mantel-Haenszel in MG-ADL/QMG Responder – Composite Variable Strategy by Antibody Status	ITT	A	X			EFT08
14.2.1.5.4	MG-ADL/QMG: Frequency tabulation of MG-ADL/QMG Responders by Antibody Status and Overall	ITT	A	X			EFT07a
14.2.1.5.5	MG-ADL/QMG: Characterization of MG-ADL/QMG Responders by Antibody Status and Overall	ITT	A	X			DMT01
14.2.1.6.1	MG-QoL15r: Mixed Model for Repeated Measurements in MG-QoL15r Total Score	ITT	A				EFT06
14.2.1.6.2	MG-QoL15r: Descriptive Statistics of Actual Values and Changes from Baseline in MG-QoL15r Score by Analysis Visit and Cycle	ITT/SAF	A/A+B		A+B		EFT03a
14.2.1.7.1	EQ-5D-5L: Descriptive Statistics of Actual Values and Changes from Baseline in VAS Score by Analysis Visit and Cycle	ITT/SAF	A/A+B		A+B		EFT03a
14.2.1.7.2	EQ-5D-5L: Cross-Tabulation of Individual Items by Analysis Visit and Cycle	ITT	A				EFT07h
14.2.1.7.3	EQ-5D-5L: Frequency Tabulation of Change Categories of Individual Items by Analysis Visit and Cycle	ITT	A				EFT07d
14.2.1.8	MGC: Descriptive Statistics of Actual Values and Changes from Baseline in MGC Score by Analysis Visit and Cycle	ITT/SAF	A		A+B		EFT03a
14.2.1.9	Neuro-QoL: Descriptive Statistics of Actual Values and Changes from Baseline in Neuro-QoL Short Form - Fatigue T-Score by Analysis Visit and Cycle	ITT/SAF	A		A+B		EFT03a

Table number	Title	PAS	PA	Topline	FA	IDMC	Mock ID
[redacted]							
14.2.1.11.1	PGI: Frequency Tabulation of PGI-S by Analysis Visit and Cycle	ITT/SAF	A		A+B		EFT07d
14.2.1.11.2	PGI: Frequency Tabulation of PGI-C by Analysis Visit and Cycle	ITT/SAF	A		A+B		EFT07d
14.2.1.11.3	PGI: Cross-Tabulation of PGI-S by Analysis Visit and Cycle	ITT	A				EFT07h
14.2.1.11.4	PGI: Frequency Tabulation of Change Categories of PGI-S by Analysis Visit and Cycle	ITT	A				EFT07d
14.2.1.12.1	TSQM-9: Descriptive Statistics of Actual Values of TSQM-9 Domain Scores by Analysis Visit and Cycle	ITT/SAF	A		A+B		EFT03a
PHARMACOKINETICS (14.2.2.X)							
14.2.2.1	Descriptive Statistics of Efgartigimod Serum Concentrations (ug/mL) by Analysis Visit	PK	A				PKT01
14.2.2.2	Descriptive Statistics of Efgartigimod Serum Concentrations (ug/mL) by Analysis Visit by Antibody Status	PK	A				PKT01
PHARMACODYNAMICS (14.2.3.X)							
14.2.3.1	Total IgG: Descriptive Statistics of Actual Values and Percent Changes From Baseline in Total IgG Level (ug/mL) by Analysis Visit and Cycle	SAF	A	X	A+B		PDT01
14.2.3.1 [IDMC]	Descriptive Statistics of Actual Values in Total IgG Level (ug/mL) by Analysis Visit and Cycle	SAF				A/A+B	PDT01
14.2.3.2	Total IgG: Descriptive Statistics of Actual Values and Percent Changes From Baseline in Total IgG Level (ug/mL) by Analysis Visit and Cycle by Antibody status	SAF	A	X			PDT01

Table number	Title	PAS	PA	Topline	FA	IDMC	Mock ID
IMMUNOGENICITY (14.2.4.X)							
14.2.4.1.1	Number and Percentage of Participants With ADA Against Efgartigimod by Analysis Visit and by Overall ADA Against Efgartigimod Participant Classification	SAF	A+B		A+B		IMT01a
14.2.4.1.2	Prevalence and Incidence of ADA Against Efgartigimod	SAF	A+B		A+B		IMT02a
14.2.4.1.3	Descriptive Statistics of ADA Against Efgartigimod Titer Values by Overall ADA Participant Classification Against Efgartigimod by Analysis Visit and Cycle	SAF	A+B		A+B		IMT03
14.2.4.2.1	Number and Percentage of Participants With Nab Against Efgartigimod by Analysis Visit and Cycle by Overall NAb Against Efgartigimod Participant Classification	SAF	A+B		A+B		IMT01b
14.2.4.2.2	Prevalence and Incidence of NAb Against Efgartigimod	SAF	A+B		A+B		IMT02b
14.2.4.2.3	Number and Percentage of NAb Against Efgartigimod Positive Participants by Overall ADA Against Efgartigimod Participant Classification	SAF	A+B		A+B		IMT04
14.2.4.3.1	Descriptive Statistics of Actual Values and Changes from Baseline in MG-ADL Total Score by Analysis Visit and Cycle by Cycle ADA Against Efgartigimod Participant Classification	SAF	A+B		A+B		EFT03b
14.2.4.3.2	Descriptive Statistics of Actual Values and Changes from Baseline in MG-ADL Total Score by Analysis Visit and Cycle by Cycle NAb Against Efgartigimod Participant Classification	SAF	A+B		A+B		EFT03b
14.2.4.4.1	Descriptive Statistics of Efgartigimod Serum Concentrations (ug/mL) by Analysis Visit and Cycle by Cycle ADA Against Efgartigimod Participant Classification	SAF	A+B		A+B		IMT05a
14.2.4.4.2	Descriptive Statistics of Efgartigimod Serum Concentrations (ug/mL) by Analysis Visit and Cycle by Cycle NAb Against Efgartigimod Participant Classification	SAF	A+B		A+B		IMT05a

Table number	Title	PAS	PA	Topline	FA	IDMC	Mock ID
14.2.4.5.1	Descriptive Statistics of Actual Values and Percent Changes From Baseline in Total IgG by Analysis Visit and Cycle by Cycle ADA Against Efgartigimod Participant Classification	SAF	A+B		A+B		PDT01
14.2.4.5.2	Descriptive Statistics of Actual Values and Percent Changes From Baseline in Total IgG by Analysis Visit and Cycle by Cycle NAb Against Efgartigimod Participant Classification	SAF	A+B		A+B		PDT01
14.2.4.6.1	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Cycle ADA Against Efgartigimod Participant Classification	SAF	A+B		A+B		IMT06
14.2.4.6.2	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Cycle NAb Against Efgartigimod Participant Classification	SAF	A+B		A+B		IMT06
14.2.4.6.3	Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Cycle ADA Against Efgartigimod Participant Classification	SAF	A+B		A+B		IMT06
14.2.4.6.4	Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Cycle NAb Against Efgartigimod Participant Classification	SAF	A+B		A+B		IMT06
14.2.4.6.5	Infusion-Related Reactions by MedDRA System Organ Class and Preferred Term by Cycle ADA Against Efgartigimod Participant Classification	SAF	A+B		A+B		IMT06
14.2.4.6.6	Infusion-Related Reactions by MedDRA System Organ Class and Preferred Term by Cycle Nab Against Efgartigimod Participant Classification	SAF	A+B		A+B		IMT06
14.3 SAFETY DATA							
14.3.1 DISPLAYS OF ADVERSE EVENTS (14.3.1.X)							
14.3.1.1	Adverse Events Overview by Cohort and Overall	SAF	A/A+B	X	A+B	A/A+B	AET01a/ AET01b
14.3.1.2	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Cohort and Overall	SAF	A/A+B	X	A+B	A/A+B	AET02a/ AET02b

Table number	Title	PAS	PA	Topline	FA	IDMC	Mock ID
14.3.1.3	Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Cohort and Overall	SAF	A/A+B	X	A+B	A/A+B	AET02a/ AET02b
14.3.1.4	Nonserious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	A/A+B		A+B		AET02a/ AET02b
14.3.1.5	Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Cohort and Overall	SAF	A/A+B	X	A+B	A/A+B	AET02a/ AET02b
14.3.1.6	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Worst Toxicity Grade	SAF	A/A+B		A+B		AET03a/ AET03b
14.3.1.7	Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	A/A+B	X	A+B		AET02a/ AET02b
14.3.1.8	Procedure-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	A		A+B		AET02a/ AET02b
14.3.1.9	Serious Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	A/A+B	X	A+B		AET02a/ AET02b
14.3.1.10	Treatment-Emergent Adverse Events Leading to IMP Discontinuation by MedDRA System Organ Class and Preferred Term by Cohort and Overall	SAF	A/A+B	X	A+B	A/A+B	AET02a/ AET02b
14.3.1.11	Treatment-Emergent Adverse Events Leading to IMP Interruption by MedDRA System Organ Class and Preferred Term	SAF	A	X	A+B		AET02a/ AET02b
14.3.1.12	Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class and Preferred Term by Cohort and Overall	SAF	A/A+B	X	A+B	A/A+B	AET02a/ AET02b
14.3.1.13 [IDMC]	Grade 3 or Higher Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class and Preferred Term	SAF				A/A+B	AET02a/ AET02b
14.3.1.14	Infusion-Related Reactions by MedDRA System Organ Class and Preferred Term	SAF	A/A+B	X	A+B	A/A+B	AET02a/ AET02b

Table number	Title	PAS	PA	Topline	FA	IDMC	Mock ID
14.3.1.15	Serious Infusion-Related Reactions by MedDRA System Organ Class and Preferred Term	SAF	A		A+B		AET02a/ AET02b
14.3.4 ABNORMAL LABORATORY VALUE LISTING (EACH PARTICIPANT)							
LABORATORY DATA (14.3.4.1.X)							
14.3.4.1.1	Descriptive Statistics of Laboratory Test Actual Values and Changes From Baseline by Analysis Visit and Cycle	SAF	A		A+B		SFT01
14.3.4.1.2	Cross-Tabulation of Laboratory Abnormalities Versus Baseline by Analysis Visit and Cycle	SAF	A/A+B		A+B		SFT02
14.3.4.1.3	Cross-Tabulation of Laboratory Toxicity Grades Versus Baseline by Analysis Visit and Cycle	SAF	A/A+B	X	A+B	A/A+B	SFT03
VITAL SIGNS (14.3.4.2.X)							
14.3.4.2.1	Descriptive Statistics of Vital Signs Actual Values and Changes From Baseline by Analysis Visit and Cycle	SAF	A		A+B		SFT01
14.3.4.2.2	Cross-Tabulation of Vital Signs Abnormalities Versus Baseline by Analysis Visit and Cycle	SAF	A/A+B		A+B		SFT02
ECG (14.3.4.3.X)							
14.3.4.3.1	Descriptive Statistics of ECG Actual Values and Changes From Baseline by Analysis Visit and Cycle	SAF	A		A+B		SFT01
14.3.4.3.2	Cross-Tabulation of ECG Abnormalities Versus Baseline by Analysis Visit and Cycle	SAF	A/A+B	X	A+B		SFT02/ SFT03
14.3.4.3.2 [IDMC]	Cross-Tabulation of QTcF Abnormalities Versus Baseline by Analysis Visit and Cycle	SAF				A/A+B	SFT03
14.3.4.3.3	Tabulation of QTcF Change Abnormalities by Analysis Visit and Cycle	SAF	A/A+B	X	A+B	A/A+B	SFT04

Table number	Title	PAS	PA	Topline	FA	IDMC	Mock ID
SUICIDALITY (14.3.4.4.X)							
14.3.4.4.1	Tabulation of Suicidality Results by Analysis Visit and Cycle	SAF	A/A+B		A+B		SFT05

8.2 LISTINGS

Listings will be created only once, with all available data (Part A and Part B) relevant for the specific listing, except if specified differently.

Listing number	Title	PAS	PA	FA	IDMC
	16.1.7 RANDOMIZATION SCHEME AND CODES				
16.1.7	Treatment Allocation and Stratification Factors	ITT	A		
	16.2.1 DISCONTINUED PARTICIPANTS				
16.2.1.1	Participant Analysis Sets	ENR	All	All	
16.2.1.2	Treatment and Study Discontinuation	SAF (A)	All	All	All
	16.2.2 PROTOCOL DEVIATIONS				
16.2.2.1	Protocol Deviations	ITT	All	All	
16.2.2.2	Eligibility Criteria Violations	SAF (A)	All	All	
	16.2.3 PARTICIPANTS EXCLUDED FROM THE EFFICACY ANALYSIS				
16.2.3.1	Non-Randomized Participants	ENR minus ITT	A		
	16.2.4 DEMOGRAPHIC DATA				
16.2.4.1	Demographic Data	ITT	All	All	
16.2.4.2	Baseline Disease Characteristics	ITT	All	All	

Listing number	Title	PAS	PA	FA	IDMC
16.2.4.3	Medical History and Concomitant Disease	SAF (A)	All	All	
16.2.4.4	Hospitalizations	SAF (A)	All	All	
16.2.4.5	Prior and Concomitant Therapies	SAF (A)	All	All	
16.2.4.6	Rescue Therapies	SAF (A)	All	All	
16.2.4.7	Prior and Concomitant Procedures	SAF (A)	All	All	
16.2.5 COMPLIANCE AND/OR DRUG CONCENTRATION DATA (IF AVAILABLE)					
16.2.5.1	IMP Administration	SAF (A)	All	All	
16.2.5.2	Participants with Overdose	SAF (A)	All	All	
16.2.5.3	Individual Efgartigimod Serum Concentrations and Actual Blood Sampling Times	PK	A		
16.2.6 INDIVIDUAL EFFICACY RESPONSE DATA					
16.2.6.1	Total IgG	SAF (A)	All	All	
[redacted]					
16.2.6.3	Intercurrent Events	ITT	A	A	
16.2.6.4	MG-ADL: Total Score and Derived Variables	ITT	All	All	
16.2.6.5	MG-ADL: AUEC of Change from Baseline	ITT	A		
16.2.6.6	QMG: Total Score and Derived Variables	ITT	All	All	
16.2.6.7	QMG: AUEC of Change from Baseline	ITT	A		
16.2.6.8	MG-QoL15r: Total Scores	ITT	All	All	
16.2.6.9	EQ-5D-5L: Dimensions and VAS Score	ITT	All	All	
16.2.6.10	MGC: Total Scores	ITT	All	All	
16.2.6.11	Neuro-QoL: Short Form - Fatigue T-Score	ITT	All	All	

Listing number	Title	PAS	PA	FA	IDMC
[redacted]					
16.2.6.13	PGI: PGI-S and PGI-C Scores	ITT	All	All	
16.2.6.14	TSQM-9: Item and Domain Scores	ITT	All	All	
16.2.6.15	Efgartigimod ADA and Neutralizing Antibodies	SAF (A+B)		All	
16.2.7 ADVERSE EVENTS LISTINGS					
16.2.7.1	Adverse Events	SAF (A)	All	All	All
16.2.7.2	Serious Adverse Events	ENR	All	All	All
16.2.7.3	Fatal Adverse Events	ENR	All	All	All
16.2.7.4	Treatment-Emergent Adverse Events Leading to IMP Discontinuation	SAF (A)	All	All	All
16.2.7.5	Treatment-Emergent Adverse Events Leading to Interruption of IMP	SAF (A)	All	All	
16.2.7.6	Treatment-Emergent Adverse Events of Special Interest	SAF (A)	All	All	All
16.2.7.7	Infusion-Related Reactions	SAF (A)	All	All	All
16.2.7.8	Adverse Events: Coding Information	SAF (A)	All	All	
16.2.8 LISTING OF INDIVIDUAL LABORATORY MEASUREMENTS BY PARTICIPANT, WHEN REQUIRED BY REGULATORY AUTHORITIES					
16.2.8.1	Laboratory Test Results for Participants with Abnormal Values	SAF (A)	All	All	
16.2.8.1 [IDMC]	Laboratory Test Results for Participants with Grade 3 or 4 Toxicities	SAF (A)			All
16.2.8.2	Liver Test Results for Participants Meeting Hy's Law Criteria	SAF (A)	All	All	
16.2.8.3	Vital Signs Results for Participants with Abnormal Values	SAF (A)	All	All	
16.2.8.4	ECG Results for Participants with Abnormal Values	SAF (A)	All	All	

Listing number	Title	PAS	PA	FA	IDMC
16.2.8.4 [IDMC]	ECG Results for Participants with QTc Abnormal Values	SAF (A)			All
16.2.8.5	Suicidality Assessment for Participants with Abnormal Values	SAF (A)	All	All	

8.3 FIGURES

Figures will be created for IDMC analyses only.

		PAS	IDMC
LABORATORY DATA (14.3.4.1.X)			
14.3.4.1.1 [IDMC]	Box Plots of Laboratory Test Actual Values by Analysis Visit and Cycle	SAF	A/A+B
PARTICIPANT PROFILE PLOTS			
16.2.1.2 [IDMC]	Individual Participant Profiles Including Exposure, Medical History, AEs, Laboratory Grade 3/4 Toxicities and Co-medication	SAF	A/A+B

9. APPENDICES

9.1 NEURO-QOL SHORT FORM - FATIGUE T-SCORE

Table 10: T-Scores for Adult Fatigue 8-item Short Form

Raw Score[a]	T-Score	SE	Raw Score[a]	T-Score	SE
8	29.5	4.4	25	52.3	1.7
9	34.1	2.7	26	53.3	1.7
10	36.5	2.2	27	54.4	1.7
11	38.2	2.0	28	55.4	1.7
12	39.5	1.9	29	56.5	1.8
13	40.7	1.8	30	57.6	1.8
14	41.8	1.7	31	58.8	1.8
15	42.8	1.7	32	59.9	1.8
16	43.8	1.7	33	61.1	1.8
17	44.7	1.7	34	62.3	1.8
18	45.6	1.7	35	63.5	1.8
19	46.5	1.7	36	64.8	1.9
20	47.4	1.7	37	66.2	2.0
21	48.4	1.7	38	67.9	2.2
22	49.3	1.7	39	70.1	2.7
23	50.3	1.7	40	74.1	4.0
24	51.3	1.8			

[a] Raw scores will be rounded to the nearest integer

9.2 SAS CODE

9.2.1 MMRM model

[redacted]

9.2.2 Cochran-Mantel-Haenszel test with Klingenberg midpoint and CI

[redacted]

9.2.3 Agresti-Min CI

[redacted]

9.2.4 Satterthwaite CI

[redacted]

9.3 MG THERAPIES AND PROCEDURES

Steroids	NSIDs	AChE inhibitors	Other	Procedures
PREDNISONE	CICLOSPORIN	NEOSTIGMINE	ECULIZUMAB	PLASMAPHERESIS
PREDNISOLONE	AZATHIOPRINE	NEOSTIGMINE BROMIDE	NIPOCALIMAB	THYMECTOMY
METHYLPREDNISOLONE	MYCOPHENOLATE MOFETIL	PYRIDOSTIGMINE	RITUXIMAB	ELECTRONEUROGRAPHY
HYDROCORTISONE	MYCOPHENOLATE SODIUM	PYRIDOSTIGMINE BROMIDE	IMMUNOGLOBULINS	FEEDING TUBE USER
TRIAMCINOLONE	MYCOPHENOLIC ACID	AMBENONIUM	IMMUNOGLOBULINS NOS	GASTROSTOMY[a]
DEFLAZACORT	METHOTREXATE	AMBENONIUM CHLORIDE	IMMUNOGLOBULIN THERAPY	ELECTROMYOGRAM
METHYLPREDNISOLONE SODIUM SUCCINATE	TACROLIMUS	DISTIGMINE	IMMUNOGLOBULIN HUMAN NORMAL	ENTERAL NUTRITION
PREDNISOLONE ACETATE	CYCLOPHOSPHAMIDE	DISTIGMINE BROMIDE	IMMUNOGLOBULINS, NORMAL HUMAN	IMMUNOADSORPTION THERAPY
DEXAMETHASONE	CYTOPHOSPHANE		IMMUNOGLOBULIN G HUMAN	
PREDNISONE ACETATE	TACROLIMUS MONOHYDRATE		ZILUCOPLAN	
	MYCOPHENOLATE MOFETIL HYDROCHLORIDE		ROZANOLIXIZUMAB	
			RAVULIZUMAB	

[a] Study physician will review case by case for this procedure to decide whether MG-related or not.

9.4 TOXICITY GRADES

Below Table 11 documents how the Criteria for Adverse Events CTCAE, v5.0: November 27, 2017[7] is implemented in the statistical analysis.

Table 11: Analysis toxicity grades (CTCAE 5.0)

PARAMETER	Unit	GRADE 1	GRADE 2	GRADE 3	GRADE 4
Amylase (pancreatic)		>1.0-1.5 *ULN	>1.5-2.0 *ULN	>2.0-5.0 *ULN	>5.0 *ULN
Alanine amino transferase		>1-3 *ULN	>3-5 *ULN	>5-20 *ULN	>20 *ULN
Albumin[a]	g/L	<LLN-30	<30-20	<20	-
	g/dL	<LLN-3	<3-2	<2	-
Alkaline phosphatase		>1.0-2.5 *ULN	>2.5-5.0 *ULN	>5.0-20.0 *ULN	>20.0 *ULN
Aspartate amino transferase		>1-3 *ULN	>3-5 *ULN	>5-20 *ULN	>20 *ULN
Bilirubin (total)		>1.0-1.5 *ULN	>1.5-3.0 *ULN	>3.0-10.0 *ULN	>10.0 *ULN
Calcium (ionized) low[a]	mmol/L	<LLN-1.0	<1.0-0.9	<0.9-0.8	<0.8
	mg/dL	<LLN-4.0	<4.0-3.6	<3.6-3.2	<3.2
Calcium (ionized) high[a]	mmol/L	>ULN-1.5	>1.5-1.6	>1.6-1.8	>1.8
	mg/dL	>ULN-6.0	>6.0-6.4	>6.4-7.2	>7.2
Calcium (corrected) low[a]	mmol/L	<LLN-2.00	<2.00-1.75	<1.75-1.50	<1.50
	mg/dL	<LLN-8	<8-7	<7-6	<6
Calcium (corrected) high[a]	mmol/L	>ULN-2.9	>2.9-3.1	>3.1-3.4	>3.4
	mg/dL	>ULN-11.5	>11.5-12.5	>12.5-13.5	>13.5
Cholesterol[a]	mmol/L	>ULN-7.75	>7.75-10.34	>10.34-12.92	>12.92
	mg/dL	>ULN-300	>300-400	>400-500	>500
Creatine kinase		>1.0-2.5 *ULN	>2.5-5.0 *ULN	>5.0-10.0 *ULN	>10.0 *ULN

PARAMETER	Unit	GRADE 1	GRADE 2	GRADE 3	GRADE 4
Creatinine		>1.0-1.5 *ULN	>1.5-3.0 *ULN	>3.0-6.0 *ULN	>6.0 *ULN
Gamma-glutamyl transferase		>1.0-2.5 *ULN	>2.5-5.0 *ULN	>5.0-20.0 *ULN	>20.0 *ULN
Glucose (fasting) low[a,b]	mmol/L	<LLN-3.0	<3.0-2.2	<2.2-1.7	<1.7
	mg/dL	<LLN-55	<55-40	<40-30	<30
Lipase		>1.0-1.5 *ULN	>1.5-2.0 *ULN	>2.0-5.0 *ULN	>5.0 *ULN
Magnesium low[a]	mmol/L	<LLN-0.5	<0.5-0.4	<0.4-0.3	<0.3
	mg/dL	<LLN-1.2	<1.2-0.9	<0.9-0.7	<0.7
Magnesium high[a]	mmol/L	>ULN-1.23	-	>1.23-3.30	>3.30
	mg/dL	>ULN-3.0	-	>3.0-8.0	>8.0
Potassium low[a]	mmol/L	-	<LLN-3.0	<3.0-2.5	<2.5
	mEq/L	-	<LLN-3.0	<3.0-2.5	<2.5
Potassium high[a]	mmol/L	>ULN-5.5	>5.5-6.0	>6.0-7.0	>7.0
	mEq/L	>ULN-5.5	>5.5-6.0	>6.0-7.0	>7.0
Sodium low[a]	mmol/L	<LLN-130	-	<130-120	<120
	mEq/L	<LLN-130	-	<130-120	<120
Sodium high[a]	mmol/L	>ULN-150	>150-155	>155-160	>160
	mEq/L	>ULN-150	>150-155	>155-160	>160
Triglycerides	mmol/L	1.71-3.42	>3.42-5.70	>5.70-11.4	>11.4
	mg/dL	150-300	>300-500	>500-1000	>1000
Partial thromboplastin time (activated or not specified)		>1.0-1.5 *ULN	>1.5-2.5 *ULN	>2.5 *ULN	-

PARAMETER	Unit	GRADE 1	GRADE 2	GRADE 3	GRADE 4
CD4 count[a]	giga/L	<LLN-0.50	<0.50-0.20	<0.20-0.05	<0.05
	counts/mm3	<LLN-500	<500-200	<200-50	<50
Fibrinogen		<1.00-0.75 *LLN	<0.75-0.50 *LLN	<0.50-0.25 *LLN	<0.25 *LLN
International normalized ratio		>1.2-1.5 *ULN	>1.5-2.5 *ULN	>2.5 *ULN	-
Lymphocytes (absolute count) low[a]	giga/L	<LLN-0.80	<0.80-0.50	<0.50-0.20	<0.20
	counts/mm^3	<LLN-800	<800-500	<500-200	<200
Lymphocytes (absolute count) high	giga/L	-	>4-20	>20	-
	counts/mm^3	-	>4000-20000	>20000	-
Neutrophils (absolute count)[a]	giga/L	<LLN-1.5	<1.5-1.0	<1.0-0.5	<0.5
	counts/mm^3	<LLN-1500	<1500-1000	<1000-500	<500
Platelets[a]	giga/L	<LLN-75	<75-50	<50-25	<25
	counts/mm^3	<LLN-75000	<75000-50000	<50000-25000	<25000
White blood cells[a]	giga/L	<LLN-3	<3-2	<2-1	<1
	counts/mm^3	<LLN-3000	<3000-2000	<2000-1000	<1000

[a] Notes: In case ULN/LLN is higher/lower than the upper/lower limit of grade 1 (or even higher grades), ULN/LLN will be ignored and only the fixed values of CTCAE will be considered. In case ULN/LLN is missing, a grade will only be derived if the value leaves no doubt on which grade is to be assigned.

[b] Grade definition will also be applied when the fasting conditions into which the sample was drawn have not been declared (eg, unscheduled samples, unknown), when only (a) sporadic result(s) for the parameter was (were) non-fasting (usually unscheduled samples), and in case of scheduled post-meal samples on a same day (eg, 4 hours after dose and after a meal).

9.5 SCHEDULE OF ASSESSMENTS

9.5.1 Part A – Double-Blinded, Placebo-Controlled Period

	SCN[a]	Treatment period				Follow-up period				End of part A[b]	UNS[c]	
Study visit		**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**			
Study week		**BL**	**W1**	**W2**	**W3**	**W4**	**W5**	**W6**	**W7**	**W8**		
Study day (window)	**-35 to -1**	**D1**	**D8 (+1)**	**D15 (+1)**	**D22 (+1)**	**D29 (±2)**	**D36 (±2)**	**D43 (±2)**	**D50 (±2)**	**D57 (±2)**	**NA**	**Protocol section**
Eligibility/BL only												
Informed consent[d]	X											10.1.3
Medical history[e]	X											8.1, 8.3
Demography	X											
Weight/height[f]	X	X								X	(X)	6.6, 8.3.1
Viral screening[g]	X											5.2, 10.2.1
Serology[h]	X											10.2
Eligibility check	X	X										5.1, 5.2, 5.4, 8.1.1
Randomization		X										6.3
Efficacy												
MG-ADL[i]	X	X	X	X	X	X	X	X	X	X	X	8.2.1
QMG[j]		X	X	X	X	X	X	X	X	X		8.2.2
MGC		X	X	X	X	X				X		8.2.3
[redacted]												
MG-QoL15r		X				X				X		8.2.5

	SCN[a]	Treatment period				Follow-up period				End of part A[b]	UNS[c]	
Study visit		**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**			
Study week		**BL**	**W1**	**W2**	**W3**	**W4**	**W5**	**W6**	**W7**	**W8**		
Study day (window)	**-35 to -1**	**D1**	**D8 (+1)**	**D15 (+1)**	**D22 (+1)**	**D29 (±2)**	**D36 (±2)**	**D43 (±2)**	**D50 (±2)**	**D57 (±2)**	**NA**	**Protocol section**
Neuro-QoL Short Form – Fatigue		X	X	X	X	X				X		8.2.6
PGI-S		X		X		X				X		8.2.7
PGI-C				X		X				X		
EQ-5D-5L		X				X				X		8.2.8
TSQM-9		X				X						8.2.9
Safety												
Physical examinations[k]	X	X								X	X	8.3.1
Vital sign measurements[l]	X	X	X	X	X	X		X		X	X	8.3.2
ECG	X									X		8.3.3
Pregnancy testing [m]	X	X	X	X	X					X	X	8.3.5
PHQ-9 for SIB	X	X				X				X		8.3.6
Blood sampling												8.1.2 8.3.4 10.2
Clinical laboratory testing, including urinalysis	X	X		X		X		X		X	X	
PK[n]		X	X	X	X	X						8.5
PD[o]	X	X	X	X	X	X		X		X		8.6
Biomarkers[p]		X				X		X		X		8.8
Immunogenicity		X		X		X				X		8.9

	SCN[a]	Treatment period				Follow-up period				End of part A[b]	UNS[c]	
Study visit		**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**			
Study week		**BL**	**W1**	**W2**	**W3**	**W4**	**W5**	**W6**	**W7**	**W8**		
Study day (window)	**-35 to -1**	**D1**	**D8 (+1)**	**D15 (+1)**	**D22 (+1)**	**D29 (±2)**	**D36 (±2)**	**D43 (±2)**	**D50 (±2)**	**D57 (±2)**	**NA**	**Protocol section**
IMP infusion[q]		X	X	X	X							6
AE[r]	Continuous monitoring											8.4, 10.3
Concomitant therapy[r]	Continuous monitoring											6.9
Health economics[r]	Continuous monitoring											8.10

(X)=flexible activity, performed as needed; AChE=acetylcholinesterase; AChR-Ab=anti-acetylcholine receptor antibody; AE=adverse event; BL=baseline; D=day; ECG=electrocardiogram; ICF=informed consent form; IgG=immunoglobulin gamma; IMP=investigational medicinal product; IV=intravenous(ly); LRP4=low-density lipoprotein receptor-related protein 4; MG-ADL=Myasthenia Gravis Activities of Daily Living; MGC=Myasthenia Gravis Composite; [redacted]MG-QoL15r=Myasthenia Gravis Quality of Life–15 revised; MuSK=muscle-specific kinase; MuSK-Ab=anti-MuSK antibody(ies); NA=not applicable; PBMC=peripheral blood mononuclear cell; PD=pharmacodynamic(s); PGI-C=Patient Global Impression of Change; PGI-S=Patient Global Impression of Severity; PHQ-9=Patient Health Questionnaire item 9; PK=pharmacokinetic(s); QMG=Quantitative Myasthenia Gravis; QoL=quality of life; SCN=screening; SIB=suicidal ideation or behavior; TP=treatment period; TSQM-9=Treatment Satisfaction Questionnaire for Medication–9 items; UNS=unscheduled visit; V=visit; W=week; WOCBP=women of childbearing potential

Note: **All activities will be performed predose on dosing days**, unless otherwise indicated. Country-specific differences relevant to any parameter in the schedule of activities are described in Section 10.8.

[a] Scenarios that could result in a prolongation of the up to 5-week screening period are described in Section 5.4 and Section 8.1.1.

[b] Participants will start part B upon completion of part A. The end of part A visit and part B TP_1V1 will occur on the same day.

[c] A UNS visit may occur at the investigator or participant's request. Depending on the reason for the UNS visit, the activities indicated will be performed at the investigator's discretion. Required activities include vital sign measurements, brief physical examination, pregnancy test for WOCBP, and MG-ADL.

[d] Only after the participant provides informed consent can any other study-related activity occur.

[e] Medical history is the participant's family history and health history, including relevant prior therapies and surgeries, all emergency room visits, hospitalizations, and admissions to intensive care units during the prior 12 months. All available vaccination history will be recorded, with the most recent vaccination for those with multiple doses or boosters.

[f] Height will be measured only at screening. Participants may be reweighed any time a change in weight is detected per Section 6.6.

[g] Retesting for virology may occur as needed.

[h] Serology for eligibility includes total IgG and AChR-Ab, and anti-MuSK antibodies for stratification. A sample to evaluate anti-LRP4 antibodies will also be collected, but the results are unnecessary for inclusion.

[i] Once enrolled, the participant must complete the MG-ADL before any other activity.

[j] AChE inhibitors must be withheld for at least 12 hours before the QMG assessment.
[k] A complete physical examination will be conducted at screening and at the end of part A visit (D57); a brief physical examination will be conducted at baseline. A symptom-directed physical examination is allowed at visits when no physical examination is required.
[l] Maintaining the same method used to measure a participant's body temperature at baseline is recommended throughout the study.
[m] WOCBP will be evaluated for pregnancy using a serum pregnancy test at screening and a urine pregnancy test at all other time points. A negative pregnancy test result must be confirmed before the IMP infusion. Pregnancy testing may be repeated as necessary.
[n] Blood samples for PK analysis will be collected before the infusion and within 1-hour postinfusion on IMP administration days.
[o] The PD analysis comprises total IgG concentration [redacted]
[p] Serum and plasma will be collected for biomarker analysis. A whole blood sample to isolate PBMCs will only be collected at V1 (BL), V5 (D29), and D57 (end of part A visit).
[q] IMP will be administered as an IV infusion over 1 hour. Participants will remain at the site for at least 30 minutes after the infusion for safety monitoring.
[r] AEs, concomitant and rescue therapies, medical procedures, vaccines, emergency room visits, hospitalizations, and admissions to intensive care units will be recorded from the time the ICF is signed until the last study-related activity.

9.5.2 *Part B - Open-Label Period*

	Cycles 1 and 2			Cycle 3 onward[a]				EDV[b] EoS SFV	UNS[c]	
Study period	**TP 1 and 2**		**IP 1 and 2**	**TPn (n=3 onward)**		**IPn (n=3 onward)**				
Study visit[d]	**V1[e]**	**V2/V3/V4**	**V1**	**V1**	**V2/V3/V4**	**V1**	**Vm**			
Study day (window)	**A**	**A+7/14/21 (±2)**	**A+28 (±2)**	**A**	**A+7/14/21 (±2)**	**A+28 (±2)**	**Y+21[f] (±7)**	**NA**	**NA**	**Protocol section**
Efficacy										
MG-ADL[g]	X	X	X	X		X	X	X	X	8.2.1
QMG[h]	X	X	X							8.2.2
MGC	X	X	X	X	X (only V4)		X[i]	X		8.2.3
[redacted]										
MG-QoL15r	X		X	X		X	X	X		8.2.5
Neuro-QoL short form Fatigue	X		X	X		X	X	X		8.2.6
PGI-S	X	X (only V3)	X							8.2.7
PGI-C	X	X (only V3)	X							
EQ-5D-5L	X		X	X			X[i]	X		8.2.8
TSQM-9[j]			X (only IP2)	(X)	(X)	(X)	(X)	X		8.2.9
Safety										
Physical examination[k]	X		X	X			X[i]	X	X	8.3.1
Weight	(X)			(X)					(X)	6.6, 8.3.1
Vital sign measurements[l]	X		X	X			X[i]	X	X	8.3.2
ECG	X			X			X[i]	X		8.3.3
Pregnancy testing[m]	X			X			X[i]	X	X	8.3.5
PHQ-9 for SIB	X			X				X		8.3.6

	Cycles 1 and 2			Cycle 3 onward[a]				EDV[b] EoS SFV	UNS[c]	
Study period	**TP 1 and 2**		**IP 1 and 2**	**TPn (n=3 onward)**		**IPn (n=3 onward)**				
Study visit[d]	**V1[e]**	**V2/V3/V4**	**V1**	**V1**	**V2/V3/V4**	**V1**	**Vm**			
Study day (window)	**A**	**A+7/14/21 (±2)**	**A+28 (±2)**	**A**	**A+7/14/21 (±2)**	**A+28 (±2)**	**Y+21[f] (±7)**	**NA**	**NA**	**Protocol section**
Blood sampling										8.1.2 8.3.4 10.2
Clinical laboratory testing, including urinalysis	X		X	X			X[i]	X	X	
PD[n]	X		X							8.6
Biomarkers[o]	X		X			X[o]		X		8.8
Immunogenicity	X			X			X[i]	X		8.9
Efgartigimod IV infusion[p]	X	X		X	X					6
AE[q]	Continuous monitoring									8.4, 10.3
Concomitant therapy[q]	Continuous monitoring									6.9
Health economics[q]	Continuous monitoring									8.10

(X)=flexible activity, performed as needed; A=visit day; AE=adverse event; ECG=electrocardiogram; EDV=early discontinuation visit; EoS=end of study visit; IgG=immunoglobulin gamma; IP=intertreatment period; IPnVm=Vm in IPn (intertreatment period number) visit (visit number); IV=intravenous(ly); MG-ADL=Myasthenia Gravis Activities of Daily Living; MGC=Myasthenia Gravis Composite; [redacted] MG-QoL15r=Myasthenia Gravis Quality of Life–15 revised; MuSK-Ab=anti-MuSK antibody(ies); PBMC=peripheral blood mononuclear cell; PD=pharmacodynamic(s); PGI-C=Patient Global Impression of Change; PGI-S=Patient Global Impression of Severity; PHQ-9=Patient Health Questionnaire item 9; QMG=Quantitative Myasthenia Gravis; QoL=quality of life; SIB=suicidal ideation or behavior; SFV=safety follow-up visit; TP=treatment period; TPnVm=TP (treatment period number) visit (visit number); TSQM-9=Treatment Satisfaction Questionnaire for Medication–9 items; UNS=unscheduled visit; Vn=visit number; W=week; WOCBP=women of childbearing potential; x=can be 0 or higher; Y=prior IP visit

Note: **All activities will be performed predose on dosing days**. Country-specific differences relevant to any parameter in the schedule of activities are described in Section 10.8.

[a] Participants requiring retreatment from C3 onwards may begin another treatment period (ie, from TP4+xV1) at any IP visit if ≥7 days have elapsed since their last efgartigimod infusion in the prior cycle and enough time remains in the study to complete the TP and EoS. The evaluation for retreatment will occur before any scheduled activities for IPnV1/m to ensure the proper activities are performed based on the participant's clinical status (ie, those listed for IPnV1/m or TPn+1V1).

[b] The activities for participants discontinuing efgartigimod early will depend on the visit when discontinuation occurred. Participants who withdraw from the study should perform planned activities for the EDV if 56 (±3) days have not elapsed since the last dose. These participants will no longer receive efgartigimod infusions and will return for the SFV 56 ±3 days after their final infusion. If 56 ±3 days have already elapsed since the last infusion, the EDV becomes the SFV and the SFV activities must be performed. Participants who withdraw from the study between visits should attend the SFV at least 56±3 days after their final infusion. If 56 ±3 days have already elapsed since that infusion, the SFV will be planned as soon as possible.

[c] A UNS may occur at the investigator or participant's request. The activities indicated for this visit will depend on the reason for the UNS at the investigator's discretion. Required activities are vital signs, brief physical examination, pregnancy test for WOCBP, and MG-ADL.

[d] Mandatory on-site visits are all TP visits, IP1V1, IP2V1, IP3V1, EDV, EoS, SFV, and every fifth visit in the IP (eg, IPnV5, IPnV10, etc). All other visits may occur by phone.

[e] Except for the efgartigimod infusion that occurs at part B TP1V1, the end of part A visit and the part B TP1V1 assessments are identical and completed once.

[f] The timing of IPnVm is relative to the previous visit (eg, IPnV2 is 21 days after IPnV1 [Y]).

[g] The MG-ADL is recommended to be completed before any other study activity on days when it is assessed.

[h] AChE inhibitors must be withheld for at least 12 hours before the QMG assessment.

[i] Activities are to be performed only at on-site visits (every 5 visits [eg, IPnV5, IPnV10, etc...]).

[j] The TSQM-9 will be completed at IP2V1 and at the study visit closest to 1 year after BL. Site visits should not be scheduled solely to complete this questionnaire.

[k] A brief physical examination will be conducted. A symptom-directed physical examination is allowed at visits when no physical examination is required.

[l] Maintaining the same method used to measure a participant's body temperature at baseline is recommended throughout the study.

[m] WOCBP will be tested for pregnancy using urine collected for the urinalysis. A negative pregnancy test result must be confirmed before IMP administration infusion. Pregnancy testing may be repeated as necessary.

[n] The PD analysis comprises levels of total IgG [redacted]

[o] Serum and plasma will be collected for biomarker analysis. A whole blood sample will be collected to isolate PBMCs only at the IP3V1 on-site visit and the EoS, per local regulations (refer to Section 10.8).

[p] Efgartigimod IV will be administered as an IV infusion over 1 hour at V1, V2, V3, and V4 in a TP. Participants will remain on-site for at least 30 minutes after the end of the infusion for safety monitoring.

[q] AEs, concomitant and rescue therapies, medical procedures, vaccines, emergency room visits, hospitalizations, and admission to intensive care units will be recorded from the time the ICF is signed until the last study-related activity.