STATISTICAL ANALYSIS PLAN

A Phase 3b, Randomized, Open-label, Parallel-Group Study to Evaluate Different Dosing Regimens of Intravenous Efgartigimod to Maximize and Maintain Clinical Benefit in Patients With Generalized Myasthenia Gravis

Protocol:	ARGX-113-2003
SGS internal reference:	BE-80-2100206
Development phase:	Phase 3b
Sponsor:	Argenx BV
Analysis purpose:	Interim / Final analysis
SAP version number:	Final 2.0
SAP version date:	4NOV2025

SIGNATURE PAGE

Name and function	Signature and date (ddMMMyyyy)
SGS CR authors and reviewers:	
[redacted], Biostatistical Coordinator	Signed by: [redacted]
Sponsor's approval: The approver agrees the statistical analysis will be performed according to this statistical analysis plan.	
[redacted], MG Program Indication Lead, Clinical Development	Signed by: [redacted]
[redacted] Lead Biostatistician	Signed by: [redacted]

PROTOCOL HISTORY

Protocol:		
Version or ID	**Date (ddMMMyyyy)**	**Impact of the changes on the statistical analysis**
Final 1.0	06JUL2021	NAP
Final 2.0	25MAY2023	Vaccine Antibody Titers and PBMCs are not collected anymore. A safety follow-up visit should be performed for all participants. All specialty lipid tests were removed. AChR-Ab requirements were updated to clarify that historical results can be used for AChR screening criteria

France specific protocol:		
Version or ID	**Date (ddMMMyyyy)**	**Impact of the amendment on the statistical analysis**
Final 1.1	04FEB2022	No

Germany specific protocol:		
Version or ID	**Date (ddMMMyyyy)**	**Impact of the amendment on the statistical analysis**
Final 1.1	11MAY2022	No

This statistical analysis plan (SAP) only considers the latest version of the protocol, and of the protocol amendments, as listed above.

LIST OF ABBREVIATIONS

Ab	antibody
AChE	acetylcholinesterase inhibitors
AChR	acetylcholine receptor
ADA	anti-drug antibodies
ADaM	analysis data model
ADY	relative day
AE	adverse event
AESI	adverse event of special interest
ALP	alkaline phosphatase
ALQ	above the quantification limit
ALT	alanine aminotransferase
ANCOVA	analysis of covariance model
aPTT	activated partial thromboplastin time
AST	aspartate aminotransferase
ATC	Anatomical therapeutic chemical
AUEC	area under the effect curve
bid	bis in die (twice daily)
BLQ	below the quantification limit
BMI	body mass index
BUN	blood urea nitrogen
CI	confidence interval
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CRF	case report form
CRP	C-reactive protein
CTCAE	Common Terminology Criteria for Adverse Events
DBP	diastolic blood pressure
ECG	electrocardiogram
eGFR	estimated glomerular filtration rate
[redacted]	[redacted]
ER	emergency room
GGT	gamma-glutamyl transferase
gMG	generalized myasthenia gravis

HbA1c	glycosylated hemoglobin
hCG	human chorionic gonadotropin
HDL	high density lipoprotein
HR	heart rate
ICE	intercurrent event
ICF	informed consent form
ICH	International Council for Harmonisation
ICU	intensive care unit
IgG	immunoglobulin G
IMP	investigational medicinal product
INR	international normalized ratio
IP	intertreatment period
IRR	infusion-related reaction
IV	intravenous
LDH	lactate dehydrogenase
LDL	low density lipoprotein
LS	least square
MCH	mean corpuscular hemoglobin
MCV	mean corpuscular volume
MG-ADL	myasthenia gravis - activities of daily living
MGFA	Myasthenia Gravis Foundation of America
[redacted]	[redacted]
MedDRA	Medical Dictionary for Regulatory Activities
MG	myasthenia gravis
mITT	modified intent-to-treat
MSE	minimal symptom expression
NAP	not applicable
NCI	National Cancer Institute
[redacted]	[redacted]
NSID	nonsteroidal immunosuppressant
PD	pharmacodynamics
PK	pharmacokinetics
PLEX	plasma exchange

PP	per protocol
PTT	partial thromboplastin time
PYFU	participant years of follow-up
Q1	1st quartile
q2w	every 2 weeks
q3w	every 3 weeks
Q3	3rd quartile
q7d	every 7 days
qod	quaque altera die (every other day)
QoL	quality of life
QTc	corrected QT interval
QTcB	Bazett's corrected QT interval
QTcF	Fridericia's corrected QT interval
RBC	red blood cell count
SAP	statistical analysis plan
SAF	safety analysis set
SC	subcutaneous
SCR	all screened participants analysis set
SD	standard deviation
SE	standard error
SFU	safety follow-up
SGS CR	SGS Clinical Research
SIB	suicide ideation and behavior
SMQ	Standardized MedDRA Queries
SoA	schedule of activities
SOC	system organ class
SOP	standard operating procedure
STAT	statistics
SBP	systolic blood pressure
TEAE	treatment-emergent adverse event
[redacted]	[redacted]
VAS	visual analog scale
WHO	World Health Organization

W	week
WBC	white blood cell
WI	work instruction

DEFINITION OF TERMS

case report form (CRF)	A printed, optical, or electronic document designed to record protocol required information to be reported to the sponsor for each trial participant.
display	Analysis table or listing
intercurrent event	Events occurring after treatment initiation that affect either the interpretation or the existence of the measurements associated with the clinical question of interest.
phase	Interval of time in the planned conduct of a study associated with a specific purpose: for example, screening, treatment, follow-up.
significant digit	All digits of a number used to express it to the required degree of accuracy, starting from the first non-zero digit.
study drug	Pharmaceutical form of an active ingredient or placebo, being tested or used as a reference in a clinical study.
treatment-emergent abnormality /toxicity	Any post-baseline abnormality/toxicity that was not present at baseline (e.g. hemoglobin normal at baseline and grade 1 post-baseline; glucose low at baseline and high post-baseline; QTcF]450; 480] ms at baseline and >500 ms post-baseline)
treatment policy strategy	Strategy for handling intercurrent events: the occurrence of the intercurrent event is considered irrelevant in defining the treatment effect of interest; the values for the variable of interest are used regardless of whether the intercurrent event occurs.
while-on-treatment strategy	Strategy for handling intercurrent events: values up to the time of the intercurrent event are used.

TABLE OF CONTENTS

1. INTRODUCTION

The protocol plans an interim analysis which is described in a separate SAP. A second interim analysis was planned after all participants had completed Part A. This SAP describes the interim and final statistical analyses to be performed for the ARGX-113-2003 (BE-80-2100206) study.

This SAP covers the efficacy, safety, pharmacokinetic (PK), pharmacodynamics (PD), immunogenicity and general characteristics parts of the statistical analysis. It specifies the analysis displays to be presented and describes the methods and procedures in a more elaborated way than in the statistical methods section of the protocol.

The statistical analysis will process and present the results following the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) standards, in particular the ICH-E3, ICH-E6, and ICH-E9 guidelines.

1.1 STUDY OBJECTIVES

According to the protocol, the primary objective of this study is:

- To assess the clinical efficacy of intravenous efgartigimod (efgartigimod IV) 10 mg/kg administered in an every 2 weeks (q2w) continuous regimen compared to that administered in a cyclic regimen.

According to the protocol, the secondary objectives of this study are:

- To evaluate the safety and tolerability of both treatment regimens used throughout the study
- To assess the clinical efficacy of efgartigimod IV in both treatment regimens over time
- To compare the number of participants who achieve maximal clinical effect during different treatment regimens

According to the protocol, the exploratory objectives of this study are:

- To assess the patient treatment satisfaction of the continuous regimen compared with the cyclic regimen
- To evaluate the impact of the difference in treatment regimens on the quality of life (QoL) of the participants
- To evaluate the PD effect of the different treatment regimens
- To evaluate the PK of different treatment regimens
- To evaluate the immunogenicity of efgartigimod in both treatment regimens
- To assess the feasibility of monitoring participants virtually with the Myasthenia Gravis Activities of Daily Living (MG-ADL) scale and receiving infusions of the investigational medicinal product (IMP) off-site
- To measure the number of participants who can maintain clinical benefit while transitioning from a q2w to an every 3 weeks (q3w) regimen

1.2 STUDY DESIGN

This is a phase 3b, multicenter, randomized, open-label, parallel-group study to evaluate alternative dosing regimens for the IMP in patients with generalized myasthenia gravis (gMG). The clinical efficacy, maximum clinical effect, safety, and tolerability will be assessed for 2 treatment regimens: cyclic and continuous.

All participants will start Part A and receive efgartigimod infusions once-weekly (q7d) during a 3-week induction period for a total of 4 infusions. After the fourth infusion at week (W)3, participants will be randomized 3:1 to the continuous regimen arm or to the cyclic regimen arm. Participants from the cyclic arm will receive IMP administered q7d in 3-week treatment periods for 4 infusions, separated by 4-week intertreatment periods. Participants from the continuous regimen will receive IMP q2w continuously through W21. From W21 dosing onwards, Part B will start. Participants from the continuous regimen will continue to receive IMP in a continuous mode, either q2w or q3w depending on clinical assessment. Participants from the cyclic regimen will receive dosing at weeks 21, 22, 23 and 24 then start continuous regimen from W26 onwards, either q2w or q3w, depending on clinical assessment.

The study schema can be found in appendix 9.5. The schedule of activities (SoA) can be found in appendix 9.6.

1.3 EXPECTED SAMPLE SIZE

Approximately 72 participants will be enrolled and randomized in a 3:1 ratio to either the continuous q2w treatment arm or the cyclic regimen arm. A randomization ratio of 3:1 was chosen because the cyclic regimen is well-studied in more than 150 gMG participants in the completed study ARGX-113-1704 and the ongoing extension study ARGX-113-1705.

1.4 RANDOMIZATION AND BLINDING

This is an open-label study. Potential selection bias will be reduced by central randomization.

Approximately 72 participants will be enrolled and randomized in a 3:1 ratio to either the continuous q2w treatment arm or the cyclic regimen arm.

Participants will be assigned a unique patient identification number at screening. Upon randomization, the participant will be assigned to a treatment arm according to the randomization schedule generated before the start of the study.

1.5 INTERIM ANALYSIS

A first interim analysis was conducted once approximately 24 participants completed the W14 visit. This was described in a separate interim analysis SAP.

A second interim analysis will be conducted once all participants have completed the W21 visit (end of Part A) with the intention of performing a final analysis for all Part A data.

No formal statistical testing is performed for the interim analyses. There is no intention to stop the study for efficacy or to adjust the sample size based on the interim analyses data. As a result, no adjustment for multiplicity is necessary.

The cut-off date for the second interim analysis will be after all participants have completed the W21 visit or have discontinued the study early. All data collected up to that date will be included in the database lock and may be used for analysis.

1.6 SOFTWARE

SAS version 9.4 or later will be used for programming.

1.7 VALIDATION MODEL

SGS Clinical Research (SGS CR) – statistics (STAT) standard operating procedures (SOPs) and work instructions (WIs) as effective at the project start will be followed throughout the project, provided the applicable regulatory requirements are still met.

Subject-level Analysis Dataset (ADSL) and the primary endpoint (mean of the average MG-ADL total score change from baseline during W1-W21) will be validated according to model C, the rest of the analysis will follow validation model B (see SOP.STAT.020):

- Model B: review by an independent person
- Model C: review by an independent person and independent programming of the parameters indicated in this SAP

2. GENERAL METHODOLOGY

2.1 ANALYSIS SETS

2.1.1 Analysis sets

The following analysis sets will be considered in the statistical analysis:

All screened participants set (SCR):	Participants who *signed an informed consent* to participate in this study
All randomized participants set (RND):	Participants who were *randomized* into this study
Safety analysis set (SAF):	All randomized participants who are exposed to the IMP
Modified intent-to-treat analysis set (mITT):	All randomized participants with a total MG-ADL score at baseline and at least one post-baseline analysis visit at or before W21
Per protocol analysis set (PP):	Participants from the mITT, excluding the participants having major protocol deviations
PK analysis set (PK):	Safety analysis set including participants with at least one serum post dose PK measurement

Notes:

- Having signed an 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.

The efficacy and PD analyses will be performed on the mITT population. A supplementary analysis for the primary endpoint may be done on the PP population. General characteristics, safety and immunogenicity analyses will be performed on the SAF. PK analysis will be performed on the PK population.

2.1.2 As planned versus as actual analysis

Considering the specific design of this study, the actual treatment will be assumed to be the same as the planned treatment.

2.2 PHASES AND TIME POINTS

2.2.1 Phases

All events and assessments will be allocated to phases (see Table 1 and Table 2). In case the time of assessment is recorded to the second, these will be ignored for the phase allocation.

Table 1: Phase Definition

Phase	Start	End
Screening	Date of signing the informed consent form (ICF), with 00:00 added as time part.	First administration date/time – 1 minute or date of last contact with 23:59 added as the time part (for participants not treated)
Treatment Part A	First administration date/time	If present, administration date/time at W21[a] - 1 minute. Otherwise date of last contact[b] with 23:59 added as time part.
Treatment Part B	Administration date/time at W21[a]	Date of last contact[b], with 23:59 added as time part

[a] W21 refers to the case report form (CRF) visit.
[b] Or date of database cut-off for ongoing participants

Table 2: Phase Definition for prior and concomitant therapies

Phase	Start	End
Screening	Date of signing the ICF	First administration date – 1 day or date of last contact (for participants not treated)
Treatment Part A	First administration date	If present, administration date at W21[a] - 1 day. Otherwise date of last contact[b]
Treatment Part B	Administration date at W21[a]	Date of last contact[b]

[a] W21 refers to the CRF visit.
[b] Or date of database cut-off for ongoing participants

In case a participant does not have a W21 administration (or if no date/time is available), but the participant continues to Part B according to the CRF form 'Patient

Status Part B' or the participant has treatment administration on >W21 visits, the start date/time for Treatment Part B will be determined as follows:

- If W21 visit date is available, Treatment Part B starts on the W21 visit date + 1 day, with 00:00 added as time part.
- If no W21 visit date is available, Treatment Part B starts on the target date of the W21 visit (see section 2.2.4) + 1 day, with 00:00 added as time part.

If the start date for Part B is on or after the date of last contact, no Part B phase will be derived.

Adverse Events (AEs) and concomitant medications will be allocated to phases as described in sections 5.1.2 and 3.5.2 respectively. All other assessments will be allocated to phases 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. If this is not possible, assessments will be handled as follows:

- Treatment phase vs. screening phase: assessments will be allocated to the treatment phase unless the available parts of the assessments start or stop date(time) provide evidence for allocating to the screening phase.
- Multiple treatment phases: assessments will be allocated to treatment Part A unless the available parts of the assessments start or stop date/time provide evidence the assessments did not occur during Part A.

2.2.2 Baseline and change from baseline

The baseline value is defined as the last available non-missing value prior to first administration of the IMP in the study.

For parameters related to questionnaires, the baseline is the last value before or at the day of first administration of the IMP, independent of the time of administration.

Change from baseline at time point t = value at time point t – baseline value.

Percentage change from baseline at time point t is defined as follows:

- When baseline value is not zero: 100*((value at time point t – baseline value) / baseline value)
- When both baseline value and value at time point t are zero: 0
- When baseline value is zero and value at time point t is not zero: not calculated

2.2.3 Relative day

Relative days in the study (ADY) will be calculated according to the following rule:

- Concerned date < reference date: ADY = concerned date – reference date
- Concerned date ≥ reference date: ADY = concerned date – reference date + 1

The reference date is the date of first administration of study drug.

2.2.4 Analysis visits

All assessments, including unscheduled assessments, will be allocated to analysis windows. Tables and listings will present the analysis windows as defined below, not the CRF visits. Allocation of assessments (see Table 3) will be done using their relative day in the study (see section 2.2.3). During Treatment Part A, assessments that are scheduled weekly per protocol SoA (MG-ADL total score and suicide ideation and behavior (SIB) risk monitoring) will use different analysis windows than other assessments not scheduled weekly.

Table 3: Analysis visits

Phase	Analysis window	Target ADY	Lower limit ADY	Upper limit ADY
Screening	Screening[a]	-14	-INF	1
Treatment Part A *(assessments scheduled weekly per protocol)*				
	Baseline	1	-INF	1[b]
	Week 1	8	1[b]	11
	Week 2	15	12	18
	Week x[c]	7*x+1	7*x-2	7*x+4
	Week 21	148	145	z[d]
Treatment Part A *(other assessments)*				
	Baseline	1	-INF	1 [b]
	Week 4	29	1[b]	40
	Week 7	50	41	64
	Week 11	78	65	89
	Week 14	99	90	113
	Week 18	127	114	138
	Week 21	148	139	z[d]
Treatment Part B				
	Week 26	183	z[d]	200
	Week (26+5*y)[e]	(26+5*y)*7+1	(26+5*y)*7-16	(26+5*y)*7+18
	Week 126	883	866	INF

[a] As the interval of screening and baseline are overlapping, it may be that the same assessment will be attributed to both timepoints.
[b] An assessment at Day 1 will be attributed to Week 1/Week 4 in case it is after the first administration, to Baseline otherwise.
[c] x goes from 3 to 20.
[d] z is the relative end day of treatment part A analysis phase. Assessments on day z will be allocated to part A week 21 if prior to dosing and to part B week 26 otherwise.
[e] y goes from 1 to 20.

Baseline is defined in section 2.2.2.

Per parameter and analysis window, the value closest to the target ADY will be used in analysis tables, other values will only be listed. 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 will be removed before the selection is made. For immunogenicity, unevaluable results due to missing results will only be selected if no other results are available.

For questionnaires, the date of the total score will be used to select the value closest to the target date and the associated items of the same assessments will be used for the analysis. For immunogenicity, the anti-drug antibodies (ADA) result will be used for the selection and the associated sample parameters (titer) will be used for the analysis.

For anti-acetylcholine receptor antibodies (AChR-Ab), the original screening result can be selected as screening value for re-screened participant if no later predose result is available.

The screening analysis visit will not be shown in the tables, but will only be listed. For the tables by visit only visits expected per SoA (appendix 9.6) will be shown.

2.2.5 Worst-case

A worst-case analysis visit will be created for parameters for which abnormalities and/or toxicity grades are defined to summarize values considered as the worst-case. For abnormalities it is derived per parameter and in case both the lowest and the highest values are considered abnormal, a participant can have two worst-case analysis visits for a same parameter. For toxicity grades the worst-case is the value associated to the highest toxicity grade and is derived per parameter and toxicity direction (hypo / hyper). Worst-case values will be determined per treatment phase.

All non-missing post-baseline values including unscheduled assessments will be considered when deriving the worst-case analysis visits.

2.2.6 Best response

A best response analysis visit (ie, minimum postbaseline value and maximum drop from baseline for MG-ADL total score, [redacted], total IgG, and anti-AChR-Ab and maximum postbaseline value [redacted] will be created for part A, part B, and overall for efficacy and PD parameters listed above to summarize values considered as the best response.

All non-missing postbaseline values, including unscheduled assessments and assessments not selected for the analysis visit, will be considered when deriving the best response analysis visit.

2.3 IMPUTATION AND ROUNDING RULES

2.3.1 Missing values

No imputation will be done of missing values (ie, observed cases analysis).

2.3.2 Values below or above a threshold

Laboratory safety and anti-AChR-Ab values expressed as below/above the quantification limit (BLQ/ALQ) will be imputed by the value of the quantification limit itself.

PK concentrations below the detection limit will be flagged as BLQ in the listings. For descriptive statistics by scheduled timepoint, BLQ values will be set to zero. All ALQ values will be set to the upper limit of quantification for the descriptive statistics by scheduled timepoint.

Total immunoglobulin G (IgG) values expressed as BLQ or ALQ will not be imputed and will be excluded from analysis.

Positive ADA samples reported as 'negative titer' will be imputed by 1.

Laboratory safety, immunogenicity, PK and PD listings will always show the non-imputed values.

2.3.3 Handling partially or completely missing dates in calculations

Partially missing date of MG diagnosis will be imputed as follows:

- Missing day will be imputed with first day of the month
- Missing day and month will be imputed with 1JAN

2.3.4 Rounding

Variables will be rounded to the appropriate number of significant digits (see Definition of terms) at display level:

- Area under the effect curve (AUEC) will be rounded to the integer.
- Time since diagnosis and body mass index (BMI) will be rounded to 1 decimal.
- Estimated glomerular filtration rate (eGFR) will be rounded to 2 decimals.
- Ratios will be rounded to the number of significant digits of the parameter with the least number of significant digits.
- Safety laboratory results will be rounded to a maximum of 3 decimals.

2.3.5 Outliers

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

2.4 PRESENTATION OF RESULTS

Unless mentioned otherwise, tables will present results from Part A, then Part B then Overall (ie over the entire study) in a staggered fashion within the same output. The analysis set used for each part is specified in 2.1.1. All listings will be staggered for Part A then Part B.

2.4.1 Calculation of descriptive statistics and percentages

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

Descriptive statistics will include the number of non-missing data points, the arithmetic mean, the standard deviation (SD), the median, minimum, Q1, Q3 and maximum. In addition, for efficacy, PD and safety outputs over time, the 95% 2-sided confidence interval (based on t-distribution, without continuity correction) and standard error (SE) will be provided.

Mean, median, Q1 and Q3 will be presented with one more decimal place than the individual values. The 95% 2-sided confidence interval, SD and SE will be presented with two more decimal places than the individual values. Minimum and maximum will be presented with the same number of decimal places than the individual values.

Descriptive statistics for PK concentrations will include n (number of observed values), arithmetic mean, SD, median, minimum and maximum, and the coefficient of variation (CV%).

Efgartigimod serum concentrations will be presented with 3 significant digits in µg/mL, except values ≥1000, which will be presented without the decimals. The descriptive statistics should be rounded to the same number of significant digits as the individual values. If more than half of the values are BLQ, SD, CV% and geometric coefficient of variation will not be calculated.

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 analysis set per treatment and phase.

For frequency tabulations and cross-tabulations, the denominator will be all participants in the analysis set per treatment. For tables where results are shown by analysis visit, the denominator will be all participants in the analysis set per treatment and per analysis visit. Missing values will not be included in the denominator count when computing percentages. For cross-tabulations of post-baseline results versus baseline results, a 'missing' category will be shown for baseline results if applicable.

2.4.2 Presentation of treatments

The following treatment labels will be used in the tables and listings for Part A and overall:

- EFG IV CYCLIC
- EFG IV CONTINUOUS
- TOTAL

The following treatment labels will be used in the tables and listings for Part B:

- EFG IV CYCLIC TO CONT
- EFG IV CONTINUOUS
- TOTAL

The total treatment group will only be shown in the tables.

For Part B, some outputs will display results from the following subgroups:

- EFG IV CYCLIC TO CONT - Q2W: participants randomized to the cyclic arm who never switched to Q3W
- EFG IV CYCLIC TO CONT - Q3W: participants randomized to the cyclic arm who ever switched to Q3W
- EFG IV CYCLIC TO CONT - TOTAL
- EFG IV CONTINUOUS - Q2W: participants randomized to the continuous arm who never switched to Q3W
- EFG IV CONTINUOUS - Q3W: participants randomized to the continuous arm who ever switched to Q3W
- EFG IV CONTINUOUS - TOTAL

2.4.3 Ordering in tables and listings

All tables will be presented per treatment, unless specified otherwise. If present, worst-case will be shown last.

Listings for general characteristics, results will be ordered by part, treatment and participant, unless specified otherwise.

All other listings will be ordered by part, treatment, participant, phase, analysis visit and time point, unless specified otherwise.

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.

Efgartigimod cyclic treatment will always be shown first, and then efgartigimod continuous treatment. If applicable, the total column will be shown last.

3. GENERAL CHARACTERISTICS ANALYSES

3.1 PARTICIPANT DISPOSITION

The following participant data will be tabulated:

- The number of participants in each analysis set
- The number and percentage of participants by country and site
- The number and percentage of participants for each phase/analysis visit
- The number and percentage of participants with an on-site or off-site type of visit for each analysis visit
- Descriptive statistics and tabulation of the phase and study duration (see section 2.2.1), calculated as phase (study) end date – phase (study) start date + 1 day.
- Total participant years of exposure defined as the sum of treatment duration of all participants by part and overall.
- Study discontinuation:
    - The number and percentage of screening failures and of each screen failure reason and the number and percentage of participants who were randomized but not treated.
    - Overall and by study part, 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.
    - For Part B, the number and percentage of study discontinuations by dosing regimen received at the time of discontinuing the study (q2w or q3w).
    - The number and percentage of participants who discontinued the study prior to week 26 (yes/no)
- Treatment discontinuation:
    - Overall and by study part, the number and percentage of participants who completed or discontinued the treatment as documented on the end of treatment page and the number and percentage of participants for each treatment discontinuation reason.
    - For Part B, the number and percentage of treatment discontinuations by dosing regimen received at the time of discontinuing the treatment (q2w or q3w).
    - The number and percentage of participants who discontinued the treatment prior to week 26 (yes/no)

All information collected in the CRF concerning treatment allocation, study and treatment discontinuation and information on analysis sets and phases will be listed.

3.2 PROTOCOL DEVIATIONS AND ELIGIBILITY

The number and percentage of participants with major and minor protocol deviations will be tabulated, overall and per class of deviation.

All available information concerning major and minor 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 birth, women of childbearing potential, age at informed consent, race, ethnicity, height, weight at screening, year of birth, date of signing ICF.
- Baseline disease characteristics: date of MG diagnosis, Myasthenia Gravis Foundation of America (MGFA) classification at screening and at diagnosis, MG-ADL, [redacted] regular use of a breathing mask, any use of feeding tube for MG, hospitalization for MG, emergency room (ER) visit for MG, prior intensive care unit (ICU) visit for MG.

3.3.2 Derivation rules

The following parameters will be derived:

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

  Note: The BMI will be calculated and rounded as detailed in section 2.3.4, only when not available in the database.
- Age category: 18-64 years, ≥ 65 years.
- Weight category: <50 kg, 50-<75 kg, 75-<120 kg, ≥120 kg
- Region: country will be categorized into the following regions:
  - Europe: EU and EEA countries, EFTA countries (Norway, Iceland, Liechtenstein, and Switzerland) and UK
  - North-America: United States, Canada
  - Rest of the world: any countries not mentioned above
- MG-ADL total score at screening and at baseline: 5-7, 8-9, ≥10.
- MG-ADL total score at baseline: ≤12, >12.
- Time since diagnosis (years): (date of ICF – date of diagnosis)/365.25.

  Note: Partially missing date of diagnosis will be imputed as specified in section 2.3.3 and result will be rounded as detailed in section 2.3.4.
- Disease duration (time since diagnosis category): <1 year, 1-<5 years, 5-<10 years, >10 years

3.3.3 Presentation of results

Demographics will be presented using descriptive statistics for age, height, weight and BMI at screening and frequency tabulations for age category, sex at birth, region, race, and ethnicity.

Baseline disease characteristics will be presented using descriptive statistics for:

- time since diagnosis (years)
- MG-ADL total score (at screening and at baseline)
- [redacted]
- [redacted]
- [redacted]
- [redacted]

Baseline disease characteristics will be presented using frequency tabulations for:

- MGFA Classification (at diagnosis and at screening)
- MG-ADL total score categories (at screening and at baseline)
- regular use of breathing mask
- any use of feeding tube for MG
- any prior hospitalization for MG
- any prior emergency room visit for MG
- any prior intensive care visit for MG

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 using the medical dictionary for regulatory activities (MedDRA) into system organ classes and preferred terms. For each finding, a start and stop date or ongoing flag is collected.

3.4.2 Derivation rules

The following parameters will be derived:

- Medical history finding: not ongoing at screening, ended before date of signing informed consent.
- Concomitant disease finding: still ongoing at screening.

3.4.3 Presentation of results

Medical history (not ongoing at screening) and concomitant diseases (still ongoing at screening) will be tabulated in a separate table. The table will show:

- The number and percentage of participants with findings
- The number and percentage of participants with findings by system organ class and preferred term

All medical history and concomitant disease data will be listed. A separate listing will be created for MG medical history and for hospitalizations, ER visits, and ICU admissions.

3.5 PRIOR AND CONCOMITANT THERAPIES

3.5.1 Available data

All therapies and procedures are coded using the World Health Organization (WHO)-DRUG Dictionary. The latest version available at the time of the analysis will be used. Anatomical therapeutic chemical (ATC) selection is performed. ATC coding up to level 4 is available in the clinical database. For each therapy and procedure, 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 date, therapies and procedures will be allocated to each phase during which they were administered. A therapy or procedure can therefore be reported in more than one phase.

Phases are defined in Table 2. Therapies and procedures with (partially) missing dates will be allocated to each phase unless the available parts of the therapy start or stop date or prior and ongoing flags provide evidence the therapy or procedure was not taken during that phase.

All therapies and procedures will be allocated into one or both of the following categories:

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

A therapy or procedure that started before the first dose date and continued during the study will be classified as both prior and concomitant.

Additionally, MG-specific therapies and procedures 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

3.5.3 Presentation of results

The following medication records will be excluded from tables: medications that ended >1 year prior to signing the ICF for MG-specific therapy or >6 months prior to signing the ICF for other therapies (excl. vaccinations). All vaccination entries will be considered in the tables. All data will be listed. In case of a missing or incomplete end date, the record will be included, unless the available parts of the therapy stop date or ongoing flag provide evidence that the end date occurs 1 year/6 months prior to signing the ICF.

Prior and concomitant therapies will be summarized 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.

All prior and concomitant therapies data will be listed with detailed information about ATC classes. Prior and concomitant procedures will be listed separately.

Separate tables will be created for prior and baseline MG-specific therapies. These tables will also show the number of participants with at least 1 MG therapy, the

number of participants with at least 2 MG therapies and the number of participants with at least 3 MG therapies. For baseline MG therapies, the number of participants per medication class (steroids, nonsteroidal immunosuppressants (NSIDs), acetylcholinesterase inhibitors (AChE) inhibitors, procedures, and other: see appendix 9.4) and the combination of classes will also be shown.

The changes in dose of MG therapy will be tabulated.

A separate listing will be created of participants receiving rescue medications. Rescue medications will be identified based on a flag on the SDTM data in the CM domain (Concomitant Medications).

A listing containing the detailed information related to vaccination history will also be created.

3.6 STUDY DRUG ADMINISTRATION

3.6.1 Available data

For each study drug administration, the start and end date/times and the volumes will be recorded. Per protocol, each infusion should be administered within two days of the analysis visit target day.

3.6.2 Derivation rules

The following parameters will be derived:

- The actual dose in mg/kg will be calculated as = $\left(\frac{\text{actual volume extracted from vials (mL)} * 20\ (\text{mg/mL})}{\text{actual volume extracted from vials (mL)} + \text{actual volume of NaCl solution added to IV bag (mL)}}\right) * \left(\frac{\text{actual volume infused (mL)}}{\text{last available participant weight (kg) before or at day of dosing}}\right)$
- Actual dose (mg/kg) per administration, using categories <9 mg/kg, 9-11 mg/kg, >11 mg/kg
- Number of administrations: number and percentage of participants who had 1, 2, 3, etc. administrations
- Treatment compliance for Part A defined as (number of doses received/12)*100%
- q3w transition status:
  - transition to q3w: participants who transitioned from q2w to q3w at least once
  - no transition to q3w: participants who never transitioned from q2w to q3w

3.6.3 Presentation of results

The number and percentage of participants with an infusion, with an infusion within the allowed protocol time window (ie, 2 days before or after the target date of the CRF visit, see also SoA in appendix 9.6) and with an infusion out of the allowed protocol time window will be tabulated at each CRF visit (part A) and at each CRF visit and overall (part B).

The number and percentage of infusions performed on-site and off-site per CRF visit and overall will be tabulated. The overall number and percentage of infusions performed on-site and off-site for the sites and visits allowing off-site administrations (ie, the Netherlands and Austria) will be shown.

A frequency table for the number of administrations and the actual dose per administration will be created. Descriptive statistics of the overall number of administrations and treatment compliance will be provided.

For Part B only, a table will show the number and percentage of participants who:

- Entered Part B
- Were in a cyclic dosing regimen in Part A and have a W26 or later assessment (transition to a continuous regimen)
- Transitioned from q2w to q3w dosing regimen
- Transitioned from q3w to q2w dosing regimen

And also the total number of dosing regimen switches from q2w to q3w per participant.

For Part B only, for the participants who transitioned from q2w to q3w:

- time to first transition to q3w (days) = date of investigator's decision to transition to q3w regimen - (W21 (for participants randomized to continuous regimen) or W28 (for participants randomized to cyclic regimen) administration date) + 1

  Note: if the participant does not have a W21/W28 administration date, the target date for that visit (see section 2.2.4) will be used.
- duration of first q3w regimen (days) = date of first q2w dose after returning to q2w regimen - date of first q3w dose + 1

  Notes: if the participant does not return to the q2w regimen before the end of the study, the time will be censored and the censoring date will be set to the date of last contact. The Kaplan-Meier method will be used for this analysis. The number of events, number of censored observations, 25th percentile, median and 75th percentile with 95% CI will be presented.
- total duration in q3w regimen (days): each q3w regimen duration will be derived similar to previous parameter. The total duration is the sum of all q3w regimens.

For Part B only, treatment duration in part B will be tabulated using descriptive statistics, by q3w transition status.

All study drug administration data will be listed.

4. EFFICACY, PHARMACOKINETICS, PHARMACODYNAMICS AND IMMUNOGENICITY ANALYSES

4.1 EFFICACY

4.1.1 Available data

Efficacy will be assessed using MG-ADL total score, [redacted]

4.1.2 Endpoints and derivation rules

The efficacy analysis will be done on the mITT population (see section 2.1.1).

For all references to weeks, analysis visits are considered as described in section 2.2.4 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.

MG-ADL total score [redacted] total score will be used as collected; no recalculation will be performed.

4.1.2.1 PRIMARY ENDPOINT

The estimand for the primary endpoint is defined as follows:

- Population: mITT (see section 2.1.1)
- Variable: mean of the average MG-ADL total score change from baseline from Week 1 up to and including Week 21
- Main intercurrent events (ICE): described in Table 4
- Population-level summary: difference in treatment means of the average MG-ADL total score change from baseline

Table 4: Main intercurrent events

ICE	Analysis strategy
Early treatment discontinuation for any reason before W21.	Treatment policy: the available data (including the end of treatment visit) will be used in the analysis regardless of whether a participant experienced the ICE or not.
Post-baseline initiation of IV or subcutaneous (SC) IgG therapy or plasma exchange (PLEX) as rescue therapy[a] before W21	While-on-treatment: data before and on the ICE date will be used in the analysis. Data in part A after the date of initiation of the rescue therapy will be considered missing in efficacy derivations or tabulations, but will be included in listings.

[a] The following procedures can trigger the ICE if evaluated as recue therapy by the investigator and if initiated before the participant's W21 CRF visit (or before ADY=148 if no W21 visit is available): plasmapheresis, immunoglobulin therapy.

4.1.2.2 SECONDARY ENDPOINTS

Unless otherwise specified, the analysis of secondary efficacy endpoints will follow the same ICE strategies as described for the primary endpoint in Table 4. Note that percent of time with a reduction of the MG-ADL total score of at least 2 points will use a composite endpoint strategy as described in its derivation rules.

The following secondary efficacy endpoints are defined:

1) Changes from baseline (see section 2.2.2) in the MG-ADL total score at each analysis visit.
2) Normalized AUEC of MG-ADL total score percent changes from baseline during the following intervals: day 1 - W7, W7 - W14, W14 - W21, W7 - W21.

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

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

   The AUEC will then be normalized by dividing by the total number of days available in the interval.

   Where:

   - C_i is the percent change from baseline in MG-ADL total score at time point t_i (in days). The change from baseline on day 1 (baseline) is 0.

   Notes:

   - 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 with the exception of baseline which will be set at the date of first medication intake (relative day = 1).
   - AUEC will be rounded as detailed in section 2.3.4.
   - In case for a specific time interval the start or end visit of the interval is missing, the AUEC for that interval can still be calculated, but excluding the trapezoid with missing start or end visit.

     Example: if W7 is missing, the AUEC for day 1 - W7 will be derived as $AUEC_{day\ 1\ -\ W6} / 42$
   - In case 2 or more consecutive visits are missing within the AUEC interval, the AUEC over that specific time interval will not be derived.

3) Average MG-ADL total score change from baseline during the following intervals: W1-W7, W8-W14, W15-W21, W8-W21, W1-W21.

4) Number and percentage of participants who have a ≥ x points improvement (ie, decrease) in MG-ADL total score from baseline during the following intervals: W1-W7, W8-W14, W15-W21, W8-W21, W1-W21.

   For each participant, the magnitude of response (ie, maximum drop from baseline) in each specified interval will be derived.

   A participant achieves a magnitude of response ≥ x during an interval if at least once during the interval an MG-ADL total score change from baseline of ≤ -x was observed. Where x = 1, …, maximum drop of any participant.

5) Percentage of time participants have a reduction in MG-ADL total score of at least 2 points from baseline during W4 through W21. This is derived for each participant as follows:
   - All post-baseline assessments in part A will be used. Day (or relative day) refers to relative day in the study, see section 2.2.3.
   - Start day (onset): relative day of the first post-baseline assessment with a reduction of at least 2 points. If a reduction of at least 2 points was observed during analysis week 4 but before day 29, the start day is 29.
   - End day: relative day of the first assessment after onset with no reduction of at least 2 points – 1. If reduction continues up until analysis week 21, the end day is 148.
   - Missing assessments will be handled as follows:
     - In case of one missing assessment between two assessments with reduction, the participant continues to have a reduction.
     - In all other cases, the participant is considered to have no reduction from the target day of the missing assessment onwards, up until the day before the next assessment. These cases include: multiple consecutive missing visits, one missing assessment followed by an assessment without reduction, or a missing Week 21 assessment in Part A.
   - ICEs will be handled using a composite endpoint strategy: the ICEs are considered informative about whether the participant has a reduction of the MG-ADL total score of at least 2 points:
     - In case a participant discontinues treatment before W21, the participant will be considered as having no reduction from the day after the end of treatment visit onwards.
     - In case a participant discontinues the study, the participant will be considered as having no reduction the day after study discontinuation.
     - In case a participant initiates IgG therapy or PLEX as rescue medication, the participant will be considered as having no reduction the day after rescue therapy was initiated.

Note: After an ICE, the participant will be considered as having no reduction until the end of Part A, regardless of the actual result of any assessment.

- A participant can have multiple periods with a reduction. The time with a reduction of the MG-ADL total score of at least 2 points for each period will be summed: sum of (end day – start day + 1).
- Percentage of time with a reduction of the MG-ADL total score of at least 2 points = time with a reduction of the MG-ADL total score of at least 2 points / 120.

6) Number and percentage of participants who achieve minimal symptom expression (MSE), defined as a MG-ADL total score of 0 or 1, in the following intervals: W1-W7, W8-W14, W15-W21, W8-W21, W1-W21.

   Actual values of the MG-ADL total score will be categorized as ≤1 (MSE), >1.

4.1.2.3 EXPLORATORY ENDPOINTS

[redacted]

4.1.2.4 ADDITIONAL ENDPOINTS

[redacted]

4.1.3 Presentation of results and statistical analysis

The average MG-ADL total score change from baseline from Week 1 up to and including Week 21 will be analyzed using an analysis of covariance model (ANCOVA) with treatment as a fixed categorical effect and baseline MG-ADL total score as a covariate. This will be repeated for the PP analysis set if at least 10 % of participants are excluded from the primary analysis.

The following statistics will be presented for ANCOVA:

- Least Square (LS) Mean per treatment arm with corresponding SE and 95% CI;
- LS Mean difference with corresponding SE and 95% CI (EFG IV cyclic – EFG IV continuous).

Summary statistics will be provided for:

- MG-ADL total score and individual items actual values and changes from baseline at each analysis visit.
- Normalized AUEC during the specified intervals.
- Average MG-ADL total score change from baseline during the specified intervals.
- MG-ADL total score magnitude of response during the specified intervals.
- Percentage of time with a reduction of the MG-ADL total score of at least 2 points during W4 to W21.
- [redacted]

Frequency tables will be provided for:

- Number and percentage of participants per magnitude of response category during the specified intervals.
- Number and percentage of participants with MSE during the specified intervals.
- MG-ADL individual items and total score at each analysis visit.
- [redacted]
- [redacted]

The denominator for the percentage calculations will be the total number of participants having data for the parameter per treatment and per interval or per analysis visit in the mITT analysis set. The total treatment group will not be presented.

For Part B, the applicable tables will also be summarized by dosing regimen (see section 4.1.4).

All data on MG-ADL individual items, total score and its derived parameters will be listed. [redacted]

4.1.4 Subgroup analyses

The average MG-ADL total score change from baseline from Week 1 up to and including Week 21, and its change from baseline by analysis visit will be presented for the following subgroups (for derivations see sections 3.3.2 and 3.5.2):

- Age category at baseline
- Sex at birth
- Weight category
- Race
- Region
- MG-ADL score category at baseline
- MG prior therapy
- MG baseline therapy
- Disease duration

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 SoA (see appendix 9.6).

Time windows for PK samples are specified as follows:

- When samples are taken on dosing days, the PK samples will be taken both predose (within 1 hour of starting the infusion) and postdose (within 1 hour after the end of the infusion)
- Non-dosing days in Part A: +/- 2 days
- Non-dosing days in Part B and safety follow-up (SFU) visits: +/- 3 days

All concentration data-points with deviations outside these permitted ranges will be excluded from the descriptive statistics on concentrations by scheduled timepoint, explained by a footnote in the appropriate tables. Day 1 predose PK sample taken earlier than 1h prior to administration will not be excluded from descriptive statistics on concentrations.

The PK samples taken after a missed dose up to the next administered dose will be excluded from descriptive statistics, explained by a footnote in the appropriate tables.

4.2.2 Derivation rules

BLQ and ALQ concentrations will be imputed according to the rules mentioned in section 2.3.2.

4.2.3 Presentation of results

Descriptive statistics on concentration data will be presented in tables, per visit and per time point. Descriptive statistics will be calculated for Part A for EFG IV CYCLIC and EFG IV CONTINUOUS only.

Individual concentration data and actual blood sampling times from start of infusion (if predose) / from end of infusion (if postdose) for PK assessments will be listed. Data issues like time deviations will be mentioned in the remarks.

4.3 PHARMACODYNAMICS

4.3.1 Available data

The following PD parameters will be measured: total IgG levels and anti-AChR antibodies.

4.3.2 Derivation rules

BLQ and ALQ results will be dealt with according to the rules mentioned in section 2.3.2.

4.3.3 Presentation of results

Descriptive statistics will be presented in tables per part and analysis visit (including best response). Descriptive statistics will be provided in terms of actual values and changes from baseline for each visit. Percent changes from baseline will also be presented.

All PD data will be listed.

4.4 IMMUNOGENICITY

4.4.1 Available data

Presence of ADA to efgartigimod is measured per SoA (see appendix 9.6).

Immunogenicity samples are analyzed in a 3-tiered approach:

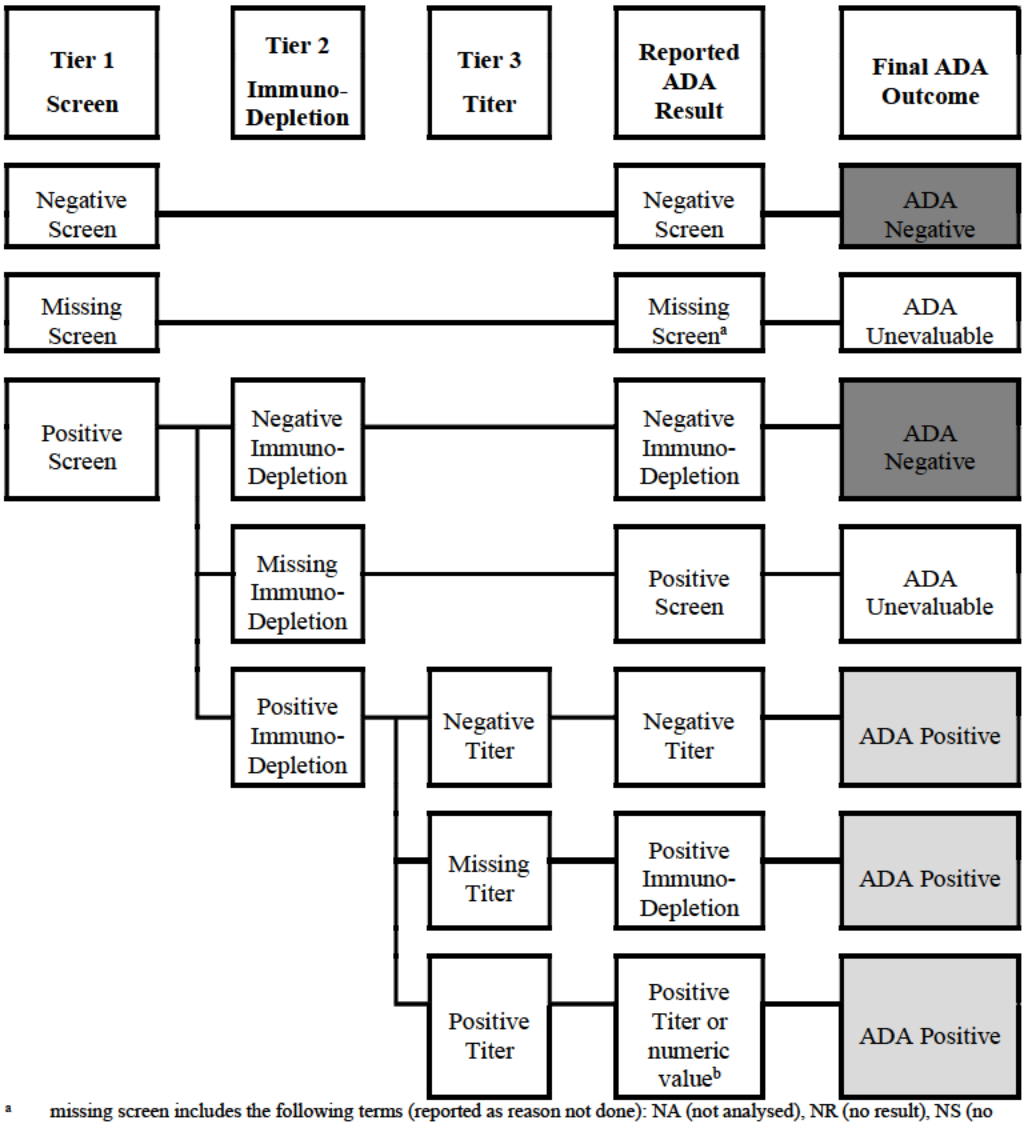
- All samples are evaluated in the ADA screening assay and are scored ADA screening positive or negative
- If a sample scored positive in the ADA screening assay, it is further evaluated in the confirmatory assay and is scored confirmed positive (positive immunodepletion) or confirmed negative (negative immunodepletion)
- If a sample is scored as confirmed positive, the samples are further characterized in the ADA titration assay (to determine titer)

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 (e.g., 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 as ADA positive.
- If a sample is negative in the titration assay, it will be reported as 'negative titer' but it should be considered as ADA positive since it was confirmed positive in the second tier.
- If a sample could not be analyzed or reported as 'positive screen', the ADA sample status is ADA unevaluable.

An overview of this 3-tiered approach and all possible ADA sample results that will be reported by the laboratory is given below. 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 analysed), 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 numeric value.

4.4.2 Derivation rules

4.4.2.1 PARTICIPANT CLASSIFICATION FOR ADA

Table 5 below gives an overview of how the ADA participant classification will be derived, starting from the participant baseline ADA sample status (see also section 4.4.1). The ADA participant classification will be done separately for part A, part B and overall.

Table 5: Participant classification for ADA against efgartigimod

Participant ADA classification	Highest[c] post baseline[e] sample status				
	ADA negative	**ADA positive (missing titer[a])**	**ADA positive (negative titer[b] or numeric titer value)**		**ADA not evaluable**
Baseline ADA sample status					
ADA negative	ADA negative	Treatment Induced ADA	Treatment Induced ADA		*ADA unevaluable*
ADA positive (missing titer[a])	Treatment Unaffected ADA	*ADA unevaluable*	*ADA unevaluable*		*ADA unevaluable*
ADA positive (negative titer[b] or positive titer)	Treatment Unaffected ADA	*ADA unevaluable*	**titer < 4 x baseline titer:** Treatment Unaffected ADA	**titer ≥ 4x baseline titer:** Treatment Boosted ADA[d]	*ADA unevaluable*
ADA not evaluable	*ADA unevaluable*	*ADA unevaluable*	*ADA unevaluable*		*ADA unevaluable*

[a] Samples with missing titer have as reported ADA result 'positive immunodepletion' or 'positive titer';
[b] Results reported as 'negative titer', ie, titer value <1 will be set to value of 1;
[c] Highest sample status (by part and overall), with order: (from low to high): ADA unevaluable, ADA negative, ADA positive (missing titer /positive immunodepletion), ADA positive with titer < 1 ('negative titer' as reported ADA result, titer value set to 1), ADA positive with titer ≥ 1 (ie, positive titer and selecting the sample with highest titer)
[d] Note: Fourfold difference in titer values is considered significant in case a twofold serial dilution is applied (= two times the dilution factor) (reference to Shankar et al., 2014).
[e] For the participant classification per part, the assessments within that part will be considered.

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', the latter two as 'ADA positive'.

ADA unevaluable participant = participant classified as ADA unevaluable or with missing baseline ADA sample or without post-baseline ADA samples

ADA incidence = percentage of participants with treatment-induced or treatment-boosted ADAs (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)

4.4.3 Presentation of results

Frequency tabulations (number and percentages) will be provided with ADA negative/positive/unevaluable samples per analysis visit. This will be repeated by ADA participant classification by part and overall. Part A table will be by treatment group, part B and total tables will be for the total treatment group only. Part A of the tables will be based on Part A ADA participant classification, Part B on Part B classification, and overall on overall classification.

Frequency tabulations (number and percentages) will be provided by phase (ie, by part) and overall on:

- participants per ADA participant classification
- prevalence and incidence of ADA
- ADA unevaluable participants
- ADA baseline positive/negative/unevaluable samples

For details on the definitions, see the above section 4.4.2.1. Part A table will be by treatment group, part B and total tables will be for the total treatment group only.

Correlation tables by ADA participant classification will be provided for the following parameters. When applicable, Part A of the tables will be based on Part A ADA participant classification, and overall on overall classification:

- mean average MG-ADL total score change from baseline from W1-W21 (only Part A)
- mean drug concentration over time (only Part A)
- mean percent change from baseline in total IgG (only Part A)
- treatment-emergent AEs (TEAEs) (Part A and overall)
- serious TEAEs (Part A and overall)
- Infusion-related reactions (IRR) (Part A and overall)

ADA titer values against efgartigimod will be summarized by means of descriptive statistics by ADA participant classification by part. Part A table will be by treatment group, part B and total tables will be for the total treatment group only.

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

5. SAFETY ANALYSES

5.1 ADVERSE EVENTS

5.1.1 Available data

AEs are coded into system organ classes and preferred terms using the MedDRA. AEs were graded using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. For each AE, start and stop date/times are collected as well as severity, a seriousness flag, treatment relatedness, relatedness to procedures, action taken towards the study drug and outcome.

5.1.2 Derivation rules

TEAEs are defined as AEs starting on or after first administration of any study drug.. In case of a (partially) missing AE start date/time, the event will be considered as treatment-emergent, unless the available parts of the AE start date/time provide evidence not to do so.

Based on their start date/time, AEs will be allocated to the phase during which they started. Each AE will therefore be reported in only one phase. Phases are defined in Table 1. In case the AE start date/time is incomplete or missing and the AE could consequently be allocated to more than one phase, a worst-case allocation will be done as detailed below:

- Treatment phase vs. screening phase: the AE will be allocated to the treatment phase unless the available parts of the AE start or stop date/time provide evidence for allocating to the screening phase.
- Multiple treatment phases: AE will be allocated to treatment Part A phase unless the available parts of the AE start or stop date/time provide evidence the assessments did not occur during Part A.

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

AEs of special interest will be defined using MedDRA system organ class (SOC) ‘Infections and infestations’.

IRR will be defined as all AEs with a MedDRA preferred terms that are listed in either:

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

AND occurring within 48 hours of an infusion, or within 2 days in case no AE start time is available.

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

Treatment relatedness will be dichotomized as follows in tables:

- Treatment-related: “related” in the CRF or missing
- Not treatment-related: “not related” in the CRF

AE onset 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 administration + 1 day
  - AE start date < date of first administration: AE start date – date of first administration
- AE onset day (vs. start of phase) = AE start date – phase start date + 1 day
- AE duration (days) =
  - AE end date – AE start date + 1 day
  - study discontinuation 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”. For ongoing participants who have an ongoing AE, the same approach will be taken using the clinical data cut-off date.

Event rates per participant years of follow-up (PYFU) will be defined as the number of events divided by the sum of follow-up time of all participants per treatment expressed in years.

5.1.3 Presentation of results

Tables will present TEAEs only and will be separated by part. Pre-treatment AEs will only be listed.

An overview table will show the number and percentage of participants with at least one event, the number of events and event rates per participant years of follow-up for the following:

- TEAEs
- Serious TEAEs
- Grade ≥ 3 TEAEs
- TEAEs of special interest (AESI)
- Fatal TEAEs
- Serious treatment-related TEAEs
- TEAEs leading to interruption of study drug
- TEAEs leading to discontinuation of study drug
- IRR events
- Treatment-related TEAEs according to the principal investigator
- Procedure-related TEAEs according to the principal investigator
- TEAEs leading to hospitalization

Summary tables by MedDRA system organ class and preferred term will show the number and percentage of participants with at least one event. The table of TEAEs will additionally show the number of events and the event rates per participant years of follow-up.

Separate tables will be prepared for the following:

- TEAEs
- Serious TEAEs
- Non-Serious TEAEs
- Grade ≥ 3 TEAEs
- AESIs
- Fatal TEAEs
- Treatment-related TEAEs
- Procedure-related TEAEs
- Serious treatment-related TEAEs
- TEAEs leading to interruption of study drug
- TEAEs leading to discontinuation of study drug
- IRR events
- Hypersensitivity reactions

Additionally, a table of all TEAEs occurring in at least 2 participants in the total group by MedDRA system organ class and preferred term in decreasing order of frequency (in the total group) will be prepared.

A table with the time to first onset and duration of TEAEs of special interest will be prepared.

The overview table and the table of TEAEs by MedDRA system organ class and preferred term will be repeated by q3w transition status (as defined in section 3.6.2).

All AEs, including pre-treatment events will be listed. Separate listings will be created for serious AEs, fatal AEs, AESIs, IRR events, hypersensitivity, TEAEs leading to interruption of study drug and TEAEs leading to discontinuation of study drug and TEAEs leading to study discontinuation. A listing showing all coding information will be prepared.

5.2 CLINICAL LABORATORY EVALUATION

5.2.1 Available data

Per protocol, the following laboratory parameters are expected:

- Biochemistry: blood urea nitrogen (BUN), creatinine, glucose (fasting for 8 hours), total calcium, glycosylated hemoglobin (HbA1c), potassium, sodium, alkaline phosphatase (ALP), lactate dehydrogenase (LDH), C-reactive protein (CRP), total protein, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), total bilirubin, direct bilirubin, albumin, lipid panel (total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), and triglycerides), international normalized ratio (INR) and activated partial thromboplastin time (aPTT).
- Hematology: platelet count, red blood cell count (RBC), hemoglobin, hematocrit, RBC indices (mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), % reticulocytes), white blood cell (WBC) count with WBC differential (% and absolute for neutrophils, lymphocytes, monocytes, eosinophils, basophils).
- Urinalysis:
  - Continuous: specific gravity, pH
  - Categorical: by dipstick (glucose, protein, blood, ketones, bilirubin, nitrite, leukocyte esterase), microscopic evaluation, highly sensitive urine human chorionic gonadotropin (hCG) pregnancy test for females of childbearing potential.
- Screening tests: pregnancy test (for female participants of childbearing potential), SARS-CoV-2 test, total hepatitis B core antibody, hepatitis B surface antibody, hepatitis B surface antigen, hepatitis C virus antibody, HIV (and CD4 count if available).

Normal ranges are available as provided by the laboratory.

5.2.2 Derivation rules

The following parameters will be derived:

- eGFR (Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)) will be derived:

$$\text{eGFR (mL/min/1.73m}^2) = 141 * \min\left(\frac{\text{creatinine (mg/dL)}}{K}\ ;\ 1\right)^{\alpha} * \max\left(\frac{\text{creatinine (mg/dL)}}{K}\ ;\ 1\right)^{-1.209} * 0.993^{\text{age (years)}} * 1.018\ \text{[if female]} * 1.159\ \text{[if black]}$$

  where K = 0.7 if female and K = 0.9 if male;
  α = -0.329 if female and α = -0.411 if male.

  Note: in case results in mg/dL are not available, results in µmol/L will be used after conversion in mg/dL: 1 µmol/L = 1/88.4 mg/dL

- Only fasted lipid samples and glucose (missing fasting status is considered as non-fasted) will be included in tabulations
- Lipid ratios will be calculated based on fasted samples only and rounded as detailed in section 2.3.3:
  - total cholesterol/HDL
  - LDL/HDL
  - HDL/LDL
- The following abnormality categories will be defined:
  - 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

  Note:
  - Classification will be done in standardized units, using non imputed values and limits.
  - For the worst-case analysis visits, as defined in section 2.2.5, an additional category low + high is defined in case there are both low and high post-baseline values.

Toxicity grades will be computed according to the CTCAE toxicity grading list. The implementation of these toxicity grades for analysis is presented in appendix 9.3. Only the parameters described in appendix 9.3 will be computed, according to the declared limits for each grade.

5.2.3 Presentation of results

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

Continuous laboratory parameters will be summarized by means of descriptive statistics by part at each analysis visit.

Laboratory abnormalities will be presented by part and overall as cross-tabulations of the abnormality at each analysis visit as well as at the worst-case analysis visit versus the baseline abnormality. Numbers of participants with treatment-emergent abnormalities (see Definition of terms) will also be shown. The denominator for the percentage is the total number of participants having data for the parameter per treatment and per analysis visit in the safety analysis set. Parameters for which toxicity grades are defined will not be included in the abnormalities tables.

Laboratory toxicity grades will be presented as cross-tabulations of the toxicity at each post-baseline analysis visit and at the worst-case analysis visit versus the baseline toxicity. 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 having data for the parameter per treatment and per analysis visit in the safety analysis set. Parameters having toxicity grades defined in both directions (hypo and hyper) will be shown by direction.

All laboratory data will be listed, but only for participants with any post-baseline abnormality / toxicity grade ≥ 3.

5.3 VITAL SIGNS

5.3.1 Available data

The following vital signs parameters are collected: systolic (SBP) and diastolic blood pressure (DBP), pulse rate, body temperature and weight.

5.3.2 Derivation rules

Abnormalities are defined in below table.

	Pulse rate (bpm)	**SBP (mmHg)**	**DBP (mmHg)**	**Temperature (°C)**
Low	<40	<90	<45	<35.8
Normal	40-100	90-150	45-90	35.8-37.5
High	>100	>150	>90	>37.5

Note: For the worst-case analysis visits, as defined in section 2.2.5, an additional category low + high is defined in case there are both low and high post-baseline values.

5.3.3 Presentation of results

Vital signs parameters supine SBP, DBP and pulse rate will be summarized by means of descriptive statistics by part at each applicable analysis visit.

Abnormalities will be presented by part and overall as cross-tabulations of the abnormality at each analysis visit as well as at the worst-case analysis visit versus the baseline abnormality. Numbers of participants with treatment-emergent abnormalities will also be shown.

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

5.4 ELECTROCARDIOGRAMS

5.4.1 Available data

The following ECG parameters will be collected: heart rate (HR), RR interval, QRS interval, PR interval, QT interval, and QTcF and QTcB.

5.4.2 Derivation rules

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

	HR (bpm)	PR (ms)	QRS (ms)
Low	<40	<120	-
Normal	40-100	120-220	0-120
High	>100	>220	>120

Note: For the worst-case analysis visit, as defined in section 2.2.5, an additional category low + high is defined in case there are both low and high post-baseline values.

For QTc interval (ms), the following categories are defined:

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

Note: The worst-case, as defined in section 2.2.5, is the highest post-baseline value and associated change.

5.4.3 Presentation of results

Uncorrected QT interval and RR will only be listed.

Continuous ECG parameters will be summarized by means of descriptive statistics by part at each analysis visit over time.

Abnormalities of the actual values will be presented by part and overall as cross-tabulations of the abnormality at each post-baseline analysis visit and at the worst-case analysis visit versus the baseline abnormality. Numbers and cumulative numbers over decreasing abnormalities (QTcF and QTcB only) of participants with treatment-emergent abnormalities will also be shown. The denominator for the percentage is the

total number of participants having data for the parameter per treatment and per analysis visit in the safety analysis set.

Abnormalities of the QTc changes will be presented by part and overall as tabulations of the change abnormality at each post-baseline analysis visit and at the worst-case analysis visit. Cumulative numbers over decreasing change abnormalities of participants will also be shown. The denominator for the percentage is the total number of participants having data for the parameter per treatment and per analysis visit in the safety analysis set.

All ECG data will be listed, but only for participants with any post-baseline abnormality.

5.5 SUICIDALITY ASSESSMENT

5.5.1 Available data

Suicidality assessment will be conducted by specifically asking the following question, derived from the PHQ-9 (reference to Simon et al. 2013): "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?" Possible outcomes are: Not at all (0), Several days (1), More than half the days (2), Nearly every day (3).

5.5.2 Presentation of results

Suicidality assessment results will be presented using a frequency tabulation by analysis visit and worst-case over time. The denominator for the percentage is the total number of participants per treatment and per analysis visit in the safety analysis set.

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

6. CHANGES TO THE PLANNED ANALYSIS

6.1 CHANGES NOT COVERED BY PROTOCOL AMENDMENTS BEFORE DATABASE LOCK

Section	Section title	Change description
2.2.2	Baseline and change from baseline	Only the overall study baseline will be used for the analyses of both parts. No separate baseline is defined for Part B.
4.1.2	Efficacy – Endpoints and derivation rules	For the purpose of this analysis, initiation of PLEX as rescue therapy is also considered an intercurrent event.

6.2 CHANGES NOT COVERED BY PROTOCOL AMENDMENTS AFTER DATABASE LOCK

NAP

6.3 CHANGES TO THE FINAL STATISTICAL ANALYSIS PLAN

Section	Section title	Change description
2.1.1	Analysis sets	SAF-B and mITT-B sets removed, as they were not used in the analysis.
2.2.6	Best response	Section was added to describe how the best response will be calculated for a selection of efficacy parameters.
4.1.2.4	Efficatcy - Additional endpoints	Section was added to describe the additional endpoints to be derived and analyzed: [redacted]
4.1.3	Efficatcy - Presentation of results	Section was updated to describe the additional analyses.
5.1.3	AEs - Presentation of results	AEs leading to study discontinuation was removed from the tables. Two subgroup tables were added.
8.1	List of tables and listings	List was updated according to above changes

7. REFERENCES

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

2 ICH Topic E6(R2) Guideline for Good Clinical Practice – Step 5: 15 December 2016.

3 ICH Topic E9 Statistical Principles for Clinical Trials – Step 4 –September 1998.

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

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

6 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.

7 ICH guideline E14: the clinical evaluation of QT/QTc interval prolongation and proarrhythmic potential for non-antiarrhythmic drugs (R3) – questions and answers, January 2016.

8 Simon, G. E., C. M. Rutter, D. Peterson, M. Oliver, U. Whiteside, B. Operskalski and E. J. Ludman (2013). "Does response on the PHQ-9 Depression Questionnaire predict subsequent suicide attempt or suicide death?" Psychiatr Serv 64(12): 1195-1202.

9 Pickard S, Law E, Jiang R, Pullenayegum E, Shaw J, Xie F, Oppe F, Boye K, Chapman R, Gong C, Balch A, Busschbach J. United States Valuation of EQ-5D-5L Health States Using an International Protocol. VALUE HEALTH. 2019; 22(8):931–941

8. LIST OF TABLES AND LISTINGS

Outputs flagged (*) will not be created for the IA2 and final analyses. Outputs flagged (**) do not need to show a total treatment group. Outputs flagged (***) will not be created for the final analyses.

8.1 TABLES

GENERAL CHARACTERISTICS

14.1.1.1	Analysis Sets	SCR
14.1.1.2	Participant Disposition by Country and Site	SAF
14.1.1.3	Participant Disposition by Analysis Visits	SAF
14.1.1.4.	Participant Disposition by Type of Analysis Visits	SAF
14.1.1.5	Study Duration and Total Participant's Exposure Time	SAF
14.1.1.6	Study Discontinuation	SCR
14.1.1.7	Treatment Discontinuation	SAF
14.1.1.8	Protocol Deviations	SAF
14.1.2.1	Demographic Data	SAF
14.1.2.2	Baseline Disease Characteristics	SAF
14.1.2.3	Medical History	SAF
14.1.2.4	Concomitant Diseases	SAF
14.1.2.5	Prior Therapies by ATC Class (Level 1 and 3) and Generic Term	SAF
14.1.2.6	Concomitant Therapies by ATC Class (Level 1 and 3) and Generic Term	SAF
14.1.2.7	Prior MG Therapies by Generic Term	SAF
14.1.2.8	Baseline MG Therapies by Generic Term	SAF
14.1.2.9	Classes of Baseline MG Therapies	SAF
14.1.2.10	Participants by Their First Change in Dose of Background MG Therapy	SAF*
14.1.2.11	Participants by Their First Change in Dose of Background MG Therapy, Split if Change in Other Direction Occurred Afterwards	SAF*
14.1.2.12	Study Drug Administration and Visit Window Deviation	SAF
14.1.2.13	Study Drug Administration by Type of Visit	SAF
14.1.2.14	Study Drug Administration and Compliance	SAF
14.1.2.15	Summary of Dosing Regimen Transitions	SAF
14.1.2.16	Time to Dosing Regimen Transitions and Duration in q3w Regimen	SAF

EFFICACY

14.2.1.1.1	MG-ADL: Average Change from Baseline in MG-ADL Total Score from Week 1 to Week 21 - mITT	mITT**
14.2.1.1.2	MG-ADL: Average Change from Baseline in MG-ADL Total Score from Week 1 to Week 21 - PP	PP**
14.2.1.1.3	MG-ADL: Average Change from Baseline in MG-ADL Total Score from Week 1 to Week 21 by Age Category at Baseline	mITT**
14.2.1.1.4	MG-ADL: Average Change from Baseline in MG-ADL Total Score from Week 1 to Week 21 by Sex at Birth	mITT**
14.2.1.1.5	MG-ADL: Average Change from Baseline in MG-ADL Total Score from Week 1 to Week 21 by Weight Category	mITT**
14.2.1.1.6	MG-ADL: Average Change from Baseline in MG-ADL Total Score from Week 1 to Week 21 by Race	mITT**
14.2.1.1.7	MG-ADL: Average Change from Baseline in MG-ADL Total Score from Week 1 to Week 21 by Region	mITT**
14.2.1.1.8	MG-ADL: Average Change from Baseline in MG-ADL Total Score from Week 1 to Week 21 by MG-ADL Total Score Category at Baseline	mITT**
14.2.1.1.9	MG-ADL: Average Change from Baseline in MG-ADL Total Score from Week 1 to Week 21 by Prior MG Therapy	mITT**
14.2.1.1.10	MG-ADL: Average Change from Baseline in MG-ADL Total Score from Week 1 to Week 21 by Baseline MG Therapy	mITT**
14.2.1.1.11	MG-ADL: Average Change from Baseline in MG-ADL Total Score from Week 1 to Week 21 by Disease Duration	mITT**
14.2.1.2	MG-ADL: Descriptive Statistics of Actual Values and Changes from Baseline in MG-ADL Total Score	mITT
14.2.1.3.1	MG-ADL: Descriptive Statistics of Changes from Baseline in MG-ADL Total Score by Age Category at Baseline	mITT**
14.2.1.3.2	MG-ADL: Descriptive Statistics of Changes from Baseline in MG-ADL Total Score by Sex at Birth	mITT**
14.2.1.3.3	MG-ADL: Descriptive Statistics of Changes from Baseline in MG-ADL Total Score by Weight Category	mITT**
14.2.1.3.4	MG-ADL: Descriptive Statistics of Changes from Baseline in MG-ADL Total Score by Race	mITT**

14.2.1.3.5	MG-ADL: Descriptive Statistics of Changes from Baseline in MG-ADL Total Score by Region	mITT**
14.2.1.3.6	MG-ADL: Descriptive Statistics of Changes from Baseline in MG-ADL Total Score by MG-ADL Total Score Category at Baseline	mITT**
14.2.1.3.7	MG-ADL: Descriptive Statistics of Changes from Baseline in MG-ADL Total Score by Prior MG Therapy	mITT**
14.2.1.3.8	MG-ADL: Descriptive Statistics of Changes from Baseline in MG-ADL Total Score by Baseline MG Therapy	mITT**
14.2.1.3.9	MG-ADL: Descriptive Statistics of Changes from Baseline in MG-ADL Total Score by Disease Duration	mITT**
14.2.1.4	MG-ADL: Normalized AUEC of MG-ADL Total Score Percent Changes from Baseline per Interval	mITT**
14.2.1.5	MG-ADL: Average Change from Baseline in MG-ADL Total Score per Interval	mITT**
14.2.1.6	MG-ADL: Magnitude of Response in MG-ADL Total Score per Interval	mITT**
14.2.1.7	MG-ADL: Frequency Tabulation of Magnitude of Response in MG-ADL Total Score per Interval	mITT**
14.2.1.8	MG-ADL: Percentage of Time Having a Reduction in MG-ADL Total Score of at Least 2 Points from Baseline from Week 4 to Week 21	mITT**
14.2.1.9	MG-ADL: Frequency Tabulation of Minimal Symptom Expression per Interval	mITT**
14.2.1.10	MG-ADL: Descriptive Statistics of Actual Values and Changes From Baseline of Individual Items of MG-ADL	mITT**
14.2.1.11	MG-ADL: Frequency Tabulation of Actual Values of Individual Items of MG-ADL	mITT**
14.2.1.12	MG-ADL: Frequency Tabulation of Actual Values of MG-ADL Total Score Over Time	mITT
14.2.1.13	MG-ADL: Frequency Tabulation of Changes from Baseline in MG-ADL Total Score Over Time	mITT
14.2.2.1	[redacted]	[redacted]

[redacted]

14.2.6.1	Intercurrent Events: Frequency Tabulation of Early Treatment Discontinuation and Rescue Therapy	mITT**
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14.2.7.1	Descriptive Statistics of Efgartigimod Serum Concentration (µg/mL) Over Time	PK**
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14.2.8.1	Descriptive Statistics of Actual Values and Changes from Baseline in Total IgG Level	mITT
14.2.8.2	Descriptive Statistics of Percent Changes from Baseline in Total IgG Level	mITT
14.2.8.3	Descriptive Statistics of Actual Values and Changes from Baseline in anti-AChR Antibodies	mITT
14.2.8.4	Descriptive Statistics of Percent Changes from Baseline in anti-AChR Antibodies	mITT
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14.2.9.1	Number and Percentage of Participants with Anti-drug Antibodies Against Efgartigimod by Analysis Visit and by ADA Against Efgartigimod Participant Classification	SAF
14.2.9.2	Prevalence and Incidence of Anti-drug Antibodies Against Efgartigimod	SAF
14.2.9.3	Descriptive Statistics of ADA Against Efgartigimod Titer Values by Analysis Visit and by ADA Against Efgartigimod Participant Classification	SAF
14.2.10.1	MG-ADL: Average Change from Baseline in MG-ADL Total Score from Week 1 to Week 21 by ADA Against Efgartigimod Participant Classification in Part A	mITT**
14.2.10.2	Descriptive Statistics of Efgartigimod Serum Concentration (µg/mL) from Week 1 to Week 21 by ADA Against Efgartigimod Participant Classification in Part A	PK**

14.2.10.3	Descriptive Statistics of Percent Changes from Baseline in Total IgG Level from Week 1 to Week 21 by ADA Against Efgartigimod Participant Classification in Part A	mITT**
14.2.10.4	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by ADA Against Efgartigimod Participant Classification	SAF
14.2.10.5	Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by ADA Against Efgartigimod Participant Classification	SAF
14.2.10.6	Infusion-Related Reactions by MedDRA System Organ Class and Preferred Term by ADA Against Efgartigimod Participant Classification	SAF

SAFETY

ADVERSE EVENTS

14.3.1.1	Adverse Events Overview	SAF
14.3.1.2	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.3	Common (≥2 Participants with the Event) Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term Sorted by Decreasing Frequency	SAF
14.3.1.4	Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.5	Non-Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.6	Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.7	Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.8	Fatal Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.9	Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.10	Procedure-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.11	Serious Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.12	Treatment-Emergent Adverse Events Leading to Interruption of Study Drug by MedDRA System Organ Class and Preferred Term	SAF

14.3.1.13	Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.14	Treatment-Emergent Adverse Events Leading to Study Discontinuation by MedDRA System Organ Class and Preferred Term	SAF***
14.3.1.15	Time to First Onset and Duration of Treatment-Emergent Adverse Events of Special Interest	SAF
14.3.1.16	Infusion-Related Reactions by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.17	Treatment-Emergent Adverse Events of Hypersensitivity by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.18	Adverse Events Overview by q3w Transition Status	SAF
14.3.1.19	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by q3w Transition Status	SAF
LABORATORY DATA		
14.3.2.1	Descriptive Statistics of Laboratory Test Actual Values and Changes from Baseline	SAF
14.3.2.2	Cross-Tabulation of Laboratory Abnormalities Versus Baseline	SAF
14.3.2.3	Cross-Tabulation of Laboratory Toxicity Grades Versus Baseline	SAF
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14.3.3.1	Descriptive Statistics of Vital Signs Actual Values and Changes from Baseline	SAF
14.3.3.2	Cross-Tabulation of Vital Signs Abnormalities Versus Baseline	SAF
ECG		
14.3.4.1	Descriptive Statistics of ECG Actual Values and Changes from Baseline	SAF
14.3.4.2	Cross-Tabulation of ECG Abnormalities Versus Baseline	SAF
14.3.4.3	Tabulation of QTc Change Abnormalities	SAF
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14.3.5.1	Suicidality Assessment	SAF

8.2 LISTINGS

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16.2.1.1	Allocation	RND

16.2.1.2	Analysis Phases	SAF
16.2.1.3	Treatment and Study Discontinuation	SAF
16.2.1.4	Dosing Regimen Transitions – Part B	SAF
16.2.2.1	Protocol Deviations	SAF
16.2.2.2	Violations on Eligibility Criteria	SAF
16.2.2.3	No-Treatment Participants	SCR minus SAF
16.2.4.1	Demographic Data	SAF
16.2.4.2	Baseline Disease Characteristics	SAF
16.2.4.3	Medical History and Concomitant Diseases	SAF
16.2.4.4	MG Medical History	SAF
16.2.4.5	Hospitalizations	SAF
16.2.4.6	Prior and Concomitant Therapies	SAF
16.2.4.7	Rescue Therapies	SAF
16.2.4.8	Vaccination History	SAF
16.2.4.9	Prior and Concomitant Procedures	SAF
16.2.5.1	Study Drug Administration	SAF
PHARMACOKINETICS		
16.2.5.2	Individual Efgartigimod Serum Concentrations and Actual Blood Sampling Times for PK Assessments	PK
EFFICACY		
16.2.6.1	MG-ADL Total Score	mITT
16.2.6.2	MG-ADL Individual Items	mITT
16.2.6.3	MG-ADL Derived Variables	mITT
16.2.6.4	[redacted]	[redacted]
16.2.6.5	[redacted]	[redacted]
16.2.6.6	[redacted]	[redacted]
16.2.6.7	[redacted]	[redacted]
PHARMACODYNAMICS		
16.2.6.8	Total IgG and anti-AChR Antibodies	mITT
SAFETY		
ADVERSE EVENTS		
16.2.7.1	Adverse Events	SAF
16.2.7.2	Serious Adverse Events	SAF

16.2.7.3	Fatal Adverse Events	SCR
16.2.7.4	Treatment-Emergent Adverse Events Leading to Interruption of Study Drug	SAF
16.2.7.5	Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug	SAF
16.2.7.6	Treatment-Emergent Adverse Events of Special Interest	SAF
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16.2.7.8	Adverse Events: Coding Information	SAF
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16.2.8.1	Laboratory Test Results for Participants with Abnormal Values	SAF
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16.2.9.1	Vital Signs Results for Participants with Abnormal Values	SAF
ECG		
16.2.10.1	ECG Results for Participants with Abnormal Values	SAF
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16.2.11.1	Suicidality Assessment for Participants with Abnormal Values	SAF
IMMUNOGENICITY		
16.2.12.1	Anti-Drug Antibodies Against Efgartigimod	SAF

9. APPENDICES

9.1 SAS CODE

[redacted]

9.2 [redacted]

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9.3 TOXICITY GRADES

Below table documents how the Common Terminology Criteria for Adverse Events CTCAE, v5.0: November 27, 2017 is implemented in the statistical analysis.

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 [1]	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 [1]	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 [1]	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 [1]	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 [1]	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 [1]	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
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 low [1]	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 [1]	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 [1]	mmol/L	>ULN-1.23	-	>1.23-3.30	>3.30
	mg/dL	>ULN-3.0	-	>3.0-8.0	>8.0
Potassium low [1]	mmol/L	-	<LLN-3.0	<3.0-2.5	<2.5
	mEq/L	-	<LLN-3.0	<3.0-2.5	<2.5
Potassium high [1]	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 [1]	mmol/L	<LLN-130	-	<130-120	<120
	mEq/L	<LLN-130	-	<130-120	<120
Sodium high [1]	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	-

CD4 count [1]	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 [1]	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) [1]	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 [1]	giga/L	<LLN-75	<75-50	<50-25	<25
	counts/mm^3	<LLN-75000	<75000-50000	<50000-25000	<25000
White blood cells [1]	giga/L	<LLN-3	<3-2	<2-1	<1
	counts/mm^3	<LLN-3000	<3000-2000	<2000-1000	<1000

[1] 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.

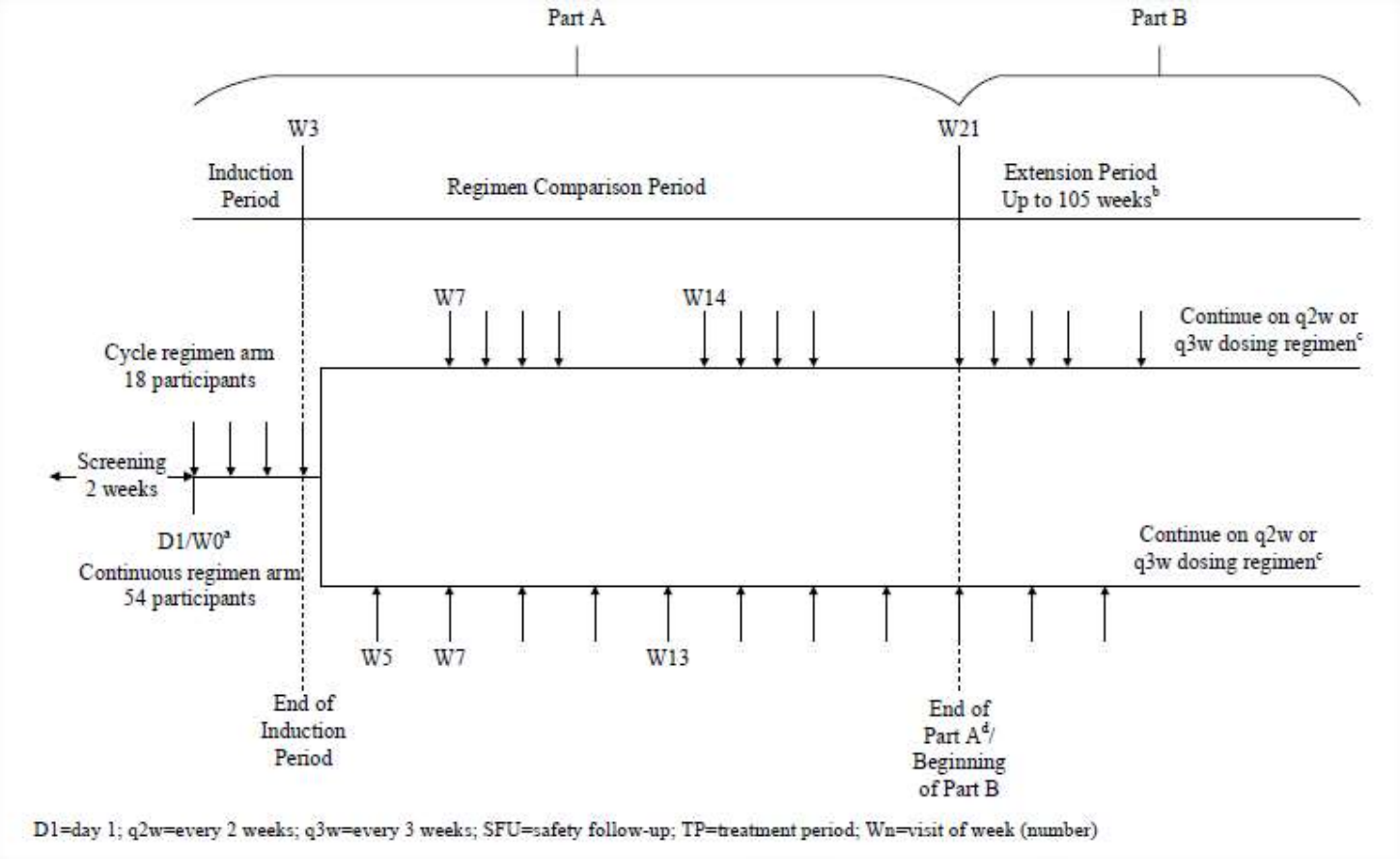
In case ULN/LLN is missing and the grade cannot be determined using the fixed values of CTCAE, no grade will be derived.

9.4 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	ACETYLCHOLINE CHLORIDE	
CORTISONE ACETATE	CYTOPHOSPHANE		IMMUNOGLOBULIN G HUMAN	
	TACROLIMUS MONOHYDRATE			
	AZATHIOPRINE SODIUM			

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

9.5 STUDY SCHEMA



[a] At day 1, participants will be randomized 3:1 to the continuous dosing regimen arm or the cyclic regimen arm, respectively.
[b] Study duration is up to 128 weeks.
[c] Participants in the cyclic regimen arm will start Part B with 1 additional TP of 3 weeks during W21 through week 24 as bridging doses before switching to continuous dosing starting during week 26. Participants in the continuous regimen arm will continue with the continuous dosing regimen. During Part B, participants who maintain clinical improvement receiving the q2w dosing regimen can switch to the q3w dosing regimen. Participants in Part B who do not maintain clinical improvement on the q3w dosing regimen will be able to switch back to the q2w dosing regimen.
[d] If efgartigimod becomes commercially available for patients with gMG or available through another patient program for gMG, participants will have the choice to switch to one of these options after completing Part A of the study. If participants continue receiving efgartigimod through either of these other means instead of continuing to Part B, they will not receive the scheduled dose at W21 and no SFU will be performed. If participants do not continue to Part B and will not continue receiving IMP through these other means, they may receive the scheduled dose at W21 and a SFU visit will be performed after 60 days (±3 days).

9.6 SCHEDULE OF ACTIVITIES

9.6.1 Part A (study start through week 21)

	Screening	Induction Period			Regimen Comparison Period											ET[a]	SFU[a]	UNS[b]
		D1 (W0)	W1 W2	W3	W4	W5 W6	W7	W8 W9 W10	W11	W12 W13	W14	W15 W16 W17	W18	W19 W20	End of Part A (W21)			
Study Day (± days)	-14 to -1	1	8 15 (±2)	22 (±2)	29 (±2)	36 43 (±2)	50 (±2)	57 64 71 (±2)	78 (±2)	85 92 (±2)	99 (±2)	106 113 120 (±2)	127 (±2)	134 141 (±2)	148 (±2)	NA	NA	NA
Required on-site visits[c]	X	X	X		X		X				X				X	X	X	
Informed consent[d]	X																	
Eligibility criteria	X	X																
Demographic characteristics	X																	
Medical and surgical history	X																	
Pregnancy test (WOCBP only)[e]	X	X			X		X				X				X	X	X	X
Viral screening[f]	X																	
SARS-CoV-2 test[g]	X														X[h]			X
Randomization		X																
Height and weight[i]	X	X			X		X				X				X	X		X
MG-ADL	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X
[redacted]																		

	Screening	Induction Period			Regimen Comparison Period											ET[a]	SFU[a]	UNS[b]
		D1 (W0)	W1 W2	W3	W4	W5 W6	W7	W8 W9 W10	W11	W12 W13	W14	W15 W16 W17	W18	W19 W20	End of Part A (W21)			
Study Day (± days)	-14 to -1	1	8 15 (±2)	22 (±2)	29 (±2)	36 43 (±2)	50 (±2)	57 64 71 (±2)	78 (±2)	85 92 (±2)	99 (±2)	106 113 120 (±2)	127 (±2)	134 141 (±2)	148 (±2)	NA	NA	NA
Required on-site visits[c]	X	X	X		X		X				X				X	X	X	
[redacted]																		
SIB risk monitoring[k]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Physical examination	X	X			X		X				X				X	X	X	X
Vital signs	X	X			X		X				X				X	X	X	X
ECG	X	X			X		X				X				X	X	X	X
Blood sampling[l]																		
Clinical safety laboratory tests[m]	X	X			X		X				X				X	X	X	X
[redacted]																		
Urinalysis	X	X			X		X				X				X	X	X	X

	Screening	Induction Period			Regimen Comparison Period										ET[a]	SFU[a]	UNS[b]
		D1 (W0)	W1 W2	W3	W4	W5 W6	W7	W8 W9 W10	W11	W12 W13	W14	W15 W16 W17	W18	W19 W20	End of Part A (W21)			
Study Day (± days)	-14 to -1	1	8 15 (±2)	22 (±2)	29 (±2)	36 43 (±2)	50 (±2)	57 64 71 (±2)	78 (±2)	85 92 (±2)	99 (±2)	106 113 120 (±2)	127 (±2)	134 141 (±2)	148 (±2)	NA	NA	NA
Required on-site visits[c]	X	X	X		X		X				X				X	X	X	
IMP administration[q]		X	X	X	Based on treatment regimen[r]										X[s]			
Prior/concomitant therapy and procedures[t]	Continuous monitoring																	
Adverse events[t]	Continuous monitoring																	

AChR-Ab=anti-acetylcholine receptor antibody; ADA=antidrug antibodies; AE=adverse event; ECG=electrocardiogram; EoS=end of study; ET=early termination; gMG=generalized myasthenia gravis; ICF=informed consent form; IgG=immunoglobulin γ; IMP=investigational medicinal product; IV=intravenous; MG-ADL=Myasthenia Gravis Activities of Daily Living; NA=not applicable; Nab=neutralizing antibodies; PD=pharmacodynamics; PHQ-9=9-item Patient Health Questionnaire; PK=pharmacokinetic; q2w=every 2 weeks; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; SFU=safety follow-up; SIB=suicide ideation and behavior; SoA=schedule of activities; UNS=unscheduled; WOCBP=women of childbearing potential; Wn=visit of week (number)

Note: At visits when the participant receives efgartigimod, all scheduled activities will be performed before the start of the infusion except for the postdose PK blood sample.

Note: Part A ends after all predose assessments have been performed at W21. Part B begins with the infusion at W21.

[a] Any participant who discontinues the study will immediately stop receiving efgartigimod and should attend an ET visit 7 (± 3) days after the early discontinuation decision and a SFU visit 60 (± 3) days, after their last dose of efgartigimod. An SFU visit 60 ± 3 days after the last dose of IMP should always occur for participants who complete the EoS visit. When a participant continues efgartigimod via commercial access or through another patient access program for gMG, this SFU visit may be done by a phone call, assessing only AEs and concomitant therapy and procedures.

[b] A UNS visit may occur at the request of the participant or the investigator. During the UNS visit, activities listed in the SoA may be performed at the investigator's discretion. Depending on the reason that prompted the visit, the UNS visit may be virtual if feasible.

[c] These indicated visits must occur at the study site. All other infusion visits (W3, W5, W8-W11, W13, W15-W17, and W19) may occur off-site (if permitted by local regulations, see Section 10.7 for country-specific requirements) or at the study site, depending on the participant's preference and regional availability of off-site infusion services. All other visits may be performed virtually.

[d] No study-related activities will be initiated before the participant signs the ICF.

[e] Pregnancy testing will be a highly sensitive serum test at screening, and a urine test at all subsequent visits. Local regulations will be followed if they require more stringent or frequent testing. See Section 8.2.7.

[f] The virology screen tests for those infections described in exclusion criteria 8. See Section 10.2.1.

[g] Additional tests may be performed as needed based on local regulations. See Section 8.2.6.4.

[h] Participants who enter part B will have a SARS-CoV-2 test if the COVID-19 pandemic is ongoing where the participant resides.

[i] Height will be measured at screening only.

[j] The baseline assessment refers to background medication administered for gMG.

[k] The SIB risk monitoring assessment is based on question 9 of the PHQ-9.

[l] At dosing visits, all blood samples will be taken predose unless otherwise specified.

[m] Blood samples for clinical laboratory safety assessments will be taken while the participant is in the fasted condition. See Section 8.2.6.1..

[n] ADA samples will be stored for potential testing of Nab against efgartigimod if PK/PD results are inconclusive. See Section 8.2.8.

[o] The PD analysis comprises total IgG and AChR-Ab levels. See Section 8.1.1.

[p] On dosing days, PK samples will be collected both predose (within 1 hour before the start of infusion) and at the end of the infusion (within 1 hour after the end of infusion). On nondosing days, 1 PK sample will be collected.

[q] Efgartigimod IV infusions will be administered either at the site or off-site by a home nurse as indicated by the visits schedule (see Section 10.7 for country-specific requirements). The home nurse's tasks at an off-site visit may be performed by another qualified person (see Section 6.2.1). Participants will be monitored for at least 30 minutes (see Section 10.7 for country-specific requirements) after the end of the infusion. Off-site administrations will be permitted based on the investigator's judgment. There should be at least 3 IMP administrations received by the patient on-site before decision to start with off-site administration will be taken by the investigator.

[r] Participants randomized to the cyclic regimen arm will receive weekly infusions of IMP on W7-W10, and W14-W17. Participants randomized to the continuous treatment arm will receive IMP q2w from W5-W21.

[s] The infusion at W21 is the first activity of part B. The infusion is only performed if the participant is eligible to enter part B.

[t] Adverse events, use of concomitant therapies, use of rescue therapy, vaccinations received, and medical procedures performed on the participants will be collected from the time the ICF is signed until the last study-related activity. All available vaccination history should be recorded as part of the participant's prior medication for vaccinations received in the past, or as concomitant medication for vaccines received during the study. Vaccination history and relevant prior therapy will be collected at screening.

9.6.2 *Part B (after week 21 through end of the study)*

Visit Type	Abridged Visit[a]	On-site Visit	End of Study	Early Termination	Safety Follow-Up	Unscheduled
	AVn	OVn	EoS[b]	ET[c]	SFU[c]	UNS[d]
Study Week	26, 31, 41, 46, 56, 61, 71, 76, 86, 91, 101, 106, 116, 121	36, 51, 66, 81, 96, 111	126	NA	NA	NA
Study Day (± days)	183, 218, 288, 323, 393, 428, 498, 533, 603, 638, 708, 743, 813, 848 (±3)	253, 358, 463, 568, 673, 778 (±3)	833 (±3)	NA	NA	NA
Required on-site visits[e]		X	X	X	X	
Weight		X	X	X		X
MG-ADL	X	X	X	X		X
[redacted]						
SIB risk monitoring[f]	X	X	X	X	X	X
Physical examination		X	X	X	X	X
Vital signs		X	X	X	X	X
ECG		X	X	X	X	X
Blood Sampling[g]						
Clinical laboratory tests[h]		X	X	X	X	X
[redacted]						

Visit Type	Abridged Visit[a]	On-site Visit	End of Study	Early Termination	Safety Follow-Up	Unscheduled
	AVn	OVn	EoS[b]	ET[c]	SFU[c]	UNS[d]
Study Week	26, 31, 41, 46, 56, 61, 71, 76, 86, 91, 101, 106, 116, 121	36, 51, 66, 81, 96, 111	126	NA	NA	NA
Study Day (± days)	183, 218, 288, 323, 393, 428, 498, 533, 603, 638, 708, 743, 813, 848 (±3)	253, 358, 463, 568, 673, 778 (±3)	833 (±3)	NA	NA	NA
Required on-site visits[e]		X	X	X	X	
Urinalysis		X	X	X	X	X
Urine pregnancy test (WOCBP only)[l]		X	X	X	X	X
SARS-CoV-2 test[m]						X
IMP administration[n]	Based on treatment regimen[o]					
Concomitant therapy and procedures[p]	Continuous monitoring					
Adverse events[p]	Continuous monitoring					

AChR-Ab=anti-acetylcholine receptor antibody; ADA=antidrug antibodies; AE=adverse event; AVn=abridged visit (number); EoS=end of study; [redacted] ET=early termination; IgG=immunoglobulin γ; IMP=investigational medicinal product; IV=intravenous; MG-ADL=Myasthenia Gravis – Activities of Daily Living; [redacted] NA=not applicable; Nab=neutralizing antibodies; [redacted] OVn=on-site visit (number); PD=pharmacodynamics; PHQ-9=9-item Patient Health Questionnaire; PK=pharmacokinetic; q2w=every 2 weeks; q3w=every 3 weeks; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; SFU=safety follow-up; SIB=suicide ideation and behavior; SoA=schedule of activities; TP=treatment period; [redacted] UNS=unscheduled; WOCBP=women of childbearing potential; Wn=visit of week (number)

Note: At visits when the participant receives efgartigimod, all scheduled activities will be performed before the start of the infusion except for the postdose PK blood sample.

Note: Part B begins with the infusion at W21. Refer to for the "IMP administration" row under the W21 column in Table 1 for this activity.

[a] Abridged visits are visits that can be performed virtually or at the study site.

[b] At the end of the study, argenx will comply with all local regulations for ensuring continued access to IMP medically identified as essential.

[c] Any participant who discontinues the study will immediately stop receiving efgartigimod and should attend an ET visit 7 (± 3) days after the early discontinuation decision and a SFU visit 60 (± 3) days, after their last dose of efgartigimod. A SFU visit 60 ± 3 days after the last dose of IMP should always

occur for participants who complete the EoS visit. When a participant continues efgartigimod via commercial access or through another patient access program for gMG, this SFU visit may be done by a phone call, assessing only AEs and concomitant therapy and procedures.

[d] A UNS visit may occur at the request of the participant or the investigator. During the UNS visit, activities listed in the SoA may be performed at the investigator's discretion. Depending on the reason that prompted the visit, the UNS visit may be virtual if feasible.

[e] These indicated visits must occur at the study site. All other infusion visits may occur off-site (if permitted by local regulations, see Section 10.7 for country-specific requirements) or at the study site, depending on the participant's preference and regional availability of off-site services. All other visits may be performed virtually.

[f] The SIB risk monitoring assessment is based on question 9 of the PHQ-9.

[g] At dosing visits, all blood samples will be taken predose unless otherwise specified.

[h] Blood samples for clinical laboratory safety assessments will be taken while the participant is in the fasted condition. See Section 8.2.6.1.

[i] ADA samples will be stored for potential testing of Nab against efgartigimod if PK/PD results are inconclusive. See Section 8.2.8.

[j] The PD analysis comprises total IgG and AChR-Ab levels. See Section 8.1.1.

[k] On dosing days, PK samples will be collected both predose (within 1 hour before the start of infusion) and at the end of the infusion (within 1 hour after the end of infusion). On nondosing days, 1 PK sample will be collected.

[l] Local regulations will be followed if they require more stringent or frequent pregnancy testing.

[m] Additional tests may be performed as needed based on local regulations. See Section 8.2.6.4.

[n] Efgartigimod IV infusions will be administered either at the site or off-site by a home nurse at the indicated visits (see Section 10.7 for country-specific requirements). The home nurse's tasks at an off-site visit may be performed by another qualified person (see Section 6.2.1). Participants will be monitored by the study staff for at least 30 minutes (see Section 10.7 for country-specific requirements) after the end of the infusion. Off-site administrations will be permitted based on the investigator's judgment. There should be at least 3 IMP administrations received by the participant on-site before decision to start with off-site administration will be taken by the investigator.

[o] Participants will either be on the q2w or q3w treatment regimen, based on clinical judgment. Participants who were randomized to the cyclic dosing regimen will receive 1 more TP starting on W21, followed by a transition to a continuous dosing regimen starting at W26. Participants may switch to the q3w dosing regimen, based on clinical judgment and guided by the MG-ADL scale. If participants on the q3w dosing regimen do not maintain clinical effect, they will switch back to the q2w dosing regimen, with another opportunity to switch to the q3w dosing regimen in 1 year.

[p] Adverse events, use of concomitant therapies, use of rescue therapy, vaccinations received, and medical procedures performed on the participants will be collected from the time the informed consent form is signed until the last study-related activity. Vaccinations received during the study should be recorded as concomitant medication.