STATISTICAL ANALYSIS PLAN

A Long-Term, Single-Arm, Open-label, Multicenter Phase 3 Study to Evaluate the Safety and Tolerability of Multiple Subcutaneous Injections of Efgartigimod PH20 SC in Patients With Generalized Myasthenia Gravis

Protocol:	ARGX-113-2002
SGS CR number:	BE-80-2000508
Development phase:	Phase 3
Sponsor:	Argenx
Analysis purpose:	Final Analysis
SAP version number:	Final 5.0
SAP version date:	31Jan2025

System Version: 1.0, Status: Approved, Document ID: VV-TMF-218994

SIGNATURE PAGE

Name and function	Signature and Date (ddMMMyyyy)
SGS CR author:	
[redacted] Biostatistical Coordinator	Signed by: [redacted]
Sponsor's approval: The approver agrees the statistical analysis will be performed according to this statistical analysis plan.	
[redacted] Biostatistical Lead's Functional Manager	Signed by: [redacted]
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PROTOCOL HISTORY

Protocol:		
Version or ID	**Date (ddMMMyyyy)**	**Impact of the changes on the statistical analysis**
Final 1.0	14DEC2020	Not applicable
Final 2.0	10MAY2021	Minor: additional optional pharmacokinetic samples and additional clinical chemistry laboratory assessments
Final 3.0	02FEB2023	Extension of study duration; Changes in SoA to reduce frequency of efficacy and safety assessments for second year on and to limit on-site visits when the participant does not need treatment; From the second year on, there is no longer a 28-day restriction between treatment periods.

Protocol amendments:		
Version or ID	**Date (ddMMMyyyy)**	**Applicable country of the amendment**
Amendment 1.1	19MAY2021	Germany
Amendment 1.2	02JUN2021	Germany
Amendment 1.3	10JUN2021	Germany
Amendment 1.4	07JUL2021	Germany
Amendment 1.5	02AUG2021	Germany
Amendment 2.1	22SEP2021	Germany
Amendment 2.2	08JUN2022	Germany

This statistical analysis plan (SAP) only considers the approved version 3.0 of the protocol and the protocol amendments, as listed above.

LIST OF ABBREVIATIONS

1705	ARGX-113-1705
2001	ARGX-113-2001
Ab	Antibody
AChR	acetylcholine receptor
ADA	anti-drug antibodies
ADaM	analysis data model
APADY	relative day in period
AE	adverse event
AESI	adverse event of special interest
ALQ	above the limit of quantification
bpm	beats per minute
CI	confidence interval
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CnB	cycle n baseline
CRF	case report form
CTCAE	Common Terminology Criteria for Adverse Events
DBP	diastolic blood pressure
DSMB	data safety monitoring board
ECG	Electrocardiogram
eGFR	estimated glomerular filtration rate
EoS	end of study
EQ-5D-5L	EuroQoL 5 Dimensions 5 Levels
EU	European Union
SFU	safety follow-up
gMG	generalized myasthenia gravis
HR	heart rate
ICF	informed consent form
ICH	International Council for Harmonisation
IgG	immunoglobulin G
IMP	investigational medicinal product
IP	intertreatment period
IRR	injection-related reaction

ISR	injection site reaction
ITT	intent-to-treat
mITT	modified intent-to-treat
MAA	marketing authorisation application
[redacted]	[redacted]
MedDRA	Medical Dictionary for Regulatory Activities
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
OLE	open-label extension
PK	pharmacokinetic(s)
PD	pharmacodynamic(s)
PYFU	patient years of follow-up
QTc	corrected QT interval
QTcB	Bazett's corrected QT interval
QTcF	Fridericia's corrected QT interval
RO	Rollover
SAP	statistical analysis plan
SAF	safety analysis set
SBP	systolic blood pressure
SD	standard deviation
SE	standard error
SGS CR	SGS Clinical Research
SOP	standard operating procedure
STAT	Statistics
TEAE	treatment-emergent adverse event
[redacted]	[redacted]
VS	vital signs
WHO	World Health Organisation
WI	work instruction

DEFINITION OF TERMS

AChR-Ab seronegative participants	AChR-Ab seronegative participants refers to participants in whom the anti-AChR-Ab could not be detected at screening in 1705/2001
case report form (CRF)	A printed, optical, or electronic document designed to record protocol required information to be reported to the sponsor for each trial subject.
Cohort	In the context of analysis by cohorts, cohort n is defined as all participants in at least n efgartigimod PH20 SC cycles
Display	Analysis table, figure or listing
MG therapy	Any therapy falling in one of the following categories per appendix 9.3: steroids, NSIDs or AChE inhibitors
Phase	Interval of time in the planned conduct of a study 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 that was not present at baseline (eg, hemoglobin normal at baseline and grade 1 post-baseline; glucose low at baseline and high post-baseline; QTcFri]450; 480] ms at baseline and >500 ms post-baseline)

TABLE OF CONTENTS

1. INTRODUCTION

This Statistical Analysis Plan (SAP) describes the final statistical analysis to be performed for the ARGX-113-2002 (BE-80-2000508) study.

This SAP covers the safety, efficacy, pharmacokinetic(s) (PK), pharmacodynamic(s) (PD), immunogenicity, and general characteristics parts of the final statistical analysis. It specifies the analysis displays to be presented and describes the methods and procedures in a more elaborate way than in the statistical methods section of the protocol. The analysis displays to be produced for this final analyses are presented in section 8.

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

1.1 STUDY OBJECTIVES

According to the protocol, the objectives and endpoints of this study are:

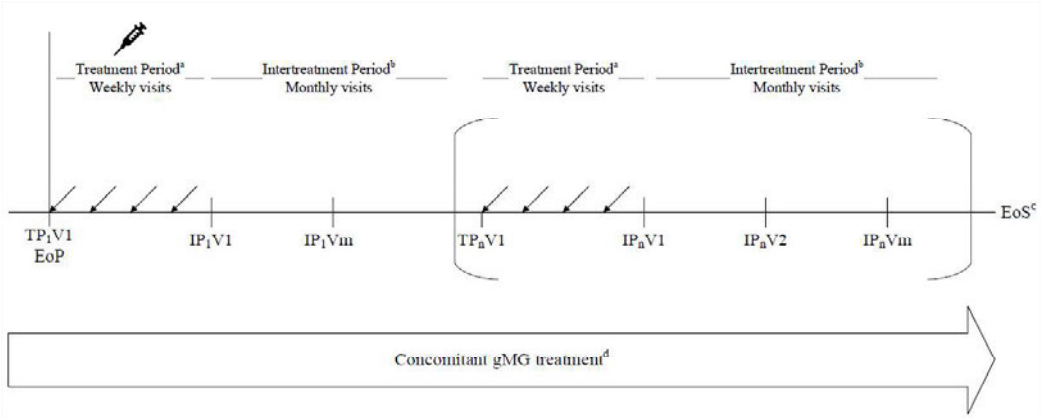
Objectives	**Endpoints**
Primary	
To evaluate the long-term safety and tolerability of efgartigimod PH20 SC in participants with gMG	Incidence and severity of adverse events (AEs), incidence of serious adverse events (SAEs) and AEs of special interest (AESIs) and changes in laboratory test results, physical examination results, vital signs, and electrocardiogram results
Secondary	
To evaluate the impact of efgartigimod PH20 SC on disease severity	Myasthenia Gravis Activities of Daily Living (MG-ADL) total score changes from baseline and cycle baseline over time by cycle
To evaluate the effect of efgartigimod PH20 SC on pharmacodynamics (PD)	Percentage reduction in levels of total immunoglobulin G (IgG) from baseline and cycle baseline over time by cycle Percentage reduction of acetylcholine receptor binding autoantibodies (AChR-Ab) from baseline and cycle baseline over time by cycle in AChR-Ab seropositive participants
To evaluate the PK of efgartigimod PH20 SC	Efgartigimod serum concentrations
To evaluate the immunogenicity of efgartigimod PH20 SC	Incidence and prevalence of anti-drug antibodies (ADAs) to efgartigimod over time Incidence and prevalence of neutralizing antibodies (NAbs) against efgartigimod over time Incidence and prevalence of ADAs to rHuPH20 over time Incidence and prevalence of NAbs against rHuPH20 over time
To evaluate the impact of efgartigimod PH20 SC on the quality of life (QoL) of the participants	Changes in total Myasthenia Gravis Quality of Life Questionnaire (15-item scale revised) (MG-

	QoL15r) from baseline and cycle baseline by cycle Changes in EuroQoL 5 Dimensions 5-Level (EQ-5D-5L) visual analog scale (VAS) score from baseline and cycle baseline over time by cycle EQ-5D-5L responses to 5 dimensions (ie, mobility, self-care, usual activities, pain/discomfort, anxiety/depression) over time by cycle
To evaluate feasibility of self-administration of efgartigimod PH20 SC	Number and percentage of participants who performed self-administration at home over time by cycle Number and percentage of caregivers who administered the injection to the participant at home over time by cycle Number of training visits needed for the participant or caregiver to be competent to start administering efgartigimod PH20 SC Number and percentage of self- or caregiver-supported study drug administration among all study treatment visits at home
Exploratory	
[redacted]	[redacted]

1.2 STUDY DESIGN

This is an ongoing long-term, single-arm, open-label, multicenter, safety study in acetylcholine receptor binding antibody (AChR-Ab) seropositive and seronegative participants with gMG. Participants will have entered the study from either study ARGX-113-2001 or study ARGX-113-1705. The aim is to evaluate the long-term safety and tolerability of efgartigimod PH20 SC 1000 mg; the clinical efficacy, pharmacodynamics (PD), pharmacokinetics (PK), immunogenicity; and impact on participant quality of life (QoL), treatment satisfaction, and preferred method of administration; and the feasibility of self- and caregiver-supported SC injection administration.

Figure 1 Study Schematic for Participants in Need of Retreatment at Study Entry



EoP=end of study/early discontinuation visit for antecedent studies ARGX-113-2001 or ARGX-113-1705; EoS=end of study; gMG=generalized myasthenia gravis; IMP=investigational medicinal product; IPnVm=intertreatment period (period number) visit (visit number); PH20=recombinant human hyaluronidase PH20 (rHuPH20); q7d=every 7 days; SC=subcutaneous(ly); SoA=schedule of activities; TP=treatment period; TPnVm=treatment period (period number) visit (visit number)

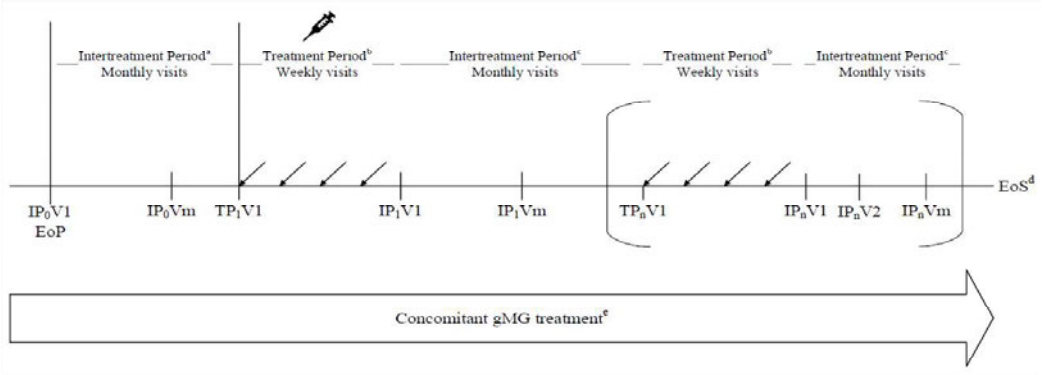
[a] Participants will receive efgartigimod PH20 SC 1000 mg q7d for a total of 4 injections in a TP. A new TP can be started if the participant is in need of retreatment as determined by the investigator, however during the first year, at least 28 days must have elapsed since the last dose of efgartigimod. During the second year onward, it is recommended to have at least 28 days between TPs. However, a subsequent treatment period can be administered earlier based on clinical evaluation at the discretion of the investigator, with a minimum interval of 7 days after the last IMP administration. In case of retreatment, there must be at least 4 weeks left in the study for the participant, so that a full TP and the EoS visit can be performed.

[b] For the visit schedule, see CTP SoA (Section 1.3).

[c] Participants will remain in the study for at least 1 year, until efgartigimod PH20 SC becomes commercially available or available through another continued access program for gMG, or until 31 Dec 2024, whichever comes first.

[d] Dose reduction or changes to the dose are allowed as described in Section 6.8.2 of the CTP. Concomitant gMG treatment can be tapered completely.

Figure 2 Study Schematic for Participants not in Need of Retreatment at Study Entry



EoP=end of study/early discontinuation visit for antecedent studies ARGX-113-2001 or ARGX-113-1705; EoS=end of study; gMG=generalized myasthenia gravis; IMP=investigational medicinal product; IPnVm=intertreatment period (period number) visit (visit number); PH20=recombinant human hyaluronidase PH20 (rHuPH20); q7d=every 7 days; SoA=schedule of activities; TP=treatment period; TPnVm=treatment period (period number) visit (visit number)

[a] During the intertreatment period, visits will occur every 21 days. TP1V1 will occur when a participant is eligible for retreatment.

[b] Participants will receive efgartigimod PH20 SC 1000 mg q7d for a total of 4 injections in a TP. A new TP can be started if the participant is in need of retreatment as determined by the investigator, however during the first year, at least 28 days must have elapsed since the last dose of efgartigimod. During the second year onward, it is recommended to have at least 28 days between TPs. However, a subsequent treatment period can be administered earlier based on clinical evaluation at

the discretion of the investigator, with a minimum interval of 7 days after the last IMP administration. In case of retreatment, there must be at least 4 weeks left in the study for the participant, so that a full TP and the EoS visit can be performed.

[c] For the visit schedule, see CTP SoA (Section 1.3).

[d] Participants will remain in the study for at least 1 year, until efgartigimod PH20 SC becomes commercially available or available through another continued access program for gMG, or until 31 Dec 2024, whichever comes first.

[e] Dose reduction or changes to the dose are allowed as described in Section 6.8.2 of the CTP. Concomitant gMG treatment can be tapered completely.

Once a participant has clinical need of retreatment, they will be administered efgartigimod PH20 SC 1000 mg every 7 days (q7d) for a total of 4 injections. The 3-week period in which efgartigimod PH20 SC 1000 mg will be administered q7d for 4 administrations constitutes a treatment period (TP). Depending on the clinical effect, participants may be retreated as needed using a variable number of treatment periods (TP), separated by an intertreatment period (IP) of at least 28 days (year1). From year 2 onward, it is recommended to have IPs of at least 28 days, but a subsequent treatment period can be administered earlier based on clinical evaluation at the discretion of the investigator. A minimal interval of 7 days after the last investigational medicinal product (IMP) administration of the previous cycle must be maintained. Participants and their caregivers will be trained in administration of the SC injection, and once they are sufficiently competent to perform the injection, all administrations, except the first administration of a TP, may be performed at home. For participants who have not previously received efgartigimod PH20 SC, administration during the first TP must be performed on-site, irrespectively whether the caregiver or participant is ready for self-administration or not. The time between each TP will depend on the clinical effect as assessed by the investigator.

STUDY ENTRY AND ROLL OVER FROM ANTECEDENT STUDIES ARGX-113-2001 AND ARGX-113-1705

At the end of study (EoS) visit on day 71 of study ARGX-113-2001 or the EoS visit of study ARGX-113-1705, eligible participants will be offered the option to roll over into this study. The first visit of study ARGX-113-2002 will coincide with the last visit of study ARGX-113-2001/ARGX-113-1705 for each participant. Overlapping assessments will not be repeated.

If the investigator has determined that the participant's condition has deteriorated due to gMG symptoms, then the investigator may decide to start a new TP at the first visit in study ARGX-113-2002. The activities of TP1V1 will be completed along with the study entry assessments. Otherwise, the participant will start study ARGX-113-2002 with an intertreatment period (IP) visit and complete IP0V1 on-site along with the study entry assessments. Subsequent IP visits in this IP can alternate between phone visits and on-site visits.

RETREATMENT

If the investigator has determined that the participant's condition has deteriorated due to gMG symptoms, the investigator may decide to start a new TP during an on-site IP visit or the participant may contact the investigator for an unscheduled visit. In this instance, the IP visit or the unscheduled visit will become the first TP visit. No activities will be duplicated.

A new TP with efgartigimod PH20 SC can be started at an on-site visit when all the following criteria are met:

- The participant completed the previous treatment period
- The participant could benefit from retreatment according to the judgement of the investigator
- There is no clinical evidence of any concomitant disease that could confound the results of the study or put the participant at undue risk
- For year 1: At least 28 days (minimum 4 weeks) has elapsed between treatment periods (ie, between the last administration of efgartigimod and TP(n+1)V1).
  From year 2 onward: At least 7 days has elapsed between treatment periods (ie, between the last dose of the previous TP and the first dose of the next TP). It is recommended to have IPs of at least 28 days, but a subsequent treatment period can be administered earlier based on clinical evaluation at the discretion of the investigator.

TIME BETWEEN TREATMENT PERIODS

The first IP visit after a TP will occur on-site 1 week (±2 days) after the last administration of efgartigimod PH20 SC. Thereafter, IP visits will occur every 3 weeks (+7 days). The second IP visit after a TP must also be performed on-site. The third IP visit may be performed by phone. All remaining IP visits may alternate between on-site visits and phone visits (eg, the fourth visit will be done on-site, the fifth visit may be done by phone, etc.) (for year 1). From year 2 onward, on-site IP visits are required for TPnV1 and for every 5 visits (IPnV5/10/15 etc). In year 1, the length of the IP may vary from participant to participant and each IP may vary in length for an individual participant from period to period, as long as there is at least 28 days between the last dose of the previous TP and the first dose of the next TP. From year 2 onward, it is recommended to have IPs of at least 28 days, but a subsequent treatment period can be administered earlier based on clinical evaluation at the discretion of the investigator. A minimal interval of 7 days after the last IMP administration of the previous cycle must be maintained. If activities at an IP visit performed by phone indicate a need for retreatment, then a TPnV1 visit will be scheduled.

The schedule of assessments is in appendix 9.4.

1.3 EXPECTED SAMPLE SIZE

Up to 201 patients may be enrolled from the antecedent studies ARGX-113-2001 and ARGX-113-1705.

1.4 RANDOMISATION AND BLINDING

Not applicable.

1.5 INTERIM ANALYSIS

Interim analyses were performed. These are described in separate SAPs.

1.6 SOFTWARE

SAS version 9.4 or later will be used for programming.

1.7 VALIDATION MODEL

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

2. GENERAL METHODOLOGY

2.1 ANALYSIS SETS

2.1.1 Analysis sets

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

Roll-over set (RO):	participants who rolled over in this study
Safety analysis set (SAF):	all participants who are exposed to IMP in this study
Modified safety analysis set (mSAF)	all participants who are exposed to IMP in this study and have signed the protocol v3.0 (dated 2Feb2023) specific informed consent form (ICF).

All analyses will be performed on the safety analysis set, unless specified otherwise.

A patient is considered to have rolled over if he/she has signed the ARGX-113-2002 specific informed consent, defined as having a complete informed consent signature date in the database.

The AChR-Ab seropositive subset population will be defined based on the actual AChR-Ab status of the parent studies, not the 'as stratified'.

2.1.2 As planned versus as actual analysis

The actual treatment of the patient will be considered for all studies (see section 2.4.2).

2.2 PHASES, PERIODS AND TIME POINTS

2.2.1 Phases and periods

All events and assessments will be allocated to phases and periods (see Table 1). Each period coincides with a cycle and includes the 4 injections of efgartigimod PH20 SC 1000 mg q7d and the intertreatment period (IP) visits. The length of the IP is patient-specific and can differ between the different periods. The number of participants can decline for each subsequent cycle.

Table 1: phase/period definition

Phase	Period	Start	End
[IP0][a]		Earliest of (date of signing the ICF and date of the rollover), with 00:00 added as time part.	First injection date/time in cycle 1 – 1 minute or date of last contact with 23:59 added as the time part (for participants not treated)
Treatment + Follow-up	Cycle 1	First injection date/time in cycle 1	First injection date/time in next cycle – 1 minute or if last cycle: date of last contact [b], with 23:59 added as time part

	Cycle n	First injection date/time in cycle n	First injection date/time in next cycle – 1 minute or if last cycle: date of last contact [b], with 23:59 added as time part
	Cycle x	First injection date/time in cycle x	Date of last contact [b], with 23:59 added as time part

[a] If the investigator has determined that the participant's condition has deteriorated due to gMG symptoms, then the investigator may decide to start a new TC at the first visit in study ARGX-113-2002
[b] Date of interim cutoff for ongoing participants

Additionally for participants allocated in the mSAF, all events and assessments will be reallocated to phases and periods (see Table 2).

Table 2: phase/period definition for analysis on mSAF

Phase	Period	Start	End
[IP0][a]		Earliest of (date of signing the ICF and date of the rollover), with 00:00 added as time part.	First injection date/time in the study – 1 minute or date of last contact with 23:59 added as the time part (for participants not treated)
Pre-amended Treatment + Follow-up		First injection date/time in the study	First injection date/time of the cycle wherein the ICF for protocol v3.0 was signed - 1 minute or date of last contact with 23:59 added as the time part (for participants who discontinued/completed the study before CTP v3.0)
Amended Treatment + Follow-up	Amended cycle 1	First injection date/time of the cycle wherein the ICF for protocol v3.0 was signed[b]	First injection date/time in next cycle – 1 minute or if last cycle: date of last contact [a], with 23:59 added as time part
	Amended cycle n	First injection date/time in cycle n	First injection date/time in next cycle – 1 minute or if last cycle: date of last contact [a], with 23:59 added as time part
	Amended cycle x	First injection date/time in cycle x	Date of last contact [a], with 23:59 added as time part

[a] Date of interim cutoff for ongoing participants
[b] If participant signed ICF for protocol v3.0 multiple times, the first date of signature will be used.

AEs and concomitant medications will be allocated to phases and periods as described in sections 5.1.2 and 3.5.2 respectively. All other assessments will be allocated to phases and periods 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 and period. If this is not possible, assessments will be

allocated to the first possible cycle unless the available parts of the assessments start or stop date/time provide evidence the assessments did not occur during that period.

In addition and to complement the analyses by cycle, a set of phases will be derived for analyses of adverse events over time (by 3-monthly periods) (see Table 3), independent of cycles of treatment.

Table 3: Phase definition by 3-monthly periods

Phase	Start	End
(Amended) 0-3 Months	First injection date/time in (amended) cycle 1	Minimum of (First injection date in (amended) cycle 1 + 90 days, date of last contact[a]), with 23:59 added as time part
(Amended) 4-6 Months	End date/time of Phase 0-3 Months + 1 minute	Minimum of (First injection date in (amended) cycle 1 + 180 days, date of last contact[a]), with 23:59 added as time part
(Amended) n*3-2 - n*3 Months (n≥3)	End date/time of previous phase + 1 minute	Minimum of (First injection date in (amended) cycle 1 + n*90 days, date of last contact[a]), with 23:59 added as time part

Where n is 3 for the third 3-monthly period, 4 for the fourth, etc.
[a] Date of last contact or cutoff date of interim analysis for participants ongoing in study 2002, whichever is earlier

Adverse events will be allocated to these 3-monthly phases for an analysis over time in which participants are on efgartigimod treatment (either actively in one or more cycles or in follow-up).

In case of (partially) missing date/time fields, events will be allocated to the first 3-monthly phase that is possible based on the available parts of the AE start and stop date/time.

2.2.2 Baseline and change from baseline

Two baselines are defined:

- Baseline is the last available value prior to first administration of efgartigimod in the first cycle in 2002.
- Cycle n Baseline (CnB) is the last available value prior to first administration of efgartigimod in (amended) cycle n, with n=1, 2, 3, etc.

Note: for questionnaires, all assessments on the day of first administration of the IMP in cycle n are considered in the baseline selection, also those post-administration.

For immunogenicity, evaluable sample will be given priority when deriving the baseline or cycle 1 baseline. The cycle baseline for cycle 2 or higher will correspond to the value from the last visit in the previous cycle without any derivation.

Change can be calculated from baseline or CnB. Note: baseline coincides with C1B. Baseline will be considered for analyses that assess across all cycles and the CnB will be used for analyses restricted to a specific cycle, n, unless specified otherwise.

Change for safety parameters will be calculated from baseline only.

For efficacy and PD, a (percent) change can be calculated from baseline or CnB, according to the analysis.

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.

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

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

2.2.3 Relative day

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

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

The reference date for APADY is the date of the first administration of the study drug in the specific period. The reference date for ADY is the date of the first administration of the study drug in the (amended) treatment + follow-up phase of the study.

2.2.4 Analysis visits

All assessments (from first ARGX-113-2002 cycle onwards), 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.

Two types of analysis windows will be used:

- Analyses by cycle: allocation of assessments will be done using their relative day in the *period* (APADY, see section 2.2.3), as defined in Table 4 below.
- Analyses over time: allocation of assessments will be done using their relative day in the (amended) treatment + follow-up phase of the *study* (ADY, see 2.2.3), as defined in Table 5 below.

Table 4: Analysis visits for analysis by cycle

Phase/Period	Analysis window	Target APADY	Lower limit APADY	Upper limit APADY
	Study entry[b]	1	[-INF]	30
Treatment/(Amended) cycle$_n$				
	CnB	1	[-INF]	1[a]
	Week 1	8	1[a]	11
	Week 2	15	12	18

Phase/Period	Analysis window	Target APADY	Lower limit APADY	Upper limit APADY
	Week 3	22	19	25
	Week 4	29	26	39
	Week 4 + (3*x)	29 + (x*21)	29 + (x*21) - 10	29 + (x*21) + 10
	Around 1 year after study entry[b]	366	183	[INF]

[a] An assessment on day 1 will be considered for baseline in case it is before the administration of the IMP, for Week 1 otherwise, unless the assessment is related to questionnaires for which time will not be important and therefore to be considered for baseline.
[b] Analysis windows only apply to [redacted] and are based on ADY instead of APADY

Baseline is defined in section 2.2.2.

For those participants who will start a new cycle, the last assessment in a cycle, prior to the administration of the new cycle, will be allocated to the appropriate visit within the previous cycle and will also be allocated as the cycle base (CB) visit of the new cycle.

Table 5: Analysis visits for analyses over time

Phase	Analysis window	Target ADY	Lower limit ADY	Upper limit ADY
(Amended) Treatment + FU	Baseline	1	-INF	1[a]
	Week 1	8	1[a]	11
	Week 2	15	12	18
	Week 3	22	19	25
	Week 4	29	26	39
	Week 7	50	40	60
	Week 10	71	61	81
	Week y[b]	y*7+1	y*7-9	y*7+11

[a] An assessment on day 1 will be considered for baseline in case it is before the administration of the IMP, for Week 1 otherwise, unless the assessment is related to questionnaires for which time will not be important and therefore to be considered for baseline.
[b] From Week 10 on, analysis visits will be defined every 3 weeks

Per parameter and analysis window, the value closest to the target APADY/ADY will be used in analysis tables and figures, other values will only be listed. If more than one value is located at the same distance from the target, then the latest in time will be selected. The value latest in time will be identified using, in order of preference, the assessment time, the visit label or the group identifier (if applicable). Missing values will be removed before the selection is made.

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. Abnormalities are derived per parameter, and if both the lowest and the highest values

are considered abnormal, then two worst-case analysis visits for the same parameter will be presented for the participant. For toxicity grades, the worst-case value of toxicity grades is associated with the highest toxicity grade and is derived per parameter and by toxicity direction (hypo/hyper).

All non-missing post-baseline values within the treatment and follow-up phase, including unscheduled assessments will be considered when deriving the worst-case analysis visit.

2.3 IMPUTATION AND ROUNDING RULES

2.3.1 Missing values

No missing values will be imputed (ie, observed cases analysis).

2.3.2 Values below or above a threshold

Laboratory safety and AChR-Ab values expressed as below/above the quantification limit (BLQ/ALQ) will be imputed by the value of the quantification limit itself. For total IgG, BLQ and ALQ values will not be imputed and will be excluded from the statistical analysis. 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. 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 time between first administration in the study and the first administration of the cycle wherein the ICF for protocol v3.0 was signed will be rounded to 1 decimal.
- Estimated glomerular filtration 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

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

2.4 PRESENTATION OF RESULTS

To support the J-MAA submission, all descriptive outputs (except for analysis by average treatment duration per year) described in this SAP will be repeated by region (Japanese / non-Japanese as defined in the study protocol). The definition of Japanese in the protocol is a participant whose parents and 4 grandparents are Japanese, who has 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 be excluded from 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 analyses, the 95% 2-sided confidence interval may be provided. For immunogenicity, geometric mean and geometric coefficient of variation (CV%) will be added.

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

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

Serum concentrations will be presented with 3 significant digits in the original concentration units, except values ≥ 1000, which will be rounded to an integer. 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 and CV% 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 cycle. All cycles will be shown, even if no events are present.

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. Similarly for immunogenicity correlation tables, a "missing ADA/NAb classification" category will be shown if applicable.

2.4.2 Presentation of treatments

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

- EFG SC (2001) – EFG SC
- EFG IV (2001) – EFG SC
- EFG IV (1705) – EFG SC
- TOTAL EFG IV – EFG SC
- TOTAL

2.4.3 Presentation of treatment in modified safety analysis set

After signing ICF for protocol version 3.0 (dated 2Feb2023), a subsequent treatment period can be administered at least 7 days after the last IMP administration of the previous cycle instead of 28 days, based on the clinical evaluation at the discretion of the investigator. Due to this protocol amendment, the number of injections per year can go up to 52 per year from year 2 onward, compared to 30 in year 1 of the study.

To evaluate the safety and efficacy across different groups with increased exposure, an additional participant classification will be created for the participants in the modified safety analysis set, based on their average weeks of treatment per year in the amended treatment + follow-up phase. Separate tables will be created for this "by average treatment duration per year" classification based upon the data since the cycle wherein the IC of the amended protocol was signed (ie, since the first amended cycle; see Table 2, section 2.2.1). All data will be listed, including the amended cycle number (where applicable).

For each participant, the average treatment duration per year will be calculated as follows:

- First, the number of completed cycles since the first amended cycle will be calculated.
- Completed cycles are cycles that were not cut off by study discontinuation or data cutoff date. For participants with a single (incomplete) cycle, the cycle will be considered a complete cycle in case the cycle duration up to data cutoff date is no less than 28 days.
- Based on these completed cycles, the total duration of completed cycles will be calculated as end date of last completed cycle – start date of first completed cycle + 1 day.
- The average treatment duration per year is then calculated as 365*(number of completed cycles)/(total duration of completed cycles)*4.
- Based on the average treatment duration per year, participants are categorized as follows:
- ≤30 weeks of treatment per year: these participants correspond to the participants with (on average) a cycle duration of at least 50 days.
- >30 to ≤38 weeks of treatment per year: these participants correspond to participants with shorter cycles, but not as short as (on average) weekly or nearly weekly treatment.
- >38 weeks of treatment per year: these participants correspond to the participants with shorter cycles, reflecting (on average) weekly or nearly weekly treatment.

Tables by average treatment duration per year will not be shown by treatment group (in section 2.4.2), but by average treatment duration category only. The following labels will be used:

- <= 30 WEEKS OF TREATMENT/YEAR
- >30 to <=38 WEEKS OF TREATMENT/YEAR
- >38 WEEKS OF TREATMENT/YEAR
- TOTAL

The time (years) between first administration in the study and the first administration of the cycle wherein the ICF for protocol v3.0 was signed will be calculated as: (date of first administration of the cycle wherein the ICF for protocol v3.0 was signed - date of first administration in the study + 1 day)/365.25

2.4.4 Cohorts

Immunogenicity analyses will be performed on all participants included in the safety analysis set over the whole observation period, but also by cycle. Due to the difference in length of the observational periods, the number of participants will be different across cycles. The number of participants in the first cycle will be higher than the number of participants in the second cycle and so forth. To account for this attrition, cohorts of participants with at least 2 cycles, with least 3 cycles, etc. will be created. The analyses performed on the safety analysis set using all available data will be repeated for each of these cohorts to evaluate immunogenicity over cycles within similar cohorts. A cohort will need to contain at least 10 participants to be shown in the results (eg, if the total number of participants with at least 6 cycles is less than 10, data for this cohort will not be presented in the tables).

In tables by cycle, analyses will first be performed on the total safety analysis set using all available data (ie, cohort of all participants) and will then be repeated (as applicable) for each of these cohorts per cycle and, if applicable, for any cycle:

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

2.4.5 Ordering in tables, figures and listings

For presentations by analysis visits, IP0 visits will not be considered in the tables.

All tables will be presented per treatment and cycle unless specified otherwise. If present, the worst-case will be shown last. Cycles will be indicated as a subtitle or

within the table like “Cycle n”. A selection of results will also be presented by cohort (‘cohort of participants with at least x cycles’; see section 2.4.4). A cohort should contain at least 10 participants to be shown.

Listings for general characteristics, results will be ordered by treatment labels (as defined above) and patient, unless specified otherwise.

All other listings will be ordered by treatment, patient, period, 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.

The ordering of groups will be done as shown in section 2.4.2.

3. GENERAL CHARACTERISTICS ANALYSES

3.1 SUBJECT DISPOSITION

The following patient data will be tabulated:

- The number of participants in each analysis set.
- The number and percentage of participants by country and investigator.
- The number and percentage of participants for each period/analysis visit.
- The number and percentage of participants for each period with on-site and phone call visits.
- Descriptive statistics of the cycle duration (see section 2.2.1), calculated as cycle end date – cycle start date + 1 day. Frequency tabulation of the cycle duration in weeks.
- Descriptive statistics of the study duration and of each analysis phase. Study duration is calculated as study end date (date of last contact) – study start date (date of informed consent) + 1 day. Data for ongoing participants are censored at the cutoff date for interim analysis. Analysis phases are defined in section 2.2.1.
- The number and percentage of participants who completed or discontinued the study as documented on the study termination page and the number and percentage of participants for each study discontinuation reason.
- The number and percentage of participants who completed or discontinued the study as documented on the study termination page and the number and percentage of participants for each study discontinuation reason by cycle.
- The number and percentage of participants who completed or discontinued the treatment as documented at the end of the treatment page and the number and percentage of participants for each treatment discontinuation reason.
- The number and percentage of participants who completed or discontinued the treatment as documented at the end of the treatment page and the number and percentage of participants for each treatment discontinuation reason by cycle.
- Frequency tabulation of the treatment and follow-up duration per 6-monthly category, showing the number and percentage in each category and additionally cumulative number and percentages. Categories are defined as follows: <6 months (< 168 days); 6 to <12 months (168 - 350 days); 12 to <18 months (351 - 532 days); 18 to <24 months (533-715 days); 24 to <30 months (716-897 days); 30 to <36 months (898 - 1080 days); 36 to <42 months (1081-1263 days); 42 to <48 months (1264 - 1445 days).

Additionally, the following patient data will be provided by average treatment duration per year:

- The number and percentage of participants by country and investigator.
- Descriptive statistics of the cycle duration (see section 2.2.1), calculated as cycle end date – cycle start date + 1 day. Frequency tabulation of the cycle duration in weeks.

- The number and percentage of participants who completed or discontinued the study as documented on the study termination page and the number and percentage of participants for each study discontinuation reason.
- The number and percentage of participants who completed or discontinued the study as documented on the study termination page and the number and percentage of participants for each study discontinuation reason by cycle.
- The number and percentage of participants who completed or discontinued the treatment as documented at the end of the treatment page and the number and percentage of participants for each treatment discontinuation reason.
- The number and percentage of participants who completed or discontinued the treatment as documented at the end of the treatment page and the number and percentage of participants for each treatment discontinuation reason by cycle.
- Frequency tabulation of the treatment and follow-up duration per 6-monthly category, showing the number and percentage in each category and additionally cumulative number and percentages.
- Frequency tabulation of the cycle wherein the ICF for protocol v3.0 was signed.

All information collected in the CRF concerning study and treatment discontinuation will be listed, including information related to discontinuation during IP0. Listings with all COVID-19-related comments and COVID-19-related remote visits will also be prepared.

3.2 PROTOCOL DEVIATIONS

The number and percentage of patients with major and minor protocol deviations will be tabulated, by type (major/minor) and overall, and per class of deviation.

All available information concerning minor and major protocol deviations will be listed.

3.3 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

3.3.1 Available data

The following parameters will be collected during the roll-over visit:

- Demographics: sex, women of childbearing potential, age (at signing of ICF of 2002), race, ethnicity, height, baseline weight, baseline body mass index, date of birth, date of signing informed consent form (ICF).
- Baseline disease characteristics: MG-ADL questionnaire (MG-ADL total score) at baseline (see 2.2.2), MG-QoL15r questionnaire (MG-QoL15r total score), EQ-5D-5L VAS score and AChR-Ab status (actual value from 2001 and 1704).

3.3.2 Derivation rules

The following parameters will be derived:

- Age category:18-<65, ≥ 65 years
- Japanese vs non-Japanese: as defined in parent study protocol, from SDTM SUPPDM dataset of parent study.
- Region: Japan; US; rest of the world
- Baseline MG-ADL total score categories: <5, 5-7, 8-9, ≥10
- Baseline eGFR category (derivation of eGFR is detailed in section 5.2.2):
  - Normal: ≥ 90 mL/min/1.73m²
  - Mildly impaired: 60 mL/min/1.73m² ≤ eGFR < 90 mL/min/1.73m²
  - Moderately impaired: 30 mL/min/1.73m² ≤ eGFR < 60 mL/min/1.73m²
  - Severely impaired: < 30 mL/min/1.73m²

Following subgroups are defined:

- AChR-Ab status: seropositive, seronegative
- Age category: 18-<65 years, ≥65 years
- Race: white, Asian, Other
- Region: United States, Japan, rest of the world
- Sex: male, female
- eGFR category at baseline: normal, mildly impaired, moderately impaired, severely impaired (as defined above)

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, region, ethnicity, Japanese/non-Japanese participants.

Baseline disease characteristics will be presented using descriptive statistics for baseline scores and a frequency tabulation for AChR-Ab status, baseline eGFR categories, and baseline MG-ADL total score categories.

Demographics and baseline disease characteristics tables will be generated by the subgroups mentioned above.

Demographics and baseline disease characteristics tables (except subgroup tables) will be repeated by average treatment duration per year.

All demographic data and baseline disease characteristics will be listed. The demographics listing will also show the date ICF for CTP v3.0 was signed, the average treatment duration per year (see section 2.4.3) and the time between first administration in the study and the first administration of the cycle wherein the ICF for protocol v3.0 was signed (see section 2.4.3).

3.4 MEDICAL HISTORY AND CONCOMITANT DISEASES

Medical history and concomitant diseases are not collected in this open-label extension study. A separate listing will be created for hospitalizations.

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.

3.5.2 Derivation rules

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

Analysis periods are defined in section 2.2.1. Therapies with (partially) missing dates will be allocated to each period 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 period.

Concomitant therapies are defined as therapies taken on or after the first OLE dose date. Prior therapies are not in the scope of this interim analysis.

MG-specific therapies that were administered during the first year will be considered separately. First year is defined as the period starting from first dose in study 2002 until day 365 relative to first dose.

3.5.3 Presentation of results

Concomitant therapies will be tabulated, by ATC class (level 1 and level 3) and generic term. This table will be provided overall, not by cycle. The table for concomitant therapies will include MG therapies.

All concomitant therapies data will be listed with detailed information about ATC classes. Concomitant procedures will be listed seperately.

For MG therapies during the first year, the number of participants per medication class (steroids, NSIDs and AChE inhibitors: appendix 9.3) and the combination of classes will 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).

Vaccination history will only be listed.

3.6 STUDY DRUG ADMINISTRATION

3.6.1 Available data

For each study drug administration, the start and end date/times and the volumes will be recorded, as well as data on self-administration.

3.6.2 Derivation rules

The following parameters will be derived:

- Number of administrations: number and percentage of patients who had 1, 2, etc. administrations (in decreasing order) per treatment cycle and overall.
- Compliance (%) per treatment cycle: 100*(number of doses received/number of doses expected). For completed cycles, the expected number of doses is 4; for the last cycle of ongoing participants, the number of expected doses is based on the number of treatment visits performed.
- Actual dose (mg): Actual total volume of IMP extracted from the vials (mL)*[redacted] mg/mL per administration.

  If the question: 'Was the correct volume administered as per protocol?' is answered as 'Yes', the actual dose will be set to 1000 mg.
- Actual dose for EFG SC per administration, using categories < 900 mg, and 900-1000 mg

3.6.3 Presentation of results

A frequency table for the number of administrations per cycle and overall, and the actual dose per administration will be created.

Descriptive statistics of the overall number of administrations and treatment compliance.

In addition, a frequency tabulation will be provided showing:

- Number and percentage of participants who performed self-administration at home or onsite, or caregivers who administered the injection to the participant at home or onsite over time by cycle.
- Number of training visits needed for the participant or caregiver to be competent to start administering efgartigimod PH20 SC. This is defined by the number of trainings received in study 2002 until the first visit where patient/caregiver is considered adequately trained (collected in FA dataset). When both staff demonstration and self-administration under supervision occurs at the same visit, this visit is considered as 1 training. For participants already considered as adequately trained in study 2001, the number of training visits needed is set to zero.
- Number and percentage of self- or caregiver-supported study drug administration at home across participants and cycles. The denominator is the total number of treatment visits in the study.

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

4. EFFICACY, PHARMACOKINETICS, PHARMACODYNAMICS AND ANTI-DRUG ANTIBODIES ANALYSES

4.1 EFFICACY AND QOL

4.1.1 Available data

Efficacy will be assessed using MG-ADL. 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).

4.1.2 Endpoints and derivation rules

1) Actual values and change from baseline and CnB in MG-ADL total score will be analyzed 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.
Of note, minimum symptom expression (MSE) is a MG-ADL total score of 0 or 1.

Categories to be used for changes from baseline and CnB 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, following timepoints will be shown for each cycle:

- Maximum drop from baseline and CnB in MG-ADL
- Minimum MG-ADL score: descriptively and categorically

Missing data will not be imputed.

Analysis will be done by AChR-Ab status (repeat for AChR-Ab seropositive participants, then for AChR-Ab seronegative participants), by type of visit (on-site visit vs by-phone visit), by region, and overall.

2) Actual values and change from baseline and CnB in MG-QoL15r total score.

3) Actual values and change from baseline and CnB in EQ-5D-5L VAS score.

4.1.3 Statistical analysis

Summary statistics will be provided in terms of absolute values and changes from baseline (overall) and CnB (for each cycle) for MG-ADL total scores on the overall safety population and by AChR-Ab status. Both tables will be repeated by average treatment duration per year. Additionally, summary statistics will be provided in terms of absolute values and change from baseline over time by average treatment duration per year.

The table on overall safety population by cycle will be repeated by type of visit and by region (see 3.3.2).

Absolute values and changes from baseline (overall) and CnB (for each cycle) in MG-ADL total scores will also be shown categorized, including the number of participants within each category, the percentage and the cumulative percentage. This

will be done for the overall safety population and by AChR-Ab status. Both analyses on the actual values will be repeated by average treatment duration per year

Summary statistics will be provided in terms of absolute values and changes from baseline (overall) and CnB (for each cycle) for MG-QoL15r total score and EQ-5D-5L VAS score in the overall safety population and by AChR-Ab status.

See section 8 for a list of tables and listings.

4.2 MEDICAL RESOURCE UTILIZATION AND HEALTH ECONOMICS

4.2.1 Available data

[redacted]

4.2.2 Presentation of results

[redacted]

4.3 PHARMACOKINETICS

4.3.1 Available data

Blood samples for determination of serum concentrations of efgartigimod will be collected at the time points indicated in the schedule of assessment (Section 9.4).

PK samples will be allocated to the analysis visit windows defined in section 2.2.4.

Time windows for PK samples are specified as follows:

- On TPnV1: prior to the injection;
- On visits for additional PK sampling (ie, PK1 and PK2): +/- 1 day
- On IPnV1: +/-2 days;
- End of Study / Early Discontinuation: +/- 7 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.

4.3.2 Derivation rules

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

4.3.3 Presentation of results

Efgartigimod concentration actual values will be summarized by means of descriptive statistics at each analysis visit.

Individual concentration data and actual blood sampling times for PK assessments will be listed.

4.4 PHARMACODYNAMICS

4.4.1 Available data

The following pharmacodynamic parameters will be analyzed: total IgG level and autoantibodies (anti-AChR antibodies for the AChR-Ab seropositive participants).

4.4.2 Endpoint and derivation rules

1) Actual value and percent change (compared to Baseline and CnB) in total IgG level at each visit.

Analysis will be done by AChR-Ab status and overall.

2) Actual value and percent change (compared to Baseline and CnB) in anti-AChR antibodies (in AChR-Ab seropositive participants) at each visit.

See section 2.2.2 for calculation of percent change from baseline.

4.4.3 Statistical analysis

Summary statistics will be provided in terms of absolute values and percent changes from baseline and CnB for each treatment cycle. IgG tables will be done by AChR-Ab status and on the overall safety population, AChR-Ab tables will be done in AChR-Ab seropositive participants only.

A sensitivity analysis will be done for the descriptive table on total IgG, excluding the IgG values per cycle after an immunoglobulin related MG therapy or a plasmapheresis procedure during that cycle period.

All data will be listed.

4.5 IMMUNOGENICITY

4.5.1 Available data

Blood samples will be collected to assess the serum levels of ADA against efgartigimod and plasma levels to assess antibodies against rHuPH20. Sampling will be done predose on IMP administration visits.

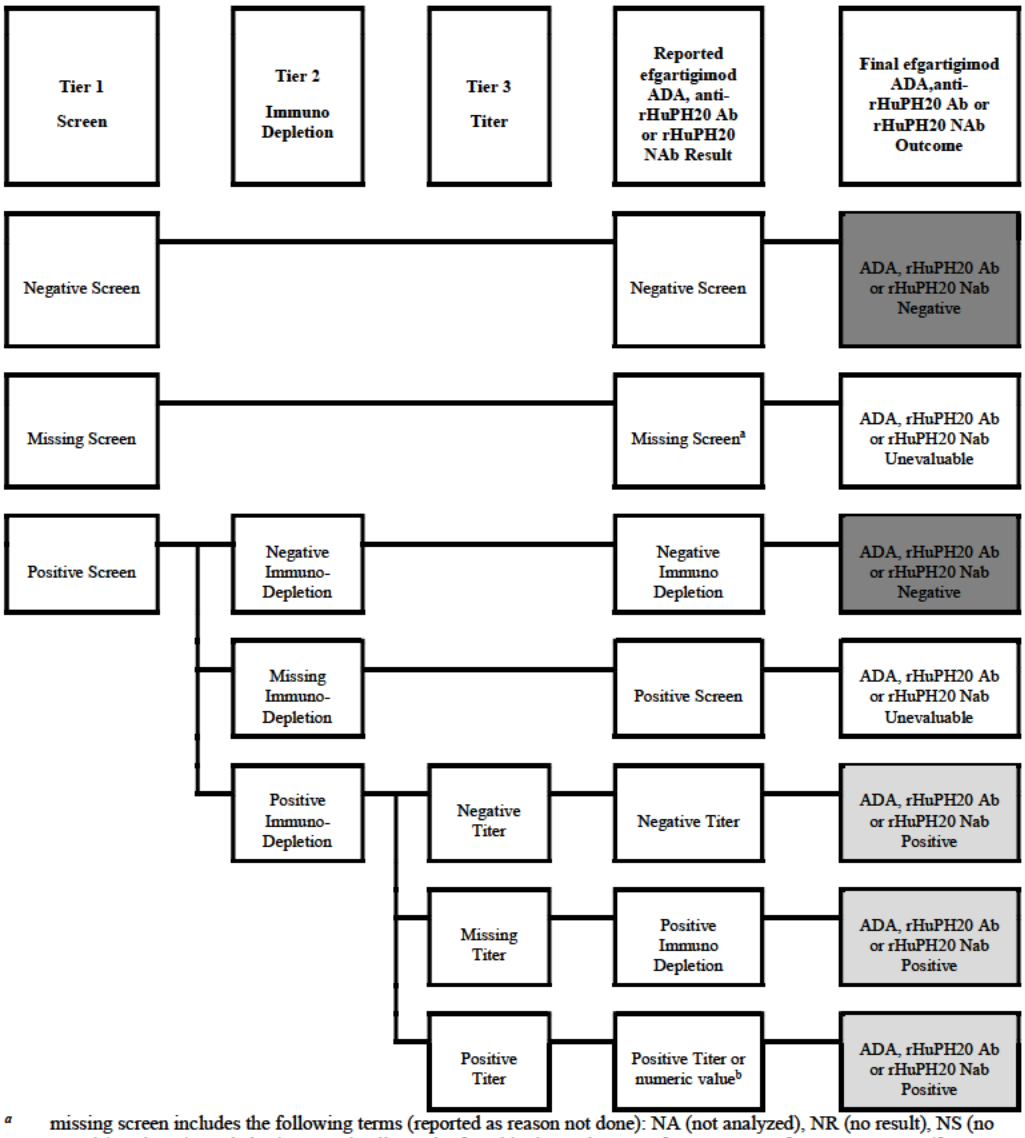
Immunogenicity samples are analyzed in a 3-tiered approach:

- 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 same 3-tiered approach is implemented: the screening NAb assay, followed by a NAb confirmatory assay, and a titer NAb assay. .

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 (eg, due to insufficient sample volume/quality to perform the titer analysis), the result will be described as ‘positive immuno-depletion’ and the sample should be considered 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 or anti-rHuPH20 Ab sample results a final ADA 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 agreements from SGS France (for ADA against efgartigimod) and Labcorp Indianapolis (for antibodies against rHuPH20 and rHuPH20 NAb) to SGS SD office.

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

4.5.2 *Derivation rules*

4.5.2.1 *Conversion of Interpolated Titers to End-Point Titers*

Due to a difference in reporting of ADA titer values in study ARGX-113-1705 and ARGX-113-2001/ARGX-113-2002, the titer values at the roll-over visit of participants rolling over from ARGX-113-1705 will be converted to the lower bound of the interval as follows:

Reported value	[1;2[	[2;4[	[4;8[	[8;16[	[16;32[	[32;64[	[64;128[	[128;256[	Etc.
Analysis value	1	2	4	8	16	32	64	128	Etc.

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

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

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

In case no ADA data is available at all, the participant can not be classified.

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).

4.5.2.3 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 numeric titer value)**		**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 numeric titer value)	Treatment Unaffected rHuPH20 Ab	rHuPH20 Ab *unevaluable*	**titer < 2 x baseline titer:** Treatment Unaffected rHuPH20 Ab	**titer ≥ 2x baseline titer:** Treatment Boosted rHuPH20 Ab[d]	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' or 'positive titer';
[b] Results reported as 'negative titer', ie, 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 (ie, positive titer and selecting the sample with highest titer)
[d] Note: Twofold difference in titer values is considered significant in case a twofold serial dilution is applied (reference to Shankar et al., 2014).

rHuPH20 Ab evaluable participant = participant classified as any of following categories: ADA 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

In case no rHuPH20 Ab data is available at all, the participant can not be classified.

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).

4.5.2.4 PARTICIPANT CLASSIFICATION FOR NAB AGAINST EFGARTIGIMOD

All ADA confirmed positive samples will also be evaluated in the NAb assay. All samples that were not analyzed in the NAb assay (ie, the ADA negatives) are per default NAb negative. 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 subjects 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

In case no NAb data is available at all, the participant can not be classified.

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).

4.5.2.5 PARTICIPANT CLASSIFICATION FOR NAB AGAINST RHUPH20

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

For NAb against rHuPH20, all samples evaluated in this NAb assay will be reported by the lab and scored as per Section 4.5.1. 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[c] post baseline sample status				
	rHuPH20 NAb negative	rHuPH20 NAb positive (missing titer[a])	rHuPH20 NAb positive ('negative titer'[b] or numeric titer value)		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[a])	Treatment Unaffected rHuPH20 NAb	*rHuPH20 NAb unevaluable*	*rHuPH20 NAb unevaluable*		*rHuPH20 NAb unevaluable*
rHuPH20 NAb positive ('negative titer'[b] or numeric titer value)	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] Samples with missing titer have as reported rHuPH20 NAb result 'positive immunodepletion' or 'positive titer';
[b] Results reported as 'negative titer', ie, titer value <100 will be set to value of 100;
[c] 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 (ie, 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

In case no rHuPH20 NAb data is available at all, the participant can not be classified.

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).

4.5.3 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 overall ADA or rHuPH20 Ab participant classification.

Frequency tabulations (number and percentages) will be provided by cycle and overall 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 (study 2002) positive/negative/unevaluable samples

For details on the definitions, see the above sections 4.5.2.2 and 4.5.2.3.

The ADA or rHuPH20 Ab participant category of the applicable cycle will be used for all tables. The baseline used for the ADA or rHuPH20 Ab participant classifications (the cycle and overall participant classification), is the 2002 study baseline.

The above frequency tabulations will be repeated for NAb assay using the definitions as defined in section 4.5.2.4 and 4.5.2.5.

Analysis will be performed for the overall safety population. The frequency tabulations on prevalence and incidence of ADA and NAb against efgartigimod will be repeated by cycle cohort (see section 2.4.4).

The frequency tabulations on prevalence and incidence of ADA against efgartigimod, and rHuPH20 Ab will also be shown by MG therapies (see section 3.5.2 and 3.5.3). Following categories will be shown: NSIDS, steroids, NSIDS+steriods, no NSIDS or steroids.

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

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

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

The duration of ADA response against Efgartigimod will also be tabulated during the pre-amended treatment + follow-up phase by presenting the number of consecutive and number of total cycles of treatment induced or boosted ADA in ADA positive participants during that phase. This analysis will also be done for rHuPH20 Ab.

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
- mean changes from baseline in total MG-ADL
- treatment-emergent adverse events
- serious treatment-emergent adverse events
- injection-related reactions (see Section 5.1.2)
- injection site reactions (see Section 5.1.2)

For final analysis, correlation tables will be prepared showing the cycle participant classification for the total treatment group.

Correlation tables by cycle NAb against efgartigimod participant classification only need to be provided as soon as there are at least 5 participants in the sum of baseline negative – postbaseline positive and baseline positive – postbaseline positive (NAb positive categories) in (one of) the treatment arms.

All available data on ADA and NAb against efgartigimod, rHuPH20 Ab and rHuPH20 NAb will be listed, showing also 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 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

Based on their start date/time, AEs will be allocated to the analysis period during which they started. Each AE will therefore be reported in only one period. Periods 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 period, AE will be allocated to the first possible cycle unless the available parts of the AE start or stop date/time provide evidence the assessments did not occur during that period. An AE started prior to ICF and ongoing at ICF will be indicated as 'pre-study'.

Event rates per 100 patient years of follow-up (PYFU) will be defined as the number of events divided by the sum of follow-up time (treatment + follow-up phase) of all participants per treatment expressed in 100 years.

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

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

Injection-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 injection, or within 2 days in case no AE start time is available. In case of a partially missing start date, the event will be considered to have occurred within 48 hours of an injection, unless the available dateparts provide evidence not to do so.

Injection site reactions (ISR) will be defined as all AEs with a MedDRA high level term "Injection site reaction", regardless of the time of AE onset relative to an injection.

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

Treatment-relatedness will be shown as follows in tables:

- Treatment-related: related or missing
- Not treatment-related

Imputation rules for AE onset and duration:

- Missing AE start day will be imputed as follows:
  - In case the AE start date is before date of ICF the missing AE start day will be imputed with 1
  - If no first efgartigimod administration in cycle 1 that month: with 1 or with the start date of the screening phase, whichever comes last
  - If first efgartigimod administration in cycle 1 that month: with the date of the first efgartigimod administration in cycle 1 or AE end date, whichever comes first.
- Missing AE start day and month will be imputed as follows:
  - If no first efgartigimod administration in cycle 1 that year: with January 1 or with the start date of the screening phase, whichever comes last
  - If first efgartigimod administration in cycle 1 that year with the date of the first efgartigimod administration in cycle 1 or AE end date, whichever comes first.
- Missing AE end day of resolved events (outcome fatal, recovered/resolved with sequelae or recovered/resolved) will be imputed with the last day of the month or with the end date of the treatment+FU phase or with cut-off date, whichever comes first.
- Missing AE end day and month of resolved events (outcome fatal, recovered/resolved with sequelae or recovered/resolved) will be imputed with December 31 or with the end date of the treatment+FU phase or with the cut-off date, whichever comes first.

AE onset and duration will be calculated as follows when (imputed) start and stop dates are fully known

- AE onset day (vs. first administration in the study/first administration of the cycle wherein the ICF for protocol v3.0 was signed)
  - AE start date ≥ date of first administration: AE start date – date of first administration + 1 day
  - AE start date < date of first administration: AE start date – date of first administration
- AE onset day (vs. start of period) = AE start date – analysis period start date + 1 day
- AE duration (days) =
  - AE end date – AE start date + 1 day
  - study discontinuation date – AE start date + 1 day (when the AE start date is fully known but the AE is not resolved at the end of the study)

    In this case the duration will be presented as ">x days". For ongoing participants who have an ongoing AE, the same approach will be taken using the clinical data cutoff date.

Following subgroups are defined:

- AChR-Ab status: seropositive, seronegative
- Age category: 18-<65 years, ≥65 years
- Race: white, Asian, Other
- Region: United States, Japan, rest of the world
- Sex: male, female
- eGFR category at baseline: normal, mildly impaired, moderately impaired, severely impaired (see section 3.3.2)
- Nadir IgG category (AESIs only): categories as quartiles based on the range of post-baseline nadir IgG values for all participants within the cycle or phase

5.1.3 Presentation of results

Adverse events occurring in IP0 will only be listed. AEs will be tabulated by cycle and overall.

An overview table will show the number and percentage of participants with at least one event, 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 events
- 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 for which the study drug was discontinued
- TEAEs leading to study drug interruption

The overview table will be repeated specifically for ISR events, omitting the records related to TEAEs of special interest, IRR and ISR events. The overview table will also be repeated by average treatment duration per year, as well as, to show any pre-amended cycle and any postamended cycle by average treatment duration per year.

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.

Separate tables will be prepared for the following TEAEs:

- Serious TEAEs
- Non-serious TEAEs
- Grade ≥ 3 TEAEs
- TEAEs of special interest
- IRR events
- ISR events
- Fatal TEAEs
- Treatment-related TEAEs
- Procedure-related TEAEs
- Serious treatment-related TEAEs
- TEAEs leading to study drug discontinuation
- TEAEs leading to study drug interruption

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

The overview table and the summary table of TEAE by SOC and PT (excluding the one in decreasing order) will be complemented by an analysis over time (per 3-monthly periods) while participants are on treatment but independent of datetime of efgartigimod administrations. Both tables will also be generated by the subgroups mentioned above and by cycle cohort (see section 2.4.4). Tables of serious TEAEs and TEAEs of grade 3 or above will also be generated by eGFR category at baseline. Subgroup tables will be limited to the total treatment group.

All adverse events tables will be repeated by average treatment duration per year, except for the subgroup tables and the tables of procedure-related TEAEs, ISR events, and fatal TEAEs.

The following summaries will also be provided for AESI:

- By SOC and PT by worst outcome
- By SOC and PT by nadir IgG category
- By SOC and PT within first 56 days of the cycle by nadir IgG category.
- Time of first onset and duration of treatment-emergent AESI (overall only)

The following summaries will also be provided for IRR by SOC and PT:

- By worst outcome
- By worst toxicity grade

The following summaries will also be provided for ISR:

- By SOC and PT by worst outcome
- By SOC and PT worst toxicity grade
- By SOC and PT by worst time of onset (within 24 hrs, more than 24 hrs after injection)
  Note: If the AE start time is not available, then events occurring on the day of IMP administration or one day after IMP administration will be considered 'within 24 hrs' unless the AE end date/time provides evidence that the event did not occur within 24 hrs. If the AE start date is missing, the event will be considered 'within 24 hrs'. If the AE start date is partially missing, the event will be considered 'within 24 hrs' unless the available part of the AE start date provides evidence that the event did not occur within 24 hrs.
- Time of first onset and duration in days of treatment-emergent ISRs (overall only)
- How many participants have ISRs in only 1 cycle, 2 cycles, … X cycles

All AEs, including pre-treatment events, will be listed. A separate listing will show pneumonia-related adverse events (see appendix 9.5).

COVID related events (events with MedDRA COVID-19 SMQ narrow selection) will be listed. This listing will include all collected AE information and additionally the cycle, 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), gamma-glutamyl transferase (GGT), total bilirubin, direct bilirubin, albumin, lipid panel (total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), and triglycerides), international normalized ratio (INR), prothrombin time (PT), and activated partial thromboplastin time (aPTT).
- Hematology: platelet count, red blood cell count (RBC), hemoglobin, hematocrit, RBC indices (mean corpuscular volume (MCV), % reticulocytes), white blood cell (WBC) count with WBC differential (% and absolute for neutrophils, lymphocytes, monocytes, eosinophils, basophils).
- Urinalysis:
  - Continuous: specific gravity, pH
  - Categorical: glucose, protein, blood, ketones, bilirubin, nitrite, leukocyte esterase, microscopic evaluation, highly sensitive urine human chorionic gonadotropin (hCG) pregnancy test for females of childbearing potential.
- Other: Serum and urine human chorionic gonadotrophin (ß-HCG), Follicle-stimulating hormone (FSH) test, SARS-CoV-2 testing
- Specialty laboratory tests: may include but not be limited to apolipoprotein B (apoB), lipoprotein A, fibrinogen, von Willebrand factor, d-dimer.

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
- The following lipid ratios will be calculated based on fasted samples only (missing fasting status is considered as non-fasted) 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 standardised 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 based on the 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

The statistical analysis will present results in standardised 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 by cycle and over time. Actual values and changes from baseline will be shown in the same table. Categorical urinalysis 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. Numbers of participants with treatment-emergent abnormalities (see Definition of terms) will also be shown. The denominator for the percentage is the total number of participants having data for the parameter per treatment and per analysis visit in the safety analysis set.

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.

Both cross-tabulations will be repeated by average treatment duration per year.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 semi-supine position, pulse rate, body temperature and weight (only fixed on few visits, at other visits only in case of obvious weight change).

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 analysis visit by cycle and over time. Actual values and changes from baseline will be shown in the same table.

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. Numbers of participants with

treatment-emergent abnormalities will also be shown. The cross-tabulation will be repeated by average treatment duration per year.

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), QRS interval, PR interval, QT interval, QTcF and QTcB.

5.4.2 Derivation rules

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

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

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

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

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

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

5.4.3 Presentation of results

Uncorrected QT interval and RR will only be listed.

Continuous ECG parameters will be summarized by means of descriptive statistics at each analysis visit by cycle and over time. Actual values and changes from baseline will be shown in the same table.

Abnormalities of the actual values 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.

The cross-tabulation and the tabulation of QTc change will be repeated by average treatment duration per year.

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

5.5.2 Presentation of results

Suicidality assessment results will be presented using a frequency tabulation by analysis visit within cycle and worst over time across all cycles. The denominator for the percentage is the total number of participants per treatment and 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

NAP

6.2 CHANGES NOT COVERED BY PROTOCOL AMENDMENTS AFTER DATABASE LOCK

NAP

6.3 CHANGES TO THE FINAL STATISTICAL ANALYSIS PLAN

The following updates were done on sponsor's request to final version 4.0 to accommodate to this final analysis:

Section	Section title	Change description
1.5	Interim analysis	Details on the purpose of the third interim analysis were removed.
2.2.3	Relative day	Relative day in the study (ADY) was added.
2.2.4	Analysis visits	A table was added to define analysis visits for analyses over time
3.2	Protocol deviation	Section was added.
3.3.2	Subject disposition - Derivation rules	Baseline eGFR category and subgroup definitions were added.
4.1.3	Efficacy and QoL - Statistical analysis	Descriptive tables over time and frequency tables by average treatment duration per year were added.
4.5.3	Immunogenicity - Presentation of results	Correlation tables by overall classification were removed. A rule was added on the minimum number of participants needed to show the NAb correlation tables.
5.1.2	Adverse events - Derivation rules	PYFU was changed into 100 PYFU and imputation rules and subgroup definitions were added.
5.1.3	Adverse events - Presentation of results	Subgroup and by cohort analyses were added.
5.2.3 5.3.3 5.4.3	Presentation of results sections of Clinical laboratory evaluation, Vital signs and ECG	Descriptive tables over time were added.
8	List of tables and listings	Additional outputs were added and the IA3 flag was removed. Outputs not of interest for the final analysis were flagged.

7. REFERENCES

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8. LIST OF TABLES AND LISTINGS

8.1 TABLES

Tables not to be created for the final analysis are flagged with *.

GENERAL CHARACTERISTICS

14.1.1.1	Analysis Sets	RO
14.1.1.2	Subject Disposition by Country and Site	SAF
14.1.1.2B	Subject Disposition by Country and Site by Average Treatment Duration per Year	mSAF
14.1.1.3	Subject Disposition by Analysis Visits	SAF
14.1.1.4	On-Site Visits and Phone Call Visits	SAF
14.1.1.5	Cycle Duration in Days	SAF
14.1.1.5B	Cycle Duration in Days by Average Treatment Duration per Year	mSAF
14.1.1.6	Cycle Duration in Weeks	SAF
14.1.1.6B	Cycle Duration in Weeks by Average Treatment Duration per Year	mSAF
14.1.1.7	Study Duration	SAF
14.1.1.8	Treatment Discontinuation by Cycle and Overall	SAF
14.1.1.8B	Treatment Discontinuation by Cycle and Overall by Average Treatment Duration per Year	mSAF
14.1.1.9	Study Discontinuation by Cycle and Overall	SAF
14.1.1.9B	Study Discontinuation by Cycle and Overall by Average Treatment Duration per Year	mSAF
14.1.1.10	Treatment and Follow up Duration in 6-Monthly Periods	SAF
14.1.1.10B	Treatment and Follow up Duration in 6-Monthly Periods by Average Treatment Duration per Year	mSAF
14.1.1.11	Frequency Tabulation of Amended Cycle Start by Average Treatment Duration per Year	mSAF
14.1.1.12	Protocol Deviations	SAF
14.1.2.1	Demographic Data	SAF
14.1.2.1B	Demographic Data by Average Treatment Duration per Year	mSAF
14.1.2.1.1	Demographic Data by AChR-Ab status	SAF
14.1.2.1.2	Demographic Data by Age Category	SAF
14.1.2.1.3	Demographic Data by Race	SAF
14.1.2.1.4	Demographic Data by Region	SAF
14.1.2.1.5	Demographic Data by Sex	SAF
14.1.2.1.6	Demographic Data by eGFR Category	SAF
14.1.2.2	Baseline Disease Characteristics	SAF
14.1.2.2.1	Baseline Disease Characteristics by AChR-Ab status	SAF
14.1.2.2.2	Baseline Disease Characteristics by Age Category	SAF

14.1.2.2.3	Baseline Disease Characteristics by Race	SAF
14.1.2.2.4	Baseline Disease Characteristics by Region	SAF
14.1.2.2.5	Baseline Disease Characteristics by Sex	SAF
14.1.2.2.6	Baseline Disease Characteristics by eGFR Category	SAF
14.1.2.2B	Baseline Disease Characteristics by Average Treatment Duration per Year	mSAF
14.1.2.3	Concomitant Therapies by ATC Class (Level 1 and 3) and Generic Term	SAF
14.1.2.4	MG Therapies During the First Year by Generic Term	SAF
14.1.2.5	Classes of MG Therapies During the First Year	SAF
14.1.2.6	Study Drug Administration	SAF
14.1.2.6B	Study Drug Administration by Average Treatment Duration per Year	mSAF
14.1.2.7	Self-Administration of Efgartigimod PH20 SC Training	SAF
14.1.2.8	Self-Administration of Efgartigimod PH20 SC	SAF
EFFICACY		
14.2.1.1.1	MG-ADL: Descriptive Statistics of Actual Values and Changes from Baseline and Cycle Baseline in MG-ADL Total Score	SAF
14.2.1.1.1B	MG-ADL: Descriptive Statistics of Actual Values and Changes from Baseline and Cycle Baseline in MG-ADL Total Score by Average Treatment Duration per Year	mSAF
14.2.1.1.1C	MG-ADL: Descriptive Statistics of Actual Values and Changes from Baseline in MG-ADL Total Score Over Time by Average Treatment Duration per Year	mSAF
14.2.1.1.2	MG-ADL: Descriptive Statistics of Actual Values and Changes from Baseline and Cycle Baseline in MG-ADL Total Score by AChR-Ab Status	SAF
14.2.1.1.2B	MG-ADL: Descriptive Statistics of Actual Values and Changes from Baseline and Cycle Baseline in MG-ADL Total Score by AChR-Ab Status by Average Treatment Duration per Year	mSAF
14.2.1.1.2C	MG-ADL: Descriptive Statistics of Actual Values and Changes from Baseline in MG-ADL Total Score by AChR-Ab Status Over Time by Average Treatment Duration per Year	mSAF
14.2.1.1.3	MG-ADL: Descriptive Statistics of Actual Values and Changes from Baseline and Cycle Baseline in MG-ADL Total Score by Region	SAF
14.2.1.1.4	MG-ADL: Descriptive Statistics of Actual Values and Changes from Baseline and Cycle Baseline in MG-ADL Total Score by Type of Visit	SAF
14.2.1.2.1	MG-ADL: Frequency Tabulation of Actual Values in MG-ADL Total Score	SAF
14.2.1.2.1B	MG-ADL: Frequency Tabulation of Actual Values in MG-ADL Total Score by Average Treatment Duration per Year	mSAF
14.2.1.2.2	MG-ADL: Frequency Tabulation of Actual Values in MG-ADL Total Score by AChR-Ab Status	SAF
14.2.1.2.2B	MG-ADL: Frequency Tabulation of Actual Values in MG-ADL Total Score by AChR-Ab Status by Average Treatment Duration per Year	mSAF

14.2.1.2.3	MG-ADL: Frequency Tabulation of Changes from Baseline and Cycle Baseline in MG-ADL Total Score	SAF
14.2.1.2.4	MG-ADL: Frequency Tabulation of Changes from Baseline and Cycle Baseline in MG-ADL Total Score by AChR-Ab Status	SAF
14.2.2.1	QoL: Descriptive Statistics of Actual Values and Changes from Baseline and Cycle Baseline in MG-QoL15r Score	SAF
14.2.2.2	QoL: Descriptive Statistics of Actual Values and Changes from Baseline and Cycle Baseline in EQ-5D-5L VAS	SAF
14.2.2.3	QoL: Descriptive Statistics of Actual Values and Changes from Baseline and Cycle Baseline in MG-QoL15r Score by AChR-Ab Status	SAF
14.2.2.4	QoL: Descriptive Statistics of Actual Values and Changes from Baseline and Cycle Baseline in EQ-5D-5L VAS by AChR-Ab Status	SAF
14.2.3.1	[redacted]	SAF
14.2.3.2	[redacted]	SAF
14.2.3.3	[redacted]	SAF
14.2.3.4	[redacted]	SAF

PHARMACOKINETICS

14.2.4.1	Descriptive Statistics of Efgartigimod Serum Concentration (ng/mL) over Time per Cycle	SAF
14.2.4.2	Descriptive Statistics of Efgartigimod Serum Concentration (ng/mL) over Time per Cycle by AChR-Ab Status	SAF

PHARMACODYNAMICS

14.2.5.1.1	IgG: Descriptive Statistics of Actual Values and Percent Changes from Baseline and Cycle Baseline in Total IgG Level	SAF
14.2.5.1.2	IgG: Descriptive Statistics of Actual Values and Percent Changes from Baseline and Cycle Baseline in Total IgG Level - Sensitivity Analysis	SAF
14.2.5.1.3	IgG: Descriptive Statistics of Actual Values and Percent Changes from Baseline and Cycle Baseline in Total IgG Level by AChR-Ab status	SAF
14.2.5.1.4	IgG: Descriptive Statistics of Actual Values and Percent Changes from Baseline and Cycle Baseline in Total IgG Level by AChR-Ab status – Sensitivity Analysis	SAF
14.2.5.2.1	AChR: Descriptive Statistics of Actual Values and Percent Changes from Baseline and Cycle Baseline in anti-AChR Antibodies (AChR-Ab seropositive)	SAF
14.2.5.2.2	AChR: Descriptive Statistics of Actual Values and Percent Changes from Baseline and Cycle Baseline in anti-AChR Antibodies (AChR-Ab seropositive) - Sensitivity Analysis	SAF

IMMUNOGENICITY

14.2.6.1	ADA: Number and Percentage of Participants with Anti-Drug Antibodies Against Efgartigimod by Analysis Visit	SAF

14.2.6.2	ADA: Number and Percentage of Participants with Anti-Drug Antibodies Against by Analysis Visit by Overall ADA Participant Classification Against Efgartigimod	SAF
14.2.6.3	ADA: Participant Classification, Prevalence and Incidence of Anti-Drug Antibodies Against Efgartigimod by Cycle and Overall	SAF
14.2.6.4	ADA: Participant Classification, Prevalence and Incidence of Anti-Drug Antibodies Against Efgartigimod by Cycle Cohort	SAF
14.2.6.5*	ADA: Participant Classification, Prevalence and Incidence of Anti-Drug Antibodies Against Efgartigimod by MG Therapies	SAF
14.2.6.6	ADA: Descriptive Statistics of ADA Against Efgartigimod Titer Values by Overall ADA Participant Classification Against Efgartigimod	SAF
14.2.6.7	rHuPH20 Antibody: Number and Percentage of Participants with Anti-rHuPH20 Antibodies by Analysis Visit	SAF
14.2.6.8	rHuPH20 Antibody: Number and Percentage of Participants with Anti-rHuPH20 Antibodies by Analysis Visit by Overall rHuPH20 Ab Participant Classification	SAF
14.2.6.9	rHuPH20 Antibody: Participant Classification, Prevalence and Incidence of anti-rHuPH20 Antibodies by Cycle and Overall	SAF
14.2.6.10*	rHuPH20 Antibody: Participant Classification, Prevalence and Incidence of anti-rHuPH20 Antibodies by MG Therapies	SAF
14.2.6.11	rHuPH20 Antibody: Number and Percentage of Anti-rHuPH20 Antibodies Positive Participants by Overall ADA Participant Classification Against Efgartigimod	SAF
14.2.6.12	rHuPH20 Antibody: Descriptive Statistics of rHuPH20 Ab Titer Values by Overall rHuPH20 Ab Participant Classification	SAF
14.2.6.13	NAb against Efgartigimod: Number and Percentage of Participants with NAb Against Efgartigimod by Analysis Visit	SAF
14.2.6.14	NAb against Efgartigimod: Number and Percentage of Participants with NAb Against Efgartigimod by Analysis Visit by Overall Nab Participant Classification Against Efgartigimod	SAF
14.2.6.15	NAb against Efgartigimod: Number and Percentage of NAb Against Efgartigimod Positive Participants by Overall ADA Participant Classification Against Efgartigimod	SAF
14.2.6.16	NAb against Efgartigimod: Participant Classification, Prevalence and Incidence of Nab Against Efgartigimod by Cycle and Overall	SAF
14.2.6.17	NAb against Efgartigimod: Participant Classification, Prevalence and Incidence of NAb Against Efgartigimod by Cycle Cohort	SAF
14.2.6.18	NAb Against rHuPH20: Number and Percentage of Participants with NAb Against rHuPH20 by Analysis Visit	SAF
14.2.6.19	NAb Against rHuPH20: Number and Percentage of Participants with NAb Against rHuPH20 by Analysis Visit by Overall NAb Participant Classification Against rHuPH20	SAF
14.2.6.20	NAb against rHuPH20: Participant Classification, Prevalence and Incidence of NAb Against rHuPH20 by Cycle and Overall	SAF
14.2.6.21	ADA: Duration of Response of Anti-Drug Antibodies Against Efgartigimod During the Pre-Amended Treatment + Follow-up Phase	SAF

14.2.6.22	rHuPH20 Antibodies: Duration of Response of Antibodies Against rHuPH20 During the Pre-Amended Treatment + Follow-up Phase	SAF
14.2.7.1.1*	PK Correlation: Descriptive Statistics of Efgartigimod Serum Concentration (ng/mL) over Time by Overall ADA Participant Classification Against Efgartigimod	SAF
14.2.7.1.2	PK Correlation: Descriptive Statistics of Efgartigimod Serum Concentration (ng/mL) over Time by Cycle ADA Participant Classification Against Efgartigimod	SAF
14.2.7.1.3*	PK Correlation: Descriptive Statistics of Efgartigimod Serum Concentration (ng/mL) over Time by Overall NAb Participant Classification Against Efgartigimod	SAF
14.2.7.1.4	PK Correlation: Descriptive Statistics of Efgartigimod Serum Concentration (ng/mL) over Time by Cycle NAb Participant Classification Against Efgartigimod	SAF
14.2.7.1.5*	PK Correlation: Descriptive Statistics of Efgartigimod Serum Concentration (ng/mL) over Time by Overall rHuPH20 Ab Participant Classification	SAF
14.2.7.1.6	PK Correlation: Descriptive Statistics of Efgartigimod Serum Concentration (ng/mL) over Time by Cycle rHuPH20 Ab Participant Classification	SAF
14.2.7.2.1*	PD Correlation: Descriptive Statistics of Actual Values and Percent Changes from Baseline in Total IgG Level by Overall ADA Participant Classification Against Efgartigimod	SAF
14.2.7.2.2	PD Correlation: Descriptive Statistics of Actual Values and Percent Changes from Baseline in Total IgG Level by Cycle ADA Participant Classification Against Efgartigimod	SAF
14.2.7.2.3*	PD Correlation: Descriptive Statistics of Actual Values and Percent Changes from Baseline in Total IgG Level by Overall NAb Participant Classification Against Efgartigimod	SAF
14.2.7.2.4	PD Correlation: Descriptive Statistics of Actual Values and Percent Changes from Baseline in Total IgG Level by Cycle NAb Participant Classification Against Efgartigimod	SAF
14.2.7.2.5*	PD Correlation: Descriptive Statistics of Actual Values and Percent Changes from Baseline in Total IgG Level by Overall rHuPH20 Ab Participant Classification	SAF
14.2.7.2.6	PD Correlation: Descriptive Statistics of Actual Values and Percent Changes from Study Cycle Baseline in Total IgG Level by Cycle rHuPH20 Ab Participant Classification	SAF
14.2.7.3.1*	Clinical Efficacy Correlation: MG-ADL: Descriptive Statistics of Actual Values and Changes from Baseline in MG-ADL Total Score by Overall Anti-Drug Antibodies Participant Classification Against Efgartigimod	SAF
14.2.7.3.2	Clinical Efficacy Correlation: MG-ADL: Descriptive Statistics of Actual Values and Changes from Baseline in MG-ADL Total Score by Cycle Anti-Drug Antibodies Participant Classification Against Efgartigimod	SAF
14.2.7.3.3*	Clinical Efficacy Correlation: MG-ADL: Descriptive Statistics of Actual Values and Changes from Baseline in MG-ADL Total Score by Overall Neutralizing Antibodies Participant Classification Against Efgartigimod	SAF

14.2.7.3.4	Clinical Efficacy Correlation: MG-ADL: Descriptive Statistics of Actual Values and Changes from Baseline in MG-ADL Total Score by Cycle Neutralizing Antibodies Participant Classification Against Efgartigimod	SAF
14.2.7.3.5*	Clinical Efficacy Correlation: MG-ADL: Descriptive Statistics of Actual Values and Changes from Baseline in MG-ADL Total Score by Overall rHuPH20 Ab Participant Classification	SAF
14.2.7.3.6	Clinical Efficacy Correlation: MG-ADL: Descriptive Statistics of Actual Values and Changes from Baseline in MG-ADL Total Score by Cycle rHuPH20 Ab Participant Classification	SAF
14.2.7.4.1*	AE Correlation: Treatment-Emergent Adverse Events by Overall ADA Participant Classification Against Efgartigimod	SAF
14.2.7.4.2	AE Correlation: Treatment-Emergent Adverse Events by Cycle ADA Participant Classification Against Efgartigimod	SAF
14.2.7.4.3*	AE Correlation: Treatment-Emergent Adverse Events by Overall NAb Participant Classification Against Efgartigimod	SAF
14.2.7.4.4	AE Correlation: Treatment-Emergent Adverse Events by Cycle NAb Participant Classification Against Efgartigimod	SAF
14.2.7.4.5*	AE Correlation: Treatment-Emergent Adverse Events by Overall rHuPH20 Ab Participant Classification	SAF
14.2.7.4.6	AE Correlation: Treatment-Emergent Adverse Events by Cycle rHuPH20 Ab Participant Classification	SAF
14.2.7.4.7*	AE Correlation: Serious Treatment-Emergent Adverse Events by Overall ADA Participant Classification Against Efgartigimod	SAF
14.2.7.4.8	AE Correlation: Serious Treatment-Emergent Adverse Events by Cycle ADA Participant Classification Against Efgartigimod	SAF
14.2.7.4.9*	AE Correlation: Serious Treatment-Emergent Adverse Events by Overall NAb Participant Classification Against Efgartigimod	SAF
14.2.7.4.10	AE Correlation: Serious Treatment-Emergent Adverse Events by Cycle NAb Participant Classification Against Efgartigimod	SAF
14.2.7.4.11*	AE Correlation: Serious Treatment-Emergent Adverse Events by Overall rHuPH20 Ab Participant Classification	SAF
14.2.7.4.12	AE Correlation: Serious Treatment-Emergent Adverse Events by Cycle rHuPH20 Ab Participant Classification	SAF
14.2.7.4.13*	AE Correlation: Treatment-Emergent Adverse Events of Injection-Related Reactions by Overall ADA Participant Classification Against Efgartigimod	SAF
14.2.7.4.14	AE Correlation: Treatment-Emergent Adverse Events of Injection-Related Reactions by Cycle ADA Participant Classification Against Efgartigimod	SAF
14.2.7.4.15*	AE Correlation: Treatment-Emergent Adverse Events of Injection-Related Reactions by Overall NAb Participant Classification Against Efgartigimod	SAF
14.2.7.4.16	AE Correlation: Treatment-Emergent Adverse Events of Injection-Related Reactions by Cycle NAb Participant Classification Against Efgartigimod	SAF
14.2.7.4.17*	AE Correlation: Treatment-Emergent Adverse Events of Injection-Related Reactions by Overall rHuPH20 Ab Participant Classification	SAF

14.2.7.4.18	AE Correlation: Treatment-Emergent Adverse Events of Injection-Related Reactions by Cycle rHuPH20 Ab Participant Classification	SAF
14.2.7.4.19*	AE Correlation: Treatment-Emergent Adverse Events of Injection Site Reactions by Overall ADA Participant Classification Against Efgartigimod	SAF
14.2.7.4.20	AE Correlation: Treatment-Emergent Adverse Events of Injection Site Reactions by Cycle ADA Participant Classification Against Efgartigimod	SAF
14.2.7.4.21*	AE Correlation: Treatment-Emergent Adverse Events of Injection Site Reactions by Overall rHuPH20 Ab Participant Classification	SAF
14.2.7.4.22	AE Correlation: Treatment-Emergent Adverse Events of Injection Site Reactions by Cycle rHuPH20 Ab Participant Classification	SAF
14.2.7.4.23*	AE Correlation: Treatment-Emergent Adverse Events of Injection Site Reactions by Overall NAb Participant Classification Against Efgartigimod	SAF
14.2.7.4.24	AE Correlation: Treatment-Emergent Adverse Events of Injection Site Reactions by Cycle NAb Participant Classification Against Efgartigimod	SAF

SAFETY

ADVERSE EVENTS

14.3.1.1	Adverse Events Overview by Cohort and Overall	SAF
14.3.1.1B	Adverse Events Overview by Average Treatment Duration per Year	mSAF
14.3.1.1.1	Adverse Events Overview by AChR-Ab status	SAF
14.3.1.1.2	Adverse Events Overview by Age Category	SAF
14.3.1.1.3	Adverse Events Overview by Race	SAF
14.3.1.1.4	Adverse Events Overview by Region	SAF
14.3.1.1.5	Adverse Events Overview by Sex	SAF
14.3.1.1.6	Adverse Events Overview by eGFR Category at Baseline	SAF
14.3.1.2	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Cohort and Overall	SAF
14.3.1.2B	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Average Treatment Duration per Year	mSAF
14.3.1.2.1	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by AChR-Ab status	SAF
14.3.1.2.2	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Age Category	SAF
14.3.1.2.3	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Race	SAF
14.3.1.2.4	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Region	SAF
14.3.1.2.5	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Sex	SAF
14.3.1.2.6	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by eGFR Category at Baseline	SAF

14.3.1.3	Treatment-Emergent Adverse Events by MedDRA Preferred Term by Decreasing Frequency	SAF
14.3.1.3B	Treatment-Emergent Adverse Events by MedDRA Preferred Term by Decreasing Frequency by Average Treatment Duration per Year	mSAF
14.3.1.4	Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.4B	Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Average Treatment Duration per Year	mSAF
14.3.1.4.1	Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by eGFR Category at Baseline	SAF
14.3.1.5	Non-serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.6	Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.6B	Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Average Treatment Duration per Year	mSAF
14.3.1.6.1	Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by eGFR Category at Baseline	SAF
14.3.1.7	Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.7B	Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Average Treatment Duration per Year	mSAF
14.3.1.8	Procedure-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.9	Serious Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.9B	Serious Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Average Treatment Duration per Year	mSAF
14.3.1.10	Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.10B	Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term by Average Treatment Duration per Year	mSAF
14.3.1.11	Treatment-Emergent Adverse Events Leading to Study Drug Interruption by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.11B	Treatment-Emergent Adverse Events Leading to Study Drug Interruption by MedDRA System Organ Class and Preferred Term by Average Treatment Duration per Year	mSAF
14.3.1.12	Injection-Related Reactions by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.12B	Injection-Related Reactions by MedDRA System Organ Class and Preferred Term by Average Treatment Duration per Year	mSAF

14.3.1.12.1	Injection-Related Reactions by MedDRA System Organ Class and Preferred Term by Worst Outcome	SAF
14.3.1.12.2	Injection-Related Reactions by MedDRA System Organ Class and Preferred Term by Worst Toxicity Grade	SAF
14.3.1.13	Injection Site Reactions by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.13B	Injection Site Reactions by MedDRA System Organ Class and Preferred Term by Average Treatment Duration per Year	mSAF
14.3.1.14.1	Adverse Events Overview for Injection Site Reactions	SAF
14.3.1.14.2	Injection Site Reactions by MedDRA System Organ Class and Preferred Term by Worst Outcome	SAF
14.3.1.14.3	Injection Site Reactions by MedDRA System Organ Class and Preferred Term by Worst Toxicity Grade	SAF
14.3.1.14.4	Injection Site Reactions by MedDRA System Organ Class and Preferred Term by Worst Time of Onset	SAF
14.3.1.14.5	Time of First Onset and Duration of Treatment-Emergent Injection Site Reactions	SAF
14.3.1.14.6	Number of Participants Having Injection Site Reactions in Only 1 Period, 2 Periods, ... X Periods by Cohort	SAF
14.3.1.15	Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.15B	Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class and Preferred Term by Average Treatment Duration per Year	mSAF
14.3.1.15.1	Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class and Preferred Term by Worst Outcome	SAF
14.3.1.15.2	Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class and Preferred Term by Nadir IgG Category	SAF
14.3.1.15.3	Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class and Preferred Term Within First 56 Days of the Cycle by Nadir IgG Category	SAF
14.3.1.15.4	Time of First Onset and Duration of Treatment-Emergent Adverse Events of Special Interest	SAF
14.3.1.16	Fatal Adverse Events by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.17	Adverse Events Overview per 3-Monthly Periods	SAF
14.3.1.17B	Adverse Events Overview per 3-Monthly Periods by Average Treatment Duration per Year	mSAF
14.3.1.18	Treatment-Emergent Adverse Events per 3-Monthly Periods by MedDRA System Organ Class and Preferred Term	SAF
14.3.1.18B	Treatment-Emergent Adverse Events per 3-Monthly Periods by MedDRA System Organ Class and Preferred Term by Average Treatment Duration per Year	mSAF
LABORATORY DATA		
14.3.2.1	Descriptive Statistics of Laboratory Test Actual Values and Changes from Baseline	SAF

14.3.2.1.1	Descriptive Statistics of Laboratory Test Actual Values and Changes from Baseline Over Time	SAF
14.3.2.2	Cross-Tabulation of Laboratory Abnormalities Versus Baseline	SAF
14.3.2.2B	Cross-Tabulation of Laboratory Abnormalities Versus Baseline by Average Treatment Duration per Year	mSAF
14.3.2.3	Cross-Tabulation of Laboratory Toxicity Grades Versus Baseline	SAF
14.3.2.3B	Cross-Tabulation of Laboratory Toxicity Grades Versus Baseline by Average Treatment Duration per Year	mSAF
VITAL SIGNS		
14.3.3.1	Descriptive Statistics of Vital Signs Actual Values and Changes From Baseline	SAF
14.3.3.1.1	Descriptive Statistics of Vital Signs Actual Values and Changes From Baseline Over Time	SAF
14.3.3.2	Cross-Tabulation of Vital Signs Abnormalities Versus Baseline	SAF
14.3.3.2B	Cross-Tabulation of Vital Signs Abnormalities Versus Baseline by Average Treatment Duration per Year	mSAF
ECG		
14.3.4.1	Descriptive Statistics of ECG Actual Values and Changes From Baseline	SAF
14.3.4.1.1	Descriptive Statistics of ECG Actual Values and Changes From Baseline Over Time	SAF
14.3.4.2	Cross-Tabulation of ECG Abnormalities Versus Baseline	SAF
14.3.4.2B	Cross-Tabulation of ECG Abnormalities Versus Baseline by Average Treatment Duration per Year	mSAF
14.3.4.3	Tabulation of QTc Change Abnormalities	SAF
14.3.4.3B	Tabulation of QTc Change Abnormalities by Average Treatment Duration per Year	mSAF
SUICIDALITY ASSESSMENT		
14.3.5.1	Suicidality assessment	SAF

8.2 LISTINGS

GENERAL CHARACTERISTICS		
16.2.1.1	Study and Treatment Discontinuation	RO
16.2.1.2	COVID-19-Related Comments	SAF
16.2.1.3	COVID-19-Related Remote Visits	SAF
16.2.2.1	Protocol Deviations	SAF
16.2.4.1	Demographic Data	SAF
16.2.4.2	Baseline Disease Characteristics	SAF
16.2.4.3	Concomitant Therapies	SAF
16.2.4.4	Concomitant Procedures	SAF
16.2.4.5	Rescue Therapies	SAF
16.2.4.6	Hospitalizations	SAF

16.2.4.7	Vaccination History	SAF
16.2.4.8	Procedures	SAF
16.2.5.1	Administration of study drug	SAF
16.2.5.2	Self-Administration of Efgartigimod PH20 SC	SAF
PHARMACOKINETICS		
16.2.5.3	Individual Efgartigimod Serum Concentrations and Actual Blood Sampling Times	SAF
EFFICACY		
16.2.6.1	MG-ADL: Total Score and Derived Variables	SAF
16.2.6.2	MG-QoL15r: Total Scores	SAF
16.2.6.3	EQ-5D-5L: 5 Dimensions and VAS Score	SAF
16.2.6.4	[redacted]	SAF
16.2.6.5	[redacted]	SAF
PHARMACODYNAMICS		
16.2.6.6	Total IgG	SAF
16.2.6.7	Anti-AChR Antibodies	SAF
SAFETY		
ADVERSE EVENTS		
16.2.7.1	Adverse Events	SAF
16.2.7.2	Serious Adverse Events	SAF
16.2.7.3	Fatal Adverse Events	RO
16.2.7.4	Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug	SAF
16.2.7.5	Treatment-Emergent Adverse Events Leading to Interruption of Study Drug	SAF
16.2.7.6	Treatment-Emergent Adverse Events of Special Interest	SAF
16.2.7.7	Injection-Related Reactions	SAF
16.2.7.8	Injection Site Reactions	SAF
16.2.7.9	Pneumonia-Related Adverse Events	SAF
16.2.7.10	Adverse Events: Coding Information	SAF
16.2.7.11	COVID-19-Related Adverse Events	SAF
LABORATORY DATA		
16.2.8.1	Laboratory Test Results for Subjects with Abnormal Values	SAF
VITAL SIGNS		
16.2.9.1	Vital Signs Results for Subjects with Abnormal Values	SAF
ECG		
16.2.10.1	ECG Results for Subjects with Abnormal Values	SAF
SUICIDALITY ASSESMENT		
16.2.11.1	Suicidality Assessment for Subjects with Abnormal Values	SAF

IMMUNOGENICITY

16.2.12.1	Anti-Drug Antibodies and Neutralizing Antibodies to Efgartigimod	SAF
16.2.12.2	Antibodies and Neutralizing Antibodies to rHuPH20	SAF

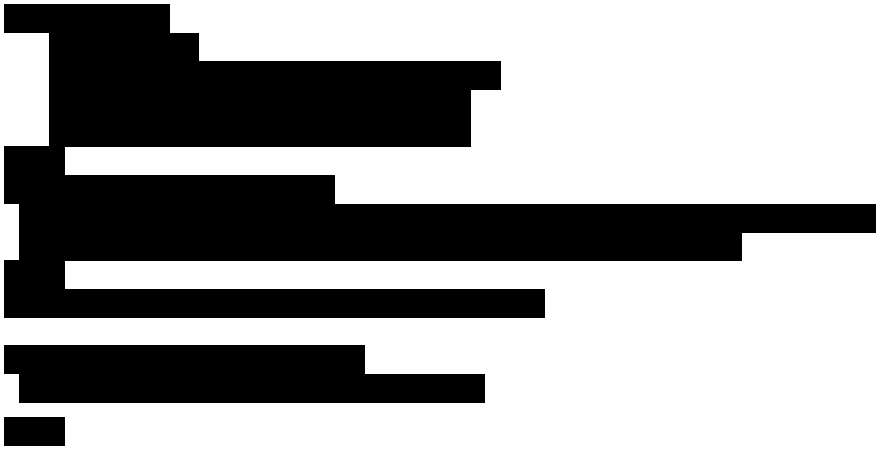
PHYSICAL EXAMINATION

16.2.13.1	Physical Examination Results for Subjects with Abnormal Values	SAF

9. APPENDICES

9.1 SAS CODE

9.1.1 [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 [1]	mmol/L	<LLN-3.0	<3.0-2.2	<2.2-1.7	<1.7
	mg/dL	<LLN-55	<55-40	<40-30	<30
Lipase		>1.0-1.5 *ULN	>1.5-2.0 *ULN	>2.0-5.0 *ULN	>5.0 *ULN
Magnesium low	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/mm^3	<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[a]
DEFLAZACORT	METHOTREXATE	AMBENONIUM CHLORIDE	IMMUNOGLOBULIN THERAPY	ELECTROMYOGRAM
METHYLPREDNISOLONE SODIUM SUCCINATE	TACROLIMUS	DISTIGMINE	IMMUNOGLOBULIN HUMAN NORMAL	ENTERAL NUTRITION
PREDNISOLONE ACETATE	CYCLOPHOSPHAMIDE	DISTIGMINE BROMIDE	IMMUNOGLOBULIN G HUMAN	IMMUNOADSORPTION THERAPY
	CYTOPHOSPHANE			
	TACROLIMUS MONOHYDRATE			

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

9.4 GENERAL SCHEDULE OF ASSESSMENTS

9.4.1 For Year 1

Visit Type	Treatment Period						Intertreatment Period		End of Treatment/ Safety Follow-up	End of Study	Unscheduled
	TP_nV1[a,b]	PK1[b,c]	TP_nV2	TP_nV3	TP_nV4	PK2[b,c]	IP_nV1[b]	IP_0V1[a,b]/ IP_nVm[d]	ET/SFU[b,e]	EoS[b,f]	UNS[g]
Study Day (Visit Window)	A	A+2 (±1)	A+7 (±2)	A+14 (±2)	A+21 (±2)	A+23 (±1)	A+28 (±2)	Y+21 (+7)	NA	730 (±7)	NA
Informed consent	X[h]							X[h]			
Inclusion/ exclusion criteria	X[h]							X[h]			
Demographic characteristics	X[h]							X[h]			
Weight	X[h]							X[h]	X	X	X
MG-ADL[i]	X		X[j]	X[j]	X[j]		X	X[j]	X	X	X
MG-QoL15r[k]	X		X[j]	X[j]	X[j]		X	X[j]	X	X	X
EQ-5D-5L[k]	X						X	X[j]	X	X	X
[redacted]											
SIB risk monitoring[o]	X		X[j]	X[j]	X[j]		X	X[j]	X	X	X
Single 12-lead ECG	X						X	X	X	X	X

Physical examination	X						X	X	X	X	X
Vital signs	X						X	X	X	X	X
Blood sampling											
Safety laboratory tests[p]	X						X	X	X	X	X
Specialty laboratory tests[q]	X						X	X			
Vaccination antibody titers and PBMCs[r]	(X)		(X)	(X)	(X)		(X)	(X)	(X)	(X)	(X)
Immunogeni-city[s]	X						X	X	X	X	X
Pharmaco-dynamics[t]	X						X	X	X	X	X
Pharmaco-kinetics[u]	X	X				X	X		X	X	X
SARS-CoV-2 test[v]											X
Urinalysis	X						X	X	X	X	X
Urine pregnancy test[w]	X						X	X	X	X	X
Efgartigimod PH20 SC administration training[x]	X		(X)	(X)	(X)		X	(X)			X

Efgartigimod PH20 SC administration[y]	X		X[j]	X[j]	X[j]						
Administration compliance monitoring[z]	Continuous monitoring[j]										
Assessment of injection site[aa]	Continuous monitoring[j]										
Hospitalization monitoring[bb]	Continuous monitoring[j]										
Adverse events[bb]	Continuous monitoring[j]										
Prior/concomitant therapy and procedures[bb]	Continuous monitoring[j]										

A=day 1 of a treatment period; AChR-Ab= anti-acetylcholine receptor antibody; ADA=anti-drug antibodies; AE=adverse event; eCRF=electronic case report form; EoS=end of study; EQ-5D-5L=EuroQoL 5-Dimension 5-Level; ECG=electrocardiogram; ET=end of treatment; FSH=follicle-stimulating hormone; IP_nVm=intertreatment period (number) visit (number); [redacted]MG-ADL=Myasthenia Gravis Activities of Daily Living; MG-QoL15r=Myasthenia Gravis Quality of Life 15 item scale revised; NAb=neutralizing antibody; NA=not applicable; PBMC=peripheral blood mononuclear cell; PD=pharmacodynamics; PHQ-9=9-item Patient Health Questionnaire; PH20=recombinant human hyaluronidase PH20; PK=pharmacokinetics; PKn=pharmacokinetic sample visit (number); SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; SC=subcutaneous(ly); SFU=safety follow-up; SIB=Suicide Ideation and Behavior; SoA=schedule of assessments; TP_nVn=treatment period (number) visit (number); [redacted]UNS=unscheduled; (X)=optional activity, only done under specified conditions; Y=previous intertreatment period visit

Note: All activities will be performed predose on dosing days, unless otherwise indicated.

[a] The transition from the antecedent studies ARGX-113-1705 or ARGX-113 2001-to study ARGX-113-2002 can either be IP0V1 or TP1V1, depending on the need for retreatment. The first visit of study ARGX 113 2002 will always coincide with the last visit from studies ARGX 113 2001 or ARGX 113 1705. Overlapping activities performed for the last visit of these antecedent studies will not be repeated for the first visit of ARGX 113 2002.

[b] This visit must always be performed at the site. All other visits can be performed by phone if IMP administration occurs at home.

[c] These are optional visits to collect additional PK samples from consenting participants. These additional visits can only be performed when all of the injections of that treatment cycle are given at the site. Sampling will only be performed during a participant's first and/or second treatment cycles.

[d] These IP visits will occur every 21 days. The visit denominator ("m") will start at 2 for each IP after a TP. At each of these IP visits performed on-site, an evaluation of the need for retreatment will be done prior to performing any activities so that only activities listed for IPnVm or TPnV1 are performed. The first of these IP visits will occur on-site and the next IP visit may be done by phone. All subsequent IP visits may alternate between on-site visits and phone visits. If activities at an IP visit performed by phone indicate a need for retreatment, then a TPnV1 visit will be scheduled.

[e] For participants who discontinue early from the study, the activities will depend on the visit at which the participant had to discontinue. Participants who discontinue early from the study at either a TP visit or an IP visit should perform planned activities for the ET visit if 49 (±2 days) days has not elapsed since the last dose of efgartigimod. These participants will not receive any further administration of efgartigimod PH20 SC during the study and will return for the SFU visit 49 ±2 days after the last dose administration. If 49 ±2 days has already elapsed since the last administration of efgartigimod PH20 SC, then this visit becomes the SFU visit and the SFU visit activities must be performed. Participants who discontinue early from the study between visits should perform the SFU visit at least 49 ±2 days after the last dose administration. If 49 ±2 days has already elapsed since the last administration of efgartigimod, then the SFU visit will be planned as soon as possible.

[f] The study will last for 2 years from the participant's first visit in this study. If efgartigimod becomes commercially available for patients with gMG or available through another patient program for gMG, participants will have the choice to switch to 1 of these options after 1 year of participation in this long-term safety study. No treatment-free follow-up will be performed in this study, except for participants who do not want to continue receiving efgartigimod.

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

[h] These activities are only performed at study entry.

[i] It is recommended to perform the MG-ADL scale prior to all other activities.

[j] When a visit is performed by phone, only these activities must be performed.

[k] These activities will only be performed in the first year of the study for each participant.

[l] [redacted]

[m] [redacted]

[n] [redacted]

[o] The SIB Risk Monitoring assessment is based on question 9 of the PHQ-9.

[p] Blood samples for clinical laboratory (hematology/clinical chemistry and FSH, if applicable) safety assessments will be collected. See Section 10.2. On dosing days, the samples will be taken predose. Participants will need to be fasted for each on-site visit at which safety laboratory assessments are collected. Fasted is defined as no food or drink at least 8 hours prior to each sampling. Permitted medications that the participant normally takes can be taken as usual before a visit.

[q] Samples for specialty laboratory tests will be taken at the baseline, the IP_1V1 visit, and the next on-site visit that is at least 4 weeks after the participant's fourth dose (TP_1V4). See Section 10.2.1.

[r] Additional blood samples (serum/PBMC) may need to be taken for additional/optional/future/vaccination research if the participant consents. If a participant that consents to this additional sampling receives a vaccination during the study, a baseline serum sample prior to the vaccination will be taken and a serum sample will be taken at least 4 weeks after the vaccine was administered. The closest visit that is at least 4 weeks after the vaccine was administered may be used. If this visit does not coincide with IP_nV1, then another sample will also be taken at this visit. Serum samples only need to be taken when a vaccination is planned or after a vaccination has occurred. In addition, a whole-blood sample to isolate PBMCs will be collected at study entry and then approximately every 3 months throughout the study during a scheduled on-site visit, regardless of the vaccines a participant has received.

[s] Titers of ADA and the presence of NAbs against efgartigimod will be measured in serum. Blood samples for plasma titer levels of ADA and NAbs against rHuPH20 will also be taken. A titer for ADA and the presence of NAbs against PH20 must be measured at study entry for participants coming from ARGX-113-1705. If no sample is taken, the reason will be recorded.

[t] The PD assessments comprises levels of total IgG, and autoantibody levels (AChR-Ab levels for AChR-Ab positive participants).

[u] The PK assessments will only be taken at TP1V1. The assessment should be performed predose.

9.4.2 For Year 2 Onward

Visit Type	Treatment Period		Intertreatment Period[a]		ET/EoS/SFU[b,c,d]	UNS[e]
	TP_nV1[b,c]	$TP_nV2/V3/V4$	IP_nV1	IP_nVm[b,c]		
Study Day (Visit Window)	A	A+7/14/21 (±2)	A+28 (±2)	Y+21 (+7)	NA	NA
MG-ADL[f]	X		X	X	X	X
SIB risk monitoring[g]	X		X	X	X	X
Single 12-lead ECG	X			X[h]	X	X
Vital signs	X			X[h]	X	X
Physical examination	X			X[h]	X	X
Weight					X	X
Safety laboratory tests[i]	X			X[h]	X	X
Vaccination antibody titers and PBMCs[j]	(X)	(X)	(X)	(X)	(X)	X
Immunogenicity[k]	X			X[h]	X	X
SARS-CoV-2 test[l]						X
Urinalysis	X			X[h]	X	X
Urine pregnancy test[m]	X			X[h]	X	X
Efgartigimod PH20 SC administration training[n]	(X)	(X)	(X)	(X)	(X)	X
Efgartigimod PH20 SC administration[o]	X	X				
Administration compliance monitoring[p]	Continuous monitoring					
Assessment of injection site[q]	Continuous monitoring					
Hospitalization monitoring[r]	Continuous monitoring					

Visit Type	Treatment Period		Intertreatment Period[a]		ET/EoS/SFU[b,c,d]	UNS[e]
	TP_nV1[b,c]	$TP_nV2/V3/V4$	IP_nV1	IP_nVm[b,c]		
Study Day (Visit Window)	A	A+7/14/21 (±2)	A+28 (±2)	Y+21 (+7)	NA	NA
Adverse events[f]	Continuous monitoring					
Prior/concomitant therapy and procedures[f]	Continuous monitoring					

A=day 1 of a TP; ADA=antidrug antibodies; AE=adverse event; eCRF=electronic case report form; ECG=electrocardiogram; EoS=end of study; ET=end of treatment; FSH=follicle-stimulating hormone; gMG=generalized myasthenia gravis; ICF=informed consent form; IMP=investigational medicinal product; IP=intertreatment period; IP_nVm=IP (period number) visit (visit number); MG-ADL=Myasthenia Gravis Activities of Daily Living; NA=not applicable; NAb=neutralizing antibody; PBMC=peripheral blood mononuclear cell; PH20=recombinant human hyaluronidase PH20 (rHuPH20); PHQ-9=9-item Patient Health Questionnaire; SC=subcutaneous(ly); SFU=safety follow-up; SIB=Suicidal Ideation and Behavior; SoA=schedule of activities; TP=treatment period; TP_nVm=TP (period number) visit (visit number); UNS=unscheduled; (X)=optional activity, only done under specified conditions; Y=previous IP period visit
Note: All activities will be performed predose on dosing days, unless otherwise indicated. If a participant enters year 2 of the study during a TP, the remaining TP visits and subsequent IPnV1 must be completed according to the year 1 SoA (refer to Table 1).

[a] IPnV1 can become a TPn+1V1 if there are at least 7 days past the last IMP administration in the previous TP, and the participant is in need of retreatment. All IPnVm visits may also become a new TP, if the investigator determines there is a need for retreatment. The need for retreatment will be assessed prior to performing any activities, so that only activities listed for IPnV1/m or TPn+1V1 are performed, respectively. The visit denominator ("m") will start at 2 for each IP after a TP.

[b] Participants will remain in the study for at least 1 year, until efgartigimod PH20 SC becomes commercially available or available through another continued access program for gMG, or until 31 Dec 2024, whichever comes first.

[c] On-site visits are required for TPnV1, for IPnV5/10/15, etc, (ie, every 5 visits), and for ET, EoS, and SFU visits. All other visits in Table 2 can be performed by phone, including TPnV2/3/4 in case of IMP home administration.

[d] For participants who discontinue early from the study, the activities will depend on the visit at which the participant had to discontinue. Participants who discontinue early from the study at either a TP visit or an IP visit should perform planned activities for the ET visit if 49 (±2 days) days has not elapsed since the last dose of efgartigimod. These participants will not receive any further administration of efgartigimod PH20 SC during the study and will return for the SFU visit 49 ±2 days after the last dose administration. If 49 ±2 days has already elapsed since the last administration of efgartigimod PH20 SC, then this visit becomes the SFU visit and the SFU visit activities must be performed. Participants who discontinue early from the study between visits should perform the SFU visit at least 49 ±2 days after the last dose administration. If 49 ±2 days has already elapsed since the last administration of efgartigimod, then the SFU visit will be planned as soon as possible.

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

[f] It is recommended to perform the MG-ADL scale prior to all other activities.

[g] The SIB Risk Monitoring assessment is based on question 9 of the PHQ-9.

[h] These assessments will only be performed every 5 visits (IPnV5, IPnV10, etc).

[i] Blood samples for clinical laboratory (hematology/clinical chemistry/coagulation panel and FSH, if applicable) safety assessments will be collected. See Section 10.2. Participants will need to be fasted for each on-site visit at which safety laboratory assessments are collected. Fasted is defined as no food or drink at least 8 hours prior to each sampling. Permitted medications that the participant normally takes can be taken as usual before a visit.

[j] Additional blood samples (serum/PBMC) may need to be taken for additional/optional/future/vaccination research if the participant consents. If a participant who consents to this additional sampling receives a vaccination during the study, samples referred to in Section 8.2.9 should be taken. The closest visit that is at least 4 weeks after the vaccine was administered may be used. If this visit does not coincide with IPnV1, then another sample will also be taken at this visit. Serum samples only need to be taken when a vaccination is planned or after a vaccination has occurred. In addition, a whole-blood sample to isolate PBMCs will be collected at study entry and then approximately every 3 months throughout the study during a scheduled on-site visit, regardless of the vaccines a participant has received.

[k] Titers of ADA and the presence of NAbs against efgartigimod will be measured in serum. Blood samples for plasma titer levels of ADA and NAbs against rHuPH20 will also be taken, but these will only be analyzed if needed for safety purposes.

[l] A nasopharyngeal swab will be performed to sample nasal and throat mucosal cells. Participants should only be tested for SARS-CoV-2 if they have symptoms of COVID-19 or if they were in contact with a person who tested positive for SARS-CoV-2, unless local or site regulations have more stringent testing requirements. Participants may be retested as needed. See Section 10.6.

[m] This activity is only for women of childbearing potential. See Section 10.5.2.1.

[n] Training can continue until the participant or caregiver is ready to administer efgartigimod PH20 SC, to the satisfaction of the site staff (a minimum of 1 visit) before performing an administration under the supervision of site staff. Therefore, a minimum of 2 visits is required for a participant or caregiver to be considered competent to administer efgartigimod PH20 SC at home. Caregivers must sign the ICF before being trained in IMP administration.

[o] The first dose administration of all TPs (TPnV1) must be performed on-site, even if the dose is self-administered or administered by the caregiver. Subsequent administrations in any TP (TPnV2/3/4) may be performed at home, if the participant or caregiver has been trained and is competent to perform IMP administration. When IMP administration is performed at home, the associated visit will be performed by phone.

[p] When administration is performed at home, participant compliance with the efgartigimod PH20 SC dosing and administration schedule will be assessed by direct questioning at each phone visit. Any deviations from the planned dosage must be recorded. See Section 6.4.

[q] When a participant is not on-site, they must record any observed injection site reaction in the patient diary. The investigator will evaluate all reported injection site reactions and decide whether the site reaction is classified and reported as an AE.

[r] Adverse events (including ongoing AEs from the antecedent studies), use of concomitant therapies, use of rescue therapy, medical procedures performed on the participants, and hospitalizations will be collected from ICF signature until the last study-related activity. All vaccines received during the study should be recorded as concomitant medication. See Section 6.8 and Section 8.3.

9.5 PNEUMONIA-RELATED EVENTS

Preferred Terms		
Pneumonia anthrax	Pneumonia acinetobacter	Haemorrhagic pneumonia
Pneumonia bordetella	Pneumonia proteus	Paracancerous pneumonia
Pneumonia chlamydial	Pneumonia serratia	Pneumonia helminthic
Pneumonia escherichia	Pneumonia blastomyces	Pneumonia toxoplasmal
Pneumonia haemophilus	Candida pneumonia	Parasitic pneumonia
Pneumonia klebsiella	Pneumonia fungal	Pneumonia adenoviral
Pneumonia legionella	Pneumonia cryptococcal	Pneumonia cytomegaloviral
Pneumonia moraxella	Pneumocystis jirovecii pneumonia	Pneumonia herpes viral
Pneumonia pneumococcal	Atypical pneumonia	Pneumonia influenzal
Pneumonia pseudomonal	Pneumonia	Pneumonia measles
Pneumonia salmonella	Pneumonia mycoplasmal	Pneumonia parainfluenzae viral
Pneumonia staphylococcal	Enterobacter pneumonia	Pneumonia respiratory syncytial viral
Pneumonia streptococcal	Miliary pneumonia	Pneumonia viral
Pneumonia tularaemia	Pneumonia necrotising	Herpes simplex pneumonia
Pneumonia bacterial	Embolic pneumonia	Varicella zoster pneumonia
Atypical mycobacterial pneumonia	Post procedural pneumonia	COVID-19 pneumonia