STATISTICAL ANALYSIS PLAN

An Open-label Extension Study of ARGX-113-2009 to Evaluate the Long-term Safety, Tolerability, and Efficacy of Efgartigimod PH20 SC in Adult Participants With Bullous Pemphigoid

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LIST OF ABBREVIATIONS

ABQOL	autoimmune bullous disease quality of life
ADA	anti-drug antibodies
ADaM	analysis data model
ADY	ADaM variable to indicate relative day in the study
AE	adverse event
AESI	adverse events of special interest
AIS	aggregate improvement score
AQL	above the upper quantification limit
ATC	anatomical therapeutic chemical
AWADY	ADaM variable to indicate relative day in a study subperiod
BP	bullous pemphigoid
BPDAI	bullous pemphigoid disease area index
BQL	below the lower quantification limit
BMI	body mass index
bpm	beats per minute
CDA	control of disease activity
C-GTI	composite glucocorticoid toxicity index
CR	complete remission
CRF	case report form
CRmin	complete remission on minimal OCS therapy
CRoff	complete remission off OCS therapy
CTCAE	Common Terminology Criteria for Adverse Events
CTP	clinical trial protocol
CWS	cumulative worsening score
DBP	diastolic blood pressure
DLQI	dermatology life quality index
ECG	electrocardiogram
eCRF	electronic case report form
EDV	early discontinuation visit
EFG	efgartigimod
eGFR	estimated glomerular filtration rate
EoTP	end of treatment period

EQ-5D-5L	EuroQoL 5 Dimensions 5 Levels
FU	follow-up
GM	geometric mean
GSD	geometric standard deviation
GTI	glucocorticoid toxicity index
GTI-SL	glucocorticoid toxicity index - specific list
HR	heart rate
ICF	informed consent form
ICH	International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
ID	identification
IGA-BP	investigator global assessment of bullous pemphigoid
[redacted]	[redacted]
IMP	investigational medicinal product
IRR	injection-related reaction
ISR	injection site reaction
MedDRA	Medical Dictionary for Regulatory Activities
NAb	neutralizing antibody
NA	not applicable
NCI	National Cancer Institute
OCS	oral corticosteroids
OLE	open-label extension
PAS	participant analysis set
PD	pharmacodynamic(s)
PI	principal investigator
PRO	patient-reported outcome
PT	preferred term
PYFU	patient years of follow-up
QoL	quality of life
QTc	corrected QT interval
QTcB	Bazett's corrected QT interval
QTcF	Fridericia's corrected QT interval
rHuPH20	recombinant human hyaluronidase PH20
ROL	rollover analysis set

SAE	serious adverse event
SAF	safety analysis set
SAP	statistical analysis plan
SBP	systolic blood pressure
SC	subcutaneous(ly)
SDTM	study data tabulation model
SGS CR	SGS Clinical Research
SoA	schedule of activities
SoC	standard of care
SOC	system organ class
SOP	standard operating procedure
SMQ	Standardized MedDRA Queries
STAT	statistics
TCS	topical corticosteroids
TEAE	treatment-emergent adverse event
TLF	tables, listings, and figures
VS	vital signs
WHO	World Health Organization
WI	work instruction

DEFINITION OF TERMS

CRF	A printed, optical, or electronic document designed to record protocol required information to be reported to the sponsor for each study participant.
Complete remission on minimal OCS therapy (CRmin)	Being in complete remission (CR) for ≥ 8 weeks and have been on minimal OCS therapy (≤ 0.10 mg/kg/day of prednisone or an equivalent dose of another OCS) for ≥ 8 weeks
Complete remission off OCS therapy (CRoff)	Being in CR for ≥8 weeks and have been off OCS therapy for ≥8 weeks.
display	Analysis table, listing, or figure
IMP	Pharmaceutical form of an active ingredient or placebo, being tested or used as a reference in a clinical study.
missing data	Data that would be meaningful for the analysis of a given endpoint but were not collected. They should be distinguished from data that do not exist.
standardized unit	unit populating --STRESU in the clinical database
treatment-emergent abnormality / toxicity	Any postbaseline* abnormality/toxicity which was not present at the study baseline or worsened after the study baseline (e.g., hemoglobin normal or grade 1 at baseline and grade 2 postbaseline; glucose low at baseline and high postbaseline; QTcF]450; 480] ms at baseline and >500 ms postbaseline). If baseline is missing, any postbaseline abnormality/toxicity will be considered emergent. *Note: postbaseline records on or after the first administration of IMP in ARGX-113-2010 and up to and including 60 days after the last IMP administration before the assessment will be considered for treatment-emergence.

1. INTRODUCTION

This SAP describes the statistical analyses to be performed for the final analysis of study ARGX-113-2010 (BE-80-2200433). It is based on the most recent version of the protocol, version 4.0 of 02 May 2024. Table, figure and listing specifications will follow the argenx generic mock TLF library, unless mentioned otherwise.

This SAP describes the safety, efficacy, pharmacodynamics (PD), immunogenicity and general characteristics sections of the statistical analysis. It specifies the analysis displays to be presented and elaborates on the methods and procedures described in the statistical methods section of the protocol.

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

1.1 STUDY OBJECTIVES AND ENDPOINTS

Table 1: Objectives and endpoints

Objectives	Endpoints
Primary	
To assess the long-term safety and tolerability of treatment with efgartigimod PH20 SC in participants with BP	• Incidence and severity of treatment-emergent AEs, SAEs, and AESIs • Rate of treatment discontinuation because of safety concerns
Secondary	
To assess the long-term efficacy and durability of response with efgartigimod PH20 SC treatment in participants with BP	• Proportions of participants achieving[a]: ○ CR while off OCS for ≥8 weeks ○ CR or PR while off OCS for ≥8 weeks ○ CR while on minimal OCS therapy for ≥8 weeks. (Minimal OCS therapy is defined as ≤0.10 mg/kg/day of prednisone [or an equivalent dose of another OCS]) ○ CR while off both OCS and efgartigimod PH20 SC for ≥8 weeks[b] ○ CR or PR while off both OCS and efgartigimod PH20 SC for ≥8 weeks[b] • Duration of sustained remission • Proportion of participants who relapse • Time to relapse • Incidence and severity of relapse • BPDAI activity scores, IGA-BP scores, and itch NRS over time • Rate of treatment failure

Additional secondary	
To evaluate the impact of efgartigimod PH20 SC treatment in reducing long-term glucocorticoid-associated toxicity in participants with BP	• GTI-related scores, including the GTI-AIS, GTI-CWS, and GTI-SL over time
To evaluate the impact of efgartigimod PH20 SC treatment on QoL in participants with BP	• EQ-5D-5L, DLQI, and ABQOL scores over time
To evaluate the PD and immunogenicity of efgartigimod PH20 SC in participants with BP	• Percent change from baseline over time for anti-BP180 and anti-BP230 antibody levels • Incidence and prevalence of ADA against efgartigimod (serum levels)
Exploratory	
[redacted]	• [redacted]

[a] These endpoint criteria can only be met when participants are off rescue therapy.
[b] The endpoint applies only to participants who have stopped receiving efgartigimod PH20 SC before protocol amendment 2 is effective.

1.2 STUDY DESIGN

This is a phase 3, open-label, prospective, global, multicenter, OLE study.

The total study duration is approximately 56 weeks comprising a treatment period of up to 48 weeks and a follow-up of approximately 8 weeks.

The study population is adult patients with BP who have completed ARGX-113-2009.

At rollover, all participants will receive efgartigimod PH20 SC after protocol amendment 2 (dated 26 April 2024) is effective. The treatment allocation of ARGX-113-2009 will remain blinded.

Participants who received placebo in ARGX-113-2009 and participants who have reinitiated efgartigimod PH20 SC treatment will receive [redacted] of efgartigimod PH20 SC [redacted] followed by once-weekly maintenance doses of efgartigimod PH20 SC1000 mg.

Participants who received efgartigimod PH20 SC in ARGX-113-2009 will continue to receive once-weekly efgartigimod PH20 SC 1000 mg maintenance doses.

In earlier protocol versions (before protocol amendment 2 was effective), participants had to stop receiving efgartigimod PH20 SC after achieving CR or PR while off concurrent BP therapy for ≥8 weeks. For these participants, reinitiation of efgartigimod PH20 SC treatment will be at the investigator's discretion unless the participant relapses. Participants who relapse will initiate efgartigimod PH20 SC treatment.

Participants will visit the site at weeks 0 (baseline), 1, 2, 4, and 8. Thereafter, participants will attend site visits every 4 weeks. Participants not receiving efgartigimod PH20 SC will attend site visits every 8 weeks.

The schedule of assessments is in appendix 9.3.

1.3 STATISTICAL HYPOTHESIS

No formal hypothesis testing will be conducted in this open-label study.

1.4 EXPECTED SAMPLE SIZE

The maximum number of participants in this study is the number of participants who complete the week 36/EoTP visit in ARGX-113-2009 and meet the eligibility criteria to roll over to this study.

1.5 RANDOMIZATION AND BLINDING

ARGX-113-2010 is open-label. The blinded allocation to efgartigimod PH20 SC or placebo from ARGX-113-2009 will be maintained until the database lock of ARGX-113-2009. Therefore, at rollover, participants receiving [redacted] on days 1 and 8 will receive 2 blinded injections with efgartigimod PH20 SC or 1 with efgartigimod PH20 SC and 1 with placebo. This will be handled via interactive response technology.

The blinding of immunogenicity data for ARGX-113-2010 will also be maintained until the database lock of ARGX-113-2009.

BP autoantibody data and albumin and total protein data collected from baseline through week 4 will remain blinded.

1.6 INTERIM ANALYSIS

No interim analyses are foreseen.

1.7 SOFTWARE

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

1.8 VALIDATION MODEL

SGS STAT Standard Operating Procedures (SOPs) and Work Instructions (Wis) as effective at the project start will be followed throughout the project, provided the applicable regulatory requirements are still met.

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

2. GENERAL METHODOLOGY

2.1 ANALYSIS SETS

2.1.1 Analysis sets

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

Rollover (ROL) analysis set:	All participants who rolled over from ARGX-113-2009 and *provided informed consent* for participation in ARGX-113-2010
Safety (SAF) analysis set:	All participants from the ROL analysis set who *received at least one dose* of IMP

Notes:

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

2.1.2 As planned versus as actual analysis

Not applicable. All endpoints will be analyzed for the total group of participants, regardless of previous treatment in ARGX-113-2009 (placebo or efgartigimod PH20 SC).

2.2 PHASES, PERIODS AND TIME POINTS

2.2.1 Analysis phases, periods and subperiods

All assessments and events will be allocated to analysis phases, periods and subperiods as defined in below table.

Table 2: Analysis phase, period and subperiod definition

Phase	Period/Subperiod	Start	End
For participants who don't receive the first IMP administration at the ARGX-113-2010 baseline visit[a], the first phase will be the observation phase. **For participants who receive the first IMP administration at the ARGX-113-2010 baseline visit[a], the first phase will be the treatment phase.**			
Observation		Date of baseline visit in ARGX-113-2010, with 00:00 added as time part	**For participants with a subsequent treatment period:** First IMP administration date/time – 1 minute. **For other participants:** Date of week 48 or EDV visit[c], with 23:59 added as time part. For participants who don't have a week 48 or EDV visit: date of last contact, with 23:59 added as time part.

Phase	Period/Subperiod	Start	End
Treatment	Treatment period 1/ On IMP treatment	**For participants with first IMP administration at the baseline visit:** Date of baseline visit in ARGX-113-2010, with 00:00 added as time part. **For participants with a previous observation phase and who initiate treatment:** First IMP administration date/time	**For participants with a subsequent Off IMP subperiod:** Last IMP administration date/time in treatment period 1. **For other participants:** Date of week 48 or EDV visit[c], with 23:59 added as time part. For participants who don't have a week 48 or EDV visit: date of last contact, with 23:59 added as time part.
	Treatment period 1/ Off IMP treatment	Last IMP administration date/time in treatment period 1 + 1 minute	**For participants with a subsequent treatment period:** First IMP administration date/time in next treatment period – 1 minute. **For other participants:** Date of week 48 or EDV visit[c], with 23:59 added as time part. For participants who don't have a week 48 or EDV visit: date of last contact, with 23:59 added as time part.
	Treatment period 2 is applicable for participants who re-initiate IMP administration after a previous Off IMP subperiod[b].		
	Treatment period 2/ On IMP treatment	First IMP administration date/time in treatment period 2	**For participants with a subsequent Off IMP subperiod**: Last IMP administration date/time in treatment period 2. **For other participants:** Date of week 48 or EDV visit[c], with 23:59 added as time part. For participants who don't have a week 48 or EDV visit: date of last contact, with 23:59 added as time part.
	Treatment period 2/ Off IMP treatment	Last IMP administration date/time in treatment period 2 + 1 minute	Date of week 48 or EDV visit[c], with 23:59 added as time part. For participants who don't have a week 48 or EDV visit: date of last contact, with 23:59 added as time part.

Phase	Period/Subperiod	Start	End
Follow-up		End of previous phase + 1 minute	Date of last contact, with 23:59 added as time part.

[a] First IMP administration is considered to occur on the ARGX-113-2010 baseline visit if the date of first IMP administration equals the scheduled baseline visit start date (SVSTDTC) or end date (SVENDTC), or if the first IMP administration occurs on an unscheduled baseline visit. In either case, the first phase starts with SVSTDTC of the first scheduled or unscheduled baseline visit.

[b] A new treatment period is considered for participants with relapse after achieving CR or PR while being off concurrent BP therapy for ≥ 8weeks before protocol amendment 2 was effective, or at the investigator's discretion after protocol amendment 2 was effective. For programming purposes, a new treatment period will be considered if a participant has a gap of at least 4 weeks (28 days) between two consecutive IMP administrations that cannot be attributed to missed visits or non-efficacy related reasons documented on the study drug administration eCRF form.

[c] SVENDTC of the last scheduled or unscheduled week 48 or early discontinuation visit will be used.

Adverse events will be allocated to phases as described in section 5.1.2. Concomitant therapies and procedures will be allocated to phases and (sub)periods as described in section 3.3.2. All other assessments will be allocated to phases and (sub)periods based on the assessment date/time. In case of (partially) missing date/time fields disabling allocation of an assessment to phases or (sub)periods, information from the visit label, time point label and the protocol schedule of activities will be used to allocate to the correct phase.

For efficacy assessments without time part, an assessment on the day of switch from observation phase to treatment phase will be considered as part of the treatment phase. Likewise, an assessment on the day of switch from treatment period 1 to treatment period 2 will be considered as part of treatment period 2.

2.2.2 Baseline and change from baseline

Study baseline is defined as the first available and nonmissing value at the baseline visit (scheduled or unscheduled) in ARGX-113-2010. This value corresponds with the value at the EoTP visit in ARGX-113-2009 (and is copied over into the database of ARGX-113-2010 at SDTM level).

Change from baseline is defined as:

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

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

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

For immunogenicity assessments, the study baseline selection will be performed by sample (not by parameter) in order to keep the ADA and NAb results of a sample together. Furthermore, values resulting in an unevaluable ADA status are given the lowest priority when the selection is made.

For evaluation of PD parameters, a treatment period-specific baseline (TPnB) will be defined:

- For a treatment period, TPnB is the last available and non-missing value prior to the first IMP administration in the treatment period. Assessments on day 1 of a treatment period without time collection or with time information exactly equal to the time of first IMP administration and which are planned predose will be considered as predose.
- For the observation phase, TPnB corresponds with the study baseline.
- For the follow-up phase, TPnB corresponds with TPnB of the preceding phase/period.

2.2.3 Relative day

The relative day in the study is calculated as follows:

- ADY = assessment date – baseline visit date, if assessment date is before the baseline visit date
- ADY = assessment date – baseline visit date +1, if assessment date is on or after the baseline visit date

The relative day in a subperiod (refer to Section 2.2.1) is calculated as:

AWADY = assessment date – subperiod start date + 1

For the observation phase, AWADY corresponds with ADY. For the follow-up phase, AWADY will be calculated with reference to the follow-up phase start date.

2.2.4 Analysis visits

All assessments, including unscheduled assessments, will be allocated to analysis visit windows. Tables and listings will present the analysis visit as defined below, not the eCRF visits. Allocations of assessments will be performed using AWADY (see section 2.2.3) according to Table 3 below:

Table 3: Analysis visits

Phase/Period/ Subperiod	Analysis visit	Target AWADY	Lower limit AWADY	Upper limit AWADY
Observation phase	Baseline[a]	-	-	-
	Week 2[d]	15	1	22
	Week 4	29	23	43
	Week 8	57	44	85
	Week x[b]	T=7*x+1	integer[(T + Tp)/2]+1[c]	integer[(T + Tn)/2][c]
Treatment phase/ Treatment period 1/ On IMP treatment	Baseline[a] / TP1B	-/ Relative day of first IMP admini-stration	-/-Inf	-/ Relative day of first IMP administration
	Week 2[d]	15	1/ Relative day of first IMP administration	22
	Week 4	29	23	43
	Week 8	57	44	71
	Week x[b]	T=7*x+1	integer[(T + Tp)/2]+1[c]	integer[(T + Tn)/2][c]

Phase/Period/ Subperiod	Analysis visit	Target AWADY	Lower limit AWADY	Upper limit AWADY
Treatment phase/ Treatment period 1/ Off IMP treatment	Week 8	57	1	85
	Week x[b]	T=7*x+1	integer[(T + Tp)/2]+1[c]	integer[(T + Tn)/2][c]
Treatment phase/ Treatment period 2/ On IMP treatment	TP2B	1	-Inf	1
	Week 2[d]	15	1	22
	Week 4	29	23	43
	Week 8	57	44	71
	Week x[b]	T=7*x+1	integer[(T + Tp)/2]+1[c]	integer[(T + Tn)/2][c]
Treatment phase/ Treatment period 2/ Off IMP treatment	Week 8	57	1	85
	Week x[b]	T=7*x+1	integer[(T + Tp)/2]+1[c]	integer[(T + Tn)/2][c]
Follow-up phase	FU Week 4	29	1	43
	FU Week 8	57	44	End day of FU phase

[a] The baseline analysis visit will be assigned to the first phase that is applicable for a participant, either the observation phase or the treatment phase. The baseline visit is defined in section 2.2.2 and does not require definition of analysis visit limits.
[b] x increases in steps of 4 weeks (On IMP subperiods) or 8 weeks (observation phase or Off IMP subperiods) up till the point where the upper limit of the analysis visit window exceeds the end day of the phase/subperiod. In this case the upper limit will be cut at the end day of the phase/subperiod. The maximum value of x is week 48.
[c] T = target day of current analysis visit, Tn = target day of next window, Tp = target day of previous window.
[d] An assessment on AWADY = 1 that is not selected as Baseline/TPnB will be assigned to Week 2.

Baseline and TPnB are defined in section 2.2.2.

Per parameter and analysis visit, the nonmissing value closest to the target AWADY will be used in analysis tables, other values will only be listed. If more than one nonmissing value is located at the same distance from the target, then the one latest in time will be selected for analysis. The value latest in time will be identified using, in order of preference, the assessment date(time), the visit label, the database group identifier or sequence number.

For immunogenicity assessments, the selection will be performed by sample (not by parameter) and analysis visit in order to keep the ADA and NAb results of a sample together. Furthermore, values resulting in an unevaluable ADA status are given the lowest priority when the selection is made.

Missing assessment dates will be imputed with the corresponding visit date. If there is no corresponding visit date available, the assessment will not be allocated to an analysis visit.

2.2.5 Worst-case

A worst-case analysis visit will be created for parameters with defined abnormalities and/or toxicity grades (e.g., labs, vital signs, ECGs). For abnormalities, the worst-case is derived per parameter and if both the lowest and highest values are considered abnormal, a participant can have two worst-case analysis visits for the same

parameter. For toxicity grades, the worst-case is the value associated with the highest toxicity grade and is derived per parameter and toxicity direction (hypo/hyper).

All nonmissing postbaseline values on or after the first administration of IMP in ARGX-113-2010 and up to and including 60 days after the last IMP administration before the assessment will be considered when deriving the worst-case analysis visit. This may include unscheduled assessments, assessments not selected for the analysis visit and assessments during the follow-up phase.

2.2.6 Last assessment

A last assessment analysis visit will be created as the last available postbaseline assessment with a nonmissing value.

The last assessment will be created for the following parameters:

- BPDAI total and activity score
- IGA-BP
- Itch NRS 24-hour average and worst scores
- ABQOL, DLQI and EQ-5D-5L questionnaires
- GTI AIS and CWS
- Numeric parameters of safety lab, vital signs and ECG

For PD parameters, a last assessment analysis visit will be created per treatment period as the last available post-TPnB assessment with a nonmissing value in the treatment period. Assessments during the follow-up phase will be considered in the selection of the last assessment of the preceding treatment period.

2.3 IMPUTATION AND ROUNDING RULES

2.3.1 Missing values

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

2.3.2 Handling partially or completely missing dates in calculations

OCS administration start dates with partially missing data will be imputed as follows:

- Missing day will be imputed with first day of the month or start date of the first phase, whichever comes latest.
- Missing day and month will be imputed with 1JAN or start date of the first phase, whichever comes latest.
- Completely missing date will be imputed with start date of the first phase.

OCS administration end dates with partially missing data will be imputed as follows:

- Missing day will be imputed with the last day of the month or the end date of the last phase, whichever comes first.
- Missing day and month will be imputed with 31DEC or the end date of the last phase, whichever comes first.
- Completely missing end date will be imputed with the end date of the last phase.

2.3.3 Values below or above a threshold

Safety values expressed as BQL or AQL will be imputed by the value of the quantification limit itself.

[redacted] values expressed as BQL or AQL will not be imputed.

For anti-BP180 and anti-BP230, see section 4.2.2.

Anti-drug antibodies (ADA) against efgartigimod: titer of positive ADA samples reported as ‘negative titer’, i.e. '<1' will be imputed by 1.

For all the above cases, listings will always present the reported (non-imputed) result.

2.3.4 Rounding

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

- OCS dose will be rounded to 0 decimals.
- BMI and percent changes from baseline will be rounded to 1 decimal.
- OCS dose per body weight will be rounded to 2 decimals.
- Safety laboratory results will be rounded to a maximum of 3 decimals.

2.3.5 Outliers

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

2.4 PRESENTATION OF RESULTS

2.4.1 Calculation of descriptive statistics and percentages

Descriptive statistics for continuous variables will include the number of nonmissing observations, arithmetic mean, standard deviation (SD), standard error (SE), median, minimum, Q1, Q3 and maximum.

Descriptive statistics for immunogenicity titer values will also include geometric mean (GM) and geometric standard deviation (GSD).

Mean, median, Q1, Q3, GM and GSD will be presented with one more decimal place than the reported values. SE and SD will be presented with two more decimal places than the reported values. Minimum and maximum will be presented with the same number of decimal places as the reported values.

Event-type safety data will be summarized by presenting the number and percentage of participants with an event, and the number of events. The denominator will be all participants in the PAS.

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

Percentages will be presented with one decimal place.

2.4.2 Presentation of treatments

The following treatment arm label will be used in displays in the ROL analysis set:

- Total

The following treatment arm label will be used in displays in the SAF analysis set:

- Total Efgartigimod PH20 SC

2.4.3 Ordering in tables, listings, and figures

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.

Listings will be ordered by participant identifier and, if applicable, by phase/period/subperiod, analysis visit, and time point, unless specified otherwise.

3. GENERAL CHARACTERISTICS ANALYSES

3.1 PARTICIPANT DISPOSITION

Participant disposition will be presented for the ROL analysis set, unless mentioned otherwise. The following participant data will be tabulated:

- The number of participants in each PAS .
- The number of participants with 1 treatment period and with 2 treatment periods respectively in the SAF analysis set.
- Descriptive statistics of each phase duration, calculated as phase end date – phase start date + 1 day.
- Descriptive statistics of each period and subperiod duration in the SAF analysis set, calculated as (sub)period end date – (sub)period start date + 1 day.
- The number and percentage of participants who completed or discontinued the treatment as documented on the treatment termination page and the number and percentage of participants for each treatment discontinuation reason. This table will be presented for the SAF analysis set
- 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 with protocol deviations, by important/non-important deviations, and by class of deviation.

Listings will be created for:

- Indication of analysis sets in which a participant is included.
- All information collected in the CRF concerning study and treatment discontinuation.
- Visits (scheduled and unscheduled) performed by the participant, with visit date and indication whether the visit occurred at site or at home.
- Protocol deviations.

3.2 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

3.2.1 Available data

The following parameters will be available:

- Demographics: sex at study start, childbearing potential, year of birth, age at informed consent, race, ethnicity, height, body weight and BMI at study baseline, date of signing ICF
- Baseline disease characteristics: disease status at study baseline (no CDA, CDA, CR, PR, Relapse, Treatment failure), BPDAI activity and total score at study baseline, IGA-BP at study baseline, itch NRS 24-hour average and worst score at study baseline

- Study entry status: date of protocol version at entry, participant receiving rescue therapy at study baseline (yes, no), type of rescue therapy at study baseline (ATC class level 3), participant receiving OCS at study baseline (yes, no), and if yes, OCS dose at study baseline (mg) and OCS dose per body weight at study baseline (mg/kg)

3.2.2 Derivation rules

The following parameters will be derived:

- Age at informed consent, categorized (18 - <65, 65 - <75, 75 - <85, >=85)
- Height: if height is not available in the database of ARGX-113-2010, the height at screening of ARGX-113-2009 will be taken.
- BMI at study baseline (kg/m²) = (body weight (kg) at study baseline) / (height (m))².
- BMI at study baseline, categorized (Underweight: < 18.5 kg/m2, Normal weight: 18.5 -< 25 kg/m2, Overweight: 25 -< 30 kg/m2, Obese: >= 30 kg/m2)
- Race, categorized (Asian, Black or African American, White, Other)
- Geographical region: Asia (Japan, China), North America (US, Canada), EU region+UK (EU/EEA/EFTA/UK), Rest of world
- BPDAI activity score at study baseline, categorized: <20, 20-56, >56
- OCS at study baseline: any use of systemic OCS on study day 1, i.e.. any record from any eCRF page with medication class = 'GLUCOCORTICOIDS' and route = 'ORAL' for which the available information indicates that the medication is taken on study day 1.
- Rescue therapy at study baseline: any use of therapy that is indicated as rescue therapy by the investigator on the eCRF page and for which the available information indicates that the medication is taken on study day 1.

3.2.3 Presentation of results

Demographics will be presented using descriptive statistics for age at informed consent, height, weight and BMI at study baseline and frequency tabulations for age category, BMI category, sex at study start, childbearing potential, geographical region, race category and ethnicity.

Baseline disease characteristics and study entry status will be presented using descriptive statistics for BPDAI activity and total score at study baseline, itch NRS 24-hour average and worst score at study baseline, OCS dose and OCS dose per body weight at study baseline and frequency tabulations for all other parameters.

All demographic data and baseline disease characteristics will be listed.

Displays will be based on the ROL analysis set.

3.3 CONCOMITANT THERAPIES AND PROCEDURES

3.3.1 Available data

All therapies are coded using World Health Organization Drug Dictionary (WHO DD). Anatomical-Therapeutic-Chemical (ATC) selection is performed to select the

most appropriate medication class. For the selected class, ATC coding up to level 4 is available in the clinical database. For each therapy, a start and stop date are collected.

Procedures are coded using the medical dictionary for regulatory activities (MedDRA) into preferred terms. For each finding, the indication and a start and stop date are collected.

3.3.2 Derivation rules

Based on their start and stop dates, therapies and procedures will be allocated to each phase, period and subperiod during which the participant received the therapy.

Therapies/procedures with (partially) missing dates will be allocated to each possible phase/(sub)period unless the available parts of the therapy/procedure start or stop date provide evidence not to do so.

Concomitant therapies/procedures are therapies/procedures for which the available information indicates that the therapy/procedure is taken/performed on or after study day 1. In case of doubt (e.g. partially missing dates), it will be assumed that the therapy/procedure is concomitant.

OCS therapy is defined as any record from any eCRF page with medication class = 'GLUCOCORTICOIDS' and route = 'ORAL'.

TCS therapy is defined as any record from any eCRF page where medication class contains 'CORTICOSTEROIDS' and route = 'TOPICAL'.

Rescue therapy is defined as any therapy that is indicated as rescue therapy by the investigator on the eCRF page.

3.3.3 Presentation of results

Concomitant therapies will be tabulated by ATC class (level 1 and 3) and generic term. Tables will be presented per phase and within the treatment phase data will be summarized overall and per subperiod.

Separate tables will be created for the number and percentage of participants with:

- Concomitant therapies, excluding OCS, TCS and rescue therapies
- Concomitant OCS therapies
- Concomitant TCS therapies
- Concomitant rescue therapies

Displays will be based on the ROL analysis set. All concomitant therapies data will be listed with detailed information about ATC classes.

3.4 EXPOSURE TO IMP AND OCS

3.4.1 Available data

For each IMP administration and OCS administration, the start and end date, doses (per administration), dose units and the volume with units (for IMP only) will be recorded.

3.4.2 Derivation rules

The total number of IMP administrations in the study will be derived as the sum of all administrations of IMP.

OCS is defined in section 3.3.2. OCS dose (mg) and OCS dose per body weight (mg/kg) will be calculated for each day in the study and will be based on prednisone equivalent dose.

Prednisone equivalent dose is calculated as [dose of ATC]*[equivalence factor prednisone]/[equivalence factor ATC]. Following [equivalence factors] are used:

- Betamethasone [1.5]
- Cortisone [37.5]
- Deflazacort [15]
- Dexamethasone [1.5]
- Fluocortolone [10]
- Hydrocortisone [30]
- Hydrocortisone sodium phosphate [30]
- Methylprednisolone [8]
- Methylprednisolone acetate [8]
- Methylprednisolone sodium succinate [8]
- Paramethasone [4]
- Prednisolone [10]
- Prednisone [10]
- Prednisolone acetate [10]
- Prednisone acetate [10]
- Prednisolone sodium succinate [10]
- Prednylidene [12]
- Rimexolone [20]
- Triamcinolone [8]

Example: calculation of equivalent dosage of 12 mg methylprednisolone: 12*10/8= 15 mg prednisone.

Following rules will be applied to calculate the daily OCS dose (per body weight):

- Records with (partially) missing dates will be imputed as detailed in section 2.3.2.
- If dates of administration records overlap, the overlapping reported doses will be added together.

- If for a given day, no record exists in the eCRF indicating OCS use that day, the dose will be assumed to be 0 mg.
- If an administration is reported as dose per administration with frequency, then the doses should be allocated to the correct dates, taking the start date and the frequency into account.

  Example:
  - Dose: 40 mg
  - Frequency: every other day
  - Start - Stop date: 01JAN2022 - 03JAN2022

  This will result in:
  - 40 mg be allocated to 01JAN2022
  - 0 mg allocated to 02JAN2022
  - 40 mg allocated to 03JAN2022
- OCS dose per body weight will be calculated based on the most recent assessment of body weight available for a study day.

3.4.3 Presentation of results

Exposure information will be presented using descriptive statistics for the total number of IMP administrations, based on the SAF analysis set.

OCS dose (per body weight) at study baseline will be included in the tabulation of baseline disease characteristics, based on the ROL analysis set.

All exposure data to IMP and OCS will be listed.

4. EFFICACY, PHARMACODYNAMIC, AND IMMUNOGENICITY ANALYSES

4.1 EFFICACY AND QUALITY OF LIFE

All efficacy endpoints are secondary endpoints in this OLE study and will be evaluated descriptively.

4.1.1 Available data

Investigators report the participant's best disease status in episodes with start and end date (no CDA, CDA, CR, PR, Relapse and Treatment failure). Furthermore, BPDAI activity and total score, IGA-BP scores and itch NRS are collected over time.

Quality of life is assessed over time using the ABQOL, DLQI and EQ-5D-5L questionnaires.

The health impact of long-term glucocorticoid use is assessed via the Aggregate Improvement Score (AIS) and Cumulative Worsening Score from the Glucocorticoid Toxicity Index (GTI) and via the GTI Specific List (GTI-SL).

4.1.2 Derivation rules

The following endpoints will be derived **for each treatment period separately**:

1) Participants achieving CR while off OCS for ≥8 weeks (CRoff). A participant will be considered a CRoff responder if the following criteria are met simultaneously for ≥8 weeks (56 days):
   - The participant's reported disease status is CR
   - The participant is off OCS therapy
   - The participant does not receive any rescue therapy (as indicated by the investigator on the eCRF)

   Else, the participant will be considered a CRoff non-responder. Participants who already have the disease status CR at day 1 of the treatment period or who are off OCS therapy at day 1 of the treatment period or who receive rescue therapy at day 1 of the treatment period, will be considered non-evaluable for this endpoint and will be excluded from this analysis for the corresponding treatment period.

   Note: the rules for assessing the OCS dose on a given day are described in section 3.4.2. Similarly, these rules can be used to assess whether rescue therapy is received on a given day. Additionally for rescue therapy, a frequency of PRN (pro re nata, or 'as needed') will be interpreted as a dose of 1 time per week.
2) Participants achieving CR or PR while off OCS for ≥8 weeks (CR/PRoff). A participant will be considered a CR/PRoff responder if the following criteria are met simultaneously for ≥8 weeks (56 days):
   - The participant's reported disease status is CR or PR (continuously or alternately)
   - The participant is off OCS therapy
   - The participant does not receive any rescue therapy (as indicated by the investigator on the eCRF)

Else, the participant will be considered a CR/PRoff non-responder. Participants who already have the disease status CR or PR at day 1 of the treatment period or who are off OCS therapy at day 1 of the treatment period or who receive rescue therapy at day 1 of the treatment period, will be considered non-evaluable for this endpoint and will be excluded from this analysis for the corresponding treatment period.

3) Participants achieving CR while on minimal OCS therapy for ≥8 weeks (CRmin). A participant will be considered a CRmin responder if the following criteria are met simultaneously for ≥8 weeks (56 days):
   - The participant's reported disease status is CR
   - The participant receives ≤0.10 mg/kg/day of prednisone (or an equivalent dose of another OCS)
   - The participant does not receive any rescue therapy (as indicated by the investigator on the eCRF). OCS used as rescue therapy will not be considered as rescue therapy if the above criterium of minimal OCS therapy is still met.

   Else, the participant will be considered a CRmin non-responder. Participants who already have the disease status CR at day 1 of the treatment period or who are on minimal (≤0.10 mg/kg/day) OCS therapy at day 1 of the treatment period or who receive rescue therapy at day 1 of the treatment period, will be considered non-evaluable for this endpoint and will be excluded from this analysis for the corresponding treatment period.
4) Participants with treatment failure.

The following endpoints will be derived **for each treatment period separately and additionally for the observation phase**:

5) Participants achieving CR while off both OCS and efgartigimod PH20 SC for ≥8 weeks (CRoff without IMP). A participant will be considered a responder for CRoff without IMP if the following criteria are met simultaneously for ≥8 weeks (56 days):
   - The participant's reported disease status is CR
   - The participant is off OCS therapy
   - The participant is off IMP
   - The participant does not receive any rescue therapy (as indicated by the investigator on the eCRF)

   Else, the participant will be considered a non-responder for CRoff without IMP. Participants who enter the ARGX-113-2010 study under protocol version 3 (26 April 2024) or 4 (02 May 2024) will be considered non-evaluable for this endpoint. Furthermore, participants who were randomized to the placebo arm in the ARGX-113-2009 study and who enter the ARGX-113-2010 study in the observation phase, will be considered non-evaluable for this endpoint in the observation phase.
6) Participants achieving CR or PR while off both OCS and efgartigimod PH20 SC for ≥8 weeks (CR/PRoff without IMP). A participant will be considered a

responder for CR/PRoff without IMP if the following criteria are met simultaneously for ≥8 weeks (56 days):

- The participant's reported disease status is CR or PR (continuously or alternately)
- The participant is off OCS therapy
- The participant is off IMP
- The participant does not receive any rescue therapy (as indicated by the investigator on the eCRF)

Else, the participant will be considered a non-responder for CR/PRoff without IMP. A participant will be considered non-evaluable for this endpoint using the same rules as for CRoff without IMP.

7) Duration of sustained remission will be calculated for participants achieving CR while off both OCS and efgartigimod PH20 SC for ≥8 weeks (i.e., responders for CRoff without IMP) within a treatment period.
   - Start date of sustained remission is 1 week (7 days) after the last IMP administration in the treatment period
   - End date of sustained remission is:
     - the start date of first relapse after achieving CRoff without IMP
     - the start date of a (next) treatment period
     - the start date of OCS therapy after achieving CRoff without IMP
     - the start date of a rescue therapy after achieving CRoff without IMP

     whichever comes first. If none of the above occurs, the participant will be censored at the end date of the study (end date of last phase).
   - Duration of sustained remission (in days) = end date - start date + 1
8) Relapse will be evaluated for participants having or achieving CDA, CR or PR during the treatment period (or observation phase). The evaluation period for relapse is till the end of the treatment period (or observation phase) in case a (next) treatment period starts, or else till the end of the study. Only the first relapse in a treatment period (or observation phase) will be considered.
9) Time to relapse:
   - Start date is the first day with status CDA, CR or PR in the treatment period (or observation phase)
   - End date is:
     - the start date of first relapse after having or achieving CDA, CR or PR
     - the end date of the study (end date of last phase), if no relapse
   - Time to relapse (in days) = end date - start date + 1
10) For participants with relapse, severity of (first) relapse will be calculated as the BPDAI total score at the onset of relapse (use the first available nonmissing BPDAI total score in the interval of relapse) minus the BPDAI total score at the preceding visit (use the most recent preceding visit for which a nonmissing BPDAI total score is available). Severity of relapse will be categorized as <0, 0-<10, 10-<20, 20-<30, or >30.

The following endpoints will be derived **overall:**

11) Changes and percent changes from study baseline will be calculated for BPDAI activity and total score.
12) Changes from study baseline will be calculated for itch NRS 24-hour average and worst scores.
13) C-GTI: Composite Glucocorticoid Toxicity Index comprises the Aggregate Improvement Score (AIS) and the Cumulative Worsening Score (CWS). Details of AIS and CWS derivations are specified in appendix 9.1.
14) A total ABQOL score is calculated as the sum of all 17 items score 0 to 3 with higher score indicating worse condition. Missing items are imputed with the average score of the present items if at least half (9) of the items are present. The total score is rounded to the highest integer.
15) Changes from study baseline will be calculated for EQ-5D-5L VAS score, DLQI score and total ABQOL score.

4.1.3 Presentation of results

Efficacy results will be presented for the ROL analysis set, unless mentioned otherwise. For tables by analysis visit, only the study baseline and last assessment analysis visits will be shown. Other analysis visits will be included in listings.

A frequency tabulation will be created for the number and percentage of participants who achieved CRoff at least once during the study (i.e., in any treatment period). The table will also present the number of participants who are evaluable for the endpoint at least once during the study. This number will serve as denominator for the percentage calculation. This table will be based on the SAF analysis set.

Similar frequency tabulations will be created for the number and percentage of participants who achieved:

- CR/PRoff
- CRmin
- Treatment failure

Similar frequency tabulations, based on the ROL analysis set, will be created for:

- CRoff without IMP
- CR/PRoff without IMP
- Relapse

Duration of sustained remission and time to relapse will be descriptively presented with median times, quantiles and number and percentage of censored observations and observations with event. Only the participant's first evaluation during the study will be included as observation.

Duration of sustained remission will be presented for the SAF analysis set.

A frequency tabulation will be created for categorized severity of relapse, for the participant's first relapse during the study.

Descriptive statistics will present the actual values, changes and percent changes from study baseline of the BPDAI activity and total scores per analysis visit (baseline and last assessment).

Frequency tabulations will be provided for the outcome of IGA-BP per analysis visit (baseline and last assessment). Additionally, cumulative percentages (starting with the best outcome result) will be calculated.

Descriptive statistics will present the actual values and changes from study baseline of the itch NRS 24-hour average and worst scores per analysis visit (baseline and last assessment).

Descriptive statistics will be provided for the C-GTI scores AIS and CWS at the last assessment.

Frequency tabulations will be provided for the outcomes of the ABQOL (17 items), EQ-5D-5L (5 dimensions) and DLQI (10 items), similar to the frequency tabulations of the IGA-BP outcomes. Descriptive statistics on absolute values and changes from study baseline for EQ-5D-5L VAS score, DLQI score and Total ABQOL score will be calculated per analysis visit (baseline and last assessment), similar to the descriptive statistics of the itch NRS scores.

Listings will be created for:

- Disease status, including the derived response variables (CRoff, CR/PRoff, CRmin, etc.)
- Duration of sustained remission and time to relapse, including the reason for censoring (if applicable) and the severity of relapse
- Lesion assessments
- BPDAI assessments
- IGA-BP assessments
- Itch NRS assessment
- Calculated C-GTI scores and complementary GTI specific list (GTI-SL)
- ABQOL, EQ-5D-5L and DLQI data

4.2 PHARMACODYNAMICS

4.2.1 Available data

The following PD parameters will be measured:

- [redacted]
- Anti-BP180 antibodies and anti-BP230 antibodies

4.2.2 Derivation rules

BQL or AQL values will be handled as described in section 2.3.3.

Samples for anti-BP180 antibodies and anti-BP230 antibodies will be diluted until the result falls within the reportable range of [20-200 RU/mL]. For anti-BP180 antibodies:

- The value for analysis will be the result with the lowest dilution factor and with value ≤200 RU/mL, multiplied by the dilution factor.
- If the result is <20 RU/mL, the value for analysis will be imputed by 20 RU/mL, multiplied by the dilution factor.
- If at a dilution factor (D1) the result is above 200 RU/mL, and at the next higher dilution factor (D2) the result is < 20 RU/mL, the value for analysis will be derived as D1 x 200 RU/mL.
- If all the results up to dilution factor 32 are above 200 RU/mL, then the value for analysis will be imputed by 6400 RU/mL (32 * 200), even if the result at a higher dilution factor gives a value below 6400 RU/mL.
- If the result is above 200 RU/mL in the original non-diluted sample and no higher dilution factors are available, the value for analysis will be imputed by 200 RU/mL.
- Multiplication by the dilution factor will be done at analysis level if not yet done by the lab.

For anti-BP230 antibodies:

- If in the original (non-diluted) sample the result is above 200 RU/mL, then the value for analysis will be imputed by 200 RU/mL, even if the result at a higher dilution factor is ≤200 RU/mL.
- If the result in the original sample is <20 RU/mL, the value for analysis will be imputed by 20 RU/mL.

Changes and percent changes versus TPnB will be calculated. Treatment periods with a TPnB value below the limit of quantification (BLQ) or with a result <20 RU/mL (for anti-BP180 and anti-BP230 antibodies) will be excluded when presenting the actual values, the changes from TPnB and the percent changes from TPnB. This will be explained by a footnote in the appropriate tables.

In addition, for all pharmacodynamic endpoints, descriptive statistics of the actual values and percent changes from baseline will also include GM and GSD. GM and GSD of percent changes from baseline are calculated as $100X\{\exp(\theta)-1\}$ where θ is respectively the arithmetic mean and arithmetic SD of a variable calculated as log(aval)-log(base). GM and GSD are not applicable for descriptive statistics of the absolute changes from baseline.

4.2.3 Presentation of results

The SAF analysis set will be used for the PD evaluation. For tables by analysis visit, only the TPnB and last assessment analysis visits in a treatment period will be shown. Results for treatment period 2 will only be presented if at least 10 participants have a post-TP2B PD assessment.

All pharmacodynamic endpoints will be summarized by means of descriptive statistics at each analysis visit of interest in a treatment period. Actual values, changes from TPnB and percent changes from TPnB will be tabulated. Descriptive statistics of the actual values and percent changes from TPnB will also include GM and GSD. GM and GSD are not applicable for descriptive statistics of the absolute changes from TPnB.

Listings will be created for [redacted] and anti-BP antibodies results over time, based on the ROL analysis set. Listings will always show the non-imputed results.

4.3 IMMUNOGENICITY

4.3.1 Available data

ADA to efgartigimod and rHuPH20 Ab is measured per schedule of assessment (see section 9.3). ADA to rHuPH20 is only analyzed in case of safety concerns and is not in scope of this SAP.

Immunogenicity samples are analyzed in a 3-tiered approach:

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

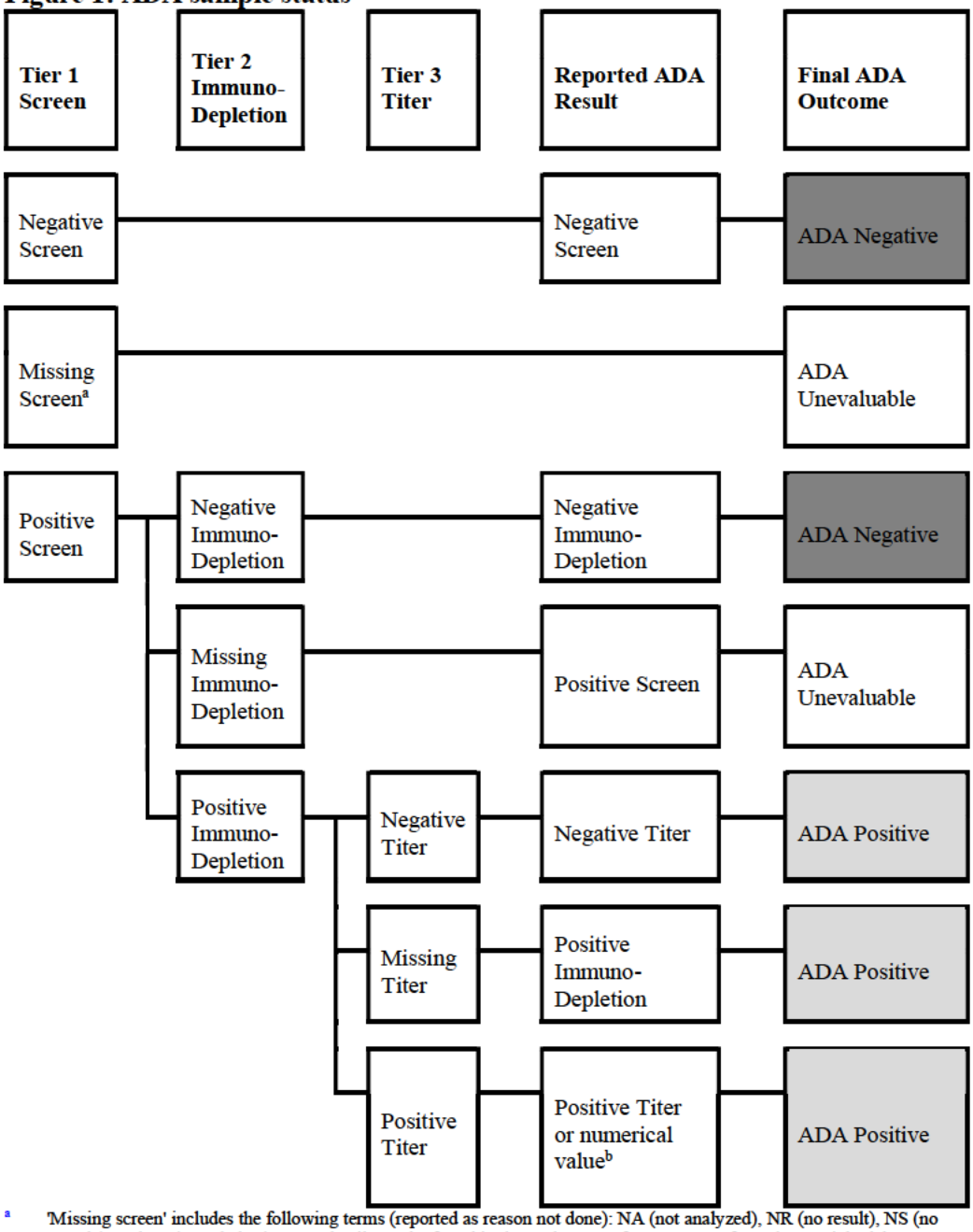
If a sample could not be analyzed or is reported as 'positive screen', the ADA sample status is ADA unevaluable.

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

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

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

Figure 1: ADA sample status



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

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

4.3.2 Derivation rules

4.3.2.1 Participant Classification for ADA against Efgartigimod

Table 4 below gives an overview of how the ADA participant classification will be derived, starting from the ADA sample status at the study baseline.

Table 4: Participant classification for ADA against efgartigimod

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

ADA = antidrug antibodies

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

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

[c] Results reported as 'negative titer' i.e. titer value '<1' will be set to value of 1.

[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).

The following definitions will be used in the summary tables:

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

4.3.2.2 PARTICIPANT CLASSIFICATION FOR NAB AGAINST EFGARTIGIMOD

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

All samples evaluated in the NAb assay will be scored as NAb positive, NAb negative, or NAb unevaluable by the laboratory. Based on these results, the participants will be categorized according to their study baseline and postbaseline sample status, as detailed in Table 5.

Table 5: Participant classification for NAb against efgartigimod

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

NAb = neutralizing antibody; neg = negative; pos = positive
[a] Highest sample status in order: (from low to high): NAb unevaluable, NAb negative, NAb positive.

The following definitions will be used in the summary tables:

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

4.3.3 Presentation of results

The safety analysis set will be used for the immunogenicity evaluation. For tables by analysis visit, analysis visits during the observation or follow-up phase will not be shown (but will be included in listings). Only analysis visits for which an assessment of the applicable parameter is scheduled per SoA will be included.

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

Frequency tabulations (number and percentages of participants) for efgartigimod will be provided in 1 table for:

- ADA evaluable and unevaluable participants
- ADA study baseline sample status

- ADA participant classification
- incidence and prevalence of ADA

The above frequency tabulations will be repeated for the NAb assay.

In addition, a frequency tabulation (number and percentages of participants) will be provided for:

- NAb against efgartigimod positive participants within efgartigimod ADA participants classification (treatment-unaffected ADA, treatment-induced ADA, treatment-boosted ADA, ADA negative and ADA unevaluable).

ADA titer values against efgartigimod titer values will be summarized by means of descriptive statistics by ADA participant classification at each analysis visit.

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

5. SAFETY ANALYSES

5.1 ADVERSE EVENTS

5.1.1 Available data

Adverse events will be coded into system organ classes (SOC) and preferred terms (PT) using the latest version of the MedDRA dictionary available at the time of the database lock of ARGX-113-2009.

For each AE, start and stop date/times will be collected as well as severity, a seriousness flag, relationship to IMP, prednisone (or equivalent) and procedures, action taken towards IMP and prednisone (or equivalent) and outcome.

The grade (severity) of AEs will be assessed by the investigator according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.

5.1.2 Derivation rules

TEAEs are defined as AEs with onset on or after the first administration of IMP in ARGX-113-2010 up to and including 60 days after the last IMP administration before the event. Figure 2 depicts an example of the assessment of TEAEs for a participant with two treatment periods.

Figure 2: Treatment-emergent adverse events

D1-D40	D41-D199		D200-D260	D261-D337		FU
IMP	No IMP		IMP	No IMP		No IMP
TEAE: D1-D40	TEAE: D40+60 days	Non-TEAE: D101-199	TEAE: D200-D260	TEAE: D260+60 days	Non-TEAE: >D320	Non-TEAE

IMP = investigational medicinal product; TEAE = treatment-emergent AE

AEs will be considered treatment-emergent based on their start date(time). If the AE start date(time) is incomplete or missing, the AE will be considered treatment-emergent unless the available parts of the AE start or stop date(time) provide evidence that the event did not occur in the interval during which an event is considered treatment-emergent. No imputation of missing/incomplete dates will be done.

Based on their start date/time, AEs will be allocated to the phase in which they started. Each AE will therefore be reported in only one phase. Phases are defined in section 2.2.1. In case the AE start date/time is incomplete or missing, and the AE could consequently be allocated to more than one phase, a worst-case allocation will be done and the AE will be allocated to the treatment phase, unless the available parts of the AE start and stop date/time provide evidence for allocating to the observation or follow-up phase.

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

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

AEs with missing relatedness to treatment, prednisone (or equivalent) or procedures will be considered as treatment-related, prednisone-related or procedure-related respectively.

AEs with missing seriousness will be considered as serious AEs.

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

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

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

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

ISRs are defined as AEs with MedDRA PT in the MedDRA high level term of "Injection site reactions", regardless of the time of onset relative to an administration.

AE onset and day since last administration will be calculated as follows when start date is fully known:

- AE onset day in the study (vs baseline visit) =
  - AE start date ≥ date of baseline visit: AE start date – date of baseline visit + 1 day
  - AE start date < date of baseline visit: AE start date – date of baseline visit
- Day since last administration: AE start date - date of last IMP before AE start date

AE duration will be calculated as follows when start and stop date are fully known:

- AE duration (days) =
  - AE end date – AE start date + 1 day
  - End date of the last phase – AE start date + 1 day (when the AE start date is fully known but the AE is not resolved at the end of the study). In this case the duration will be presented as ">x days" in listings.

Event rates per 100 participant years of follow-up (PYFU) will be calculated as 100 * the number of events/PYFU, with:

- PYFU overall (in years) will be calculated as [the sum over all participants of the study duration calculated as (last phase end date - first phase start date + 1)]/365.25
- PYFU for TEAEs (in years) will be calculated as the sum over all participants of the follow-up time during which an event is considered treatment-emergent divided by 365.25.

5.1.3 Presentation of results

The SAF analysis set will be used for the reporting of AEs, unless mentioned otherwise. Tables will present the combined treatment and follow-up phase and will present TEAEs only, unless mentioned otherwise.

An overview table will show the number and percentage of participants with at least one event, the number of events and the event rates per 100 PYFU for the following:

- TEAEs
- Treatment-related TEAEs
- Serious TEAEs
- Serious treatment-related TEAEs
- Serious prednisone-related TEAEs
- Grade ≥ 3 TEAEs
- Treatment-related grade ≥ 3 TEAEs
- TEAEs related to prednisone (or equivalent)
- TEAEs related to study procedures
- TEAEs for which the IMP was discontinued
- TEAEs for which the IMP was interrupted
- TEAEs of special interest *
- Treatment-related TEAEs of special interest *
- TEIRRs *
- Serious TEIRRs *
- TEISRs *
- Fatal TEAEs *

This overview table will be repeated for:

- Overall AEs: all AEs during the study, also including non-TEAEs. This table will be based on the ROL analysis set.
- Treatment-emergent ISR events (TEISRs), excluding the event categories marked with "*" in the above list.

Summary tables by MedDRA SOC and PT will include the number and percentage of participants with at least one event, the number of events and the event rates per 100 PYFU. Each AE record in the clinical database is considered as a distinct adverse event and is counted as such. Summary tables by SOC and PT will be sorted alphabetically.

These tables will be provided for:

- TEAEs
- Overall AEs (based on the ROL analysis set)
- Treatment-related TEAEs
- Serious TEAEs

- Serious treatment-related TEAEs
- Serious prednisone-related TEAEs
- Grade ≥ 3 TEAEs
- Treatment-related Grade ≥ 3 TEAEs
- TEAEs related to prednisone (or equivalent)
- TEAEs related to study procedures
- TEAEs for which the IMP was discontinued
- TEAEs of special interest
- Treatment-related TEAEs of special interest
- TEIRRs
- Serious TEIRRs
- TEISRs
- Fatal TEAEs
- Common TEAEs (PT occurring in at least 5% of the Total Efgartigimod PH20 SC treatment arm; the cut-off is applied after rounding to the nearest integer. System organ class will be presented if any preferred term within it is selected.)

All AEs, including non-TEAEs will be listed for the ROL analysis set (but excluding AEs that started during ARGX-113-2009). Separate listings will be prepared for SAEs, fatal AEs, TEAEs leading to IMP discontinuation (in the SAF analysis set) and AESIs. A listing showing all coding information will be prepared as well.

5.2 CLINICAL LABORATORY EVALUATION

5.2.1 Available data

Per protocol, the following safety laboratory parameters are expected:

Laboratory test	**Parameters**		
Hematology	RBC count platelet count hemoglobin hematocrit	RBC indices: MCV MCH	WBC count with differential: neutrophils lymphocytes monocytes basophils eosinophils
Biochemistry	ALT AST ALP albumin bilirubin (total and direct) BUN sodium	calcium creatinine CRP GGT glucose HbA1c potassium	total protein Lipid panel: total cholesterol HDL LDL (measured, not calculated) triglycerides

Laboratory test	Parameters
Routine urinalysis	Specific gravity pH, glucose, protein, blood, ketones, bilirubin, urobilinogen, nitrite, leukocyte esterase Microscopic examination (if blood or protein is abnormal)
Specialty laboratory tests	INR

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

5.2.2 Derivation rules

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

Notes:

- Abnormalities will be derived for hematology and biochemistry parameters for which no toxicity grading is defined.
- Classification will be performed in standardized units, using nonimputed values and limits.
- For the worst-case analysis visit, as defined in section 2.2.5, an additional category low + high is defined if there are both low and high postbaseline values

Toxicity grades will be computed according to the NCI 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 SAF analysis set will be used for the clinical laboratory evaluation. For tables by analysis visit, only the baseline and last assessment analysis visits will be shown. Cross-tabulations will also include the worst-case analysis visit. All other analysis visits will be included in listings.

Only continuous laboratory parameters expected per protocol will be tabulated, except for INR. The statistical analysis will present results in standardized units, except for creatinine clearance (adjusted for BSA), which will be reported in $mL/min/1.73m^2$.

Continuous laboratory parameters will be summarized using descriptive statistics at each analysis visit of interest. Actual values and changes from study baseline will be shown in the same table.

Laboratory abnormalities will be presented as cross-tabulations of the abnormality at each postbaseline analysis visit of interest versus the study baseline abnormality. The number of participants with treatment-emergent abnormalities will also be shown (see Definition of terms). The denominator for the percentage is the total number of

participants with nonmissing data for the parameter and analysis visit in the SAF analysis set.

Laboratory toxicity grades will be presented as cross-tabulations of the toxicity at each postbaseline analysis visit of interest versus the study 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 with nonmissing data for the parameter and analysis visit in the SAF analysis set. Parameters with toxicity grades defined in both directions (hypo and hyper) will be shown by direction.

All laboratory data will be listed for the ROL analysis set, including laboratory tests not foreseen per protocol, but only for participants with any postbaseline abnormality or toxicity grade ≥1.

5.3 VITAL SIGNS

5.3.1 Available data

Body temperature, pulse rate, respiratory rate, and blood pressure are recorded. Blood pressure and pulse are assessed with the participant rested.

For each vital sign record, assessment date, parameter name, test result and unit are collected.

5.3.2 Derivation rules

Abnormalities are defined in Table 6 below.

Table 6: Criteria to define vital signs abnormalities

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

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

BMI (kg/m²) will be derived as = (body weight (kg)) / (height at screening (m))² in function of C-GTI derivations.

5.3.3 Presentation of results

The SAF analysis set will be used for the evaluation of vital signs. For tables by analysis visit, only the baseline and last assessment analysis visits will be shown. Cross-tabulations will also include the worst-case analysis visit. All other analysis visits will be included in listings.

Vital signs parameters will be summarized using descriptive statistics at each analysis visit of interest. Actual values and changes from study baseline will be shown in the same table.

Abnormalities will be presented as cross-tabulations of the abnormality at each postbaseline analysis visit of interest versus the study baseline abnormality. The number of participants with treatment-emergent abnormalities will also be shown.

The denominator for the percentage is the total number of participants with nonmissing data for the parameter and analysis visit in the SAF analysis set.

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

5.4 ELECTROCARDIOGRAMS

5.4.1 Available data

At a minimum, interval data (PR, QT, QTcF, QTcB and QRS intervals); ventricular rate; and overall interpretation will be recorded for each ECG. For each ECG record, parameter name, test result and unit, assessment date(time) are collected.

5.4.2 Derivation rules

When the ECG assessment date/time is registered down to the level of seconds, the part in seconds will not be considered for analysis purposes (e.g. allocation to phases/(sub)periods).

Abnormalities for HR, QRS, and PR interval are defined in Table 7 below.

Table 7: ECG normal ranges

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

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

For QTcB and QTcF interval (ms), the following categories are defined:

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

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

5.4.3 Presentation of results

The SAF analysis set will be used for the ECG evaluation. For tables by analysis visit, only the baseline and last assessment analysis visits will be shown. Tabulations of abnormalities will also include the worst-case analysis visit. All other analysis visits will be included in listings.

Uncorrected QT interval and RR interval will only be listed.

Continuous ECG parameters will be summarized using descriptive statistics at each analysis visit of interest. Actual values and changes from study baseline will be shown in the same table.

Abnormalities of the actual values will be presented as cross-tabulations of the abnormality at each postbaseline analysis visit of interest versus the study baseline abnormality. Numbers and cumulative numbers over decreasing abnormalities (QTcF and QTcB only) of participants with treatment-emergent abnormalities will also be shown. The denominator for the percentage is the total number of participants with nonmissing data for the parameter and analysis visit in the SAF analysis set.

Abnormalities of the QTcB and QTcF changes from study baseline will be presented as tabulations of the change abnormality at each postbaseline analysis visit of interest. Cumulative numbers over decreasing change from baseline abnormalities of participants with change abnormalities will also be shown. The denominator for the percentage is the total number of participants with nonmissing data for the parameter and analysis visit in the SAF analysis set.

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

6. VERSION HISTORY

This SAP for study ARGX-113-2010 is based on the protocol version 4.0, dated 02 May 2024.

6.1 CHANGES NOT COVERED BY PROTOCOL AMENDMENTS BEFORE DATABASE LOCK

6.2 CHANGES NOT COVERED BY PROTOCOL AMENDMENTS AFTER DATABASE LOCK

6.3 CHANGES TO THE FINAL STATISTICAL ANALYSIS PLAN

7. REFERENCES

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

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

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

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

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

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

An analysis of the time-relations of electrocardiogram. Bazett HC Heart 1920 7:353–370.

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

8. LIST OF TABLES AND LISTINGS

8.1 TABLES

The mock ID refers to the table ID in the argenx mock library.

Table number	Title	PAS / DPS	Mock ID
14.1 DEMOGRAPHIC DATA			
GENERAL CHARACTERISTICS (14.1.X)			
14.1.1.1	Participant Analysis Sets and Number of Treatment Periods	ROL	DST01
14.1.1.2	Analysis Phase Duration	ROL	DST05
14.1.1.3	Analysis Period and Subperiod Duration	SAF	DST05
14.1.1.4	Treatment Discontinuation	SAF	DST03
14.1.1.5	Study Discontinuation	ROL	DST04
14.1.1.6	Protocol Deviations	ROL	DVT01
14.1.2.1	Demographic Data	ROL	DMT01
14.1.2.2	Baseline Disease Characteristics	ROL	DMT01
14.1.2.3	Concomitant Therapies by ATC Class (Level 1 and 3) and Generic Term	ROL	CMT01
14.1.2.4	Concomitant OCS Therapies by ATC Class (Level 1 and 3) and Generic Term	ROL	CMT01
14.1.2.5	Concomitant TCS Therapies by ATC Class (Level 1 and 3) and Generic Term	ROL	CMT01
14.1.2.6	Concomitant Rescue Therapies by ATC Class (Level 1 and 3) and Generic Term	ROL	CMT01
14.1.2.7	IMP Administration	SAF	EXT01

14.2 EFFICACY DATA

EFFICACY (14.2.1.X)

14.2.1.1	CRoff: Proportion of Participants Who Achieved CRoff	SAF	EFT07b
14.2.1.2	CR/PRoff: Proportion of Participants Who Achieved PR/CRoff	SAF	EFT07b
14.2.1.3	CRmin: Proportion of Participants Who Achieved CRmin	SAF	EFT07b
14.2.1.4	CRoff Without IMP: Proportion of Participants Who Achieved CRoff Without IMP	ROL	EFT07b
14.2.1.5	CR/PRoff Without IMP: Proportion of Participants Who Achieved CR/PRoff Without IMP	ROL	EFT07b
14.2.1.6	Sustained Remission: Kaplan-Meier Estimates of Duration of Sustained Remission	SAF	EFT09a
14.2.1.7	Relapse: Proportion of Participants with Relapse	ROL	EFT07b
14.2.1.8	Relapse: Kaplan-Meier Estimates of Time to Relapse	ROL	EFT09a
14.2.1.9	Relapse: Frequency Tabulation of Severity of Relapse	ROL	EFT07a
14.2.1.10	BPDAI: Descriptive Statistics of Actual Values, Changes From Baseline, and Percent Changes From Baseline in BPDAI Activity Score over Time	ROL	PDT01
14.2.1.11	BPDAI: Descriptive Statistics of Actual Values, Changes From Baseline, and Percent Changes From Baseline in BPDAI Total Score over Time	ROL	PDT01
14.2.1.12	IGA-BP: Frequency Tabulation of IGA-BP Score Over Time	ROL	EFT07d
14.2.1.13	Itch NRS: Descriptive Statistics of Actual Values and Changes From Baseline in Itch NRS 24-hour Average Score over Time	ROL	EFT03a
14.2.1.14	Itch NRS: Descriptive Statistics of Actual Values and Changes From Baseline in Itch NRS 24-hour Worst Score over Time	ROL	EFT03a
14.2.1.15	Treatment Failure: Proportion of Participants with Treatment Failure	ROL	EFT07b
14.2.1.16	C-GTI: Descriptive Statistics of CWS and AIS over Time	ROL	EFT03a
14.2.1.17	ABQOL: Frequency Tabulation of ABQOL 17 Items Over Time	ROL	EFT07d

14.2.1.18	ABQOL: Descriptive Statistics of Actual Values and Changes From Baseline in ABQOL Total Score over Time	ROL	EFT03a
14.2.1.19	EQ-5D-5L: Frequency Tabulation of EQ-5D-5L 5 Dimensions Over Time	ROL	EFT07d
14.2.1.20	EQ-5D-5L: Descriptive Statistics of Actual Values and Changes From Baseline in EQ-5D-5L VAS Score over Time	ROL	EFT03a
14.2.1.21	DLQI: Frequency Tabulation of DLQI 10 Items Over Time	ROL	EFT07d
14.2.1.22	DLQI: Descriptive Statistics of Actual Values and Changes From Baseline in DLQI Score over Time	ROL	EFT03a
PHARMACODYNAMICS (14.2.3.X)			
14.2.3.1	Descriptive Statistics of Actual Values, Changes From Treatment-Period Baseline, and Percent Changes From Treatment-Period Baseline [redacted] over Time	SAF	PDT01
14.2.3.2	Descriptive Statistics of Actual Values, Changes From Treatment-Period Baseline, and Percent Changes From Treatment-Period Baseline in Anti-BP180 and Anti-BP230 Antibodies over Time	SAF	PDT01
IMMUNOGENICITY (14.2.4.X)			
14.2.4.1	Number and Percentage of Participants With Anti-drug Antibodies Against Efgartigimod over Time by Anti-drug Antibodies Against Efgartigimod Participant Classification	SAF	IMT01a
14.2.4.2	Prevalence and Incidence of Anti-drug Antibodies Against Efgartigimod	SAF	IMT02a
14.2.4.3	Descriptive Statistics of Anti-drug Antibodies Against Efgartigimod Titer Values over Time by Anti-drug Antibodies Against Efgartigimod Participant Classification	SAF	IMT03
14.2.4.4	Number and Percentage of Participants With Neutralizing Antibodies Against Efgartigimod over Time by Neutralizing Antibodies Against Efgartigimod Participant Classification	SAF	IMT01b
14.2.4.5	Prevalence and Incidence of Neutralizing Antibodies Against Efgartigimod	SAF	IMT02b
14.2.4.6	Number and Percentage of Neutralizing Antibodies Against Efgartigimod Positive Participants by Overall Anti-drug Antibodies Against Efgartigimod Participant Classification	SAF	IMT04

14.3 SAFETY DATA

14.3.1 DISPLAYS OF ADVERSE EVENTS (14.3.1.X)

14.3.1.1	Treatment-Emergent Adverse Events Overview	SAF	AET01a
14.3.1.2	Overall Adverse Events Overview	ROL	AET01a
14.3.1.3	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.4	Overall Adverse Events by MedDRA System Organ Class and Preferred Term	ROL	AET02b
14.3.1.5	Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.6	Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.7	Serious Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.8	Serious Prednisone-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.9	Grade 3 or More Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.10	Treatment-Related Grade 3 or More Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.11	Prednisone-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.12	Procedure-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.13	Treatment-Emergent Adverse Events Leading to IMP Discontinuation by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.14	Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class and Preferred Term	SAF	AET02b

14.3.1.15	Treatment-Related Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.16	Treatment-Emergent Injection-Related Reactions by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.17	Serious Treatment-Emergent Injection-Related Reactions by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.18	Treatment-Emergent Adverse Events Overview for Injection Site Reactions	SAF	AET01c
14.3.1.19	Treatment-Emergent Injection Site Reactions by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.20	Fatal Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.21	Common Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.4 ABNORMAL LABORATORY VALUE LISTING (EACH PARTICIPANT)			
LABORATORY DATA (14.3.4.1.X)			
14.3.4.1.1	Descriptive Statistics of Laboratory Test Actual Values and Changes From Baseline Over Time	SAF	SFT01
14.3.4.1.2	Cross-Tabulation of Laboratory Abnormalities Versus Baseline Over Time	SAF	SFT02
14.3.4.1.3	Cross-Tabulation of Laboratory Toxicity Grades Versus Baseline Over Time	SAF	SFT03
VITAL SIGNS (14.3.4.2.X)			
14.3.4.2.1	Descriptive Statistics of Vital Signs Actual Values and Changes From Baseline Over Time	SAF	SFT01
14.3.4.2.2	Cross-Tabulation of Vital Signs Abnormalities Versus Baseline Over Time	SAF	SFT02
ECG (14.3.4.3.X)			
14.3.4.3.1	Descriptive Statistics of ECG Actual Values and Changes From Baseline Over Time	SAF	SFT01
14.3.4.3.2	Cross-Tabulation of ECG Abnormalities Versus Baseline Over Time	SAF	SFT02
14.3.4.3.3	Cross-Tabulation of QTcB and QTcF Abnormalities Versus Baseline Over Time	SAF	SFT03
14.3.4.3.4	Tabulation of QTcB and QTcF Change Abnormalities Over Time	SAF	SFT04

8.2 LISTINGS

Listing number	Title	PAS / DPS
16.2.1 DISCONTINUED PARTICIPANTS		
16.2.1.1	Participant Analysis Sets	ROL
16.2.1.2	Treatment and Study Discontinuation	ROL
16.2.1.3	Study Visits	ROL
16.2.2 PROTOCOL DEVIATIONS		
16.2.2.1	Protocol Deviations	ROL
16.2.4 DEMOGRAPHIC DATA		
16.2.4.1	Demographic Data	ROL
16.2.4.2	Baseline Disease Characteristics	ROL
16.2.4.3	Concomitant Therapies	ROL
16.2.4.4	Concomitant Procedures	ROL
16.2.5 COMPLIANCE AND/OR DRUG CONCENTRATION DATA (IF AVAILABLE)		
16.2.5.1	IMP Administration	SAF
16.2.5.2	OCS Administration	ROL
16.2.6 INDIVIDUAL EFFICACY RESPONSE DATA		
16.2.6.1	Disease Status	ROL
16.2.6.2	Duration of Sustained Remission, Time to Relapse and Severity of Relapse	ROL
16.2.6.3	Lesion Assessments	ROL

16.2.6.4	BPDAI	ROL
16.2.6.5	IGA-BP	ROL
16.2.6.6	Itch NRS	ROL
16.2.6.7	C-GTI	ROL
16.2.6.8	GTI Specific List	ROL
16.2.6.9	ABQOL	ROL
16.2.6.10	EQ-5D-5L	ROL
16.2.6.11	DLQI	ROL
16.2.6.12	[redacted]	ROL
16.2.6.13	Anti-BP180 and Anti-BP230 Antibodies	ROL
16.2.6.14	Efgartigimod Anti-drug Antibodies and Neutralizing Antibodies	ROL
16.2.7 ADVERSE EVENTS LISTINGS		
16.2.7.1	Adverse Events	ROL
16.2.7.2	Serious Adverse Events	ROL
16.2.7.3	Fatal Adverse Events	ROL
16.2.7.4	Treatment-Emergent Adverse Events Leading to IMP Discontinuation	SAF
16.2.7.5	Adverse Events of Special Interest	ROL
16.2.7.6	Adverse Events: Coding Information	ROL
16.2.8 LISTING OF INDIVIDUAL LABORATORY MEASUREMENTS BY PARTICIPANT, WHEN REQUIRED BY REGULATORY AUTHORITIES		
16.2.8.1	Laboratory Test Results for Participants with Post-Baseline Abnormal Values or Toxicities	ROL
16.2.8.2	Vital Signs Results for Participants with Post-Baseline Abnormal Values	ROL
16.2.8.3	ECG Results for Participants with Post-Baseline Abnormal Values	ROL

9. APPENDICES

9.1 GTI: DERIVATION OF CWS AND AIS

9.1.1 Allocate weights

Weights per item are attributed as specified below. GTI at Wx is evaluated versus previous GTI assessment. The first time point is referred to as *start (or previous)* and the second time point within each comparison is referred to as *follow-up (or current)*.

Increase, decrease or no change in medication intake compared to previous assessment are checked in the GTI assessment. A missing evaluation, including for external data, will be considered as no change with weight=0.

External GTI data (i.e., LDL/HbA1c/BP and BMI) are allocated to a GTI assessment based on dates. The last available value of these external data since previous GTI assessment will be used.

Changes from severe to moderate do not have any impact on calculation of CWS/AIS. Severe outcome on an item however is captured on the specific list (SL).

9.1.1.1 BMI (COMPARED TO PREVIOUS ASSESSMENT)

- Moderate decrease in the direction of the normal range [<25 kg/ m2] by at least 5 BMI units -36
- Minor decrease in the direction of the normal range [<25 kg/ m2] by more than 2 but less than 5 BMI units -21
- No significant change (BMI remains within +/- 2 BMI units compared with start) OR BMI remains <25 kg/ m2 0
- Minor increase in BMI (increase by more than 2 but less than 5 BMI units,
- to above the upper limit of normal BMI [≥25kg/m2]) 21
- Moderate increase in BMI (increase by at least 5 BMI units above normal BMI [≥25kg/m2]) 36

9.1.1.2 GLUCOSE TOLERANCE (COMPARED TO PREVIOUS ASSESSMENT)

- Moderate improvement in glucose tolerance: -44
  - HbA1c declined >10% from start AND medication decrease
- Minor improvement in glucose tolerance: -32
  - HbA1c declined >10% from start AND no medication increase (unchanged or missing) AND start HbA1c ≥ 5.7
  - HbA1c within 10% of start AND decrease in diabetic medication
  - HbA1c < 5.7 AND decrease in diabetic medication AND HbA1c increased >10%
- No significant change in glucose tolerance: 0
  - HbA1c within 10% of start or (start and follow-up) HbA1c < 5.7 AND no change in medication (or missing)
  - HbA1c increased > 10% of start AND a decrease in medication AND follow-up HbA1c ≥ 5.7
  - HbA1c decreased by > 10% of start AND an increase in medication
- Minor worsening of glucose tolerance or medication status: 32
  - HbA1c increased >10% of start AND no change in medication (or missing) AND follow-up HbA1c ≥ 5.7%
  - HbA1c within 10% of start AND increase in diabetic medication
- Moderate worsening of glucose tolerance despite increased diabetic treatment: 44
  - HbA1c increased >10% of start AND an increase in diabetic medication AND follow-up HbA1c ≥ 5.7%

Note: changes in medication for glucose control, used in the above weight derivations, are assessed as a GTI specific question.

14.2.1.18	ABQOL: Descriptive Statistics of Actual Values and Changes From Baseline in ABQOL Total Score over Time	ROL	EFT03a
14.2.1.19	EQ-5D-5L: Frequency Tabulation of EQ-5D-5L 5 Dimensions Over Time	ROL	EFT07d
14.2.1.20	EQ-5D-5L: Descriptive Statistics of Actual Values and Changes From Baseline in EQ-5D-5L VAS Score over Time	ROL	EFT03a
14.2.1.21	DLQI: Frequency Tabulation of DLQI 10 Items Over Time	ROL	EFT07d
14.2.1.22	DLQI: Descriptive Statistics of Actual Values and Changes From Baseline in DLQI Score over Time	ROL	EFT03a
PHARMACODYNAMICS (14.2.3.X)			
14.2.3.1	Descriptive Statistics of Actual Values, Changes From Treatment-Period Baseline, and Percent Changes From Treatment-Period Baseline in [redacted] over Time	SAF	PDT01
14.2.3.2	Descriptive Statistics of Actual Values, Changes From Treatment-Period Baseline, and Percent Changes From Treatment-Period Baseline in Anti-BP180 and Anti-BP230 Antibodies over Time	SAF	PDT01
IMMUNOGENICITY (14.2.4.X)			
14.2.4.1	Number and Percentage of Participants With Anti-drug Antibodies Against Efgartigimod over Time by Anti-drug Antibodies Against Efgartigimod Participant Classification	SAF	IMT01a
14.2.4.2	Prevalence and Incidence of Anti-drug Antibodies Against Efgartigimod	SAF	IMT02a
14.2.4.3	Descriptive Statistics of Anti-drug Antibodies Against Efgartigimod Titer Values over Time by Anti-drug Antibodies Against Efgartigimod Participant Classification	SAF	IMT03
14.2.4.4	Number and Percentage of Participants With Neutralizing Antibodies Against Efgartigimod over Time by Neutralizing Antibodies Against Efgartigimod Participant Classification	SAF	IMT01b
14.2.4.5	Prevalence and Incidence of Neutralizing Antibodies Against Efgartigimod	SAF	IMT02b
14.2.4.6	Number and Percentage of Neutralizing Antibodies Against Efgartigimod Positive Participants by Overall Anti-drug Antibodies Against Efgartigimod Participant Classification	SAF	IMT04

14.3 SAFETY DATA

14.3.1 DISPLAYS OF ADVERSE EVENTS (14.3.1.X)

14.3.1.1	Treatment-Emergent Adverse Events Overview	SAF	AET01a
14.3.1.2	Overall Adverse Events Overview	ROL	AET01a
14.3.1.3	Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.4	Overall Adverse Events by MedDRA System Organ Class and Preferred Term	ROL	AET02b
14.3.1.5	Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.6	Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.7	Serious Treatment-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.8	Serious Prednisone-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.9	Grade 3 or More Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.10	Treatment-Related Grade 3 or More Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.11	Prednisone-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.12	Procedure-Related Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.13	Treatment-Emergent Adverse Events Leading to IMP Discontinuation by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.14	Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class and Preferred Term	SAF	AET02b

14.3.1.15	Treatment-Related Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.16	Treatment-Emergent Injection-Related Reactions by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.17	Serious Treatment-Emergent Injection-Related Reactions by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.18	Treatment-Emergent Adverse Events Overview for Injection Site Reactions	SAF	AET01c
14.3.1.19	Treatment-Emergent Injection Site Reactions by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.20	Fatal Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.1.21	Common Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	SAF	AET02b
14.3.4 ABNORMAL LABORATORY VALUE LISTING (EACH PARTICIPANT)			
LABORATORY DATA (14.3.4.1.X)			
14.3.4.1.1	Descriptive Statistics of Laboratory Test Actual Values and Changes From Baseline Over Time	SAF	SFT01
14.3.4.1.2	Cross-Tabulation of Laboratory Abnormalities Versus Baseline Over Time	SAF	SFT02
14.3.4.1.3	Cross-Tabulation of Laboratory Toxicity Grades Versus Baseline Over Time	SAF	SFT03
VITAL SIGNS (14.3.4.2.X)			
14.3.4.2.1	Descriptive Statistics of Vital Signs Actual Values and Changes From Baseline Over Time	SAF	SFT01
14.3.4.2.2	Cross-Tabulation of Vital Signs Abnormalities Versus Baseline Over Time	SAF	SFT02
ECG (14.3.4.3.X)			
14.3.4.3.1	Descriptive Statistics of ECG Actual Values and Changes From Baseline Over Time	SAF	SFT01
14.3.4.3.2	Cross-Tabulation of ECG Abnormalities Versus Baseline Over Time	SAF	SFT02
14.3.4.3.3	Cross-Tabulation of QTcB and QTcF Abnormalities Versus Baseline Over Time	SAF	SFT03
14.3.4.3.4	Tabulation of QTcB and QTcF Change Abnormalities Over Time	SAF	SFT04

8.2 LISTINGS

Listing number	Title	PAS / DPS
16.2.1 DISCONTINUED PARTICIPANTS		
16.2.1.1	Participant Analysis Sets	ROL
16.2.1.2	Treatment and Study Discontinuation	ROL
16.2.1.3	Study Visits	ROL
16.2.2 PROTOCOL DEVIATIONS		
16.2.2.1	Protocol Deviations	ROL
16.2.4 DEMOGRAPHIC DATA		
16.2.4.1	Demographic Data	ROL
16.2.4.2	Baseline Disease Characteristics	ROL
16.2.4.3	Concomitant Therapies	ROL
16.2.4.4	Concomitant Procedures	ROL
16.2.5 COMPLIANCE AND/OR DRUG CONCENTRATION DATA (IF AVAILABLE)		
16.2.5.1	IMP Administration	SAF
16.2.5.2	OCS Administration	ROL
16.2.6 INDIVIDUAL EFFICACY RESPONSE DATA		
16.2.6.1	Disease Status	ROL
16.2.6.2	Duration of Sustained Remission, Time to Relapse and Severity of Relapse	ROL
16.2.6.3	Lesion Assessments	ROL

9.1.1.3 BLOOD PRESSURE (COMPARED TO PREVIOUS ASSESSMENT)

- Moderate improvement in BP: -44
  - Decrease in either systolic or diastolic BP of >10% of start AND medication decrease AND start systolic BP ≥120 mmHg or start diastolic BP ≥ 85 mmHg
- Minor improvement in BP: -19
  - Decrease in either systolic or diastolic BP of >10% of start AND no medication increase (unchanged or missing) AND start systolic BP ≥120 mmHg or start diastolic BP ≥ 85 mmHg
  - Systolic AND diastolic BP within 10% of start AND a decrease in medication
  - Systolic BP < 120 and diastolic BP < 85 (both start and end) AND a decrease in medication
- No significant change in BP: 0
  - Systolic AND diastolic BP within 10% of start or (start and follow-up) systolic / diastolic BP < 120/85 resp AND no change in medication (or missing)
  - Increase in systolic or diastolic BP >10% of start AND a decrease in medication AND follow-up systolic BP ≥120 mmHg or diastolic BP ≥ 85 mmHg
  - Decrease in systolic or diastolic BP of > 10% of start AND an increase in medication AND start systolic BP ≥120 mmHg or diastolic BP ≥ 85 mmHg
- Minor worsening of BP: 19
  - Increase in systolic or diastolic BP >10% of start AND no change in medication (or missing) AND follow-up systolic BP ≥120 mmHg or diastolic BP ≥ 85 mmHg
  - Systolic AND diastolic BP within 10% of start AND an increase in medication
  - Systolic BP < 120 and diastolic BP < 85 (both start and end) AND an increase in medication

- Moderate worsening of BP despite treatment 44
  - Increase in systolic or diastolic BP >10% of start AND an increase in medication AND follow-up systolic BP ≥120 mmHg or diastolic BP ≥ 85 mmHg

Notes:

1. changes in medication for BP control, used in the above weight derivations, are assessed as a GTI specific question.

2. check ≥ normal range and > 10% needs to be done separately for systolic and diastolic BP. In case of both an increase and decrease occurs, this is considered as no change in BP and the score will be based on the change in medication (score = +/-19 for increase/decrease, score = 0 for no change).

3. Hypertensive Emergency = Y or PRES = Y at current visit is provided a score 44 regardless of the value at previous visit

9.1.1.3 BLOOD PRESSURE (COMPARED TO PREVIOUS ASSESSMENT)

- Moderate improvement in BP: -44
  - Decrease in either systolic or diastolic BP of >10% of start AND medication decrease AND start systolic BP ≥120 mmHg or start diastolic BP ≥ 85 mmHg
- Minor improvement in BP: -19
  - Decrease in either systolic or diastolic BP of >10% of start AND no medication increase (unchanged or missing) AND start systolic BP ≥120 mmHg or start diastolic BP ≥ 85 mmHg
  - Systolic AND diastolic BP within 10% of start AND a decrease in medication
  - Systolic BP < 120 and diastolic BP < 85 (both start and end) AND a decrease in medication
- No significant change in BP: 0
  - Systolic AND diastolic BP within 10% of start or (start and follow-up) systolic / diastolic BP < 120/85 resp AND no change in medication (or missing)
  - Increase in systolic or diastolic BP >10% of start AND a decrease in medication AND follow-up systolic BP ≥120 mmHg or diastolic BP ≥ 85 mmHg
  - Decrease in systolic or diastolic BP of > 10% of start AND an increase in medication AND start systolic BP ≥120 mmHg or diastolic BP ≥ 85 mmHg
- Minor worsening of BP: 19
  - Increase in systolic or diastolic BP >10% of start AND no change in medication (or missing) AND follow-up systolic BP ≥120 mmHg or diastolic BP ≥ 85 mmHg
  - Systolic AND diastolic BP within 10% of start AND an increase in medication
  - Systolic BP < 120 and diastolic BP < 85 (both start and end) AND an increase in medication

- Moderate worsening of BP despite treatment 44
  - Increase in systolic or diastolic BP >10% of start AND an increase in medication AND follow-up systolic BP ≥120 mmHg or diastolic BP ≥ 85 mmHg

Notes:

1. changes in medication for BP control, used in the above weight derivations, are assessed as a GTI specific question.

2. check ≥ normal range and > 10% needs to be done separately for systolic and diastolic BP. In case of both an increase and decrease occurs, this is considered as no change in BP and the score will be based on the change in medication (score = +/-19 for increase/decrease, score = 0 for no change).

3. Hypertensive Emergency = Y or PRES = Y at current visit is provided a score 44 regardless of the value at previous visit

9.1.1.4 LIPID METABOLISM (LDL COMPARED TO PREVIOUS ASSESSMENT)

- Moderate improvement in lipids: -30
  - Decrease in LDL concentration >10% of start AND medication decrease
- Minor improvement in lipids: -10
  - Decrease in LDL concentration >10% of start AND no change in medication (or missing) AND start above target range
  - LDL within 10% of start AND decrease in medication
- No significant change in lipids: 0
  - LDL within 10% of start AND no change in medication (or missing)
  - Increase in LDL > 10% of start AND decrease in medication
  - Decrease in LDL > 10% of start AND no medication change (or missing) AND start LDL below or equal target range
  - Decrease in LDL > 10% of start AND increase in medication
- Minor worsening of LDL or medication status: 10
  - Increase in LDL >10% of start AND no change in medication (or missing)
  - LDL within 10% of start of start AND increase in medication
- Worsening of LDL despite treatment: 30
  - Increase in LDL >10% of start AND an increase in medication

Notes:

1. changes in medication for lipid control, used in the above weight derivations, are assessed as a GTI specific question.
2. target range for LDL is 1.81mmol/L

9.1.1.5 GLUCOCORTICOID-INDUCED MYOPATHY (COMPARED TO PREVIOUS ASSESSMENT)

- Moderate/severe weakness to none: -63
- Moderate/severe weakness to mild weakness: -54
- Mild weakness to none: -9
- No significant change: 0
- None to mild weakness: 9
- Mild to Moderate/severe weakness: 54
- None to Moderate/severe weakness: 63

9.1.1.6 SKIN TOXICITY (COMPARED TO PREVIOUS ASSESSMENT)

Allocate weights for each of the 5 subitems: acneiform rash, easy bruising, hirsutism, atrophy/striae, erosions/tears/ulcerations

- Moderate/severe to none: -26
- Moderate/severe to minor: -18
- Minor to none: -8
- No significant change: 0
- None to minor: 8
- minor to moderate/severe: 18
- None to moderate/severe: 26

Note: minor and mild or used fully interchangeable.

For the derivation from the grading to severe, moderate, minor (or mild): see table underneath:

Minor/Mild	Moderate	Severe (Specific Domain)
Acneiform rash (Grades 1-2)	Acneiform rash (Grade 3)	Acneiform rash (Grade 4)
Easy bruising (Grade 1)	Easy bruising (Grade 2)	
Hirsutism (Grade 1)	Hirsutism (Grade 2)	
Atrophy/Striae (Grade 1)	Atrophy/Striae (Grade 2)	Atrophy/Striae (Grade 3)
Erosions/Tears/Ulcerations (Grade 1)	Erosions/Tears/Ulcerations (Grade 2)	Erosions/Tears/Ulcerations (Grade 3)

9.1.1.8 NEUROPSYCHIATRIC EFFECTS (COMPARED TO PREVIOUS ASSESSMENT)

Allocate weights for each of the 4 subitems: insomnia, mania, cognitive impairment, depression

- Moderate/severe to none: -74
- Moderate/severe to minor: -63
- Minor to none: -11
- No significant change: 0
- None to minor: 11
- Minor to moderate/severe: 63
- None to moderate/severe: 74

Notes:

1. presence of psychosis or glucocorticoid-induced violence (as captured in the GTI specific list) always has weight=74. Disappearance of psychosis or glucocorticoid-induced violence has weight=-74.

2. minor and mild or used fully interchangeable

For the derivation from the grading to severe, moderate, minor (or mild): see table underneath:

Minor/Mild	Moderate	Severe (Specific Domain)
Insomnia – (Grade 1)	Insomnia – (Grade 2)	
Mania (Grade 1)	Mania (Grade 2)	Mania (Grade 3)
Cognitive impairment (Grade 1)	Cognitive impairment (Grade 2)	Cognitive impairment (Grade 3)
Depression (Grade 1)	Depression (Grade 2)	Depression (Grade 3)

9.1.1.9 INFECTION (COMPARED TO PREVIOUS ASSESSMENT)

- No significant infection: 0
- Specific infections < Grade 3 (oral or vaginal candidiasis, uncomplicated zoster): 19
- Grade 3, 4, or 5 or complicated herpes zoster: 93

Note:

Special case domain: each infection is a distinct event, so infections only have worsening. That means that a subject may have Infection grade 3 at Wx and again at Wy and the subjects may be assigned a score of 93 for the worsening from Wx to Wy if the investigator has collected 'Infection' at Wy.

9.1.2 CWS and AIS calculation

9.1.2.1 CWS

The CWS is calculated as the sum of the worsening items: i.e., with weights >0. For the items with subitems, i.e., skin toxicity and neuropsychiatric effects, only the subitem with the highest positive weight is used. As an example, if neither insomnia nor depression were present at the start of the GTI interval but there is mild insomnia and moderate depression present at postbaseline, then only the moderate depression is used for the neuropsychiatric weight (+74 points).

In the CWS calculation, the most severe infection in every GTI interval is scored (so in case of 2 periods, the score for an infection is counted twice for the overall CWS at endpoint).

CWS is calculated at Wx as the sum of the worsening items in all postbaseline timepoints up to that timepoint respectively.

9.1.2.2 AIS

With the AIS, improvement as well as worsening is included in the calculations of the sum of the items. For the items with subitems, i.e., skin toxicity and neuropsychiatric effects, only the subitem with the highest positive weight is used as well as the subitem with the lowest negative weight is used. For example: if the highest positive skin subitem is +26 and the highest negative skin subitem is -18, then skin weight for AIS is +8.

AIS is calculated at Wx as the sum of the items in all postbaseline timepoints up to that timepoint respectively.

9.2 TOXICITY GRADES

Below Table 8 documents how the Criteria for Adverse Events CTCAE, v5.0: November 27, 2017 is implemented in the statistical analysis.

Table 8: Analysis toxicity grades (CTCAE 5.0)

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

PARAMETER	Unit	GRADE 1	GRADE 2	GRADE 3	GRADE 4
	mg/dL	>ULN-11.5	>11.5-12.5	>12.5-13.5	>13.5
Cholesterol[a]	mmol/L	>ULN-7.75	>7.75-10.34	>10.34-12.92	>12.92
	mg/dL	>ULN-300	>300-400	>400-500	>500
Creatine kinase[c]		>1.0-2.5 *ULN	>2.5-5.0 *ULN	>5.0-10.0 *ULN	>10.0 *ULN
Creatinine[c]		>1.0-1.5 *ULN	>1.5-3.0 *ULN	>3.0-6.0 *ULN	>6.0 *ULN
Gamma-glutamyl transferase[c]		>1.0-2.5 *ULN	>2.5-5.0 *ULN	>5.0-20.0 *ULN	>20.0 *ULN
Glucose (fasting) low[a,b]	mmol/L	<LLN-3.0	<3.0-2.2	<2.2-1.7	<1.7
	mg/dL	<LLN-55	<55-40	<40-30	<30
Lipase[c]		>1.0-1.5 *ULN	>1.5-2.0 *ULN	>2.0-5.0 *ULN	>5.0 *ULN
Magnesium low[a]	mmol/L	<LLN-0.5	<0.5-0.4	<0.4-0.3	<0.3
	mg/dL	<LLN-1.2	<1.2-0.9	<0.9-0.7	<0.7
Magnesium high[a]	mmol/L	>ULN-1.23	-	>1.23-3.30	>3.30
	mg/dL	>ULN-3.0	-	>3.0-8.0	>8.0
Potassium low[a]	mmol/L	-	<LLN-3.0	<3.0-2.5	<2.5
	mEq/L	-	<LLN-3.0	<3.0-2.5	<2.5
Potassium high[a]	mmol/L	>ULN-5.5	>5.5-6.0	>6.0-7.0	>7.0
	mEq/L	>ULN-5.5	>5.5-6.0	>6.0-7.0	>7.0
Sodium low[a]	mmol/L	<LLN-130	-	<130-120	<120
	mEq/L	<LLN-130	-	<130-120	<120
Sodium high[a]	mmol/L	>ULN-150	>150-155	>155-160	>160
	mEq/L	>ULN-150	>150-155	>155-160	>160

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

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

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

[c] Local laboratory assessments of this laboratory parameter can be considered in the toxicity table.

9.3 SCHEDULE OF ASSESSMENTS

Table 1: Schedule of Activities for Participants Who Have Not Received Efgartigimod PH20 SC Since Baseline and Rolled Over Before Protocol Amendment 2 Is Effective

Study period		Observation period								Follow-up period	Other visits		
Study week(s)	Baseline/ rollover (W0)[a,b]	W2	W4	W8	W16	W24	W32	W40	EoTP/W48	EoTP + 8 weeks	EDV[c]	UNS[d]	Applicable protocol section(s)
Visit window		±2 d	±2 d	±7 d	±7 d	±7 d	±7 d	±7 d	±7 d	±3 d			
Eligibility (baseline only)													
Informed consent	X												Section 10.1.3
Eligibility check	X												Section 5.1 Section 5.2
Safety													
Physical examination (complete)	X								X		X		Section 8.3.1
Physical examination (brief)			X	X						X			Section 8.3.1
Weight	X					X			X		X	X	Section 8.3.1
Vital sign measurements	X	X	X	X	X	X	X	X	X	X	X	X	Section 8.3.1
ECG	X					X							Section 8.3.3
Urine pregnancy test[e]	X		X	X	Every 4 weeks				X		X		Section 8.3.5
Urinalysis	X	X	X	X		X		X	X	X	X	X	Table 7
Clinical chemistry and hematology	X	X	X	X	X	X	X	X	X	X	X	X	Table 7
GTI assessments (GTI-AIS, GTI-CWS, GTI-SL)	X					X			X		X		Section 8.3.6

Study period		Observation period								Follow-up period	Other visits		Applicable protocol section(s)
Study week(s)	Baseline/ rollover (W0)[a,b]	W2	W4	W8	W16	W24	W32	W40	EoTP/W48	EoTP + 8 weeks	EDV[c]	UNS[d]	
Visit window		±2 d	±2 d	±7 d	±7 d	±7 d	±7 d	±7 d	±7 d	±3 d			
Concomitant therapies/procedures	Continuous monitoring												Section 6.9
AE monitoring	Continuous monitoring												Section 8.4
Efficacy/disease monitoring													
Disease assessment[b]	X	X	X	X	X	X	X	X	X	X	X	X	Section 8.2.1.1
IGA-BP	X	X	X	X	X	X	X	X	X	X	X	X	Section 8.2.1.2
BPDAI	X	X	X	X	X	X	X	X	X	X	X	X	Section 8.2.1.3
Itch NRS	X	X	X	X	X	X	X	X	X	X	X	X	Section 8.2.1.4
Blood sample collection													
Immunogenicity	X		X	X	X	X	X	X	X	X	X	X	Section 8.9
PD (anti-BP180, anti-BP230[redacted]	X	X	X	X	X	X	X	X	X	X	X	X	Section 8.6
PK	X												NA
Substudy: vaccination antibody titers (serum)	Relative to the time of vaccination in ARGX-113-2009												Section 8.3.4.1
Substudy: vaccination antibody titers (PBMCs)	Relative to the time of vaccination in ARGX-113-2009												Section 8.3.4.1
Other													
Monitoring of concurrent BP therapy (Definitions of Terms)	X	X	X	X	X	X	X	X	X	X	X	X	Section 6.9 Section 8.2.1.1

Study period	Baseline/ rollover (W0)[a,b]	Observation period								Follow-up period	Other visits		Applicable protocol section(s)
Study week(s)		W2	W4	W8	W16	W24	W32	W40	EoTP/W48	EoTP + 8 weeks	EDV[c]	UNS[d]	
Visit window		±2 d	±2 d	±7 d	±7 d	±7 d	±7 d	±7 d	±7 d	±3 d			
QoL questionnaires (EQ-5D-5L, DLQI, ABQoL)	X					X			X		X		Section 8.2.2

ABQoL=Autoimmune Bullous Disease Quality of Life; AE=adverse event; BP=bullous pemphigoid; BPDAI=Bullous Pemphigoid Disease Area Index; CDA=control of disease activity; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eCRF=electronic case report form; EDV=early discontinuation visit; efgartigimod PH20 SC=efgartigimod for SC administration coformulated with rHuPH20; EoTP=end-of-treatment period (visit); GTI=Glucocorticoid Toxicity Index; GTI-AIS=GTI Aggregate Improvement Score; GTI-CWS=GTI Cumulative Worsening Score; GTI-SL=GTI Specific List; IGA-BP=Investigator Global Assessment of Bullous Pemphigoid [redacted] IMP=investigational medicinal product; NA=not applicable; NRS=numerical rating scale; PBMC=peripheral blood mononuclear cell; PD=pharmacodynamics; PK=pharmacokinetics; QoL=quality of life; rHuPH20=recombinant human hyaluronidase PH20; SC=subcutaneous; SoA=schedule of activities; UNS=unscheduled visit; W=week

Note: Assessments indicated in gray font will only be recorded on the ARGX-113-2009 eCRF and not on the ARGX-113-2010 eCRF.

[a] Participants for whom IMP was temporarily interrupted at the time of the EoTP in ARGX-113-2009 must follow the SoA in Table 1 until the investigator has determined that it is safe for the participant to receive treatment. If the participant requires treatment with efgartigimod PH20 SC, they must follow the SoA in Table 2 as of day X (refer to Section 5.5).

[b] Participants who have not received efgartigimod PH 20 SC since baseline must follow the SoA in Table 1 until the investigator decides that efgartigimod PH20 SC should be initiated. If relapse occurs during the study, efgartigimod PH20 SC must be initiated. Participants who initiate efgartigimod PH20 SC must follow the SoA in Table 2 as of day X (refer to Section 6.3 for more details).

[c] When a participant is withdrawn from the study (for any reason listed in Section 7.2), study sites should make every effort to schedule the EDV within 7 days after the last contact with the participant and a safety follow-up visit 8 weeks after the previous contact.

[d] A UNS may be performed if the participant has (or suspects they have) new BP lesions or other issues requiring site staff intervention, such as notable weight change. At these visits, the investigator will determine whether efgartigimod PH20 SC therapy must be started/resumed and will decide which assessments to conduct based on the purpose of the UNS. If relapse occurs, IGA-BP, BPDAI, and itch NRS assessments must be performed.

[e] The urine pregnancy test is only applicable to WOCBP.

Table 2: Schedule of Activities for Participants Who Roll Over or Initiate Efgartigimod PH20 SC After Protocol Amendment 2 Is Effective, and Participants Who Stopped Receiving Efgartigimod PH20 SC After Roll Over but Before Protocol Amendment 2 Is Effective

Study period	Baseline/ rollover (W0)[a]	Day X[b]	Treatment period					Observation period[c]		Follow-up period		Other visits		Applicable protocol section(s)
Study week(s)			W1	W2	W4	W8	Every 4 W until EFG stop	Every 8 W after EFG stop	W48/ EoTP	F1[d]	F2	EDV[e]	UNS[f]	
Visit timing (relative to day X, where applicable)		X	+1 W	+2 W	+4 W	+8 W	+ Every 4 W	+ Every 8 W	W48	EoTP +4 W	EoTP +8 W			
Visit windows			±2 d	±2 d	±2 d	±7 d	±7 d	±7 d	±7 d	±3 d	±3 d			
Eligibility (baseline only)														
Informed consent	X													Section 10.1.3
Eligibility check	X													Section 5.1 Section 5.2
Safety														
Physical examination (complete)	X	X[g]							X			X		Section 8.3.1
Physical examination (brief)						X	Every 16 weeks	Every 16 weeks [h,i]		X	X		X	Section 8.3.1
Weight[j]	X	X[j]		X[j]	X[j]	X	X[j]	X	X			X	X	Section 8.3.1
Vital sign measurements	X	X		X	X	X	X	X	X	X	X	X	X	Section 8.3.1
ECG	X						Week 24	Week 24[i]	X			X		Section 8.3.3
Urine pregnancy test[k]	X	X			X	X	X	Every 4 weeks[h]	X	X	X	X		Section 8.3.5

Study period	Baseline/ rollover (W0)[a]	Day X[b]	Treatment period					Observation period[c]		Follow-up period		Other visits		Applicable protocol section(s)
Study week(s)			W1	W2	W4	W8	Every 4 W until EFG stop	Every 8 W after EFG stop	W48/ EoTP	F1[d]	F2	EDV[e]	UNS[f]	
Visit timing (relative to day X, where applicable)		X	+1 W	+2 W	+4 W	+8 W	+ Every 4 W	+ Every 8 W	W48	EoTP +4 W	EoTP +8 W			
Visit windows			±2 d	±2 d	±2 d	±7 d	±7 d	±7 d	±7 d	±3 d	±3 d			
Urinalysis	X	X		X	X	X	X	X	X	X	X	X	X	Table 7
Clinical chemistry and hematology	X	X		X	X	X	X	X	X	X	X	X	X	Table 7
GTI assessments (GTI-AIS, GTI-CWS, GTI-SL)	X					X	Every 16 weeks	Every 16 weeks [h,i]	X			X		Section 8.3.6
Concomitant therapies/procedures	Continuous monitoring													Section 6.9
AE monitoring	Continuous monitoring													Section 8.4
Substudy (selected sites): photography of BP lesions	(X)													NA
Efficacy/disease monitoring														
Disease assessment	X	X		X	X	X	X	X	X	X	X	X	X	Section 8.2.1.1
IGA-BP	X	X		X	X	X	X	X	X	X	X	X	X	Section 8.2.1.2
BPDAI	X	X		X	X	X	X	X	X	X	X	X	X	Section 8.2.1.3
Itch NRS	X	X		X	X	X	X	X	X	X	X	X	X	Section 8.2.1.4
Blood sample collection														

Study period	Baseline/ rollover (W0)[a]	Day X[b]	Treatment period					Observation period[c]		Follow-up period		Other visits		Applicable protocol section(s)
Study week(s)			W1	W2	W4	W8	Every 4 W until EFG stop	Every 8 W after EFG stop	W48/ EoTP	F1[d]	F2	EDV[e]	UNS[f]	
Visit timing (relative to day X, where applicable)		X	+1 W	+2 W	+4 W	+8 W	+ Every 4 W	+ Every 8 W	W48	EoTP +4 W	EoTP +8 W			
Visit windows			±2 d	±2 d	±2 d	±7 d	±7 d	±7 d	±7 d	±3 d	±3 d			
Immunogenicity	X	X			X	X	Every 8 weeks	X	X	X	X	X	X	Section 8.9
PD (anti-BP180, anti-BP230, [redacted]	X	X		X	X	X	X	X	X	X	X	X	X	Section 8.6
PK	X													NA
Substudy: vaccination antibody titers (serum)	Relative to the time of vaccination in ARGX-113-2009													Section 8.3.4
Substudy: vaccination antibody titers (PBMCs)	Relative to the time of vaccination in ARGX-113-2009													Section 8.3.4
Other														
Efgartigimod PH20 SC administration[l]	Once weekly								X if applicable					Section 6.3
Efgartigimod PH20 SC (self-)administration refresher training[m]	At least once during the study													Section 6.5

Study period	Baseline/ rollover (W0)[a]	Day X[b]	Treatment period					Observation period[c]		Follow-up period		Other visits		Applicable protocol section(s)
Study week(s)			W1	W2	W4	W8	Every 4 W until EFG stop	Every 8 W after EFG stop	W48/ EoTP	F1[d]	F2	EDV[e]	UNS[f]	
Visit timing (relative to day X, where applicable)		X	+1 W	+2 W	+4 W	+8 W	+ Every 4 W	+ Every 8 W	W48	EoTP +4 W	EoTP +8 W			
Visit windows			±2 d	±2 d	±2 d	±7 d	±7 d	±7 d	±7 d	±3 d	±3 d			
Monitoring of concurrent BP therapy (Definitions of Terms)	X	X	X	X	X	X	X	X	X	X	X	X	X	Section 6.9 Section 8.2.1.1
QoL questionnaires (EQ-5D-5L, DLQI, ABQoL)	X					X	Every 16 weeks	Every 16 weeks[h,i]	X			X		Section 8.2.2

ABQoL=Autoimmune Bullous Disease Quality of Life questionnaire; AE=adverse event; BP=bullous pemphigoid; BPDAI=Bullous Pemphigoid Disease Area Index; CR=complete remission; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eCRF=electronic case report form; EDV=early discontinuation visit; EFG=efgartigimod PH20 SC; efgartigimod PH20 SC=efgartigimod for SC administration coformulated with rHuPH20; EoTP=end-of-treatment period (visit); F1/F2=follow-up visits 1 and 2; GTI=Glucocorticoid Toxicity Index; GTI-AIS=GTI Aggregate Improvement Score; GTI-CWS=GTI Cumulative Worsening Score; GTI-SL=GTI Specific List; IGA-BP=Investigator Global Assessment of Bullous Pemphigoid; [redacted]NA=not applicable; NRS=numerical rating scale; OCS=oral corticosteroids; PBMC=peripheral blood mononuclear cell; PD=pharmacodynamics; PK=pharmacokinetics; PR=partial remission; QoL=quality of life; rHuPH20=recombinant human hyaluronidase PH20; SC=subcutaneous; SoA=schedule of activities; UNS=unscheduled visit; W=week

Note: Assessments indicated in gray font will only be recorded on the ARGX-113-2009 eCRF and not on the ARGX-113-2010 eCRF.

[a] The baseline visit will occur on the same day as the EoTP visit of ARGX-113-2009. All baseline assessments will be performed before administration of efgartigimod PH20 SC. Assessments do not need to be repeated if performed as part of the ARGX-113-2009 EoTP visit.

[b] Day X applies when efgartigimod PH20 SC is initiated (refer to Section 6.3). Efgartigimod PH20 SC treatment will be started on day X, which can be the same day as the day the relapse is confirmed. Subsequent visits will be relative to day X, except for the EoTP visit that will take place 48 weeks after baseline for all participants.