16.1.9. Documentation of Statistical Methods

Document	Date
Statistical Analysis Plan	01 February 2022

STATISTICAL ANALYSIS PLAN

A Phase 3, Randomized, Open-Label, Parallel-Group Study to Compare the Pharmacodynamics, Pharmacokinetics, Efficacy, Safety, Tolerability, and Immunogenicity of Multiple Subcutaneous Injections of Efgartigimod PH20 SC With Multiple Intravenous Infusions of Efgartigimod in Patients With Generalized Myasthenia Gravis

Protocol:	ARGX-113-2001
SGS CR number:	BE-80-2000507
Development phase:	Phase 3
Sponsor:	Argenx
Analysis purpose:	Final analysis
SAP version number:	Final 1.0
SAP version date:	1FEB2022

SIGNATURE PAGE

Name and function	Signature and Date (ddMMMyyyy)
SGS CR authors:	
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Sponsor's approval: The approver agrees the statistical analysis will be performed according to this statistical analysis plan.	
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PROTOCOL HISTORY

Protocol:		
Version or ID	**Date (ddMMMyyyy)**	**Impact of the changes on the statistical analysis**
Final	15OCT2020	NAP
Final 2.0	02JUL2021	NAP

Protocol amendments:		
Version or ID	**Date (ddMMMyyyy)**	**Applicable country of the amendment**
Amendment 1.1	04NOV2020	Japan specific amendment
Amendment 1.1	14MAY2021	Germany specific amendment
Amendment 2.1	09JUL2021	Germany specific amendment
Amendment 2.1	13JUL2021	Japan specific amendment

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

LIST OF ABBREVIATIONS

Ab	antibody
AChE	acetylcholinesterase
AChR	acetylcholine receptor
ADA	anti-drug antibodies
ADaM	analysis data model
AE	adverse event
AESI	adverse events of special interest
ALQ	above the limit of quantification
ANCOVA	analysis of covariance
AUEC	area under the effect curve
BLQ	below the limit of quantification
bpm	beats per minute
CI	confidence interval
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
C_{max}	maximum concentration
COVID-19	coronavirus disease-2019
CRF	case report form
CTCAE	Common Terminology Criteria for Adverse Events
C_{trough}	concentration observed predose
CV	coefficient of variation
DBP	diastolic blood pressure
DSMB	data safety monitoring board
DY	relative day
ADY	ADaM variable to indicate relative day in study
ECG	electrocardiogram
EDC	electronic data capture
EFG	Efgartigimod
EoS	end of study
EoT	end of treatment
EQ-5D-5L	EuroQoL 5 Dimensions 5 Levels
eGFR	estimated glomerular filtration rate
FSH	follicle-stimulating hormone

FU	follow-up
gMG	generalized myasthenia gravis
HR	heart rate
ICF	informed consent form
ICH	International Council for Harmonization
IgG	immunoglobin G
IMP	investigational medicinal product
IRR	infusion-related reaction
ISR	injection site reaction
ITT	Intent-To-Treat
IV	intravenous
MedDRA	Medical Dictionary for Regulatory Activities
MG	myasthenia gravis
MG-ADL	myasthenia gravis activities of daily living
MG-QoL15r	15-item Quality of life scale for Myasthenia Gravis [revised version]
NAb	neutralizing antibody
NAP	not applicable
NI	noninferiority
NSID	non-steroidal immunosuppressive drug
PD	pharmacodynamics
PK	pharmacokinetics
PYFU	patient years of follow-up
QMG	quantitative myasthenia gravis
QTc	corrected QT interval
QTcB	Bazett's corrected QT interval
QTcF	Fridericia's corrected QT interval
SAP	statistical analysis plan
SAF	safety analysis set
SBP	systolic blood pressure
SC	subcutaneous
SCR	all screened participants analysis set
SD	standard deviation
SDTM	study data tabulation model

SE	standard error
SGS CR	SGS Clinical Research
SoA	schedule of assessments
SoC	standard of care
SOP	standard operating procedure
STAT	statistics
TEAE	treatment-emergent adverse event
UN	Unstructured covariance structure
VS	vital signs
WHO	World Health Organization
WI	work instruction

DEFINITION OF TERMS

AChR-Ab seronegative participants	AChR-Ab seronegative participants refers to participants in whom the anti-AChR-Ab cannot be detected per the actual lab results.
case report form (CRF)	A printed, optical, or electronic document in which protocol required information is recorded for each trial participant.
Display	Analysis table, figure or listing
Phase	Interval of time in the planned conduct of a study that is associated with a specific purpose: for example, screening, treatment, follow-up.
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)
MG therapy	Any therapy falling in one of the following categories per appendix 9.3: steroids, NSIDs, AChE inhibitors or Other

TABLE OF CONTENTS

1. INTRODUCTION

This SAP describes the statistical analysis to be performed for the ARGX-113-2001 (BE-80-2000507) study.

This SAP covers the final statistical analysis. It specifies the analysis displays to be presented and describes the methods and procedures in a more comprehensive way than presented in the statistical methods section of the protocol.

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

1.1 STUDY OBJECTIVES

Objectives	Endpoints
Primary	
• To demonstrate that the PD effect of injections of 1000 mg efgartigimod PH20 SC, administered every 7 days (q7d) for 4 administrations, is noninferior to that of IV infusions of efgartigimod at a dose of 10 mg/kg administered q7d for 4 administrations.	• Percent reduction from baseline in total immunoglobulin G (IgG) levels at day 29, ie, 7 days after the fourth IV or SC administration
Secondary	
To compare the PD effect of efgartigimod PH20 SC and efgartigimod IV over time	• Absolute values, change from baseline, and percent reduction from baseline in total IgG levels over time • Absolute values, change from baseline, and percent reduction from baseline in acetylcholine receptor binding autoantibodies (AChR-Ab) levels over time in AChR-Ab positive patients • Absolute values, change from baseline, and percent reduction from baseline in IgG subtype levels (IgG1, IgG2, IgG3, and IgG4) over time • Area under the effect curve (AUEC) of the percentage reduction from baseline total IgG and similar AUEC for each IgG subtype per dosing interval (days 1–8, days 8–15, days 15–22, and days 22–29), days 1–29, and over the entire study (days 1–71)

• To evaluate the PK of efgartigimod PH20 SC and efgartigimod IV	• PK parameters: maximum concentration (Cmax) (after all doses for the IV treatment arm), concentration observed predose (Ctrough)
• To evaluate the safety, tolerability, and immunogenicity of efgartigimod PH20 SC and efgartigimod IV	• Incidence and prevalence of anti-drug antibodies (ADAs) against efgartigimod • Incidence and prevalence of ADAs against rHuPH20 in the SC treatment arm • Incidence and severity of adverse events (AEs), incidence of serious adverse events (SAEs), and changes in laboratory test results, physical examination results, vital signs, and electrocardiogram (ECG) results
To evaluate the clinical efficacy of efgartigimod PH20 SC and efgartigimod IV	• Number and percentage of Myasthenia Gravis Activities of Daily Living (MG-ADL) responders • Number and percentage of Quantitative Myasthenia Gravis (QMG) responders • Change from baseline in MG-ADL total score over time • Change from baseline in QMG score over time
Exploratory	
[redacted]	[redacted]

1.2 STUDY DESIGN

This is a phase 3, multicentre, randomized, open-label, parallel-group study to evaluate the noninferiority of the PD effect of efgartigimod PH20 SC 1000 mg as compared to efgartigimod IV 10 mg/kg in patients with gMG. The safety, clinical

efficacy, immunogenicity, PK of efgartigimod PH20 SC 1000 mg and efgartigimod IV 10 mg/kg will also be assessed.

The total study duration is approximately 12 weeks:

- approximately 2 weeks of screening, with an additional 5 days allowed as needed to ensure AChR-Ab test results have been received
- 3 weeks of treatment
- 7 weeks of follow-up

The primary target population is adult patients with generalized myasthenia gravis (gMG), who have an MG-ADL total score ≥5 points and greater than 50% of the total score attributed to nonocular symptoms, at screening and baseline. Participants must be receiving a stable dose of concomitant treatment for gMG.

Serum from participants will be tested to determine their AChR-Ab status. Up to 20% of the participants randomized can be seronegative for AChR-Abs in both the overall population and the Japanese participant population. A Japanese participant is defined as a participant whose parents and 4 grandparents are Japanese, who has the Japanese nationality, was born in Japan, has not lived outside of Japan for a total of >10 years, and currently lives in Japan.

Randomization will be stratified by Japanese versus non-Japanese participants. Within non-Japanese participants, randomization will be further stratified by AChR-Ab status.

After confirmation of eligibility, participants will be randomized 1:1 at the day 1 visit to receive efgartigimod IV 10 mg/kg or efgartigimod PH20 SC 1000 mg every 7 days (q7d) for 4 administrations.

Efgartigimod IV will be administered by a 1-hour IV infusion performed by the site staff.

Efgartigimod PH20 SC will be administered by injection into the abdominal subcutaneous tissue. Participants receiving efgartigimod PH20 SC or their caregivers will be trained in self-administration or caregiver-supported administration of the IMP. If the participant or the caregiver successfully completes the training to the satisfaction of the investigator and the participant, the participant or the caregiver may administer the second, third and/or fourth injections at the site under supervision.

At End of Study (EoS), eligible participants will be offered the option to roll over into an extension study ARGX-113-2002 to receive efgartigimod PH20 SC. Participants who complete this study may be eligible to participate in the extension study.

The schedule of assessments (SoA) is in appendix 9.4.

1.3 EXPECTED SAMPLE SIZE

The noninferiority (NI) evaluation will be based on percent reduction from baseline in total IgG levels at Day 29 (Week 4) using a NI margin of 10.

Based on data from the phase 3 study ARGX-113-1704 and later confirmed by data from a healthy volunteer study ARGX-113-1907, the mean percent decrease in total IgG levels with the IV formulation is expected to be approximately 62 (standard

deviation 7.5). When assuming the total IgG percent reduction from baseline with the SC formulation is 60 (2 less compared to the IV formulation) along with a standard deviation of 7.5, 20 participants per treatment arm are needed to reach 90% power to detect noninferiority using a 1-sided 2-sample t-test at a 2.5% level of significance. To account for participant discontinuation, 3 additional participants per treatment arm have been added. A sample size of 46 participants will need to be enrolled and randomized, allowing for 13% attrition rate.

However, the maximum number of 76 patients as described in the original study protocol will be randomized in the ARGX-113-2001 study to fulfill regulatory expectations to provide sufficient safety data in the license application file.

1.4 RANDOMIZATION AND BLINDING

This is an open-label study; potential selection bias will be reduced by central randomization for assigning participants to IV or SC route of administration.

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

Randomization will be stratified by Japanese versus non-Japanese participants. Within the non-Japanese participants, randomization will be further stratified by AChR-Ab status.

1.5 INTERIM ANALYSIS

Not applicable.

1.6 SOFTWARE

SAS version 9.4 or later will be used for programming.

1.7 VALIDATION MODEL

SGS statistics (STAT) standard operating procedures (SOPs) and work instructions (WIs) that were effective at the start of the project will be followed throughout the project, provided the applicable regulatory requirements are still being met.

Analysis Data Model (ADaM) datasets, analysis tables, and listings will be validated according to model B (review by an independent person), except the following datasets: ADSL (Subject-Level), ADAE (Adverse Events), ADLB1 (Pharmacodynamics) and ADLB2 (Laboratory). These datasets will follow validation model C (review by an independent person and independent programming of the parameters indicated in this SAP). Intext tables will be validated according to model A (review by the program developer [see SOP.STAT.020 and SOP.PK.020]).

PK analysis will be validated according SOP.PK.001.

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 (RAND):	participants who were randomized into this study
Intent-to-treat set (ITT):	all randomized participants who are exposed to the IMP
Modified Intent-to-treat set (mITT):	all randomized participants with a value for total IgG levels at baseline and at least 1 post-baseline timepoint, only considering lab values where LBNAM = SGS FRANCE
Per protocol (PP) analysis set:	participants from the mITT set, excluding the participants having major protocol deviations
Safety analysis set (SAF):	all randomized participants who are exposed to the IMP
PK analysis set (PK):	subset of safety analysis set with at least 1 postdose 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.

PD analyses will be done on the mITT set. Clinical efficacy analyses will be done on the ITT set. Sensitivity analysis of the primary efficacy endpoint will be done on the PP set. General characteristics, safety and immunogenicity analyses (ADA, NAb) will be performed on the SAF set. The PK analysis set will be used for the PK analysis.

The AChR-Ab seropositive subset population is defined based on the actual lab results.

2.1.2 As planned versus as actual analysis

For analyses done on the SAF and PK sets, the actual treatment the participant received will be considered. For analyses on the ITT, mITT and PP sets, the planned treatment of the participant will be considered. In case of misdosing during one IV infusion or SC injection, actual treatment will remain equal to planned treatment.

2.2 PHASES AND TIME POINTS

2.2.1 Phases

All events and assessments will be allocated to phases (see Table 1).

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 + FU	First administration date/time	Date of study termination for participants rolling over to ARGX-113-2002 or date of last contact for other participants, with 23:59 added as the time part

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 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.

2.2.2 Baseline and change from baseline

The baseline value is the last available and non-missing value before the first administration of the study drug.

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

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

Percent change from baseline at time point t = (actual value at time point t -baseline value)*100/baseline value.

Note that for immunogenicity, the baseline visit is defined per sample, i.e. for the sample of ADA/NAb against efgartigimod, and for the sample of antibodies/NAb against rHuPH20.

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 will be done using their relative day in the study (see section 2.2.3) according to the following table:

Table 2: analysis visits

Phase	Analysis window	Target ADY	Lower limit ADY	Upper limit ADY
Screening	Screening*	-14	-INF	1
Treatment + FU				
	Baseline	1	-INF	1**
	Week 1	8	1**	11
	Week 2	15	12	18
	Week 3	22	19	25
	Week 4	29	26	32
	Week 5	36	33	39
	Week 6	43	40	46
	Week 7	50	47	53
	Week 8	57	54	63
	Week 10	71	64	999

*: As the interval of screening and baseline are overlapping, it may be that the same assessment will be attributed to both timepoints.

**: An assessment on day 1 will be attributed to baseline in case it is before the administration of the IMP, to Week 1 otherwise, unless the assessment is related to questionnaires for which time will not be considered and therefore be allocated to baseline.

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 value that is the latest in time will be selected. The value latest in time will be identified using, in order of preference, the assessment time, the visit label, or the group identifier (if applicable). Missing values are removed before the selection is made. For 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.

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 scenario. 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 the 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).

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

2.3 IMPUTATION AND ROUNDING RULES

2.3.1 Missing values

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

2.3.2 Values below or above a threshold

Safety and AChRAb values expressed as below the quantification limit (BLQ) or above the quantification limit (ALQ) will be imputed as the value of the quantification limit itself. For total IgG and IgG subtypes, BLQ and ALQ values will not be imputed and will be excluded from analysis. For AChR-Ab BLQ values, a limit of 0.256 will be used if not specified in the database. For participants with a baseline PD value BLQ; the PD parameter will be excluded from the statistical analysis involving change and percent change from baseline. Listings will always show the non-imputed values.

PK concentrations BLQ will be flagged as such in the listings. For descriptive statistical analysis, all BLQ values will be set to zero. For ALQ values, all ALQ values will be set to the upper limit of quantification for descriptive analysis. Listings will always present the original value.

2.3.3 Rounding

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

- Time since diagnosis and BMI will be rounded to 1 decimal.
- AUEC will be rounded to the integer.
- Estimated glomerular filtration rate (eGRF) will be rounded to 2 decimals.
- Ratios will be rounded to the number of decimals of the parameter with the least number of decimals.
- Safety laboratory results will be rounded to a maximum of 3 decimal.

2.3.4 Outliers

Outlier detection rules will be applied on the IgG subtypes. The IgG subtype observations from a specific sample are considered to be an outlier in case the ratio of the sum of the IgG subtypes and the total IgG level observed at a specific time-point

(sum IgG subtypes / total IgG) is higher than Q3 + 1.5*IQR or lower than Q1 – 1.5*IQR.

The cut-off values of Q3 + 1.5*IQR and Q1 – 1.5*IQR are based on all samples (all individual ratios), independent of treatment or timepoint (i.e., one upper and one lower cut-off value for all samples in the study).

For the identified outliers, all 4 IgG subtype observations are to be excluded from the summary statistics by timepoint, the AUEC derivation, and the maximum drop from baseline/minimum post-baseline timepoint calculation. Participants with an IgG subtype outlier at baseline will be excluded from all statistical analyses involving change and percent change from baseline for all 4 IgG subtypes.

2.4 PRESENTATION OF RESULTS

All descriptive outputs described in this SAP will be repeated by region (Japanese / Non-Japanese as defined in the study protocol) to support the J-MAA submission. The definition of a Japanese participant in the protocol is a participant whose parents and 4 grandparents are Japanese, who has the Japanese nationality, was born in Japan, has not lived outside of Japan for a total of >10 years, and currently lives in Japan. Note that these additional outputs will not be included in the FDA/EMA submission.

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, for general and safety) or standard error (SE, for PD and efficacy), the median, minimum, Q1, Q3, and maximum. In addition, for PD and efficacy, the 95% 2-sided confidence interval will be provided.

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

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%).

Descriptive statistics for PK parameters will include n, arithmetic mean, SD, median, minimum and maximum, CV%, as well as geometric mean and geometric coefficient of variation.

Serum concentrations and PK parameters will be presented with 3 significant digits in the original concentration units, 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 never 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:

- EFG SC
- EFG IV
- 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 will show results ordered by treatment and participant, unless specified otherwise.

All other listings will be ordered by treatment, participant, 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.

For tables by AChR-Ab status, AChR-Ab seropositive participants will be shown first, and then seronegative. EFG SC treatment will always be shown first, and then EFG IV treatment.

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 by 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.
- The number and percentage of screen failures, of participants randomized but not treated and 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 (including reasons for screen failures).
- 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.
- The number and percentage of participants who roll over to study ARGX-113-2002.

All information collected in the CRF concerning treatment allocation, treatment discontinuation, and study discontinuation will be listed. Listings with all COVID-19-related comments and COVID-19-related remote visits will also be prepared.

In addition, the stratification information used in IRT randomization (Japanese, non-Japanese AChR-Ab seropositive, and non-Japanese AChR-Ab seronegative), the Japanese vs non-Japanese status (as defined in the study protocol, a Japanese is a participant whose parents and 4 grandparents are Japanese, who has the Japanese nationality, was born in Japan, has not lived outside of Japan for a total of >10 years, and currently lives in Japan), and the actual AChR-Ab status will be summarized by treatment and overall.

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, age at informed consent, race (if Asian, also subcategory is specified), ethnicity, region, Japanese/non-Japanese participants (as defined in the protocol, from SDTM SUPPDM dataset), height, baseline weight, baseline body mass index (BMI), year of birth, date of signing informed consent form (ICF).
- Baseline disease characteristics: date of diagnosis, MGFA Classification at screening and at diagnosis, thymectomy performed for MG (yes/no), time since thymectomy, AChR-Ab status, MG-ADL questionnaire (MG ADL total score), QMG questionnaire (QMG total score), MGQoL15 questionnaire (MGQoL15 total score), EQ-5D-5L VAS, regular use of a breathing mask, and any use of feeding tube for MG.

3.3.2 Derivation rules

The following parameters will be derived:

- Baseline body mass index (BMI) (kg/m²) = (baseline weight (kg)) / (height (m))²

  Note: The BMI will be calculated and rounded as detailed in section 2.3.3, only when not available in the database.
- AChR-Ab status (actual value): based on lab value (where LBNAM = PPD LABS) at screening using a validated radioimmunoassay detection method and using the normal ranges (within normal ranges is negative, outside is positive)
- Region (subgroup): country will be categorized into the following regions: Japan / USA / rest of the world
- Screening and baseline MG-ADL total score: 5-7, 8-9, ≥10
- Time since diagnosis/thymectomy (years): (date of ICF – date of diagnosis/thymectomy)/365.25. Partially missing date of diagnosis/thymectomy will be imputed as follows:
  - Missing day of diagnosis/thymectomy will be imputed with 1
  - Missing day and month of diagnosis/thymectomy will be imputed with 1JAN

    Note: Result will be rounded as detailed in section 2.3.3.

3.3.3 Presentation of results

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

Following age categories will be shown: 18-64, ≥65 years.

Baseline disease characteristics will be presented using descriptive statistics for:

- time since diagnosis (years)
- time since thymectomy (years)
- MG-ADL total score at screening
- MG-ADL total score at baseline
- QMG total score
- MG-QoL15r total score
- EQ-5D-5L VAS

Baseline disease characteristics will be presented using frequency tabulations for

- MGFA Classification (at screening and at diagnosis)
- AChR-Ab status (actual)
- MG-ADL total score categories at screening
- MG-ADL total score categories at baseline
- Thymectomy performed for MG
- Regular use of a breathing mask
- Any use of feeding tube 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 version 24.1) 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 hospitalizations, ER visits, and ICU admissions.

3.5 PRIOR AND CONCOMITANT THERAPIES

3.5.1 Available data

All therapies are coded using the September 2021 version of the WHO-DRUG. ATC selection is performed. ATC coding up to level 4 is available in the clinical database. For each therapy, a start date or prior flag and stop date or ongoing flag are collected. Note that only MG therapies taken from 1 year prior to screening and non-MG therapies taken from 6 months prior to screening are collected.

3.5.2 Derivation rules

Based on their start and stop date, therapies will be allocated to each phase during which they were administered. A therapy can therefore be reported in more than one phase.

Phases are defined in section 2.2.1. Therapies 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 was not taken during that phase.

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

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

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

Additionally, MG-specific therapies that started before the first dose 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

Prior and concomitant therapies will be tabulated (separately), by ATC class (level 1 and level 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 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, NSIDs, AChE inhibitors, procedures, and other: see appendix 9.3) and the combination of classes will also be shown.

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 EXPOSURE TO STUDY DRUG AND TREATMENT COMPLIANCE

3.6.1 Available data

For each study drug administration (EFG IV and EFG SC), the start and end date/times and the volumes will be recorded. For the EFG SC treatment arm, data on self-administration will also be collected.

3.6.2 Derivation rules

The following parameters will be derived:

- For EFG IV, the actual dose in mg/kg will be calculated as = $\left(\frac{\text{actual volume extracted from vials (mL)} * 20\ (\text{mg/mL})}{\text{actual volume extracted from vials (mL)} + \text{actual volume of NaCl solution added to IV bag (mL)}}\right) * \left(\frac{\text{actual volume infused (mL)}}{\text{last available participant weight (kg)before or at day of dosing}}\right)$

  For EFG SC, the actual dose in mg will be calculated as = $\text{actual volume extracted from vials (mL)} * 180\ (\text{mg/mL})$. If the question: 'Was the correct volume administered as per protocol?' is answered as 'Yes', the actual dose will be set to 1000 mg.

  Note: As per protocol, a variation of ± 10% of the amount of 10 mg/kg for EFG IV or 1000 mg for EFG SC will not be considered an overdose/underdose.
- Actual dose for EFG IV (mg/kg) per administration, using categories <9 mg/kg, 9-11 mg/kg, >11 mg/kg and for EFG SC per administration, using categories < 900 mg, and 900-1000 mg.
- Number of administrations: number and percentage of participants who had 1, 2, 3 etc.… administrations.
- Treatment compliance defined as (number of doses received/4)*100%.

3.6.3 Presentation of results

A frequency table for the number of administrations will be created.

Descriptive statistics of the number of administrations and treatment compliance.

For the EFG SC treatment arm, a frequency table will be created showing training information:

- [redacted]
- [redacted]
- [redacted]
- [redacted]

Another table will be prepared for the EFG SC treatment arm, showing the total number of injections and administrator (patient/caregiver/site staff/other) per analysis visit and overall.

All study drug administration and self-administration data will be listed.

4. PHARMACODYNAMIC, CLINICAL EFFICACY, PHARMACOKINETIC AND ANTIBODIES ANALYSES

4.1 PHARMACODYNAMICS

4.1.1 Available data

The following pharmacodynamic parameters will be measured: PD markers (total IgG and IgG subtypes [IgG1, IgG2, IgG3 and IgG4]), and anti-AChR antibodies for the AChR-Ab seropositive participants.

4.1.2 Endpoint and derivation rules

The **primary endpoint** is the percent change from baseline in total IgG levels at week 4.

The following main intercurrent events will be considered:

- early treatment discontinuation for any reason prior to week 4
- initiation of Ig therapy (IVIg and SCIg) as rescue therapy prior to week 4
- missed doses

In the case of early treatment discontinuation or missed doses, the last observation captured within 7 days after the last dose will be used. If Ig therapy is used as rescue therapy prior to the date of the observation selected for primary endpoint based on the rules above, this observation will not be used and the last observation prior to the initiation of Ig therapy will be used instead.

The following **secondary endpoints** on pharmacodynamics are defined:

1) Change and percent change compared to baseline in total IgG level and IgG subtypes (IgG1, IgG2, IgG3 and IgG4) at each visit.

In addition to the planned timepoints, following timepoints will be shown:

- Maximum drop from baseline
- Minimum post-baseline value

Analysis will be done on AChR-Ab seropositive participants and overall.

2) Change and percent change compared to baseline in anti-AChR antibodies (in AChR-Ab seropositive participants) at each visit.

In addition to the planned timepoints, following timepoints will be shown:

- Maximum drop from baseline
- Minimum post-baseline value

See section 2.2.2 for calculation of change and percent change from baseline and section 2.3.2 for imputation rules.

3) The area under the effect curve (AUEC) of the percent change from baseline in total IgG will be computed and similar AUEC will be computed for each IgG subtype and for anti-AChR antibodies for the following intervals:

- Days 1 - 8 (Baseline - Week 1)
- Days 8 - 15 (Week 1 - Week 2)
- Days 15 - 22 (Week 2 - Week 3)
- Days 22 - 29 (Week 3 - Week 4)
- Days 1 - 29 (Baseline - Week 4)
- Days 1 - 57 (Baseline - Week 8)
- Days 1 - 71 (Baseline - Week 10).

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

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

Where:

- C_i is the percent change in concentration at time point t_i (in days).
- Only analysis visits as used in descriptive statistics tables (i.e., with ADY closest to target ADY) will be considered.
- AUEC will be calculated in days, using actual dates of assessments.
- AUEC will be rounded as detailed in section 2.3.3.

In case for a specific time interval the start or end visit of the interval is missing, the AUEC over that specific time interval will not be derived.

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

4.1.3 Presentation of results and statistical analysis

All statistical comparisons will be made using two-sided tests at the 0.05 significance level unless specifically stated otherwise.

The primary endpoint, percent change from baseline in total IgG levels at week 4, will be analyzed using an ANCOVA model with treatment (as randomized) as a factor and total IgG levels at baseline as a covariate.

The following statistics will be presented for an ANCOVA:

- Least Square (LS) Mean per treatment arm;
- Standard error of LS Mean;
- 95% confidence interval (CI) of LS Mean;
- LS Mean Difference (EFG SC– EFG IV);
- Standard error of LS Mean Difference;
- 2-sided 95% confidence interval (CI) for LS Mean Difference;

When the lower limit of the 95% confidence interval for the difference (mean percent change with SC – mean percent change with IV) is above the margin of -10, the SC formulation will be considered noninferior to the IV formulation.

Sensitivity analyses will be done for the primary endpoint on the PP population.

ANCOVA of primary endpoint will be repeated for AChR-Ab seropositive participants.

Summary statistics will be provided in terms of absolute values, changes, and percent changes from baseline over time for total IgG, IgG subtypes and corresponding AUEC and AChR-Ab. In addition, 2-sided CI's for the percent change difference between EFG SC and EFG IV will be shown, based on a two-sample t-test using Satterthwaite's correction.

In addition, the summaries of actual value and percent change from baseline of total IgG and IgG subtypes over time and the summaries of AUEC of total IgG and IgG subtypes during the above intervals will be repeated by AChR-Ab status.

The summaries of actual value and percent change from baseline in total IgG and AChR-Ab over time and the summaries of AUEC of total IgG and AChR-Ab during the above intervals will be repeated for the following subgroups:

- Age category at baseline: 18-64, ≥65 years
- Sex at birth
- Race
- Region (US/Japan/ Rest of World (RoW))
- Baseline MG-ADL score: 5-7, 8-9, ≥10
- Thymectomy

All data will be listed. A separate listing will be created showing the IgG subtype outliers (see section 2.3.4 for more details).

4.2 CLINICAL EFFICACY AND QUALITY OF LIFE

4.2.1 Available data

Efficacy will be assessed using the MG-ADL and QMG scales, and quality of life will be measured using 15-item Quality of life scale for Myasthenia Gravis [revised version] (MG-QoL15r) and EuroQoL 5 Dimensions 5 Levels (EQ-5D-5L) VAS.

The QMG total score from the SDTM database will not be used when a grade F value is reported for a certain visit. In such a case, the vital capacity item score from the SDTM database (QS.QSTESTCD = QMG008) will be imputed with 3 and the QMG total score will be recalculated, correcting for this imputed value. Otherwise the QMG total score from the SDTM database will be used. It will be reported in the CO dataset (CO.COVAL) when a quality grade F occurs for a certain visit.

4.2.2 Derivation rules

All clinical efficacy endpoints will be analyzed on the ITT population. 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.

In case of initiation of a new MG therapy/procedure or change in SoC therapy/procedure for any reason, assessments after receipt of a new MG therapy/procedure or after a change in SoC will be considered as:

- Having no reduction of at least 2 points (in case of MG-ADL total score, or 3 points for QMG total score) at the applicable assessments to derive the response/non-response as defined below
- Missing assessments for analysis on actual values and changes from baseline (descriptive statistics)

For PLEX, IVIg, and SCIg, the above rules only apply to the assessments obtained within 30 days of the PLEX/IVIg procedure.

The following secondary clinical efficacy endpoints will be assessed:

1) Number and percentage of MG-ADL responders.

A participant is considered a responder if he/she shows a reduction of MG-ADL total score of at least 2 points (compared to baseline) at response onset and for the next 4 consecutive visits after onset (i.e. 5 consecutive measurements in a period of 4 weeks) (see section 2.2.4) with the first of these decreases occurring at the latest 1 week after the last administration. MG-ADL total score will be used as collected; no recalculation will be performed.

This response is further referred to as "MG-ADL responder" in tables and listings.

The following rules are intended for the handling of missing visit or missing values:

- Participants who drop-out or are lost-to-follow-up will be treated as non-responders, if they have not achieved a MG-ADL response before leaving the study.
- Intermittent missing data at only 1 of 4 post-onset (O) consecutive analysis windows: if the missing data follows one of the following score patterns: OXmXX, OmXXX, OXXXmX or OXXmX, then the participant will be considered as having achieved a MG-ADL response. If no such pattern is present, the participant will be considered as not having achieved a MG-ADL response.
- Intermittent missing data following onset of response at ≥2 of 4 consecutive post-onset analysis windows: the participant will be considered as not having achieved a sustained response.

Missing data at one or more consecutive analysis windows after onset of response

Reason for missing data	Score change pattern	Interpretation (binary response)
Missing data at 1 visit after onset of response	OXmXX or OXXmX, OmXXX, OXXXmX	Responder
	mOXXX, OXXXmY*	Non-responder
Missing data ≥ 2 of 4 consecutive visits after onset of response	NA	Non-responder

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

2) Number and percentage of QMG responders, defined as participants who have a decrease of at least 3 points in the QMG total score (compared to baseline) for at least 4 consecutive weeks with the first of these decreases occurring at the latest 1 week after the last administration.

The same derivation rules as for MG-ADL responses apply, including handling of missing data.

3) Actual values and change from baseline in MG-ADL total score will be analysed descriptively and categorically.

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

Categories to be used for changes from baseline in MG-ADL total score: >0, 0, -1, -2, -3, -4, -5, -6, -7, -8, -9, -10, <-10. Number of participants, percentages and cumulative percentages will be shown.

In addition to the planned timepoints, the following timepoints will be shown:

- Maximum drop from baseline in MG-ADL
- Minimum post-baseline MG-ADL score

Missing data will not be considered.

4) Actual values and change from baseline in QMG total score will be described descriptively and categorically similar to the description of the MG-ADL total score. Of note for the categorization of the QMG total score a category of ≥25 will be added.

Following additional endpoints will be assessed:

1) Characterization of response in MG-ADL:

- Onset (First drop of >=2 MG-ADL in sequence of 4 week/5 assessments)
- Magnitude of response (maximum drop from baseline)
- Minimum post-baseline MG-ADL value
- Percentage of early responders

2) Characterization of response in QMG:

The analysis is identical to the characterization of response in MG-ADL.

3) Percentage of participants who have a decrease of at least 2 points on the MG-ADL total score (compared to baseline) for at least 4 consecutive weeks with the first of these decreases occurring at the latest after 1 or a maximum of 2 administrations of IMP (early MG-ADL responders). In practice, visit 'Week 2' is the last visit the onset of response can start to be considered an early responder, even in case of a missed administration.

The same derivation rules as for MG-ADL responses apply, including handling of missing data.

This response is further referred to as "Early MG-ADL response".

4) Actual values and changes from baseline in MG-QoL15r total score and EQ-5D-5L VAS score at week 10 will be analyzed descriptively.

4.2.3 Presentation of results and statistical analysis

Summary statistics will be provided in terms of absolute values and changes from baseline for continuous parameters. In addition, 2-sided CI's for the percent change difference between EFG SC and EFG IV will be shown, based on a two-sample t-test using Satterthwaite's correction.

Absolute values and changes from baseline will also be categorized, including the number of participants within each category, the percentage, and the cumulative percentage.

Summaries and frequency tabulations of MG-ADL/QMG actual value and change from baseline over time will also be shown by AChR-Ab status.

A frequency tabulation will be provided for the percentage of MG-ADL responders by AChR-Ab status. Response rates and differences in response rate (EFG SC - EFG IV) will be shown together with the 95% Wald confidence limits.

Similar tabulations will be provided for early MG-ADL responders and QMG responders.

A sensitivity analysis will be performed using the QMG total score provided in the SDTM database. The summary table of absolute values and changes from baseline, and the frequency tabulation of QMG responders will be repeated based on this QMG total score.

A cross-tabulation of MG-ADL responders by prior thymectomy status will be provided by AChR-Ab status and overall. Another cross-tabulation will be created for QMG responders by MG-ADL response, by AChR-Ab status and overall.

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

[redacted]

For further details on the planned analyses tables and listings, see section 8.1.

4.3 PHARMACOKINETICS

4.3.1 Available data

Blood samples will be collected for the determination of efgartigimod concentration at the time points indicated in the schedule of assessments (Section 9.4)

Time windows for PK samples are specified as follows:

- Dosing days for the efgartigimod IV treatment arm: within 1 hour prior to the start of infusion for the predose PK sample; within 1 hour after end of infusion for the postdose PK sample;
- Dosing days for the efgartigimod PH20 SC treatment arm: within 1 hour prior to the injection;
- Non-dosing days: +/-2 days;
- End of Study / Early Discontinuation: +/- 3 days.

All concentration data-points with deviations outside these permitted ranges will be excluded from the descriptive statistics on concentrations, 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.

4.3.2 Derivation rules

The PK analysis will be based on actual sampling times from start of IV infusion (for the IV treatment arm) or from the time of injection (for the SC treatment arm). The following parameters from the individual serum drug concentration versus time profile for efgartigimod:

- C_{max}: maximum observed serum concentration per visit (Day1, Weeks 1, 2, and 3) (after all doses within one visit for the IV treatment arm);
- C_{trough}: Serum concentration observed pre-dose at Weeks 1, 2, 3 and 4 (in both treatment arms);

For PK analysis, the following rules will be applied:

- Concentration below limit of quantification (BLQ) will be imputed according to the rules mentioned in section 2.3.2.

If the 1h postdose sample is missing, C_{max} will not be estimated.

4.3.3 Presentation of results

Individual concentration data and actual blood sampling times from start of infusion (for the IV treatment arm) or from the time of the injection (for the SC treatment arm) for PK assessments will be listed.

Descriptive statistics on concentration data will be presented in tables, per visit and per time point. Descriptive statistics will be calculated by treatment arm.

Individual PK parameters will be listed. Descriptive statistics on PK parameters will be presented in tables per visit. Descriptive statistics will be calculated by treatment arm.

In addition, descriptive statistics on concentrations will be calculated by treatment arm and:

- ADA Participant Classification
- NAb Participant Classification
- rHuPH20 Ab Participant Classification
- AChR-Ab status

In addition, descriptive statistics on PK parameters will be calculated by treatment arm and:

- AChR-Ab status

A statistical evaluation will be performed on Ctrough (Week 1, 2 and 3) and the serum concentration at Week 4 from an ANOVA model on ln-transformed value with treatment as fixed effect. Geometric mean and its 95% CI, as well as the geometric mean ratio (SC vs IV) and its 90% CI will be presented.

4.4 IMMUNOGENICITY

4.4.1 Available data

Presence of anti-drug antibodies (ADA) against efgartigimod and presence of antibodies (Abs) against rHuPH20 is measured at baseline, Week 2, Week 4, Week 7 and Week 10.

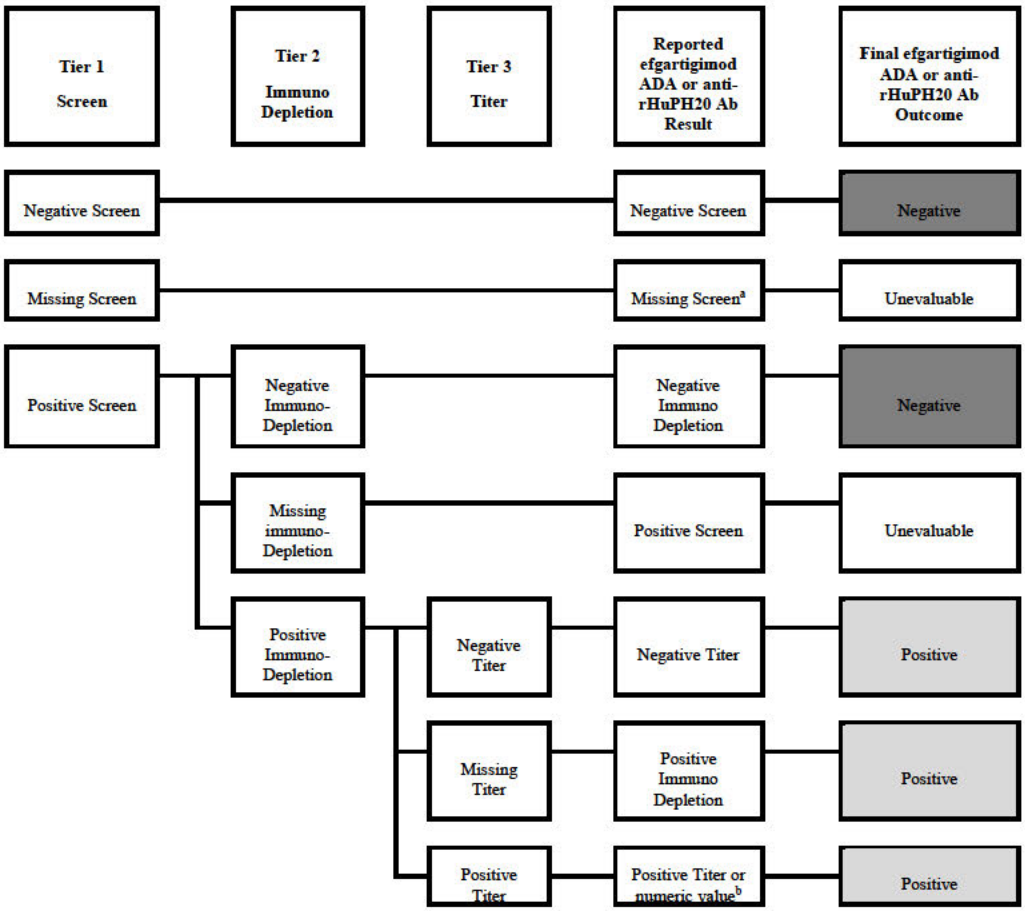
Immunogenicity samples are analyzed in a 3-tiered approach:

- All samples are evaluated in the efgartigimod ADA or anti-rHuPH20 Ab screening assay and are scored screening positive or negative
- If a sample scored screening positive, 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 titration assay (to determine titer) and are also further analyzed in the NAb (neutralizing antibodies) assay to confirm neutralizing activity. For NAb against efgartigimod, a screening assay is performed and results will be reported as negative or positive. For NAb against rHuPH20, the screening NAb assay is followed by a titer NAb assay in case the sample screened positive.

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

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

An overview of this 3-tiered approach and all possible sample results that will be reported by the laboratory is given below. From these reported efgartigimod ADA or anti-rHuPH20 Ab sample results, a final sample status needs to be derived during the statistical analysis, as presented in the final column ('Final Outcome'):



[a] missing screen includes the following terms (reported as reason not done): NA (not analyzed), NR (no result), NS (no sample) and SL (sample lost). More details can be found in the IS data transfer agreement (DTA) from SGS France (for ADA against

efgartigimod) and the DTA from Covance Indianapolis (for antibodies against rHuPH20) with SGS SDO.

[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 AGAINST EFGARTIGIMOD

Table below gives an overview of how the ADA participant classification will be derived, starting from the participant baseline ADA sample status.

Participant ADA classification	**Highest[c] post baseline sample status**				
	ADA negative	**ADA positive (missing titer[a])**	**ADA positive (negative titer[b] or positive titer)**		**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	*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';
[b] Results reported as 'negative titer', i.e. titer value <1 will be set to value of 1;
[c] Highest sample status, 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 (i.e. positive titer and selecting the sample with highest titer)

ADA evaluable participant = participant classified as any of following categories: ADA negative, treatment unaffected ADA, treatment induced ADA, treatment boosted ADA.

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

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).

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).

4.4.2.2 *PARTICIPANT CLASSIFICATION FOR ANTIBODIES AGAINST rHuPH20*

Table below gives an overview of how the anti-rHuPH20 antibody (rHuPH20 Ab) participant classification will be derived, starting from the participant baseline rHuPH20 Ab sample status.

Participant anti-rHuPH20 Ab classification	**Highest[c] post baseline sample status**				
	rHuPH20 Ab negative	**rHuPH20 Ab positive (missing titer[a])**	**rHuPH20 Ab positive (negative titer[b] or positive titer)**		**rHuPH20 Ab not evaluable**
Baseline rHuPH20 Ab sample status					
rHuPH20 Ab negative	rHuPH20 Ab negative	Treatment Induced rHuPH20 Ab	Treatment Induced rHuPH20 Ab		rHuPH20 Ab *unevaluable*
rHuPH20 Ab positive (missing titer[a])	Treatment Unaffected rHuPH20 Ab	rHuPH20 Ab *unevaluable*	rHuPH20 Ab *unevaluable*		rHuPH20 Ab *unevaluable*
rHuPH20 Ab positive (negative titer[b] or positive titer)	Treatment Unaffected rHuPH20 Ab	rHuPH20 Ab *unevaluable*	**titer < 2 x baseline titer:** Treatment Unaffected rHuPH20 Ab	**titer ≥ 2x baseline titer:** Treatment Boosted rHuPH20 Ab	rHuPH20 Ab *unevaluable*
rHuPH20 Ab not evaluable	rHuPH20 Ab *unevaluable*	rHuPH20 Ab *unevaluable*	rHuPH20 Ab *unevaluable*		rHuPH20 Ab *unevaluable*

[a] Samples with missing titer have as reported rHuPH20 Ab result 'positive immunodepletion';
[b] Results reported as 'negative titer', i.e. titer value <5 will be set to value of 5;
[c] Highest sample status, with order: (from low to high): rHuPH20 Ab unevaluable, rHuPH20 Ab negative, rHuPH20 Ab positive (missing titer/positive immunodepletion), rHuPH20 Ab positive with titer < 5 ('negative titer' as reported rHuPH20 Ab result, titer value set to 5), rHuPH20 Ab positive with titer ≥ 5 (i.e. positive titer and selecting the sample with highest titer)

rHuPH20 Ab evaluable participant = participant classified as any of following categories: rHuPH20 Ab negative, treatment unaffected rHuPH20 Ab, treatment induced rHuPH20 Ab, treatment boosted rHuPH20 Ab.

rHuPH20 Ab unevaluable participant = participant classified as rHuPH20 Ab unevaluable or with missing baseline rHuPH20 Ab sample or without post-baseline rHuPH20 Ab samples

Note: Twofold difference in titer values is considered significant in case a twofold serial dilution is applied (reference to Shankar et al., 2014).

Anti-rHuPH20 Ab incidence = percentage of participants with treatment-induced or treatment-boosted rHuPH20 Ab (denominator: number of evaluable participants).

Anti-rHuPH20 Ab prevalence = percentage of participants with treatment-unaffected rHuPH20 Ab, treatment-induced rHuPH20 Ab or treatment-boosted rHuPH20 Ab (denominator: number of evaluable participants).

4.4.2.3 PARTICIPANT CLASSIFICATION FOR NAB AGAINST EFGARTIGIMOD

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

For NAb against efgartigimod, all samples evaluated in this NAb assay will be scored as NAb positive or NAb negative by the laboratory. Based on these results, the participants will be categorized based on their baseline and post-baseline sample status as detailed in following table.

Participant NAb classification	**Highest[a] post baseline NAb sample status**		
	NAb negative	**NAb positive**	**NAb not evaluable**
Baseline NAb sample status			
NAb negative	baseline neg – post-baseline neg	baseline neg – post-baseline pos	*NAb unevaluable*
NAb positive	baseline pos - post-baseline neg	baseline pos – post-baseline pos	*NAb unevaluable*
NAb not evaluable	*NAb unevaluable*	*NAb unevaluable*	*NAb unevaluable*

a: Highest sample status in order: (from low to high): NAb unevaluable, NAb negative, NAb positive.

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

NAb incidence = percentage of participants with participant classification 'baseline neg – post-baseline pos' and 'baseline pos – post-baseline pos' (denominator: number of evaluable participants).

NAb prevalence = percentage of participants with participant classification 'baseline neg – post-baseline pos', 'baseline pos – post-baseline pos' or 'baseline pos – post-baseline neg'. (denominator: number of evaluable participants).

4.4.2.4 PARTICIPANT CLASSIFICATION FOR NAB AGAINST RHUPH20

All rHuPH20 Ab confirmed positive samples will also be evaluated in the NAb assay. All samples that were not analyzed in the NAb assay (i.e. the rHuPH20 Ab negatives) are per default NAb negative. Also, if a NAb sample is not reported, the NAb sample status is NAb unevaluable.

For NAb against rHuPH20, all samples evaluated in this NAb assay will be scored as NAb negative or NAb positive by the laboratory. In case the sample is NAb positive, a titration assay will occur, and the sample will be reported as 'negative titer', 'positive titer' or by an actual titer value. Based on these results, participants will be categorized based on their baseline and post-baseline sample status as detailed in following table.

Participant rHuPH20 NAb classification	Highest[b] post baseline sample status				
	rHuPH20 NAb negative	rHuPH20 NAb positive (missing titer)	rHuPH20 NAb positive (negative titer[a] or positive titer)		rHuPH20 NAb not evaluable
Baseline rHuPH20 NAb sample status					
rHuPH20 NAb negative	rHuPH20 NAb negative	Treatment Induced rHuPH20 NAb	Treatment Induced rHuPH20 NAb		*rHuPH20 NAb unevaluable*
rHuPH20 NAb positive (missing titer)	Treatment Unaffected rHuPH20 NAb	*rHuPH20 NAb unevaluable*	*rHuPH20 NAb unevaluable*		*rHuPH20 NAb unevaluable*
rHuPH20 NAb positive (negative titer[a] or positive titer)	Treatment Unaffected rHuPH20 NAb	*rHuPH20 NAb unevaluable*	**titer < 2 x baseline titer:** Treatment Unaffected rHuPH20 NAb	**titer ≥ 2x baseline titer:** Treatment Boosted rHuPH20 NAb	*rHuPH20 NAb unevaluable*
rHuPH20 NAb not evaluable	*rHuPH20 NAb unevaluable*	*rHuPH20 NAb unevaluable*	*rHuPH20 NAb unevaluable*		*rHuPH20 NAb unevaluable*

[a] Results reported as 'negative titer', i.e. titer value <100 will be set to value of 100;
[b] Highest sample status, with order: (from low to high): rHuPH20 NAb unevaluable, rHuPH20 NAb negative, rHuPH20 NAb positive (missing titer), rHuPH20 NAb positive with title <100 ('negative titer' as reported NAb result, titer value set to 100), rHuPH20 NAb positive (i e. actual titer value and selecting the sample with highest titer) .

rHuPH20 NAb evaluable participant = participant classified as any of following categories: rHuPH20 NAb negative, treatment unaffected rHuPH20 NAb, treatment induced rHuPH20 NAb, treatment boosted rHuPH20 NAb.

rHuPH20 NAb unevaluable participant = participant classified as rHuPH20 NAb unevaluable or with missing baseline rHuPH20 NAb sample or without post-baseline rHuPH20 NAb samples

Anti-rHuPH20 NAb incidence = percentage of participants with treatment-induced or treatment-boosted rHuPH20 NAb (denominator: number of evaluable participants).

Anti-rHuPH20 NAb prevalence = percentage of participants with treatment-unaffected rHuPH20 NAb, treatment-induced rHuPH20 NAb or treatment-boosted rHuPH20 NAb (denominator: number of evaluable participants).

4.4.3 Presentation of results

Analyses will be done for ADA against efgartigimod and antibodies against rHuPH20.

Frequency tabulations (number and percentages) will be provided with ADA or rHuPH20 Ab negative/positive/unevaluable samples per analysis visit. In addition, these tables will be repeated by ADA or rHuPH20 Ab participant classification.

Frequency tabulations (number and percentages) will be provided by treatment on:

- participants per ADA or rHuPH20 Ab participant classification
- prevalence and incidence of ADA or rHuPH20 Ab
- ADA or rHuPH20 Ab unevaluable participants
- ADA or rHuPH20 Ab baseline positive/negative/unevaluable samples

For details on the definitions, see the above section 4.4.2.1 and 4.4.2.2.

The above frequency tabulations will be repeated for NAb assay using the definitions as defined in section 4.4.2.3 and 4.4.2.4, except for the frequency tables of samples per analysis visit by participant classification.

The frequency tabulations on prevalence and incidence of ADA against efgartigimod, and rHuPH20 Ab will also be shown by baseline MG therapies (see section 3.5.2). Following categories will be shown: NSIDS, steroids, NSIDS+steriods, none.

In addition, frequency tabulations (number and percentages) will be provided for:

- NAb against efgartigimod positive participants within the ADA participant classification against efgartigimod (ADA Negative, Treatment-unaffected ADA, Treatment-induced ADA, and Treatment-boosted ADA).
- rHuPH20 Ab positive participants within the ADA participant classification against efgartigimod.

Correlation tables by ADA and NAb participant classification against efgartigimod, and by rHuPH20 Ab participant classification will be provided for the following parameters:

- mean drug concentration over time
- mean percent change from baseline in total IgG
- number and percentage of MG-ADL responders
- number and percentage of QMG responders
- treatment-emergent adverse events
- serious treatment-emergent adverse events
- MedDRA Hypersensitivity SMQ broad selection

ADA titer values against efgartigimod and rHuPH20 Ab titer values will be summarized by means of descriptive statistics by ADA participant classification against efgartigimod or rHuPH20 Ab participant classification respectively.

All available data on ADA and NAb against efgartigimod, rHuPH20 Ab and rHuPH20 NAb will be listed, also showing the sample status and participant classification.

5. SAFETY ANALYSES

5.1 ADVERSE EVENTS

5.1.1 Available data

Adverse events (AEs) are coded into system organ classes and preferred terms using the medical dictionary for regulatory activities (MedDRA) version 24.1. 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

Treatment-emergent adverse events (TEAE) are defined as AEs starting on or after first administration of any study drug.

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 section 2.2.1. 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.

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

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

Adverse events of special interest will be defined using MedDRA system organ class ‘Infections and infestations’.

Injection site reactions (ISR) and infusion-related reactions (IRR) will be defined as all AEs with a MedDRA preferred terms that are listed in either:

- MedDRA Hypersensitivity SMQ broad selection
- MedDRA Anaphylactic SMQ broad selection
- MedDRA Extravasation SMQ broad selection, excluding implants

AND occurring within 48 hours of an infusion or injection, 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 dichotomised 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 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".

5.1.3 Presentation of results

Tables will present TEAEs only. Pre-treatment AEs will only be listed.

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

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

Summary tables by MedDRA system organ class and preferred term will show the number and percentage of participants with at least one event. The below tables of TEAEs will additionally show the number of events.

In addition to all TEAEs, separate tables will be prepared for the following TEAEs:

- Serious TEAEs
- Non-Serious TEAEs
- Grade ≥ 3 TEAEs
- TEAEs of special interest
- IRR and ISR events
- Treatment-related TEAEs
- Procedure-related TEAEs
- Serious treatment-related TEAEs
- TEAEs leading to interruption of study drug
- TEAEs for which the study drug was discontinued

Additionally, a table of all TEAEs by MedDRA preferred term in decreasing order of frequency (in the all participants group) will be prepared.

Also, a table showing time to first onset and duration of TEAEs of special interest will be prepared. For the duration, all AESI will be considered, not only the first one in onset time.

All AEs, including pre-treatment events will be listed. A separate listing will show pneumonia-related adverse events (see appendix 9.5). A listing showing all coding information will be prepared as well.

COVID related events (events with preferred term COVID-19, COVID-19 pneumonia, suspected COVID-19, and coronavirus infection) will be listed. This listing will include all collected AE information and additionally onset since first efgartigimod dose, onset since last efgartigimod dose before AE onset, last total IgG before AE onset, the last percent change in total IgG before AE onset and the time when that reported total IgG was taken compared to AE onset.

5.2 CLINICAL LABORATORY EVALUATION

5.2.1 Available data

Per protocol, the following laboratory parameters are expected:

- Biochemistry: blood urea nitrogen (BUN), creatinine, creatinine clearance (unadjusted), glucose (fasting for 8 hours), total calcium, glycosylated hemoglobin (HbA1c), potassium, sodium, alkaline phosphatase (ALP), lactate dehydrogenase (LDH), C-reactive protein (CRP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ glutamyl transferase (GGT), bilirubin, total and direct albumin, cholesterol (total, LDL, HDL, triglycerides), international normalized ratio (INR), activated partial thromboplastin Time (aPTT).
- Hematology: platelet count, red blood cell (RBC) count, hemoglobin, hematocrit, RBC indices (mean corpuscular volume (MCV), %Reticulocytes), white blood cell count with differential (% and absolute numbers; neutrophils, lymphocytes, monocytes, eosinophils, basophils)
- Urinalysis:
  - Continuous: specific gravity, pH
  - Categorical: glucose, protein, blood, ketones, bilirubin, nitrite, leukocyte esterase by dipstick, highly sensitive urine human chorionic gonadotropin (hCG) pregnancy test (for female participants of childbearing potential), microscopic evaluation
- Screening tests:
  - Virology: HIV 1&2 screen/p24 antigen, hepatitis B core, hepatitis B surface, and hepatitis be surface antigen; and hepatitis C antibody, SARS-CoV-2 testing
  - Highly sensitive serum hCG pregnancy test (for female participants of childbearing potential), Follicle-stimulating hormone (FSH) (for female participants)

Normal ranges are available as provided by the laboratory.

5.2.2 Derivation rules

The following parameters will be derived:

- Estimated glomerular filtration rate (eGFR) (Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)) (mL/min/1.73m²) = 141 * minimum(creatinine (mg/dL)/ K; 1)$^{\alpha}$ * maximum(creatinine (mg/dL)/ K; 1) $^{-1.209}$ * 0.993$^{\text{age (years)}}$ * [1.018 if female] * [1.159 if race = black]

  where K = 0.7 if female and K = 0.9 if male;

  α = -0.329 if female and α = -0.411 if male

  Note: in case results in mg/dL are not available, results in µmol/L will be used after conversion in mg/dL: 1 mg/dL = 88.4 µmol/L
- Only fasted lipid samples and glucose (missing fasting status is considered as non-fasted) will be included in tabulations

- Following lipid ratios (based on fasted samples only) will be calculated (unless available in the SDTM database) 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 National Cancer Institute (NCI) common toxicity criteria for adverse events (CTCAE) toxicity grading list (version 5.0). The implementation of these toxicity grades for analysis is presented in appendix 9.2. Only the parameters described in appendix 9.2 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/1.73m2.

Continuous laboratory parameters will be summarized by means of descriptive statistics at each analysis visit. Categorical urinalysis and screening test results will be listed only.

Laboratory abnormalities will be presented as cross-tabulations of the abnormality at each post-baseline analysis visit and at the worst-case analysis visit versus the baseline abnormality. The number 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.

5.3 VITAL SIGNS

5.3.1 Available data

The following vital signs parameters are collected: systolic (SBP) and diastolic blood pressure (DBP) in supine position, pulse rate in supine position, body temperature and weight (only measured on few visits, see Schedule of assessments in appendix 9.4).

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 at each applicable analysis visit.

Abnormalities will be presented as cross-tabulations of the abnormality at each post-baseline analysis visit versus the baseline abnormality and as cross-tabulations of the worst-case abnormality versus the baseline abnormality. The number 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 electrocardiogram (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 QTcB and QTcF 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 at each analysis visit over time.

Abnormalities will be presented 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 (QTc 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 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

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

5.5.2 Presentation of results

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.

5.6 PHYSICAL EXAMINATIONS

Abnormal physical examination findings will be listed.

6. CHANGES TO THE PLANNED ANALYSIS

6.1 CHANGES NOT COVERED BY PROTOCOL AMENDMENTS BEFORE DATABASE LOCK

On sponsor's request, analysis sets were renamed as follows:

Protocol definition	Protocol analysis set	SAP
All randomized participants with a value for total IgG levels at baseline and at least 1 post-baseline timepoint	ITT	mITT
All randomized participants who are exposed to the IMP	SAF	SAF, ITT

6.2 CHANGES NOT COVERED BY PROTOCOL AMENDMENTS AFTER DATABASE LOCK

NAP

6.3 CHANGES TO THE FINAL STATISTICAL ANALYSIS PLAN

NAP

7. REFERENCES

ICH E3: Structure and Content of Clinical Study Reports, July 1996

ICH E6: Guideline for Good Clinical Practice, December 2016

ICH E9: Statistical Principles for Clinical Trials, September 1998

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

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G. E. Simon, 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.

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8. LIST OF TABLES AND LISTINGS

8.1 TABLES

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14.1.1.1	Analysis Sets	SCR	TL
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	Study Duration	SAF	TL
14.1.1.5	Treatment Discontinuation	SAF	TL
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14.1.1.7	Randomization Stratification	SAF	
14.1.1.8	Protocol Deviations	SAF	
14.1.2.1	Demographic Data	SAF	TL
14.1.2.2	Baseline Disease Characteristics	SAF	TL
14.1.2.3	Medical History	SAF	
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14.1.2.5	Prior Therapies by ATC Class (Level 1 and 3) and Generic Term	SAF	
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14.1.2.7	MG Therapies Stopped Prior to ICF by Generic Term	SAF	
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14.1.2.9	Classes of Baseline MG Therapies	SAF	TL
14.1.2.10	Study Drug Administration	SAF	TL
14.1.2.11	Self-Administration of Efgartigimod PH20 SC Training	SAF	TL
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14.2.1.1.2	IgG: Percent Change from Baseline in Total IgG Levels at Week 4 - ANCOVA - PP	PP	TL
14.2.1.1.3	IgG: Percent Change from Baseline in Total IgG Levels at Week 4 - ANCOVA - mITT (AChR-Ab Seropositive)	mITT	TL
14.2.1.2.1	IgG: AUEC of the Percent Change from Baseline in Total IgG Level and IgG Subtypes per Dosing Interval and Over Entire Study	mITT	TL

14.2.1.2.2	IgG: AUEC of the Percent Change from Baseline in Total IgG Level and IgG Subtypes per Dosing Interval and Over Entire Study by AChR-Ab Status	mITT	TL
14.2.1.3	IgG: AUEC of the Percent Change from Baseline in Total IgG Level per Dosing Interval and Over Entire Study by Subgroup	mITT	TL
14.2.1.4	IgG: Descriptive Statistics of Actual Values and Changes from Baseline in Total IgG Level and IgG Subtypes	mITT	
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14.2.3.3.1	MG-ADL: Frequency Tabulation of Actual Values in MG-ADL Total Score	ITT	
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14.2.3.3.4	MG-ADL: Frequency Tabulation of Changes from Baseline in MG-ADL Total Score by AChR-Ab Status	ITT
14.2.3.4	MG-ADL: Early MG-ADL Responders - Frequency Tabulation by AChR-Ab Status and Overall	ITT
14.2.3.5	MG-ADL: Characterization of MG-ADL Responders	ITT
14.2.3.6	MG-ADL: MG-ADL Responders - Dynamic Borrowing Using Bayesian Hierarchical Model	ITT
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14.2.8.1	Descriptive Statistics of Efgartigimod Serum Concentration (ng/mL) Over Time	PK

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14.2.9.3	ADA: Participant Classification, Prevalence and Incidence of Anti-Drug Antibodies Against Efgartigimod	SAF
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14.2.10.3.1	Clinical Efficacy Correlation: MG-ADL Responders - Frequency Tabulation by ADA Participant Classification Against Efgartigimod	ITT
14.2.10.3.2	Clinical Efficacy Correlation: MG-ADL Responders - Frequency Tabulation by NAb Participant Classification Against Efgartigimod	ITT
14.2.10.3.3	Clinical Efficacy Correlation: MG-ADL Responders - Frequency Tabulation by rHuPH20 Ab Participant Classification	ITT
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14.2.10.4.2	Clinical Efficacy Correlation: QMG Responders - Frequency Tabulation by NAb Participant Classification Against Efgartigimod	ITT
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14.2.10.5.1	AE Correlation: Treatment-Emergent Adverse Events by ADA Participant Classification Against Efgartigimod	SAF
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SAFETY

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14.3.1.1	Adverse Events Overview	SAF	TL
14.3.1.2	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	TL
14.3.1.3	Treatment-Emergent Adverse Events by MedDRA Preferred Term by Decreasing Frequency	SAF	
14.3.1.4	Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	TL
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14.3.1.8	Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	TL
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14.3.1.11	Treatment-Emergent Adverse Events Leading to Interruption of Study Drug by MedDRA System Organ Class and Preferred Term	SAF	TL
14.3.1.12	Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term	SAF	TL
14.3.1.13	Time to First Onset and Duration of Treatment-Emergent Adverse Events of Special Interest	SAF	
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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	TL
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14.3.3.2	Cross-Tabulation of Vital Signs Abnormalities Versus Baseline	SAF	
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14.3.4.3	Tabulation of QTc Change Abnormalities	SAF	TL
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14.3.5.1	Suicidality Assessment	SAF	

8.2 LISTINGS

GENERAL CHARACTERISTICS		
16.2.1.1	Allocation	RAND
16.2.1.2	Treatment and Study Discontinuation	SAF
16.2.2.1	Major Protocol Deviations	SAF
16.2.2.2	Minor Protocol Deviations	SAF
16.2.2.3	Violations on Eligibility Criteria	SAF

16.2.2.4	No-Treatment Participants	SCR minus SAF
16.2.2.5	COVID-19-Related Comments	SAF
16.2.2.6	COVID-19-Related Remote Visits	SAF
16.2.4.1	Demographic Data	SAF
16.2.4.2	Baseline Disease Characteristics	SAF
16.2.4.3	Medical History	SAF
16.2.4.4	MG Medical History	SAF
16.2.4.5	Hospitalizations	SAF
16.2.4.6	Prior and Concomitant Therapies	SAF
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16.2.4.8	Vaccination History	SAF
16.2.4.9	Procedures	SAF
16.2.5.1	Administration of Study Drug	SAF
16.2.5.2	Self-Administration Training of Efgartigimod PH20 SC	SAF
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16.2.5.3	Individual Efgartigimod Serum Concentrations and Actual Blood Sampling Times for PK Assessments	PK
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16.2.6.5	Total IgG and IgG Subtypes	mITT
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16.2.7.1	Adverse Events	SAF
16.2.7.2	Serious Adverse Events	SAF
16.2.7.3	Fatal Adverse Events	SCR

9. APPENDICES

9.1 SAS CODE

9.1.1 ANCOVA model

[redacted]

9.1.2 Bayesian logistic regression (with EFG IV arm borrowing)

[redacted]

[redacted]

9.2 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	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	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	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	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	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	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 (fasting) low	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	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	mmol/L	>ULN-1.23	-	>1.23-3.30	>3.30
	mg/dL	>ULN-3.0	-	>3.0-8.0	>8.0
Potassium low	mmol/L	-	<LLN-3.0	<3.0-2.5	<2.5
	mEq/L	-	<LLN-3.0	<3.0-2.5	<2.5
Potassium high	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	mmol/L	<LLN-130	-	<130-120	<120
	mEq/L	<LLN-130	-	<130-120	<120
Sodium high	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	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	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)	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	giga/L	<LLN-75	<75-50	<50-25	<25
	counts/mm^3	<LLN-75000	<75000-50000	<50000-25000	<25000
White blood cells	giga/L	<LLN-3	<3-2	<2-1	<1
	counts/mm^3	<LLN-3000	<3000-2000	<2000-1000	<1000

Note: 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.

9.3 MG THERAPIES AND PROCEDURES

Steroids	NSIDs	AChE inhibitors	Other	Procedures
PREDNISONE	CICLOSPORIN	NEOSTIGMINE	ECULIZUMAB	PLASMAPHERESIS
PREDNISOLONE	AZATHIOPRINE	NEOSTIGMINE BROMIDE	NIPOCALIMAB	THYMECTOMY
METHYLPREDNISOLONE	MYCOPHENOLATE MOFETIL	PYRIDOSTIGMINE	RITUXIMAB	ELECTRONEUROGRAPHY
HYDROCORTISONE	MYCOPHENOLATE SODIUM	PYRIDOSTIGMINE BROMIDE	IMMUNOGLOBULINS	FEEDING TUBE USER
TRIAMCINOLONE	MYCOPHENOLIC ACID	AMBENONIUM	IMMUNOGLOBULINS NOS	GASTROSTOMY
DEFLAZACORT	METHOTREXATE	AMBENONIUM CHLORIDE	IMMUNOGLOBULIN THERAPY	ELECTROMYOGRAM
METHYLPREDNISOLONE SODIUM SUCCINATE	TACROLIMUS	DISTIGMINE	IMMUNOGLOBULIN HUMAN NORMAL	
PREDNISOLONE ACETATE	CYCLOPHOSPHAMIDE	DISTIGMINE BROMIDE		
	CYTOPHOSPHANE			
	TACROLIMUS MONOHYDRATE			

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

9.4 SCHEDULE OF ASSESSMENTS

	Screening[b]	Treatment Period				Follow-up Period					End of Study	Unscheduled
Visit		**V1 Baseline**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**	**EoS[a]**	**UNS[b]**
Study Day (visit window)	**-14 to -1**	**1**	**8(±1)**	**15(±1)**	**22(±1)**	**29(±2)**	**36(±2)**	**43(±2)**	**50(±2)**	**57(±2)**	**71(±3)**	
Activity												
Informed consent[c]	X											
Inclusion/exclusion criteria	X	X										
SARS-CoV-2 test[d]	X											X
Medical/surgical history[e]	X											
Demographic data	X											
Height and weight[f]	X	X									X	X
MG-ADL	X	X	X	X	X	X	X	X	X	X	X	X
QMG[g]		X	X	X	X	X	X	X	X	X	X	X
MG-QoL15r		X									X	
EQ-5D-5L		X									X	
Physical examination	X	X	X	X	X	X	X	X	X	X	X	X
Vital signs[h]	X	X	X	X	X	X	X	X	X	X	X	X
SIB risk monitoring[i]	X	X	X	X	X	X	X	X	X	X	X	X

	Screening	Treatment Period				Follow-up Period					End of Study	Unscheduled
Visit		**V1 Baseline**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**	**EoS[a]**	**UNS[b]**
Study Day (visit window)	**-14 to -1**	**1**	**8(±1)**	**15(±1)**	**22(±1)**	**29(±2)**	**36(±2)**	**43(±2)**	**50(±2)**	**57(±2)**	**71(±3)**	
Activity												
Clinical laboratory tests[j]	X	X	X	X	X	X	X	X	X	X	X	X
AChR-Ab serotype	X											
Single 12-lead ECG[k]	X	X			X						X	X
Urinalysis	X	X			X	X					X	X
Pharmacokinetics[l]		X	X	X	X	X	X	X	X	X	X	X
Pharmacodynamics[m]		X	X	X	X	X	X	X	X	X	X	X
Immunogenicity[n]		X		X		X			X		X	X
Pregnancy test[o]	X	X	X	X	X	X					X	X
Viral screen[p]	X											
Randomization[q]		X										
Training for self-administration of SC IMP[r]		X	X	X	X	(X)	(X)	(X)	(X)	(X)	(X)	(X)
Administration of IMP[s]		X	X[t]	X[t]	X[t]							
Assessment of administration site[u]	Continuous monitoring											
Hospitalization monitoring[v]	Continuous monitoring											

	Screening	Treatment Period				Follow-up Period					End of Study	Unscheduled
Visit		**V1 Baseline**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**	**EoS[a]**	**UNS[b]**
Study Day (visit window)	**-14 to -1**	**1**	**8(±1)**	**15(±1)**	**22(±1)**	**29(±2)**	**36(±2)**	**43(±2)**	**50(±2)**	**57(±2)**	**71(±3)**	
Activity												
Prior/concomitant therapy[v]	Continuous monitoring											
Adverse events[v]	Continuous monitoring											

Ab= antibody; AChR-Ab=acetylcholine receptor binding autoantibody; AChE=acetylcholinesterase; ADA=anti-drug antibodies; ECG=electrocardiogram; EoS=end of study; EQ-5D-5L=EuroQoL 5 Dimensions 5 Levels; ER=emergency room; FSH= follicle-stimulating hormone; ICU=intensive care unit; IgG=immunoglobulin G; IMP=investigational medicinal product; IV=intravenous; MG-ADL=Myasthenia Gravis-Activities of Daily Living total score; MGFA=Myasthenia Gravis Foundation of America; MG-QoL15r=Myasthenia Gravis Quality of Life Questionnaire (15 item scale revised); NAb=neutralizing antibody; PD=pharmacodynamics; PHQ=Patient Health Questionnaire; PK=pharmacokinetics; PR= atrioventricular node delay interval; QMG=Quantitative Myasthenia Gravis score; QRS=duration of ventricular depolarization; QT=total duration of ventricular depolarization; QTcF=rate-corrected QT intervals using Fridericia's formula; PH20= recombinant human hyaluronidase PH20 (rHuPH20); RR= time between heartbeats; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; SC=subcutaneous; SIB=Suicide Ideation and Behavior; SoA=Schedule of Activities; UNS=unscheduled; V=visit

Note: All activities are performed predose on dosing days unless otherwise indicated. It is recommended to perform the MG-ADL scale prior to all other assessments.

[a] After a participant completes the study and all EoS visit activities, the participant will be allowed, if eligibility criteria are met, to roll over into the open-label extension study ARGX-113-2002 to receive efgartigimod PH20 SC 1000 mg.

[b] A UNS visit can occur at the request of the participant or the investigator. During the UNS visit, activities as indicated in the SoA can be performed at the discretion of the investigator, depending on the reason for the UNS visit.

[c] No study-related activities will be initiated before the participant signs the informed consent form.

[d] A nasopharyngeal swab will be performed to sample nasal and throat mucosal cells. Participants may be retested as needed (see Section 10.7)

[e] Medical history will also include all ER visits, hospitalizations, and ICU admissions that have occurred in the previous 12 months. All available vaccination history will be recorded. For vaccines where multiple doses or boosters are received, only the most recent must be recorded. See Section 8.2.5.

[f] Height will only be measured at screening and weight will be measured at screening, at baseline, at the EoS visit, and at UNS visits.

[g] AChE inhibitors must be withheld for at least 12 hours before the QMG assessment (consistent with the revised manual for the QMG test as recommended by the MGFA).

[h] It is recommended that the method used to measure body temperature at screening is maintained throughout the study for each patient.

[i] The SIB Risk Monitoring assessment is based on question 9 of the PHQ. See Section 8.2.10.

[j] Blood samples for clinical laboratory (hematology/clinical chemistry and FSH, if applicable) safety assessments will be collected predose on dosing days. In addition, total IgG at screening is to be assessed for defining eligibility. Participants need to be in a fasted state (defined as no food or drink, except for water, which is allowed until at least 4 hours prior to sampling) for at least 8 hours prior to each sampling.

[k] The following ECG intervals will be measured: RR, PR, QRS, QT, and QTcF.

[l] On dosing days, PK samples will be collected predose (within 1 hour prior to start of administration) and at the end of each infusion for IV (within 1 hour after end of infusion). No postdose PK samples will be collected in case of IMP administration by SC injection.
[m] The PD analysis comprises levels of total IgG, IgG subtypes (IgG1, IgG2, IgG3 and IgG4) and levels of AChR-Abs (for AChR-Ab seropositive participants only).
[n] Titers of ADA against efgartigimod and presence of NAbs against efgartigimod will be measured in serum in both the IV and SC treatment arms. Plasma titer levels of ADA and NAbs against rHuPH20 will be measured in the SC treatment arm only.
[o] Female participants of childbearing potential will be tested for pregnancy using a serum test at screening and a urine test at all other visits.
[p] The virology screen includes relevant tests to comply with exclusion criteria 7 and is performed on samples taken at screening.
[q] Randomization will be performed after screening within approximately 2 weeks and only after confirmation of the eligibility of the patient. If the AChR-Ab test result is not available in time (ie, within the 2 weeks screening window), the screening window can be increased by a maximum of 5 calendar days as needed.
[r] Applicable to participants in the SC treatment arm only. These participants and their caregivers will be trained in self-administration of efgartigimod PH20 SC and the training can continue until the participant or their caregiver is capable of self-administration. Training sessions marked with parentheses "(X)" are optional.
[s] The IMP (efgartigimod IV or efgartigimod PH20 SC) will be administered at visits 1, 2, 3, and 4 either as an 1-hour IV infusion or an SC injection. Participants will remain at the site for at least 1 hour following the end of the drug administration to be monitored for safety.
[t] Participants randomized to the SC treatment arm or their caregivers will be allowed to administer efgartigimod PH20 SC at the site under supervision if the self-administration/caregiver-supported administration training is completed and documented and if the site staff determine that the participant is ready to do so.
[u] The assessment of the administration site will be performed prior to dosing and 1 hour postdose on dosing days, in addition to continuous monitoring by the participant in between visits.
[v] Adverse events, use of concomitant therapies, use of rescue therapy, medical procedures performed on the participants, and hospitalizations will be collected from the time the informed consent form is signed until the last study-related activity. Relevant prior therapy and all available vaccination history will only be collected at screening. See Section 6.8 and Section 8.3.

9.5 PNEUMONIA-RELATED EVENTS

Preferred Terms

Pneumonia anthrax	Atypical pneumonia
Pneumonia bordetella	Pneumonia
Pneumonia chlamydial	Pneumonia mycoplasmal
Pneumonia escherichia	Enterobacter pneumonia
Pneumonia haemophilus	Miliary pneumonia
Pneumonia klebsiella	Pneumonia necrotising
Pneumonia legionella	Embolic pneumonia
Pneumonia moraxella	Post procedural pneumonia
Pneumonia pneumococcal	Haemorrhagic pneumonia
Pneumonia pseudomonal	Paracancerous pneumonia
Pneumonia salmonella	Pneumonia helminthic
Pneumonia staphylococcal	Pneumonia toxoplasmal
Pneumonia streptococcal	Parasitic pneumonia
Pneumonia tularaemia	Pneumonia adenoviral
Pneumonia bacterial	Pneumonia cytomegaloviral
Atypical mycobacterial pneumonia	Pneumonia herpes viral

Pneumonia acinetobacter	Pneumonia influenzal
Pneumonia proteus	Pneumonia measles
Pneumonia serratia	Pneumonia parainfluenzae viral
Pneumonia blastomyces	Pneumonia respiratory syncytial viral
Candida pneumonia	Pneumonia viral
Pneumonia fungal	Herpes simplex pneumonia
Pneumonia cryptococcal	Varicella zoster pneumonia
Pneumocystis jirovecii pneumonia	COVID-19 pneumonia