STATISTICAL ANALYSIS PLAN

ARGX-113-2009

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PROTOCOL HISTORY

ARGX-113-2009

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LIST OF ABBREVIATIONS

2009	ARGX-113-2009
2010	ARGX-113-2010
Ab	Antibody
ABQOL	Autoimmune Bullous Disease Quality of Life
AC	Adaptation Committee
ADA	anti-drug antibodies
ADaM	Analysis Data model
AE	Adverse Event
AESI	Adverse Events of Special Interest
AIS	aggregate improvement score
ALQ	above the limit of quantification
ANCOVA	Analysis of covariance
ATC	Anatomical-Therapeutic-Chemical
BMI	body mass index
BP	Bullous Pemphigoid
bpm	beats per minute
BPDAI	Bullous Pemphigoid Disease Area Index
BLQ	Below the limit of quantification
CDA	Control of Disease Activity
C-GTI	Composite Glucocorticoid Toxicity Index
CMH	Cochran-Mantel-Haenszel
COD	Cumulative OCS dose
CR	Complete Remission
CRF	Case Report Form
CRmin	complete remission on minimal OCS therapy
CRoff	complete remission off OCS therapy
CSP	Clinical Study Protocol
CTCAE	Common Terminology Criteria for Adverse Events
CWS	cumulative worsening score
DBP	Diastolic blood pressure
DLQI	Dermatology Life Quality Index

DY	relative day
ECG	Electrocardiogram
EFG	Efgartigimod
EoS	End of Study
EoTP	End of Treatment Period visit
ESD	Early Study Discontinuation visit
ETD	Early Treatment Discontinuation visit
EQ-5D-5L	EuroQol 5-Dimension 5-Level Scale
FAS	Full analysis set
FU	Follow-up
GM	Geometric mean
GSD	Geometric standard deviation
GTI	Glucocorticoid Toxicity Index
GTI-SL	Glucocorticoid Toxicity Index – Specific List
HR	Heart rate
IA	Interim Analysis
ICE	Intercurrent event
ICF	Informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IgG	Immunoglobin G
[redacted]	[redacted]
IGA-BP	Investigator Global Assessment of Bullous Pemphigoid
IMP	Investigational medicinal product
IM	intramuscular
IRR	Injection-related reaction
ISR	Injection site reaction
IV	intravenous
IVIg	immunoglobulins given intravenously
LRV	Lower reference value
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	Mixed model for repeated measurements
NAb	Neutralizing antibody

NCOD	Normalized cumulative OCS dose
NCI	National Cancer Institute
NRS	Numerical Rating Scale
OCS	Oral corticosteroid
OLE	Open-label extension
PD	Pharmacodynamics
PK	Pharmacokinetics
PBO	Placebo
PR	Partial Remission
PRO	participant-reported outcome
PT	preferred term
QoL	Quality of life
QTc	corrected QT interval
QTcF	Fridericia's corrected QT interval
rHuPH20	recombinant human hyaluronidase PH20
SAE	Serious Adverse Event
SAF	Safety analysis set
SAP	Statistical analysis plan
SBP	Systolic blood pressure
SC	Subcutaneous
SCR	all screened participants analysis set
SD	Standard deviation
SE	Standard error
SGS CR	SGS Clinical Research
SOC	system organ class
SOP	Standard operating procedure
STAT	Statistics
TEAE	Treatment-emergent adverse event
TCS	Topical corticosteroid
TV	Target value
WI	Work instruction
WHODD	World Health Organization Drug Dictionary

DEFINITION OF TERMS

case report form (CRF)	A printed, optical, or electronic document in which protocol required information is recorded for each study participant.
Complete remission (CR)	The absence of new lesions, complete healing of existing lesions, and absence of pruritus.
Complete remission on minimal OCS therapy (CRmin)	Being in 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.
Control of disease activity (CDA)	The point at which new lesions cease to form and established lesions begin to heal, and pruritic symptoms start to abate.
Display	Analysis table, figure or listing.
Minimal OCS therapy	An oral prednisone dosage of ≤0.10 mg/kg/day (or an equivalent dose of another OCS).
Phase	Interval of time in the planned conduct of a study that is associated with a specific purpose: for example, screening, treatment, follow-up.
IMP	Pharmaceutical form of an active ingredient or placebo, being tested or used as a reference in a clinical study.
Partial remission (PR)	The presence of only new transient lesions.
Relapse	Appearance of 3 or more new lesions a month (blisters, eczematous lesions, or urticarial plaques),

	or at least 1 large (>10 cm diameter) eczematous lesion or urticarial plaque that does not heal within 1 week, or extension of established lesions or daily pruritus in a participant who has achieved CDA
Transient lesions	New lesions that heal within 1 week or pruritus lasting less than 1 week.
Treatment failure	The absence of CDA after being administered oral prednisone at 0.75 mg/kg/day (or equivalent OCS) for 3 weeks. The investigator has the option to add a fourth week of therapy with oral prednisone 0.75 or 1 mg/kg/day (or equivalent) (based on clinical judgment) before declaring treatment failure
Treatment-emergent abnormality	Any post-baseline abnormality that was not present at baseline (e.g., hemoglobin normal at baseline and grade 1 post-baseline; glucose low at baseline and high post-baseline; QTcF]450; 480] ms at baseline and >500 ms post-baseline).

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1. INTRODUCTION

This statistical analysis plan (SAP) describes the interim and final statistical analyses to be performed for study ARGX-113-2009 (BE-80-2100382).

The final analysis of part A data will be performed after its last participant completes their last visit. Similarly, the final analysis of part B data will be performed after its last participant completes their last visit. Additionally, at the part B final analysis, all analyses will be performed on the pooled Part A and B data.

This SAP covers the efficacy (including participant-reported outcome [PRO] measures and quality of life [QoL]), pharmacokinetic (PK), pharmacodynamic (PD), immunogenicity, general characteristics and safety parts of the statistical analysis. It specifies the analysis displays to be presented and describes the methods and procedures in a more elaborated way than in the statistical methods section of the Clinical Study Protocol (CSP).

Analyses of exploratory endpoints or substudy endpoints are not in scope of this SAP.

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

1.1 STUDY OBJECTIVES

1.1.1 Part A

The primary objective of part A of study 2009 is to evaluate the efficacy of Efgartigimod (EFG) PH20 SC on achieving sustained remission in the treatment of participants with Bullous Pemphigoid (BP).

The secondary objectives of Part A are:

- To evaluate the corticosteroid-sparing effects of EFG PH20 SC in participants with BP
- To characterize the overall efficacy of EFG PH20 SC in the treatment of participants with BP
- To evaluate the efficacy of EFG PH20 SC in preventing relapse of BP
- To evaluate the effect of EFG PH20 SC on pruritus in participants with BP
- To assess the safety and tolerability of EFG PH20 SC administered to participants with BP
- To assess glucocorticoid-associated morbidity and evaluate the impact of EFG PH20 SC in reduction of glucocorticoid toxicity
- To evaluate the effects of EFG PH20 SC on the QoL of participants with BP
- To evaluate the pharmacokinetics of EFG PH20 SC in participants with BP
- To evaluate the pharmacodynamics of EFG PH20 SC in participants with BP
- To evaluate the immunogenicity of EFG PH20 SC in participants with BP

- To evaluate the competency of participants or caregivers to (self-)administer EFG PH20 SC

The exploratory objectives include the following:

- To further explore the pharmacodynamics of EFG PH20 SC in participants with BP

1.1.2 Part B

According to the protocol, the primary objective of part B of study 2009 is to evaluate the efficacy of EFG PH20 SC on achieving sustained remission in the treatment of participants with BP.

The secondary objectives of Part B are:

- To evaluate the corticosteroid-sparing effects of EFG PH20 SC in participants with BP
- To characterize the overall efficacy of EFG PH20 SC in the treatment of participants with BP
- To evaluate the efficacy of EFG PH20 SC in preventing relapse of BP
- To characterize the efficacy of EFG PH20 SC in the treatment of participants with BP
- To evaluate the effect of EFG PH20 SC on pruritus in participants with BP
- To further characterize the overall efficacy of EFG PH20 SC in the treatment of participants with BP
- To assess the safety and tolerability of EFG PH20 SC administered to participants with BP
- To assess glucocorticoid-associated morbidity and evaluate the impact of EFG PH20 SC in reduction of glucocorticoid toxicity
- To evaluate the effects of EFG PH20 SC on the QoL of participants with BP
- To evaluate the pharmacokinetics of EFG PH20 SC in participants with BP
- To evaluate the pharmacodynamics of EFG PH20 SC in participants with BP
- To evaluate the immunogenicity of EFG PH20 SC in participants with BP
- To evaluate the competency of participants or caregivers to (self-)administer EFG PH20 SC

The exploratory objectives include the following:

- To further explore the pharmacodynamics of EFG PH20 SC in participants with BP

1.2 STUDY DESIGN

Study 2009 is an operationally seamless 2-part, phase 2/3, prospective, global, multicenter, randomized, double-blinded, placebo (PBO) -controlled study to investigate the efficacy, safety, tolerability, immunogenicity, PRO measures (including QoL assessments), PK, and PD of EFG PH20 SC in adult participants with moderate-to-severe BP.

During both parts of the study, participants will be administered investigational medicinal product (IMP: EFG PH20 SC or PBO PH20 SC) once weekly for 36 weeks. All participants will also receive concurrent therapy with oral corticosteroids (OCS), i.e., prednisone at a starting dosage of 0.5 mg/kg/day at baseline, or an alternate OCS at an equivalent dose strength. The OCS dosage will be adjusted according to each participant's BP disease status throughout the study.

Part A is a phase 2, proof-of-concept study in which approximately 40 adult participants with moderate-to-severe BP will be randomly assigned to treatment with either EFG PH20 SC or PBO PH20 SC. The main goal of part A is to determine whether EFG PH20 SC is effective in the treatment of participants with BP via assessment of the study's primary endpoint: the proportion of participants who are in complete remission (CR) while receiving efgartigimod PH20 SC or placebo and have been off OCS therapy for ≥8 weeks at week 36. Other part A objectives and endpoints are listed in section 1.1.1.

An interim analysis (IA) will be conducted from data obtained from all part A participants through the week 26 visit. The IA will be conducted to assess the primary endpoint, assess several of the study's secondary endpoints, confirm the appropriate sample size for part B of the study, and determine whether the efficacy results observed through week 26 warrant continued study of EFG PH20 SC for the treatment of participants with BP (futility analysis).

The final analysis of part A data will be performed after its last participant completes their last visit.

Part B is a phase 3, confirmatory study in which approximately 120 adult participants with moderate-to-severe BP will be randomly assigned to treatment with either EFG PH20 SC or PBO PH20 SC. The main goal of part B is to confirm the results obtained for the primary endpoint from part A (the proportion of participants who are in CR while receiving efgartigimod PH20 SC or placebo and have been off OCS therapy for ≥8 weeks at week 36), but in a separate and larger group of participants. Other part B objectives and endpoints are listed in section 1.1.2. The proposed order of the key secondary endpoints for part B may be adjusted based on the results obtained in the IA of part A of the study.

1.3 EXPECTED SAMPLE SIZE

Part A: Approximately 40 adult participants with moderate-to-severe BP will be randomly assigned in a 1:1 ratio to one of the following study intervention groups:

- EFG PH20 SC
- PBO PH20 SC

Part B: Approximately 120 adult participants with moderate-to- severe BP will be randomly assigned in a 1:1 ratio to one of the following study intervention groups:

- EFG PH20 SC
- PBO PH20 SC

Participants who reach the End of Treatment Period (EoTP) visit (week 36) will be offered the option to either roll over into a long-term, open-label extension (OLE) study (ARGX-113-2010) or complete a 7-week treatment-free follow-up period.

1.4 INTERIM ANALYSIS

An IA will be performed during part A of the study. Results of the IA will help supporting the sponsor's decision whether to continue part B of the study as currently designed, modify the sample size for part B, or discontinue the study (both parts A and B) due to lack of efficacy.

The IA of part A will be performed using data collected from all of its participants through the data cutoff time point (defined as the last participant in part A reaching week 26).

Both part A and part B of the study are randomized and double-blinded. Section 1.4.4 provides the measures to ensure that blinding and integrity of the part A dataset is maintained while the unblinded IA is being performed.

1.4.1 Futility analysis

A futility analysis will be performed using the analysis of the primary endpoint at the IA cutoff time point.

1.4.1.1 ENDPOINT USED FOR THE FUTILITY ANALYSIS

The primary endpoint will be used for the futility analysis. The primary endpoint is a binary endpoint. A subject is considered a responder (Y) if he or she is in CR while receiving efgartigimod PH20 SC or placebo and is off OCS therapy for ≥8 weeks at week 36. Otherwise, the subject is considered a non-responder (N).

1.4.1.2 MISSING DATA IMPUTATION

All missing data imputation rules specified in Section 4.1.2.2 for the primary endpoint will be applied. At the IA cutoff time point, some subjects will have not completed the treatment period. As specified in Section 4.1.2.2, absence of data due to premature study termination or a subject failing to perform the disease assessment at week 36 will be handled using the composite strategy (i.e., subject considered as non-responder).

However, for the IA one more imputation rule is required to handle the fact that some subjects will still be ongoing by the time of data cutoff. For ongoing subjects only, a surrogate endpoint will be defined as 'being in CR while receiving efgartigimod PH20 SC or placebo and is off OCS therapy for ≥8 weeks at last visit'. Derivation of this endpoint follows the same rules and strategies planned in Section 4.1.2.2for the primary endpoint but replacing 'week 36' by 'week X' which will represent subject's last visit before cutoff time point.

For ongoing subjects, the above surrogate endpoint will be used as a proxy (substitute) of the primary endpoint at the IA.

Also, for key secondary endpoints with evaluation at week 36, a surrogate endpoint will be used replacing 'week 36' by 'week X' which will represent subject's last visit before cutoff time point.

1.4.1.3 STATISTICAL ANALYSIS

The primary endpoint will be analyzed as detailed in Section 4.1.2. The primary estimand (composite strategy) will be used. In particular, the futility decision-making algorithms will be implemented instead of the estimated Klingenberg strata-adjusted difference in proportions. For this statistic, a standard two-sided 95% confidence interval will be first produced as plan for the final analysis. However, these values are not the ones to be used by futility analysis recommendation algorithm (Frewer et al.). These other confidence interval limits will also be obtained at the IA using the same SAS code (Proc FREQ) proposed for the final analysis:

- Lower limit of the two-sided 60% confidence interval. This value will be denoted as LL80 because, if this value is interpreted using Bayesian thinking, we could say that the treatment effect (in the absolute difference scale) will be greater than LL80 with a (posterior) probability > 80%.
- Upper limit of the two-sided 80% confidence interval. This value will be denoted as UL90 because, it could be interpreted that the absolute difference (EFG vs. PBO) will be smaller than UL90 with a probability > 90%.

1.4.1.4 FUTILITY ANALYSIS RECOMMENDATION ALGORITHM

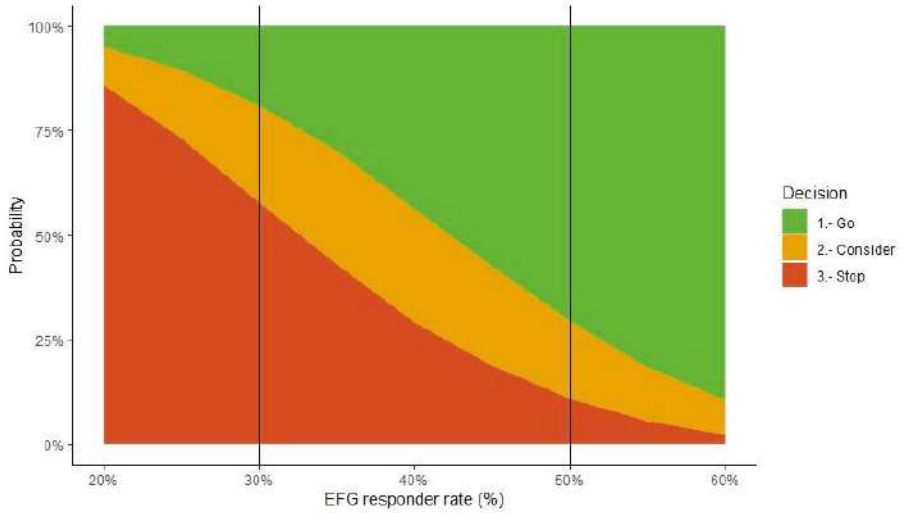
The target value (TV) was defined in the CSP as an absolute treatment difference (EFG vs. PBO) of 30%. Similarly, the lower reference value (LRV) was defined as an absolute treatment difference (EFG vs. PBO) of 10%.

The futility analysis recommendation algorithm is as follows:

- The recommendation will be to continue the study ("Go") if LL80 > LRV and UL90 > TV.
- The recommendation will be to stop the study ("Stop") if UL90 ≤ TV.
- The outcome will be considered inconclusive ("Consider") otherwise.

Figure 1 illustrates the probability of each of the planned recommendations for each value of the EFG responder rate while holding the PBO rate to 20%.

Figure 1. Probability of recommendation vs. EFG responder rate (PBO rate fixed at 20%)



In case the recommendation is 'consider', the analysis of the key secondary endpoints will be reviewed to make a final decision.

This document considers the above as recommendations and acknowledges the possibility of deviations from the above algorithm. If the recommendation is 'stop', it is also possible that the sponsor decides to not stop the study (e.g., if the analysis of key secondary endpoint suggests a clinically meaningful effect).

1.4.2 Sample size re-adjustment

1.4.2.1 STATISTICAL CALCULATION

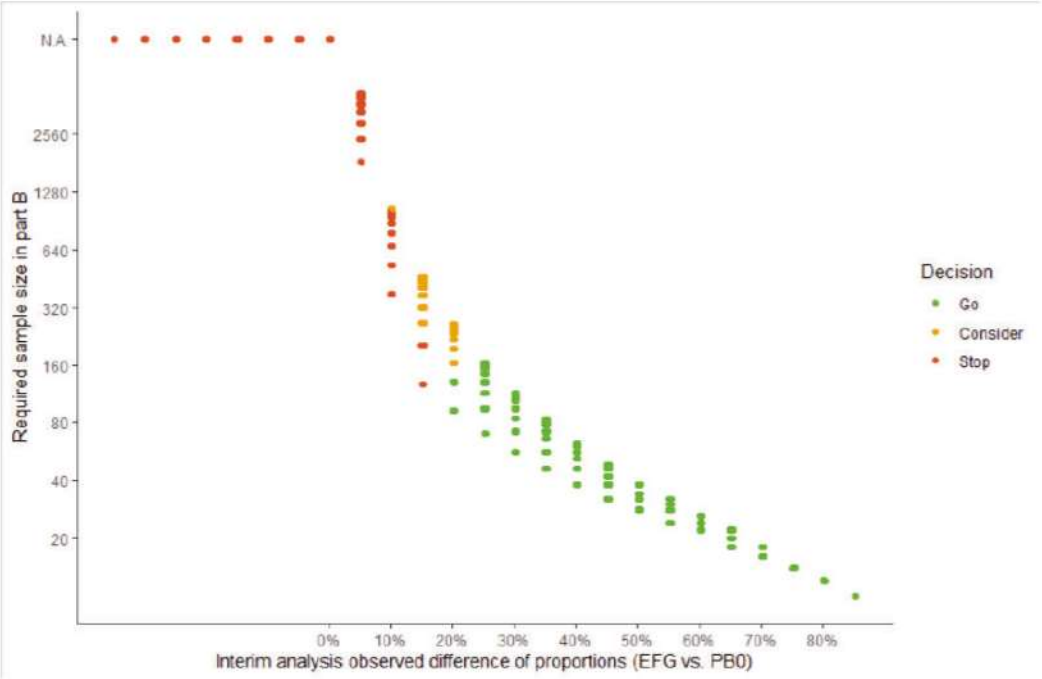
The unadjusted proportions of primary endpoint response (after implementing the proxy imputation method defined above) will be used to calculate the sample size required in part B to achieve a 90% power.

The following SAS script will be used to obtain the required sample size:

```
proc power;
 twosamplefreq test = pchi
 groupproportions = (0.X 0.Y)
 ntotal = .
 power = 0.9;
run;
```

Figure 2 illustrates the distribution of the obtained required sample sizes vs. the observed treatment difference after using 100,000 simulations of part A trial (n = 20 per arm) assuming 20% rate with PBO and 50% rate with EFG.

Figure 2. Observed absolute difference in part A and resulting required sample size in part B



1.4.2.2 SAMPLE SIZE RE-ASSESSMENT ALGORITHM

The sample-size reassessment recommendation algorithm is as follows:

- If the obtained required sample size is smaller or equal to the sample size planned in the protocol (n = 120 for part B), then the sample size of part B will be maintained as planned in the protocol
- If the obtained required sample size is > 120, then part B sample size may be increased. This document acknowledges the possibility of not expanding the sample size of part B to the number obtained if that number is too large from a feasibility perspective

1.4.3 Control of the type I error for key secondary endpoints

1.4.3.1 STATISTICAL ANALYSIS

The following five key secondary endpoints will be analyzed at the IA as planned in Section 4.1.3:

- Normalized cumulative OCS dose (NCOD) over the on IMP treatment period
- Achieving a score of 0 on Investigator Global Assessment of Bullous Pemphigoid (IGA-BP) while receiving efgartigimod PH20 SC or placebo and have been off OCS therapy for ≥8 weeks at week 36
- Achieving control of disease activity (CDA) while receiving efgartigimod PH20 SC or placebo and remain free of relapse through week 36
- Achieving CR while receiving efgartigimod PH20 SC or placebo and have been receiving minimal OCS therapy for ≥8 weeks at week 36
- Change from baseline in the 24-hour average itch score

For each of the above key secondary endpoints, the primary estimand and primary estimator will be obtained only.

1.4.3.2 Algorithm to adapt the methodology to control type I error for key secondary endpoints

The endpoints will be sorted in ascending order (i.e., smallest p-value first, largest p-value last). This order will be used in the final analysis of part B to test sequentially the key secondary endpoints (fixed sequence procedure).

1.4.4 Data access plan

To preserve the integrity of Part A data, the dissemination of IA results will be limited. In this section, further details on this are given.

1.4.4.1 Personnel who will perform the interim analyses

The biometrics contract research organization (SGS) will appoint a separate unblinded biostatistician to perform the unblinded IA and release it to the recipients as defined below.

The identity of this person will be documented and archived in the biometrics ARGX-113-2009 eTMF before executing the IA.

1.4.4.2 Personnel who will have access to interim results

Results of the IA of part A will not be shared with sites personnel and investigators. Access to the results of the IA will also be restricted within the sponsor. An unblinded Adaptation Committee (AC) will be established. No permanent members of the ARGX-113-2009 Clinical Trial Team (CTT) will be part of the AC. No members outside the AC will have access to unblinded data.

The exact list of members of the AC will be documented and archived in the Argenx ARGX-113-2009 eTMF (Veeva) before executing the IA.

1.4.4.3 Access control

SGS will install a secured transfer folder with only access for the unblinded biostatistician and the unblinded AC.

1.4.4.4 INFORMATION TO BE DISSEMINATED OUTSIDE THE AC

The AC will not share the results of the IA with any other party. Only the recommendations will be sent to the ARGX-113-2009 Clinical Trial Team (CTT) or the PV & PB Clinical Development Team (CDT).

1.4.4.5 RECIPIENT OF THE RECOMMENDATION

The ARGX-113-2009 Clinical Trial Team (CTT) or the PV & PB Clinical Development Team (CDT) are the primary recipients of the recommendations since these teams are accountable to implement them.

The recommendations (excluding the results themselves) may also be further propagated (e.g., to sites and investigators).

1.5 SOFTWARE

SAS version 9.4 or later will be used for programming the interim and final analysis.

1.6 VALIDATION MODEL

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

Analysis Data Model (ADaM) datasets (except subject-level analysis dataset [ADSL]), analysis tables, figures and listings will be reviewed by an independent person (model B validation). ADaM datasets ADSL, ADAE, ADLB and the primary endpoint will be reviewed through independent programming (model C validation).

2. GENERAL METHODOLOGY

2.1 ANALYSIS SETS

2.1.1 Analysis sets

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

All screened participants set (SCR):	participants who signed the informed consent form (ICF) to participate in the study
Full analysis set (FAS):	all participants who were randomized into the study
Safety analysis set (SAF):	all randomized participants who received at least one dose of IMP
Per Protocol set (PP):	All FAS analysis set participants who did not have an important protocol deviation impacting the efficacy results. The determination of the per-protocol population will be finalized and documented prior to database lock and unblinding.
PK analysis set (PK)	all participants in the safety analysis set for whom at least one post-baseline serum PK concentration is available, excluding placebo participants
PD analysis set (PD)	all participants in the safety analysis set for whom at least one post-baseline serum PD result is available

Note: Having signed an informed consent is defined as having a complete informed consent signature date in the database.

The efficacy analyses will be done on the FAS analysis set. Sensitivity analyses of primary and key secondary efficacy endpoints will be done on the PP analysis set. The general characteristics and safety analyses will be done on the safety analysis set. PK analysis will be performed on the PK analysis set. PD analysis will be done on the PD analysis set.

2.1.2 As planned versus as actual analysis

All analyses on the FAS and PP analysis set will be performed according to the planned randomization group. All other analyses will be performed according to the actual received IMP.

2.2 PHASES AND TIME POINTS

2.2.1 Analysis phases

All events and assessments will be allocated to phases as defined below.

Table 1: Phase and period definition

Phase	Period	Start	End[2]
Screening		Date of signing the informed consent form (ICF), with 00:00 added as time part	First IMP administration date/time – 1 minute
Treatment [1]	On IMP treatment	First IMP administration date/time	Last IMP administration date with 23:59 added as time part. For participants with ongoing treatment at the time of the interim analysis, date of database cut-off with 23:59 added as time part.
	Off IMP treatment	End of on IMP treatment period + 1 minute	For participants who roll-over to study 2010, date of trial termination (of study 2009), with 23:59 added as time part. For participants who do not roll-over to study 2010 and have an EoTP visit: date of EoTP visit, with 23:59 added as time part. For participants who do not roll-over to study 2010 and have no EoTP visit, date of trial termination (of study 2009), with 23:59 added as time part. For participants ongoing in the study at the time of the interim analysis, date of database cut-off with 23:59 added as time part.
Following phase is only applicable for participants who had the EoTP visit and who do not roll-over to study 2010.			
Follow-up (FU)		End of treatment phase + 1 minute	Date of trial termination (of study 2009), with 23:59 added as time part. For participants ongoing in the study at the time of the interim analysis, date of database cut-off with 23:59 added as time part.

[1] Although the baseline falls within the Screening phase, it will be allocated to the Treatment phase in ADaM.
[2] End of the treatment phase is the maximum of the end of the on IMP treatment period and off IMP treatment period.

Adverse events will be allocated to phases as described in section 5.1.2. Concomitant medications will be allocated to phases and periods as described in section3.4.2. All other assessments will be allocated to phases based on the assessment date/time.

In case of (partially) missing date/time fields disabling allocation, information from the visit label and the protocol schedule of activities will be used to allocate to the correct phase. If this is not possible, assessments will be allocated to the treatment

phase unless the available parts of the assessments start or stop date/time provide evidence for allocating to a non-treatment phase.

2.2.2 Baseline and change from baseline

The baseline value will be the last available and non-missing value prior to the first dose of IMP. For immunogenicity assessments, values resulting in an unevaluable ADA/NAb status are given the lowest priority when the baseline selection is made. Assessments on day 1 without time information or with time exactly equal to time of first IMP administration, and which are planned pre-dose will be considered as pre-dose. For GTI assessments, the baseline value will be the last available and non-missing assessment prior or equal to analysis relative day 7 (see section 2.2.3).

Change from baseline at time point t is defined as:

value at time point t – baseline value

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

100*([value at time point t – baseline value] / baseline value)

2.2.3 Relative day

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

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

Unless stated otherwise, the reference date is the date of first administration of IMP

2.2.4 Analysis visits

For longitudinal responses, all assessments, including unscheduled assessments, will be allocated to analysis windows as defined below. Tables and listings will present the analysis windows, not the case report form (CRF) visits. Allocation of assessments will be done using their relative day (DY, see section 2.2.3). Visit window limits are the mid-point between the scheduled study days for each visit.

Table 2: Analysis visits (for assessments other than disease status)

Phase	Analysis window	Target DY	Lower limit DY	Upper limit DY
Screening	Screening[2]	-14	-INF	1
Treatment	Baseline	1	-INF	1[1]
	Week 1	8	1[1]	11
	Week 2	15	12	18
	Week 3	22	19	25
	Week 4	29	26	43
	Week 8	57	44	71
	Week 12	85	72	99

	Week 16	113	100	127
	Week 20	141	128	155
	Week 24	169	156	176
	Week 26[2]	183	177	190
	Week 28	197	191	211
	Week 32	225	212	239
	Week 36[2]	253	240	End of treatment phase
Follow-up [3]	FU Week 3	21	1	35
	FU Week 7	49	36	End of FU phase

[1] An assessment on Day 1 will be attributed to Baseline in case it is before the first administration, to Week 1 otherwise.
[2] ECG is only captured at screening, W26, W36, ETD and ESD.
[3] The start date of the follow-up phase will be used as a reference date for the DY calculation.

Table 3: Analysis visits (for disease status assessments)

Phase	Analysis window	Target DY	Lower limit DY	Upper limit DY
Screening	Screening	-14	-INF	1
Treatment	Baseline	1	-INF	1[1]
	Week 1	8	1[1]	11
	Week 2	15	12	18
	Week 3	22	19	25
	Week 4	29	26	32
	Week 5	36	33	39
	Week 6	43	40	46
	…			
	Week X (X = 7 to 34)	X*7+1	X*7-2	X*7+4
	…			
	Week 35	246	243	249
	Week 36[2]	253	250	End of treatment phase
Follow-up [2]	FU Week 3	21	1	35
	FU Week 7	49	36	End of FU phase

[1] An assessment on Day 1 will be attributed to Baseline in case it is before the first administration, to Week 1 otherwise.
[2] The start date of the follow-up phase will be used as a reference date for the DY calculation.

Per parameter and analysis window, the value closest to the target DY will be used in analysis tables, other values will only be listed. If more than one value is located at the same distance from the target, then the latest in time will be selected. The value latest in time will be identified using, in order of preference, the assessment date and time, the visit label or the group identifier (if applicable). For immunogenicity assessments, values resulting in an unevaluable ADA/rHuPH20 Ab status are given the lowest priority when the selection is made. For other assessments, missing values are removed before 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 considered in the per-time point analysis. Note that these assessments are included in analyses on worst-case.

Special windowing is applied for some parameters:

- For Autoimmune Bullous Disease Quality of life (ABQOL), Dermatology Life Quality Index (DLQI) and EuroQoL 5-Dimension 5-Levels- (EQ-5D-5L) scale: Additional visit window: Last Assessment: last record post baseline.
- For Glucocorticoid Toxicity Index (GTI): Additional visit window: Last Assessment: last record post baseline.
- For PK, additional assessment on day 10. See also section 4.2.1.

2.2.5 Worst-case

A worst-case analysis visit will be created for parameters for which abnormalities and/or toxicity grades are defined to summarize values considered as the worst-case. For abnormalities it is derived per parameter and in case both the lowest and the highest values are considered abnormal, a participant can have 2 worst-case analysis visits for a same parameter. For toxicity grades the worst-case is the value associated to the highest toxicity grade and is derived per parameter and toxicity direction (hypo/hyper).

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

2.3 IMPUTATION AND ROUNDING RULES

2.3.1 Missing values

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

2.3.2 *Handling partially or completely missing dates in calculations*

Partially missing date of BP disease onset / diagnosis will be imputed as follows:

- Missing day of disease onset / diagnosis will be imputed with first day of the month
- Missing day and month of disease onset / diagnosis will be imputed with January 1st.

If the imputed date of diagnosis is before the date of disease onset, date of diagnosis will be imputed with date of disease onset.

If the imputed date of disease onset is after the date of diagnosis, date of disease onset will be imputed with date of diagnosis.

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, the date of trial termination, or the cut-off date, whichever comes first.
- Missing day and month will be imputed with 31DEC, the date of trial termination, or the cut-off date, whichever comes first.
- Completely missing end date will be considered as still ongoing at trial termination or the cut-off date.

2.3.3 *Values below or above a threshold*

Safety values expressed as below (or above) the detection limit will be imputed by the value of the detection limit itself. Listings will always show the non-imputed values.

Total IgG [redacted] values expressed as below or above the limit of quantification (BLQ or ALQ, respectively) will not be imputed.

For anti-BP180 and anti-BP230, see section 4.3.2.

Listings will always show the non-imputed results.

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

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

Antibodies (Ab) against rHuPH20: titer of positive rHuPH20 Ab samples reported as 'negative titer' will be imputed by 5.

Neutralizing antibodies (NAb) against rHuPH20: titer of positive rHuPH20 NAb samples reported as 'negative titer' will be imputed by 100.

Listings will always present 'negative titer'.

2.3.4 Rounding of derived variables

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

- Cumulative OCS dose and OCS dose at baseline will be rounded to 0 decimals.
- Time since diagnosis will be rounded to 1 decimal.
- Normalized cumulative OCS dose (NCOD) and OCS dose per body weight at baseline will be rounded to 2 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

To support the summary document of the J-MAA submission, all descriptive outputs described in this SAP will be repeated for the Japanese population (versus Non-Japanese / Overall population). The definition of a Japanese participant in the protocol is a participant whose parents and 4 grandparents are Japanese, who has the Japanese nationality, was born in Japan, has not lived outside of Japan for a total of >10 years, and currently lives in Japan.

To support the marketing authorization application in China, all descriptive outputs in this SAP will be repeated for the Chinese population (participants from Chinese centers).
These additional descriptive outputs for the Japanese and Chinese populations will not be included in the FDA/EMA submission.

2.4.1 Calculation of descriptive statistics and percentages

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

Descriptive statistics will include the number of non-missing data points, the arithmetic mean, the standard deviation (SD), the standard error (SE), the 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, geometric mean (GM) and geometric standard deviation (GSD) will be presented with one more decimal place than the individual values (with a maximum of 4 decimal places). SD and SE will be presented with two more decimal places than the individual values (with a maximum of 5 decimal places). Minimum and maximum will be presented with the same number of decimal places than the individual values (with a maximum of 3 decimal places).

Percent changes from baseline are presented with one decimal for the individual values, minimum and maximum, two decimals for mean, median, Q1, Q3, GM and GSD, and with 3 decimals for SD and SE.

Descriptive statistics for PK concentrations will include n (number of observed values), arithmetic mean, SD, median, minimum and maximum, the coefficient of variation (CV%), the GM, and geometric CV%. Serum concentrations will be presented with 3 significant digits. If more than half of the values are BLQ, arithmetic mean will be set to BLQ and SD and CV% will not be calculated.

For event-type safety data, the number and percentage of participants with an event, and the number of events will be shown. The denominator will be all participants in the analysis set per treatment and phase.

For frequency tabulations and cross-tabulations, the denominator will be all participants in the analysis set per treatment. For tables where results are shown by analysis visit, the denominator will be all participants in the analysis set per treatment and per analysis visit. Missing values will never be included in the denominator count when computing percentages. For cross-tabulations of post-baseline results versus baseline results, a 'missing' category will be shown for baseline results if applicable.

2.4.2 Presentation of treatments

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

- Efgartigimod PH20 SC
- Placebo

When deemed necessary for presentation purposes, treatment labels can be abbreviated to:

- EFG PH20 SC
- PBO

In the general characteristics analysis, a grand total will be added to summarize all participants over treatments. Grand totals will be shown last.

2.4.3 Order in tables and listings

All tables and figures will be presented per treatment, unless specified otherwise. In by-visit displays, worst-case will be shown last, if present. All tables and figures will be presented separately for Part A, Part B and pooled Part A and B, with Part A (or B or A+B) indicated in the first title and included in output file names as _A (or _B or _AB). Listings will be presented for Part A and Part B participants separately.

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

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

In tables showing several parameters, each parameter will begin on a new page and parameters will be sorted alphabetically, within the parameter category if applicable.

The Efgartigimod PH20 SC treatment group will always be shown first, then the Placebo treatment group.

3. GENERAL CHARACTERISTICS ANALYSES

3.1 PARTICIPANT DISPOSITION

The following participant data will be tabulated:

- The number of participants in each analysis set.
- The number and percentage of participants in each country and site.
- The number and percentage of participants for each phase and analysis visit.
- Descriptive statistics of the phase duration, calculated as phase end date – phase start date + 1 day.
- Descriptive statistics of the period duration, calculated as period end date – period start date + 1 day.
- The number and percentage of participants who completed or discontinued the study as documented on the study termination page and the number and percentage of participants for each study discontinuation reason.
- The number and percentage of participants who completed or discontinued the treatment as documented on the end of treatment page and the number and percentage of participants for each treatment discontinuation reason.
- The number and percentage of participants who roll over to study ARGX-113-2010 and the number and percentage of participants by reason not rolling over (i.e., 'not eligible', 'not willing to' and 'other').
- The number and percentage of participants with important and non-important protocol deviations.

Listings will be created for:

- Treatment allocation and 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.
- Violations on eligibility criteria.
- Screen failures (with reason for screen failure) and other non-treated participants (randomized but not treated).
- Any comments related to COVID-19 infections during the study.

3.2 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

3.2.1 Available data

The following parameters will be available:

- Demographics: sex at birth, age at informed consent, race and ethnicity (if collection permitted), childbearing potential, date of last menses (listed only), height, weight and BMI at screening, year of birth (listed only), date of signing ICF (listed only).
- Baseline disease characteristics: date of BP disease onset and diagnosis (listed only), BP disease history (newly diagnosed / relapsing), number of relapses in participant's history, Karnofsky performance status score, BPDAI activity and total score at baseline, BP disease severity at screening (moderate / severe; as determined by IGA-BP=3/4 and collected on the Disease History form), IGA-BP at baseline (collected on IGA-BP form), itch NRS 24-hour average and worst score at baseline, OCS dose at baseline (mg), OCS dose per body weight at baseline (mg/kg), anti-BP180 antibodies at baseline, anti-BP230 antibodies at baseline.

3.2.2 Derivation rules

The following parameters will be derived:

- Age at informed consent, categorized (18 - <65, 65 - <75, 75 - <85, >=85)
- BMI at screening, categorized (Underweight: < 18.5 kg/m^2, Normal weight: 18.5 -< 25 kg/m^2, Overweight: 25 -< 30 kg/m^2, Obese: >= 30 kg/m^2)
- Race, categorized (Asian, Black or African American, White, Other)
- BPDAI activity score at baseline, categorized: <20, 20-56, >56
- Anti-BP180 antibodies at baseline, categorized: positive (≥20 RU/mL), negative (<20 RU/mL)
- Anti-BP230 antibodies at baseline, categorized: positive (≥20 RU/mL), negative (<20 RU/mL)
- Both anti-BP180 and anti-BP230 antibodies positive: if both of the above are positive
- Time since BP disease diagnosis (months): (date of first IMP – date of diagnosis)*12/365.25

Notes:

  - Partially missing dates will be imputed as detailed in section 2.3.2.
  - Result will be rounded as detailed in section 2.3.4.

- Geographical region: Asia (Japan, China), North America (US, Canada), EU region+UK (EU/EEA/EFTA/UK), Rest of world
- OCS dose (per body weight) at baseline: since day 1 can be considered as a transition day, OCS dose on day 2 will be used as baseline.

3.2.3 Presentation of results

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

Baseline disease characteristics will be presented using descriptive statistics for time since diagnosis, number of relapses, BPDAI activity and BPDAI total score at baseline, itch NRS 24-hour average and worst score at baseline, Karnofsky performance score, anti-BP180 and anti-BP230 antibodies; frequency tabulations for all other parameters.

All demographic data and baseline disease characteristics will be listed.

3.3 MEDICAL HISTORY AND CONCOMITANT DISEASES

3.3.1 Available data

Medical history findings are coded using the medical dictionary for regulatory activities (MedDRA) into system organ classes (SOC) and preferred terms (PT). For

each finding, a start and stop date or ongoing flag is collected. The MedDRA version will be updated to the latest one until the database lock of 2009.

3.3.2 Derivation rules

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

Concomitant disease: medical history condition still ongoing at screening.

3.3.3 Presentation of results

Medical history and concomitant diseases will be tabulated separately. Both tables will show:

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

All medical history (not ongoing at screening) and concomitant disease (still ongoing at screening) data will be listed.

3.4 PRIOR AND CONCOMITANT THERAPIES AND PROCEDURES

3.4.1 Available data

Following therapies are collected in the CRF:

- BP therapy history (until baseline)
- Vaccination history
- OCS administration
- Prior and concomitant therapies, including BP rescue therapies
- Procedures

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 date or prior flag and stop date or ongoing flag 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.

3.4.2 Derivation rules

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

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

Based on their start and stop date, therapies and procedures will be allocated into one or both of the following categories:

- Prior: any therapy/procedure that strictly started before the first IMP.
- Concomitant: any therapy/procedure that was taken on or after the first IMP.

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

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

Under certain conditions (see CTP section 6.8.3), participants will discontinue IMP treatment and may start rescue therapy. Rescue therapy may include OCS, TCS, immunosuppressants, tetracyclines with or without nicotinamide, dapsone, or IVIg.

Intercurrent events (ICE) of disallowed therapies that may influence efficacy are defined as any of the following therapies (and that are not prescribed as rescue therapy):

- Immunosuppressants or dapsone at therapeutic doses for at least 4 weeks in total
- IVIg /SCIg at immunomodulating dose (≥1 g/kg/month)
- Tetracyclines at therapeutic dose for at least 2 weeks in total
- Rituximab or other anti-CD20 biologics, at least 1 infusion
- Plasma exchange or Immunoadsorption, at least 1 procedure
- IV or IM corticosteroids

  At least 1 administration, any dose, from week 28 to 36 (i.e., during the 8-week period required to confirm CR off OCS therapy) or

  At any time before week 28 in any of the 3 following situations:
  - More than 60 mg/day of prednisone or prednisone equivalent dose for 3 consecutive days
  - More than 40 mg/day of prednisone or prednisone equivalent dose for 4 consecutive days
  - More than 7 days in total
- Any interventional study drugs under development for BP
- Very potent topical corticosteroids (TCS) for 7 consecutive days or 14 days in total

Note: if dose is missing and/or period of intake cannot be derived, it is still considered an intercurrent event.

Details on the derivation of intercurrent events are provided in appendix 9.1. More information how these intercurrent events are handled can be found in the efficacy section 4.1.

3.4.3 Presentation of results

Therapies will be tabulated by ATC class (level 1 and 3) and generic term. Tables will be created for:

- Prior therapies (excluding therapies from the BP history CRF form)
- BP therapy history (all therapies from the BP history CRF form)
- Concomitant therapies (excluding medications from the OCS CRF form, excluding rescue therapies and excluding disallowed therapies that classify as intercurrent event)
- Concomitant OCS and equivalent medications administered for BP (all medications from the OCS CRF form, excluding OCS medications administered as rescue therapy)
- Rescue therapies (excluding medications from the OCS CRF form)
- Disallowed therapies that classify as intercurrent event (excluding rescue therapies)

Concomitant therapies and concomitant OCS therapies will be tabulated for the on IMP treatment period, off IMP treatment period, and FU phase separately.

All prior and concomitant therapies/procedures data will be listed with detailed information about ATC classes. Furthermore, separate listings will be created for BP therapy history, rescue therapies and for disallowed therapies that classify as intercurrent event.

3.5 IMP AND OCS ADMINISTRATION

3.5.1 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.

3.5.2 Derivation rules

Normalized cumulative OCS dose (NCOD) will be calculated based on prednisone equivalent doses. 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.

Only systemic use of oral medication is included.

NCOD (mg/kg/day) is calculated for different periods as [the sum of (equivalent doses taking into account daily dose frequency)/(body weight in kg)]/(period duration in days) with body weight of visit closest before or at each intake of OCS medication. If for a given day of analysis period, no record exists in the CRF indicating OCS use that day, the dose will be assumed to be 0 mg. NCOD will be calculated with and without considering main intercurrent events (see efficacy section 4.1.3.1). Additionally, the cumulative OCS dose (COD, in mg) over these periods will be calculated.

The denominator of the NCOD should cover all days on IMP treatment in the study, starting at baseline. Following periods are considered (including start and end of the period):

- Over the whole 2009 on IMP treatment period
- From first IMP administration until CDA or end of on IMP treatment period (whichever comes first)
- From first IMP administration until CR or end of on IMP treatment period (whichever comes first)

- From first IMP administration until CR while on minimal OCS therapy for ≥8 weeks or end of on IMP treatment period (whichever comes first)
- From first IMP administration until CR/PR while off OCS therapy for ≥8 weeks or end of on IMP treatment period (whichever comes first)
- From first IMP administration until CR while off OCS therapy for ≥8 weeks or end of on IMP treatment period (whichever comes first)
- From CDA onset until Relapse or end of on IMP treatment period (whichever comes first) (Only defined on the subset of participants that achieve CDA during the on IMP treatment period)
- From CR onset until Relapse or end of on IMP treatment period (whichever comes first) (Only defined on the subset of participants that achieve CR during the on IMP treatment period)

Details on how to derive the time till CDA, CR, CRmin, CR/PRoff and CRoff are included in section 4.1.4.

Following rules will be applied to allocate OCS administrations to the correct period:

- Only the start and stop date information will be considered
- Records with (partially) missing dates will be imputed as detailed in section 2.3.2.
- If dates of administration records overlap, the reported doses will be added together.
- 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

The following parameters will be derived for IMP administration:

- Number of administrations: sum of all administrations of study drug. Two administrations are expected on day 1 and day 8.
- Number of loading doses: i.e., daily doses of 2000 mg (2 administrations of 1000 mg).

The following parameters will be derived for IMP self-administration by participant and by caregiver:

- Number of participants/caregivers receiving the self-administration training.

  Number of training visits received by participant/caregiver.
- Number of participants/caregivers who were adequately trained and capable to self-administer efgartigimod.
- Number of training visits before being considered capable to self-administer.

3.5.3 Presentation of results

Number of administrations and number of loading doses will be summarized using descriptive statistics. Analysis of NCOD is described in the efficacy section 4.1.3.

All study drug administration data will be listed. Also, a detailed listing of OCS administration and NCOD will be provided including prednisone equivalent doses with body weight at intake, dates of ICE, CDA, PR, CR, CRmin, CRoff, first relapse and end of study (EoS). NCOD and OCS cumulative dose for the periods of interest will be listed.

Frequency tabulations with percentages will be produced for:

- Number of participants/caregivers receiving the self-administration training (denominator is all participants in SAF)
- Number of training visits received (denominator is number of participants/caregivers receiving training)
- Number of participants/caregivers who were adequately trained and capable to self-administer efgartigimod (denominator is number of participants/caregivers receiving training)
- Number of training visits before being considered capable to self-administer (denominator is number of participants/caregivers receiving training)
- Number of administrations by administrator (site staff, participant, caregiver, home nurse) and location (at home/onsite) per CRF visit and overall

All CRF information related to IMP self-administration and training will be listed.

4. EFFICACY, PHARMACOKINETIC, PHARMACODYNAMIC AND IMMUNOGENICITY ANALYSES

4.1 EFFICACY AND QUALITY OF LIFE

All efficacy endpoints will be analyzed on the FAS population. The primary endpoint and all 5 key secondary endpoints will also be analyzed on the PP population as sensitivity analysis.

Wherever the stratification factors will be used in the efficacy analyses, the actual values of these will be used and not the ones coming from the randomization. Also, for participants randomized without stratification, i.e., part A participants and Japanese or Chinese Part B participants, these factors will be derived in order to include these participants in the statistical models.

For all references to weeks, analysis visits are considered as described in section 2.2.4, unless specified otherwise. If multiple assessments fall within the same analysis window, only the assessment closest to the target date will be considered unless specified otherwise. Other assessments within this window will only be listed and not considered in the below analyses. Only the time to response endpoint (see section 4.1.4) will be derived using all possible measurements and not only the one closest to the target of the analysis visit. Only visits up to Week 36 analysis visit will be considered defining the different responses. For endpoints 'at week 36', the last non-missing analysis visit assessment from week 32 till week 36 will be used.

All endpoints/estimands defined as an event ‘while receiving efgartigimod PH20 SC or placebo’ should be handled as follows: treatment discontinuations not due to ‘lack of efficacy’ (but e.g., due to AE) are still considered as 'while receiving efgartigimod PH20 SC or placebo'.

Examples of SAS code for the statistical analysis procedures are provided in appendix 9.3.

4.1.1 Available data

BP Disease status is assessed weekly. Investigators report the participant’s best BP disease status in episodes with start and end date (no CDA, CDA, CR while receiving OCS therapy of more than 0.10 mg/kg/day, CR while receiving minimal OCS therapy for less than 8 weeks *or* for at least 8 weeks, CR while being off OCS therapy for less than 8 weeks *or* for at least 8 weeks, PR while receiving OCS therapy, PR while being off OCS therapy for less than 8 weeks *or* for at least 8 weeks, Relapse, Treatment failure). The BP disease status at a visit is derived as the status of the episode during which the visit occurred (and only for visits where it is confirmed that the disease status assessment occurred).

Furthermore, efficacy will be evaluated by assessments of NCOD, IGA-BP, Itch NRS and BPDAI Activity and Total Score.
Quality of life will be measured using ABQOL Questionnaire, DLQI and EQ-5D-5L Scale.

The health impact of glucocorticoid (GC) use will be measured using the Aggregate Improvement Score (AIS) from the GTI, the Cumulative Worsening Score (CWS) from the GTI and the Glucocorticoid Toxicity Index Specific List (GTI-SL).

4.1.2 Primary Endpoint

4.1.2.1 ESTIMAND ANALYSIS

- Population: adult participants with newly diagnosed or relapsing BP, regardless of whether the participant is naïve to treatment or has previously received treatment. Participants will be receiving concurrent therapy of oral prednisone (or equivalent OCS); therefore, candidates who have a known contraindication to OCS will be excluded from study participation (exclusion criterion 4).
- Subject level variable: being in CR while receiving efgartigimod PH20 SC or placebo and have been off OCS therapy for ≥8 weeks (CRoff) at week 36.
- Main intercurrent events:

  1. Intercurrent treatments before week 36 (see appendix 9.1)

  - Immunosuppressants or dapsone at therapeutic doses for at least 4 weeks in total
  - IVIg /SCIg at immunomodulating dose (≥1 g/kg/month)
  - Tetracyclines at therapeutic dose for at least 2 weeks in total
  - Rituximab or other anti-CD20 biologics, at least 1 infusion
  - Plasma exchange or Immunoadsorption, at least 1 procedure
  - IV or IM corticosteroids

    At least 1 administration, any dose, from week 28 to 36 (i.e., during the 8-week period required to confirm CR off OCS therapy) or

    At any time before week 28 in any of the 3 following situations:

    - More than 60 mg/day of prednisone or prednisone equivalent dose for 3 consecutive days
    - More than 40 mg/day of prednisone or prednisone equivalent dose for 4 consecutive days
    - More than 7 days in total

- Any interventional study drugs under development for BP
- Very potent TCS for 7 consecutive days or 14 days in total

2. Discontinuation of IMP before week 36 due to lack of efficacy

3. Death before week 36

Details on the derivation of intercurrent treatments are provided in appendix 9.1.

- Population-level summary: the odds ratio (with 95% confidence interval [CI]) under efgartigimod PH20 SC in combination with concurrent OCS therapy versus PBO PH20 SC in combination with concurrent OCS therapy.

4.1.2.2 Handling of Intercurrent Events, Rescue Therapy and Missing Data

A composite strategy approach will be taken to address all main ICEs. This implies that participants who take intercurrent treatments, participants who discontinue IMP due to lack of efficacy and participants who died before week 36 will be considered non-responders for the primary endpoint analysis.

Participants who receive rescue therapy before Week 36 will be considered non-responders for the primary endpoint analysis.

Missing values will be imputed as follows:

- Missing data for reason of one of the main ICEs will be handled as described above.
- For response 'at week 36', the last non-missing analysis visit assessment from week 32 till week 36 will be used. If all disease status assessments at the analysis windows for week 32 to week 36 are missing, then the participant is considered non-responder.
- Otherwise, if disease status information is missing for the primary endpoint, the participant will be considered a non-responder.
- Handling of missing data due to the cut-off for the Part A interim analysis is described in section 1.4.1.2.

A supplementary analysis for this primary analysis on FAS will use the 'treatment policy strategy' where the main intercurrent events are handled differently. The occurrence of the intercurrent event is irrelevant: CRoff as assessed by the investigator is used regardless of whether or not the intercurrent event occurs. Participants who received rescue therapy before Week 36 are still considered as non-responders for this supplementary analysis. Missing data at week 36 will be imputed by means of multiple imputation (fitted separately per treatment group). However, if a participant died before week 36, this is considered a non-responder (composite strategy).

4.1.2.3 PRESENTATION OF RESULTS

The primary endpoint will be analyzed on the FAS population and additionally on the PP population as sensitivity analysis.

A frequency tabulation will be provided for the disease status as collected in the CRF per analysis visit. This includes the status 'CR while being off OCS therapy for at least 8 weeks'. For participants who received rescue therapy, only assessments prior to or on the start date of rescue therapy will be considered.

Frequency tabulations will be provided of the percentage of participants who are in CR while receiving efgartigimod PH20 SC or placebo and have been off OCS therapy for ≥8 weeks at week 36 (composite strategy - primary endpoint). The table will be repeated for subgroups, including treatment differences in proportions with 95% Wald CI (with continuity correction).

The proportion of participants with BP who are in CRoff at week 36 will be tested by means of a Cochran-Mantel-Haenszel (CMH) test stratified for the 2 stratification factors of disease history (newly diagnosed versus relapsing) and disease severity as per IGA-BP at screening (moderate versus severe). The common (conditional) odds ratio will be provided, along with the exact 95% CI and 2-sided p-value from the CMH association test. In addition, the Klingenberg 95% CI for the strata-adjusted difference of proportions along with its midpoint estimate will be provided. Homogeneity of the odds ratios will be tested by means of a Breslow-Day test with Tarone's adjustment.

A sensitivity analysis will be performed on this primary endpoint using exact logistic regression with fixed effect terms for randomized treatment and stratified for the 2 stratification factors of disease history and disease severity as per IGA-BP at screening. Treatment groups will be compared in terms of the (conditional) odds ratio with 95% CI. A non-linear model with fixed effect terms for randomized treatment and the 2 stratification factors will be fitted to obtain the estimated treatment difference in proportions with 95% CI.

The same CMH test as for the primary analysis will be applied for the supplementary analysis (using a treatment policy strategy).

All sensitivity and supplementary analyses for the primary endpoint will be performed both for the analysis of study Part A, study Part B and pooled study Part A and B.

A listing will be created for the disease status at each visit, presenting the result as collected in the CRF and the result when taking into account intercurrent events (composite strategy) and rescue therapy (non-responder).

4.1.3 Key secondary endpoints (alpha controlled)

For the analysis of study Part B, the below endpoints are considered as key secondary endpoints. They will be tested in the FAS population in hierarchical order (see section 4.1.5). Additionally, the key secondary endpoints will be analysed in the PP population as a sensitivity analysis.

For the analysis of study Part A, the hierarchical testing procedure will not apply.

4.1.3.1 *Handling of Intercurrent Events, Rescue Therapy and Missing Data*

1) Normalized cumulative OCS dose (NCOD, mg/kg/day) over the on IMP treatment period.

Main intercurrent events are defined as follows, and handled in a 'while on treatment' strategy:

- Intercurrent medications (see section 3.4.2): stop calculating cumulative dose after ICE. In case 'immunosuppressants for at least 4 weeks in total' is the ICE, use end of the 4 weeks IC medication as stop for cumulative dose calculation. In case 'tetracyclines for at least 2 weeks in total' is the ICE, use end of the 2 weeks IC medication as stop for cumulative dose calculation. In case 'IV or IM corticosteroids ' is the ICE, use the first day of this IC medication as stop for cumulative dose calculation. In case 'very potent TCS for 7 consecutive days or 14 days in total ' is the ICE, use the end of the 7 or 14 days IC medication as stop for cumulative dose calculation.

Details on the derivation of intercurrent events are provided in appendix 9.1.

A supplementary analysis for this secondary endpoint will use the 'treatment policy strategy' where the occurrence of the intercurrent event is considered irrelevant: NCOD is calculated regardless of whether or not the intercurrent event occurs.

Rescue therapies will not be considered for the NCOD endpoint since rescue therapies are only permitted after discontinuation of IMP treatment and NCOD calculation is restricted to the on IMP treatment period.

2) The proportion of participants that have achieved IGA-BP score of 0 while receiving efgartigimod PH20 SC or placebo and have been off OCS therapy for ≥8 weeks at week 36: the same approach for handling the main ICEs (composite strategy), for the handling of rescue therapies and for handling missing data, as suggested for the primary analysis, will be applied.

3) The proportion of participants that have achieved control of disease activity (CDA) while receiving efgartigimod PH20 SC or placebo and remain free of relapse through week 36: the same approach for handling the main ICEs (composite strategy), for the handling of rescue therapies and for handling missing data, as suggested for the primary analysis, will be applied.

4) The proportion of participants that have achieved CR while receiving efgartigimod PH20 SC or placebo and while receiving minimal OCS therapy for ≥8 weeks (CRmin) at week 36:

A participant is considered as CRmin at week 36 when the reported disease status at week 36 is 'CR while receiving minimal OCS therapy for at least 8 weeks' or 'CR while being off OCS therapy for at least 8 weeks', or else when the reported disease status at week 36 belongs to a sequence of episodes with disease statuses 'CR while receiving minimal OCS therapy for less than 8 weeks *or* for at least 8 weeks' and' CR while being off OCS therapy for less than 8 weeks *or* for at least 8 weeks', having

started at least 56 days earlier (and for which within these 56 days the disease status provides evidence that the participant remained in CR and the minimal OCS therapy was maintained).

The same approach for handling the main ICEs (composite strategy), for handling rescue therapies and for handling missing data, as suggested for the primary analysis, will be applied.

5) The Itch NRS is measured over time and changes from baseline in the 24-hour average itch score will be analysed. A 'treatment policy' approach will be applied by ignoring the main ICEs. For participants who received rescue therapy, only assessments prior to or on the start date of rescue therapy will be included in the analysis.

4.1.3.2 PRESENTATION OF RESULTS

1) Summary statistics on NCOD and (non-normalized) cumulative OCS dose (COD) will be provided.

An ANCOVA model with factors for treatment and the stratification variables will be applied on NCOD. Least square (LS) means and standard error (SE) with 95% 2-sided CI for placebo and efgartigimod will be reported, along with the difference in LS means of IMP vs placebo (with SE), 95% 2-sided CI, and 2-sided p-value.

The supplementary analysis (using the treatment policy strategy) will be analysed in a similar way (descriptive statistics and ANCOVA). This supplementary estimator is not considered in the family wise alpha control.

2) Frequency tabulations will be provided for the percentages of participants within each outcome of IGA-BP per analysis visit. Additionally cumulative percentages (starting with the best outcome result) will be calculated. For participants who received rescue therapy, only assessments prior to or on the start date of rescue therapy will be considered.

Frequency tabulations will be provided of the percentage of participants that have achieved IGA-BP score of 0 while receiving efgartigimod PH20 SC or placebo and have been off OCS therapy for ≥8 weeks at week 36.

The same stratified CMH as for the primary endpoint will be performed.

All IGA-BP data will be listed.

3) Frequency tabulations will be provided of the percentage of participants that have achieved control of disease activity (CDA) while receiving efgartigimod PH20 SC or placebo and remain free of relapse through week 36.

The same stratified CMH as for the primary endpoint will be performed.

4) Frequency tabulations will be provided of the percentage of participants that have achieved CR while receiving efgartigimod PH20 SC or placebo and while receiving minimal OCS therapy for ≥8 weeks (CRmin) at week 36.

The same stratified CMH as for the primary endpoint will be performed.

5) Descriptive statistics will present the actual values and changes from baseline of the itch NRS 24-hour average score per analysis visit. For participants who received

rescue therapy, only assessments prior to or on the start date of rescue therapy will be considered.

Changes from baseline in the 24-hour average itch NRS score will be analysed using a mixed-effect model for repeated measurements (MMRM). The least square means on changes from baseline at week 36 will be calculated as well at the other analysis visits (with no strict control of alpha of these). The MMRM model will include treatment by visit and baseline value by visit interaction terms, and the two stratification factors as covariates. Within-subject correlation will be modeled using the R matrix. With 13 post-baseline visits during the treatment-phase, a standard unstructured covariance matrix would require 91 variance parameters. Therefore, a modified unstructured covariance matrix (UN) will be used: ANTE(1).

Least square means, SE, and 95% 2-sided CI for placebo and efgartigimod will be reported by analysis visit, along with LS means of the between-arm difference including also with SE, 95% 2-sided CI, and 2-sided p-value. If the default Newton–Raphson algorithm used by SAS PROC MIXED fails to converge, the following will be tried to avoid lack of convergence while maintaining an unstructured variance:

The Fisher scoring algorithm (via the SCORING = 5 option of the PROC MIXED statement) will be used to obtain the initial values of covariance parameters.
In the rare case where the above fails, the following covariance structures will be tested for convergence (in order): toeph, arh(1), csh, toep, ar(1) and cs).

All itch NRS data will be listed.

Subgroup tables will be created for all key secondary endpoints (not for supplementary analysis).

4.1.4 Other secondary endpoints (not alpha controlled)

All other secondary endpoints will be analyzed using the FAS population.

1) Proportion of participants who achieve an IGA-BP score of 0 or 1 while receiving efgartigimod PH20 SC or placebo and have been off OCS therapy for ≥8 weeks at week 36: same derivation and presentation as for the primary endpoint taking into account ICEs (composite strategy) and rescue therapy (non-responders).

2) Proportion of participants who achieve an IGA-BP score of 0 or 1 while receiving efgartigimod PH20 SC or placebo at any time through week 36: similar derivation and presentation as for the primary endpoint taking into account ICEs (composite strategy): a participant with IGA-BP score of 0 or 1 before ICE (if any) is considered a responder. For participants who received rescue therapy, only assessments prior to or on the start date of rescue therapy will be considered.

3) Change from baseline to week 36 in the BPDAI activity and total score will be analysed using the same MMRM model with 'treatment policy strategy' as for the analysis on the Itch NRS score. For participants who received rescue therapy, only assessments prior to or on the start date of rescue therapy will be included in the model.

Descriptive statistics on absolute values, changes from baseline and percent changes from baseline in BPDAI activity and total score will be calculated per analysis visit. For participants who received rescue therapy, only assessments prior to or on the start date of rescue therapy will be considered.

4) Time to CDA, calculated as the difference between the first date CDA was achieved and the first IMP administration date.
Time to CDA (days) = date (first CDA) - first IMP date + 1

Participants who already have CDA at the first IMP administration date (day 1) will be excluded from the analysis. Participants without any post-baseline disease assessment are censored at day 1. Participants with post-baseline disease assessment but not achieving CDA during treatment phase are censored at end of treatment phase.

Participants with a main intercurrent event prior to achieving CDA (composite strategy) and participants who received rescue therapy prior to achieving CDA, will be censored at the planned end of the treatment phase. More specifically, these participants will be censored at the maximum of:

- Day 267 (Week 36 + 2 weeks)
- The latest day CDA was achieved by any participant in the treatment phase

The first date CDA was achieved is the start date of the first episode with disease status CDA or a better disease status (CR while receiving OCS therapy of more than 0.10 mg/kg/day, CR while receiving minimal OCS therapy for less than 8 weeks *or* for at least 8 weeks, CR while being off OCS therapy for less than 8 weeks *or* for at least 8 weeks).

Time to CDA will be descriptively presented by treatment group for each stratum and overall with median times, quantiles and number and percentage of participants censored and with event. Both treatment groups will be compared using a stratified Gehan-Wilcoxon statistic.

5) Time to CR, calculated as the difference between the first date CR was achieved and the first IMP administration date. Similar calculations and censoring rules are applied as for 'time to CDA'.

The first date CR was achieved is the start date of the first episode with disease status CR while receiving OCS therapy of more than 0.10 mg/kg/day or a better disease status (CR while receiving minimal OCS therapy for less than 8 weeks *or* for at least 8 weeks, CR while being off OCS therapy for less than 8 weeks *or* for at least 8 weeks).

Time to CR will be analysed in a similar way as 'time to CDA'.

6) Time to CR while on minimal OCS therapy for ≥8 weeks, calculated as the difference between the first date CRmin was achieved and the first IMP administration date. Similar calculations and censoring rules are applied as for 'time to CDA'.

The first date CRmin was achieved is:

- the start date of the first episode with disease status CR while receiving minimal OCS therapy for at least 8 weeks or CR while being off OCS therapy for at least 8 weeks
- or else the start date of the first episode within a sequence of episodes with disease statuses CR while receiving minimal OCS therapy for less than 8 weeks *or* for at least 8 weeks and CR while being off OCS therapy for less than 8 weeks *or* for at least 8 weeks + 56 days

whichever comes first.

Time to CRmin will be analysed in a similar way as 'time to CDA', except that a stratified log-rank test will be used for comparing both treatment groups (instead of the stratified Gehan-Wilcoxon statistic).

7) Time to CR/PR while off OCS therapy for ≥8 weeks (CR/PRoff), calculated as the difference between the first date CR/PR while off OCS therapy for ≥8 weeks was achieved and the first IMP administration date. Similar calculations and censoring rules are applied as for 'time to CDA'.

The first date CR/PR while off OCS therapy for ≥8 weeks was achieved is:

- the start date of the first episode with disease status CR while being off OCS therapy for at least 8 weeks or PR while being off OCS therapy for at least 8 weeks
- or else the start date of the first episode within a sequence of episodes with alternating disease statuses CR while being off OCS therapy for less than 8 weeks and PR while being off OCS therapy for less than 8 weeks + 56 days

whichever comes first.

Time to CR/PR will be analysed in a similar way as 'time to CRmin'.

8) Time to CR while off OCS therapy for ≥8 weeks, calculated as the difference between the first date CR while off OCS therapy for ≥8 weeks was achieved and the first IMP administration date. Similar calculations and censoring rules are applied as for 'time to CDA'.

The first date CR while off OCS therapy for ≥8 weeks was achieved is the start date of the first episode with disease status CR while being off OCS therapy for at least 8 weeks.

Time to CRoff will be analysed in a similar way as 'time to CRmin'.

9) Time from CDA onset to Relapse, calculated only in participants with CDA as the difference between the first date of relapse and the first date CDA was achieved. Similar calculations and censoring rules are applied as for 'time to CDA', except for the handling of intercurrent events and rescue therapies. Main intercurrent events prior to Relapse are ignored (treatment policy strategy) and participants who received rescue therapy prior to Relapse will be censored at the start of the rescue therapy.

Time from CDA onset to Relapse will be analysed in a similar way as 'time to CRmin'.

10) Time from CR onset to Relapse, calculated only in participants with CR as the difference between the first date of relapse and the first date CR was achieved. Similar calculations and censoring rules are applied as for 'time from CDA to Relapse'.

Time from CR onset to Relapse will be analysed in a similar way as 'time to CRmin'.

11) Time from CRoff onset to Relapse, calculated only in participants with CRoff as the difference between the first date of relapse and the first date CRoff was achieved. Similar calculations and censoring rules are applied as for 'time from CDA to Relapse'.

Time from CR onset to Relapse will be analysed in a similar way as 'time to CRmin'.

12) NCOD as calculated for the different subperiods. NCOD from CDA/CR onset until relapse will only be analysed in participants with CDA/CR respectively. Same analysis will be performed as for the primary estimand of the key secondary parameter with ICEs handled according a 'while on treatment' strategy.

COD will be calculated for the on IMP treatment period and the subperiods mentioned before. Only descriptive statistics will be presented.

13) Changes from baseline at week 36 in the 24-hour worst Itch NRS score will be analysed in the same way as for the 24-hour average itch score in the key secondary analysis.

14) Proportion of participants who received rescue therapy before week 36. A 'treatment policy' approach will be applied by ignoring main ICEs. Same CMH model as proposed for the primary endpoint.

15) ABQOL (17 items), EQ-5D-5L (5 dimensions) and DLQI (10 items) are assessed by the investigator at baseline, Week 12, Week 26 and at Week 36/ETD/ESD. Frequency tabulations will be provided for the percentages of participants within each outcome of QoL questionnaire items. Additionally cumulative percentages (starting with the best outcome result) will be calculated. A 'treatment policy' approach will be applied by ignoring main ICEs. For participants who received rescue therapy, only assessments prior to or on the start date of rescue therapy will be considered.

16) EQ-5D-5L VAS score and DLQI score are assessed by the investigator at baseline, Week 12, Week 26 and at Week 36/ETD/ESD. 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. A 'treatment policy' approach will be applied by ignoring main ICEs. For participants who received rescue therapy, only assessments prior to or on the start date of rescue therapy will be considered.

Descriptive statistics on absolute values and changes from baseline for EQ-5D-5L VAS score, DLQI score and Total ABQOL score will be calculated per time point.

The same MMRM model as for the itch NRS score will be applied to analyse these changes from baseline but using a standard unstructured covariance matrix (UN) since there are only 3 post-baseline visits during the treatment-phase.

17) C-GTI: Composite Glucocorticoid Toxicity Index comprises the Aggregate Improvement Score (AIS) and the Cumulative Worsening Score (CWS) (health impact of GC) and is derived at baseline, Week 12 , Week 26, and Week 36/ETD/ESD. AIS and CWS are calculated for the first 12 weeks, 26 weeks, and 36 weeks period and overall (period till last post-baseline assessment). Details of AIS and CWS derivations are specified in appendix 9.2.

A 'treatment policy' approach will be applied by ignoring ICEs. For participants who received rescue therapy, only assessments prior to or on the start date of rescue therapy will be considered.

Descriptive statistics will be provided for the C-GTI scores AIS and CWS; treatment groups will be compared at each visit using the same ANCOVA model as for the NCOD analysis. C-GTI will be analysed on complete cases: i.e., participants with C-GTI assessment at baseline and at least one post-baseline visit. Participants where first post-baseline GTI improvements/worsening have not been obtained with respect to the baseline moment but with respect to a later moment (i.e., no GTI assessment at baseline visit) are excluded from analyses and are only listed.

Kaplan-Meier curves will be created for all 'time to event' endpoints.

Separate listings will be created for all 'time to event' endpoints, for lesion assessments, for BPDAI assessments and scores, for ABQOL, EQ-5D-5L and DLQI data, for calculated C-GTI scores and for complementary GTI specific list (GTI-SL).

4.1.5 Fixed-Sequence testing procedure

The fixed-sequence testing procedure will only apply for the analysis of study Part B.

To control the type I error for the primary and secondary endpoints (alpha controlled), the primary efficacy endpoint will be tested at the 5% 2-sided alpha level and will act as gatekeeper for the testing of the key secondary endpoints. The primary endpoint and secondary endpoints will be tested in a strict hierarchical order as per the algorithm of section 1.4.3.2 to control the type I error.

The individual per-endpoint tables will only show unadjusted p-values. A fixed-sequence testing procedure table will be produced. This table will show both unadjusted p-values and p-values adjusted for multiplicity. For a given endpoint, the adjusted-for-multiplicity p-value is calculated as the maximum between its unadjusted p-value and the highest of all unadjusted p-values tested before.

- Primary endpoint: the proportion of participants who are in CR while receiving efgartigimod PH20 SC or placebo and have been off OCS therapy for ≥8 weeks at week 36 using a 'composite strategy' approach
- Secondary endpoints:
  - NCOD using 'while on treatment strategy' approach
  - Proportion of participants achieving IGA-BP score of 0 while receiving efgartigimod PH20 SC or placebo and have been off OCS therapy for ≥8 weeks at week 36 using a 'composite strategy' approach
  - Proportion of participants achieving control of disease activity (CDA) while receiving efgartigimod PH20 SC or placebo and remain free of relapse through week 36 using a 'composite strategy' approach
  - Proportion of participants achieving CR while receiving efgartigimod PH20 SC or placebo and have been receiving minimal OCS therapy for ≥8 weeks at week 36 using a 'composite strategy' approach
  - Change from baseline to week 36 in the 24-hour average Itch NRS score using a 'treatment policy' approach

4.1.6 Subgroup analyses for efficacy

Subgroups are defined based on the following categorizing factors:

- Disease history (newly diagnosed versus relapsing)
- Disease severity as per IGA-BP at screening (moderate versus severe)
- BPDAI activity score at baseline: <20, 20-56, >56
- Geographical region (Asia, North America, EU region+UK, Rest of world)
- Sex at birth
- Age at informed consent (18 - <65, 65 - <75, 75 - <85, >=85)
- BMI at screening (Underweight: < 18.5 kg/m^2, Normal weight: 18.5 -< 25 kg/m^2, Overweight: 25 -< 30 kg/m^2, Obese: >= 30 kg/m^2)
- Race (Asian, Black or African American, White, Other)

Subgroup analyses will be performed on the primary and key secondary efficacy endpoints.

Following table summarizes the analyses:

Table 4: Summary of (subgroup/supplementary) analyses

Subject level variable	Estimand	Estimator
CRoff at week 36	Composite	CMH [1,p,s] Logistic regression
	Treatment policy	MI + CMH
NCOD	While on treatment	ANCOVA [2,p,s]
	Treatment policy	ANCOVA
IGA-BP score of 0 at week 36 while off OCS therapy for ≥8 weeks	Composite	CMH [2,p,s]
CDA and remain free of relapse through week 36	Composite	CMH [2,p,s]
CRmin at week 36	Composite	CMH [2,p,s]
Itch NRS 24-hour average score	Treatment policy	MMRM [2,p,s]
IGA-BP score of 0 or 1 at week 36 while off OCS therapy for ≥8 weeks	Composite	CMH
IGA-BP score of 0 or 1 at any time through week 36	Composite	CMH
BPDAI activity and total score/Itch NRS worst score	Treatment policy	MMRM
Time to CDA/CR	Composite	Gehan-Wilcoxon
Time to relapse from CDA/CR/CRoff	Treatment policy	Log-rank
Other time to event	Composite	Log-rank
NCOD for subperiods	While on treatment	ANCOVA
Received rescue therapy before week 36	Treatment policy	CMH
QoL	Treatment policy	MMRM
C-GTI	Treatment policy	ANCOVA

[1] Primary endpoint
[2] Key secondary endpoint for study Part B
[p] Also analysis on PP analysis set will be performed.
[s] Also subgroup analyses will be performed. No inferential statistics will be calculated for the subgroup analyses.

4.2 PHARMACOKINETICS

4.2.1 Available data

Blood samples will be collected for the determination of efgartigimod concentration at the time points indicated in the schedule of assessments (see appendix 9.5). Sampling will be done predose on IMP administration visits (within 2 hours before IMP).

In Part A only, 1 additional PK sample will be collected from all participants on day 10 (±1 day; should be collected at least 2 days after the second IMP dose is administered at week 1).

Following PK samples will be excluded from the descriptive statistics based on time since previous IMP:

- When PK sampling is deviating more than 2 days from scheduled sample visit: i.e., if PK sample is not within last IMP+7 days ± 2 days.
- For the Day 10 visit when PK sampling is deviating more than 1 day from scheduled sample visit: i.e., if PK sample is not within second IMP+2 days ± 1 day.
- When a predose sample is taken after IMP administration.
- When the IMP administration prior to the scheduled PK sample is missed (not applicable for Day 1).

A remark with reason for exclusion of the time point will be added in the appropriate listing.

4.2.2 Derivation rules

PK concentrations will be reported in ng/mL by the lab and will be converted to ug/mL for analyses.

4.2.3 Presentation of results

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

Descriptive statistics per time point on concentration data will be presented in tables.

4.3 PHARMACODYNAMICS

4.3.1 Available data

The following pharmacodynamic parameter will be measured: total IgG serum levels, anti-BP180 antibodies, anti-BP230 antibodies [redacted] serum levels.

4.3.2 Derivation rules

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.

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.

Total IgG [redacted] results expressed as below or above the limit of quantification (BLQ or ALQ, respectively) will not be imputed.

Changes and percent changes vs baseline will be calculated. Participants with a baseline 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 baseline and the percent changes from baseline. This will be explained by a footnote in the appropriate tables. Limits of quantification are provided by the lab.

In addition, for all pharmacodynamic endpoints, descriptive statistics of the actual vales will also include GM, and GSD. GM and GSD are not applicable for descriptive statistics of the absolute changes from baseline. For these selected endpoints, descriptive statistics of 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).

4.3.3 Presentation of results

All pharmacodynamic endpoints will be summarized by means of descriptive statistics at each analysis visit. Actual values, changes from baseline and percent changes from baseline will be tabulated.

Tables with descriptive statistics will be presented including all available data and will be repeated for a subset of data in which samples are excluded if taken later than 2 weeks (14 days) after the previous IMP administration.

Also, the same subgroup analyses will be performed as for efficacy. For the final analysis of Part A data, only the following subgroups are of interest:

- Disease history (newly diagnosed versus relapsing)
- Disease severity as per IGA-BP at screening (moderate versus severe)
- BPDAI activity score at baseline: <20, 20-56, >56
- Age at informed consent (18 - <65, 65 - <75, 75 - <85, >=85)

Listings will be created for total IgG, [redacted] and anti-BP antibodies results over time. Listings will always show the non-imputed results.

4.4 IMMUNOGENICITY

4.4.1 Available data

Blood samples will be collected for the determination of anti-drug antibodies (ADA) to efgartigimod (in serum samples) and antibodies against rHuPH20 (in plasma samples) at the time points indicated in the schedule of assessments (see appendix 9.5).

Immunogenicity samples are analysed in a 3-tiered approach:

- All samples are evaluated in the ADA screening assay and are scored as ADA screening positive or negative.
- If a sample scored positive in the ADA screening assay, it is further evaluated in the confirmatory assay and is scored confirmed positive (positive immunodepletion) or confirmed negative (negative immunodepletion).
- If a sample is scored as confirmed positive, the samples are further characterized in the ADA titration assay (to determine titer) and are also further analyzed in the Neutralizing antibody (Nab) assay to confirm neutralizing activity (positive or negative). For NAb against efgartigimod, a screening assay is performed and results will be reported as negative or positive. For NAb against rHuPH20, the same 3-tiered approach is implemented: the screening NAb assay, followed by a NAb confirmatory assay, and a titer NAb assay, according to the above described 3-tiered approach.

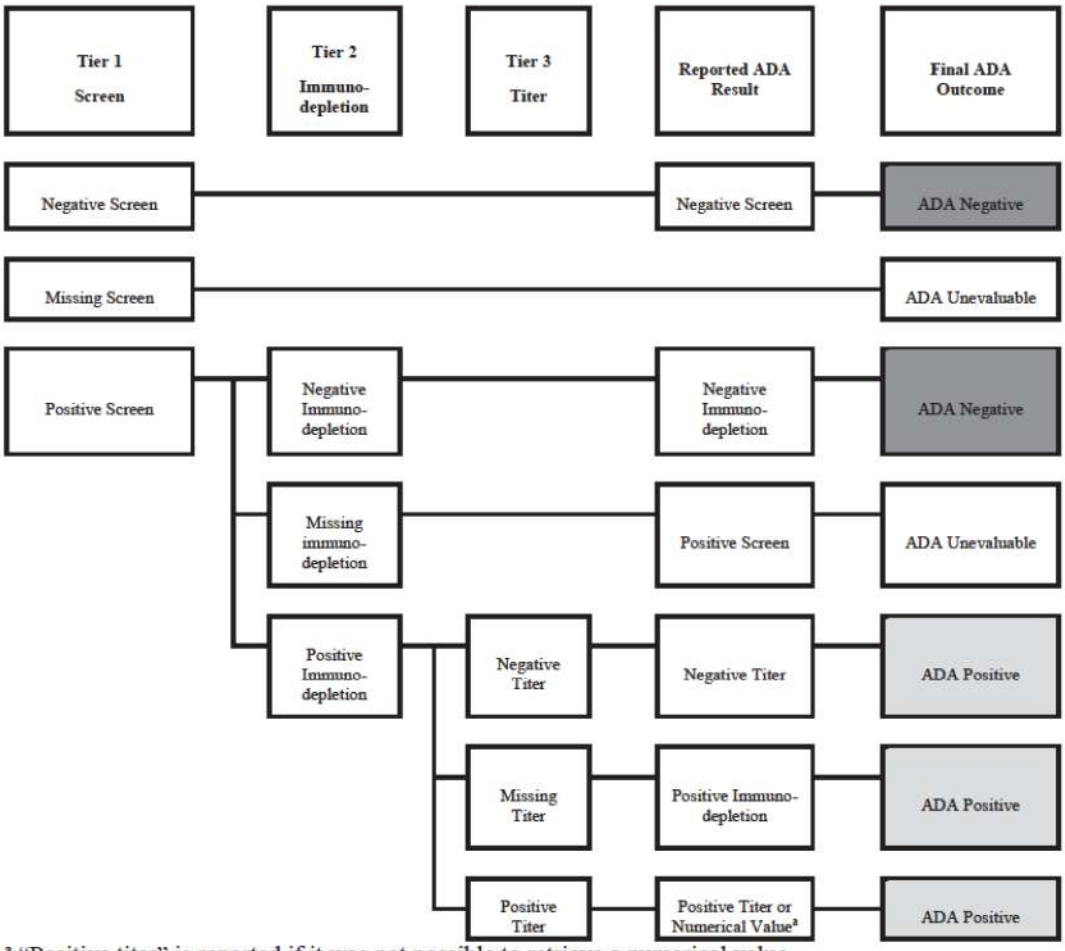
If available, a titer result will be reported for the ADA confirmed positive samples. However, a titer result is not always available:

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

This is also applicable to rHuPH20 Ab and rHuPH20 NAb results.

An overview of this 3-tiered approach and all possible ADA or rHuPH20 Ab or rHuPH20 NAb sample results that will be reported by the laboratory is given below. From these reported ADA or rHuPH20 Ab or rHuPH20 NAb sample results a final ADA or rHuPH20 Ab or rHuPH20 NAb 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] "Positive titer" is reported if it was not possible to retrieve a numerical value.

4.4.2 Derivation rules

4.4.2.1 PARTICIPANT CLASSIFICATION FOR ADA AGAINST EFGARTIGIMOD

Table 5 below gives an overview of how the ADA participant classification will be derived, starting from the participant baseline ADA sample status.

Table 5: Participant classification for ADA against Efgartigimod

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

[a] Samples with missing titer have as reported ADA result 'positive immunodepletion' or 'positive titer;'
[b] Results reported as 'negative titer,' i.e., titer value <1 will be set to value of 1;
[c] Highest sample status, with order: (from low to high): ADA unevaluable, ADA negative, ADA positive (missing titer /positive immunodepletion), ADA positive with titer <= 1 ('negative titer' as reported ADA result, titer value set to 1), ADA positive with titer >1 (i.e., numeric titer and selecting the sample with highest titer)

ADA evaluable participant = participant classified as any of following categories: ADA negative, treatment-unaffected ADA, treatment-induced ADA, treatment-boosted ADA. The first 2 categories are classified as 'ADA negative', the latter 2 as 'ADA positive'.

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

Note: Fourfold difference in titer values is considered significant in case a twofold serial dilution is applied (= 2 times the dilution factor) (reference to Shankar et al., 2014).

ADA incidence = percentage of participants with treatment-induced or treatment-boosted ADAs (denominator: number of evaluable participants).

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

4.4.2.2 PARTICIPANT CLASSIFICATION FOR ANTIBODIES AGAINST RHUPH20

Table 6 below gives an overview of how the anti-rHuPH20 antibody (rHuPH20 Ab) participant classification will be derived, starting from the participant baseline rHuPH20 Ab sample status.

Table 6: Participant classification for antibodies against rHuPH20

Participant anti-rHuPH20 Ab classification	**Highest[c] post-baseline sample status**				
	rHuPH20 Ab **negative**	rHuPH20 Ab **positive (missing titer[a])**	rHuPH20 Ab **positive (negative titer[b] or numeric titer value)**		rHuPH20 Ab **not evaluable**
Baseline rHuPH20 Ab sample status					
rHuPH20 Ab negative	rHuPH20 Ab negative	Treatment-Induced rHuPH20 Ab	Treatment-Induced rHuPH20 Ab		rHuPH20 Ab *unevaluable*
rHuPH20 Ab positive (missing titer[a])	Treatment-Unaffected rHuPH20 Ab	rHuPH20 Ab *unevaluable*	rHuPH20 Ab *unevaluable*		rHuPH20 Ab *unevaluable*
rHuPH20 Ab positive (negative titer[b] or numeric titer value)	Treatment-Unaffected rHuPH20 Ab	rHuPH20 Ab *unevaluable*	**titer < 4 x baseline titer:** Treatment-Unaffected rHuPH20 Ab	**titer ≥ 4x baseline titer:** Treatment-Boosted rHuPH20 Ab	rHuPH20 Ab *unevaluable*
rHuPH20 Ab not evaluable	rHuPH20 Ab *unevaluable*	rHuPH20 Ab *unevaluable*	rHuPH20 Ab *unevaluable*		rHuPH20 Ab *unevaluable*

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

rHuPH20 Ab evaluable participant = participant classified as any of following categories: rHuPH20 Ab negative, treatment-unaffected rHuPH20 Ab, treatment-induced rHuPH20 Ab, treatment-boosted rHuPH20 Ab. The first 2 categories are classified as 'rHuPH20 Ab negative', the latter 2 as 'rHuPH20 Ab positive'.

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

Note: A 4-fold difference in titer values is considered significant in case a twofold serial dilution is applied (reference to Shankar et al., 2014).

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

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

4.4.2.3 PARTICIPANT CLASSIFICATION FOR NAB AGAINST EFGARTIGIMOD

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

For NAb against efgartigimod, all samples evaluated in 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 based on their baseline and post-baseline sample status as detailed in table 7.

Table 7: Participant classification for NAb against Efgartigimod

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

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

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

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

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

4.4.2.4 PARTICIPANT CLASSIFICATION FOR NAB AGAINST RHUPH20

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

participants will be categorized based on their baseline and post-baseline sample status as detailed in following table 8.

Table 8: Participant classification for NAb against rHuPH20

Participant rHuPH20 NAb classification	Highest[c] post baseline sample status				
	rHuPH20 NAb negative	rHuPH20 NAb positive (missing titer[a])	rHuPH20 NAb positive (negative titer[b] or numeric titer value)		rHuPH20 NAb not evaluable
Baseline rHuPH20 NAb sample status					
rHuPH20 NAb negative	rHuPH20 NAb negative	Treatment Induced rHuPH20 NAb	Treatment Induced rHuPH20 NAb		*rHuPH20 NAb unevaluable*
rHuPH20 NAb positive (missing titer[a])	Treatment Unaffected rHuPH20 NAb	*rHuPH20 NAb unevaluable*	*rHuPH20 NAb unevaluable*		*rHuPH20 NAb unevaluable*
rHuPH20 NAb positive (negative titer[b] or numeric titer value)	Treatment Unaffected rHuPH20 NAb	*rHuPH20 NAb unevaluable*	**titer < 4 x baseline titer:** Treatment Unaffected rHuPH20 NAb	**titer ≥ 4x baseline titer:** Treatment Boosted rHuPH20 NAb	*rHuPH20 NAb unevaluable*
rHuPH20 NAb not evaluable	*rHuPH20 NAb unevaluable*	*rHuPH20 NAb unevaluable*	*rHuPH20 NAb unevaluable*		*rHuPH20 NAb unevaluable*

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

rHuPH20 NAb evaluable participant = participant classified as any of following categories: rHuPH20 NAb negative, treatment-unaffected rHuPH20 NAb, treatment-induced rHuPH20 NAb, treatment-boosted rHuPH20 NAb. The first 2 categories are classified as 'rHuPH20 NAb negative', the latter 2 as 'rHuPH20 NAb positive'.

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

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

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

4.4.3 Presentation of results

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

Frequency tabulations (number and percentages) will be provided with ADA or rHuPH20 Ab negative/positive/unevaluable samples per analysis visit. These tables will be presented by ADA or rHuPH20 Ab participant category.

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

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

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

The above frequency tabulations will be repeated for NAb assay using the definitions as defined in section 4.4.2.3. and 4.4.2.4.

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

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

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

- Mean (SD) drug concentration over time
- Mean (SE) percent change from baseline in total IgG
- Overall Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Overall Anti-Drug Antibodies Participant Classification (All Participants)
- Overall Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Overall Anti-Drug Antibodies Participant Classification (All Participants)
- Overall Injection related reactions (IRR) by Overall Anti-Drug Antibodies Participant Classification (All Participants)
- Overall Injection site reactions (ISR) by Overall Anti-Drug Antibodies Participant Classification (All Participants)
- Proportion of participants being in CRoff at week 36*

* Difference in proportion responders (primary endpoint) between each of the 4 categories versus ADA Negative, NAb baseline neg – post-baseline neg and rHuPH20 Ab Negative, including 95% exact confidence interval will be calculated.

Correlation tables by NAb against efgartigimod participant classification only need to be provided as soon as there are $N \geq 5$ participants in the sum of baseline negative – postbaseline positive and baseline positive – postbaseline positive NAb positive categories in (one of) the treatment arms. Correlation tables of mean drug concentration over time, correlation with efficacy, and mean percent change from baseline in total IgG can be restricted to the efgartigimod-administered participants only. The other correlation tables must be provided for efgartigimod- and placebo-administered participants.

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

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

5. SAFETY ANALYSES

5.1 ADVERSE EVENTS

5.1.1 Available data

Adverse events (AEs) are coded into system organ classes and preferred terms using the latest version of the MedDRA available at the database lock. For each AE, start and stop date/times are collected as well as severity according to the National Cancer Institute (NCI) common terminology criteria for adverse events (CTCAE) toxicity grading list (version 5.0), a seriousness flag, treatment relatedness, relatedness to procedures, action taken towards the IMP, outcome, and AE of special interest (AESI) category (infection).

5.1.2 Derivation rules

Treatment-emergent adverse events (TEAE) are defined as AEs starting within 60 days of an administration of IMP. Post-TEAEs are AEs starting after first administration of IMP that are not TEAEs.

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

- Treatment phase vs. non-treatment phase: the AE will be allocated to the treatment phase unless the available parts of the AE start or stop date/time provide evidence for allocating to the non-treatment phase.

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

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

AEs with missing treatment, prednisone or procedure relatedness will be considered as treatment-related, prednisone-related, or procedure-related respectively.

AEs with missing seriousness will be considered as serious AEs.

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

Injection-related reactions (IRRs) will be defined as all AEs with MedDRA preferred terms that are 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 occurring within 48 hours of an administration, or within 2 days in case no AE start time is available. In case of (partially) missing AE start date, 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.

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

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

- AE onset day (vs. first administration) =
  - AE start date ≥ date of first administration: AE start date – date of first IMP administration + 1 day
  - AE start date < date of first administration: AE start date – date of first IMP administration
- AE duration (days) =
  - AE end date – AE start date + 1 day
  - Study completion date or Study discontinuation date – AE start date + 1 day (when the AE start date is fully known but the AE is not resolved at the end of the study)

  In this case the duration will be presented as ">x days".

Event rates per 100 participant years of follow-up (PYFU) will be calculated as 100*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 IMP date + 1 day)]/365.25.
- PYFU for TEAEs (in years) will be calculated as above for PYFU overall with study duration cut off at 60 days after last IMP (i.e., last IMP date + 60 included) since AEs starting more than 60 days after last administration of IMP are not considered as TEAE.
- PYFU for post-TEAEs (in years) will be calculated as [the sum over all participants of all period durations during which an AE is considered to be post-treatment-emergent]/365.25.

Time to onset of first treatment-emergent adverse event (in days) will be calculated as date of the first treatment-emergent AE – date of first IMP administration + 1.

Participants without any TEAE will be censored at the date of the last IMP administration + 60 days or end date of the last analysis phase, whichever comes first. This info will be provided in the ADaM dataset (ADTTE); no tabulation is foreseen.

Similar time-to-event calculations will be done for:

- Time to onset of first serious TEAE
- Time to onset of fatal TEAE

5.1.3 Presentation of results

Unless mentioned otherwise, tables will present TEAEs only.

The TEAE tables will be presented for the treatment and follow-up phase combined.

An overview table will show the number and percentage of participants with at least one event and the number of events and number of events per 100 participant years of follow-up for the following:

- TEAEs
- Treatment-related TEAEs
- Serious TEAEs
- Serious treatment-related TEAEs
- Serious prednisone-related TEAEs
- Grade $\geq$ 3 TEAEs
- Treatment-related Grade $\geq$ 3 TEAEs
- TEAEs related to prednisone (or equivalent OCS)
- 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
- TE IRRs
- Serious TE IRRs
- TE ISR events
- Fatal TEAEs

This overview table will be repeated for:

- Post-TEAEs (AEs starting after first IMP administration but not considered treatment-emergent)
- All AEs during the treatment + follow-up phase (overall AEs)

A similar overview table will be created specifically for treatment-emergent ISR events and will show the number and percentage of participants with at least one event, the number of events and number of events per 100 participant years of follow-up for the following:

- Treatment-emergent ISRs (TEISRs)
- Treatment-related TEISRs
- Serious TEISRs
- Serious treatment related TEISRs
- Serious prednisone related TEISRs
- Grade $\geq$ 3 TEISRs
- Treatment-related Grade $\geq$ 3 TEISRs
- TEISRs related to prednisone (or equivalent OCS)
- TEISRs related to study procedures
- TEISRs for which the IMP was discontinued

- TEISRs for which the IMP was interrupted

A summary table of TEAEs by MedDRA system organ class and preferred term will show the number and percentage of participants with at least one event, the number of events and number of events per 100 participant years of follow-up.

This summary table will be repeated for:

- Post-TEAEs (AEs starting after first IMP administration but not considered treatment-emergent)
- All AEs during the treatment + follow-up phase (overall AEs)

Separate tables by MedDRA system organ class and preferred term will be prepared for the following, showing the number and percentage of participants with at least one event, the number of events and number of events per 100 participant years of follow-up:

- 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
- TEAEs related to study procedures
- TEAEs for which the IMP was discontinued
- TEAEs of special interest
- Treatment-related TEAEs of special interest

- TE IRRs
- Serious TE IRRs
- TE ISR events
- Fatal TEAEs
- Common TEAEs (preferred terms occurring in at least 10% [5% for the analyses using pooled Part A and Part B data] of participants in either treatment group; the cut-off is applied after rounding to the nearest integer. System organ class will be presented if any preferred term within is selected.)

All AEs, including pre-treatment events will be listed. Furthermore, separate listings will be created for SAEs, fatal AEs, TEAEs leading to discontinuation of IMP and AESIs. A coding listing will indicate how individual terms have been coded to MedDRA system organ classes and preferred terms.

5.2 CLINICAL LABORATORY EVALUATION

5.2.1 Available data

Per protocol, the following safety laboratory parameters are expected:

- Biochemistry: sodium, potassium, calcium (total), HbA1c, creatinine, creatinine clearance, CRP, GGT, glucose, blood urea nitrogen (BUN), alanine aminotransferase (ALT/SGPT), aspartate aminotransferase (AST/SGOT), bilirubin (total and direct), low-density lipoprotein-cholesterol (LDL), high-density lipoprotein-cholesterol (HDL), total cholesterol, triglycerides, alkaline phosphatase (ALP), total protein, and albumin.
- Hematology: hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), % reticulocytes, red blood cell (RBC) count, platelet count, white blood cell (WBC) count with differential.
- Special laboratory tests: aPTT, INR.
- Urinalysis: specific gravity, pH, protein, glucose, ketones, blood, bilirubin, urobilinogen, nitrite, leukocyte esterase, and microscopic examination.

Normal ranges are available as provided by the laboratory.

5.2.2 Derivation rules

Toxicity grades will be computed according to the NCI CTCAE v5.0 grading list. The implementation of these toxicity grades for analysis is presented in appendix 9.4. Only the parameters described in appendix 9.4 will be computed, according to the declared limits for each grade.

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:

- Classification will be done by using non-imputed values and limits as reported in standardized units in the clinical database: a value <X where X equals the lower limit of normal range will be classified as low. A value X with normal range <X will be classified as high.
- For the worst-case analysis visits, an additional category low + high is defined in case there are both low and high post-baseline values.

The creatinine clearance or estimated glomerular filtration rate (eGFR) will be derived by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula if not already provided as such by the central lab:

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

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

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

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

5.2.3 Presentation of results

The statistical analysis will present results in standardized units, except for eGFR that will be presented in mL/min/1.73m².

Continuous laboratory parameters will be summarized by means of descriptive statistics at each analysis visit. Actual values and changes from baseline will be shown in the same table. For albumin and low-density lipoprotein-cholesterol (LDL-C) also percent changes vs baseline will be shown.

Laboratory abnormalities for biochemistry and hematology parameters will be presented as a cross-tabulation (shift table) of the abnormality at each post-baseline analysis visit and at the worst-case analysis visit versus the baseline abnormality. This table will also show numbers of participants with treatment-emergent abnormalities (see Definition of terms). The denominator for the percentage is the total number of participants per treatment and per analysis visit in the safety analysis set. Tables for laboratory abnormalities will be restricted to biochemistry and hematology parameters.

Laboratory toxicity grades will be presented as a cross-tabulation (shift table) of the toxicity (NCI-CTCAE grades) at each post-baseline analysis visit and at the worst-case analysis visit versus the baseline toxicity. This table will also show numbers and cumulative numbers over decreasing toxicity grading of participants with treatment-emergent toxicities. The denominator for the percentage is the total number of

participants per treatment and per analysis visit in the safety analysis set. Parameters having toxicity grades defined in both directions (hypo and hyper) will be shown by direction.

All laboratory data will be listed, but only for participants with any post-baseline abnormality or toxicity or any overall interpretation of blood sample determined as clinically significant by the investigator, based on the sample for biochemistry or hematology parameters.

5.3 VITAL SIGNS

5.3.1 Available data

The following vital signs parameters are collected over time: supine systolic (SBP) and diastolic blood pressure (DBP), heart rate, body temperature, BMI and weight.

5.3.2 Derivation rules

Abnormalities are defined in below table.

	SBP (mmHg)	DBP (mmHg)	Temperature (°C)
Low	<90	<45	<35.8
Normal	90-150	45-90	35.8-37.5
High	>150	>90	>37.5

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

BMI (kg/m^2) will be derived as = (body weight (kg)) / (height at screening (m))^2. Post-baseline values will only be used in the C-GTI derivations.

5.3.3 Presentation of results

Vital signs parameters (without BMI) will be summarized by means of descriptive statistics at each analysis visit. Actual values and changes from baseline will be shown in the same table.

Abnormalities will be presented as a cross-tabulation of the abnormality at each post-baseline analysis visit and at the worst-case analysis visit versus the baseline abnormality. This table will also show numbers of participants with treatment-emergent abnormalities (see Definition of terms).

All vital signs data (without BMI) will be listed, but only for participants with any post-baseline abnormality or any reading determined as clinically significant by the investigator.

5.4 ELECTROCARDIOGRAMS

5.4.1 Available data

At a minimum, the following electrocardiogram (ECG) parameters will be collected over time: QRS interval, PR interval, RR interval, QT interval, QTcF, QTcB, ventricular rate (HR), and overall interpretation (by investigator and by ECG vendor).

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. selection of baseline assessment, allocation to phases/periods).

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

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

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

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

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

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

5.4.3 Presentation of results

Uncorrected QT interval and RR interval will only be listed.

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

Abnormalities of the actual values will be presented as a cross-tabulation of the abnormality at each post-baseline analysis visit, and at the worst-case analysis visit

versus the baseline abnormality. This table will also show numbers and cumulative numbers over decreasing abnormalities (QTcF and QTcB only) of participants with treatment-emergent abnormalities. The denominator for the percentage is the total number of participants per treatment and per analysis visit in the safety analysis set.

Abnormalities of the QTcF and QTcB changes from baseline will be presented as a tabulation of the change from baseline abnormality at each post-baseline analysis visit and at the worst-case analysis visit. This table will also show cumulative numbers over decreasing change from baseline abnormalities of participants. The denominator for the percentage is the total number of participants per treatment and per analysis visit in the safety analysis set.

All ECG data will be listed, but only for participants with any post-baseline abnormality or any overall interpretation determined as clinically significant by the investigator.

6. CHANGES TO THE PLANNED ANALYSIS

6.1 CHANGES NOT COVERED BY PROTOCOL AMENDMENTS BEFORE DATABASE LOCK

1.) The protocol specifies the NCOD calculation as:

Normalized cumulative OCS dose (NCOD) will be calculated normalized by weight and by number of days in study. The following formula will be adopted to calculate NCOD for each participant.

$$NCOD = \frac{Cumulative\ Dose\ of\ OCS\ from\ baseline\ to\ the\ week\ 36\ visit}{(Weight\ of\ the\ patient\ at\ baseline)\ x\ (number\ of\ days\ in\ study)}$$

Instead of the weight at baseline, it was chosen to use the most recent weight assessment instead. NCOD (mg/kg/day) is calculated for different periods as [the sum of (equivalent doses taking into account daily dose frequency)/(body weight in kg)]/(period duration in days) with body weight of visit closest before or at each start of prednisone equivalent medication instead of using weight at baseline.

2.) This SAP defines intercurrent medications in more detail than the protocol:

- Immunosuppressants or dapsone at therapeutic doses for at least 4 weeks:
  - Doses considered as therapeutic dose are specified in SAP appendix 9.1
  - Only considered as intercurrent medication if administered in the last 12 weeks before Week 36
- Tetracyclines at therapeutic dose for at least 2 weeks:
  - Doses considered as therapeutic dose are specified in SAP appendix 9.1
  - Only considered as intercurrent medication if administered in the last 10 weeks before Week 36
- Very potent TCS with a weekly dose >20 g for 1 week:
  - Since the dose of TCS cannot be derived from the eCRF data, very potent TCS is considered as intercurrent medication when it is applied for 7 consecutive days or 14 days in total.

3.) Per protocol, death before week 36 is not considered as main intercurrent event in the efficacy analysis. It is added as main intercurrent event in this SAP.

6.2 CHANGES NOT COVERED BY PROTOCOL AMENDMENTS AFTER DATABASE LOCK

Not applicable.

6.3 CHANGES TO THE FINAL STATISTICAL ANALYSIS PLAN

Not applicable.

7. REFERENCES

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Liu, D., Ahmet, A., Ward, L., Krishnamoorthy, P., Mandelcorn, E. D., Leigh, R., Brown, J. P., Cohen, A., & Kim, H. (2013). A practical guide to the monitoring and management of the complications of systemic corticosteroid therapy. Allergy, asthma, and clinical immunology: official journal of the Canadian Society of Allergy and Clinical Immunology, 9(1), 30.

8. LIST OF TABLES AND LISTINGS

8.1 TABLES

Note: tables to be produced for the IA and final topline results (TL) are indicated in last 2 columns.

Tables that are only to be produced for the interim analysis of study Part A are indicated with a hash mark (#). Tables that are only to be produced at the time of the final analysis are indicated with an asterix (*). At the final analysis, all tables will be created separately based on Part A data, based on Part B data and based on the pooled Part A and B data. Separate listings will be created for the Part A and Part B data.

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14.2.1.2.1.5	NCOD: Descriptive Statistics - Supplementary Analysis - FAS	FAS		
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14.2.1.2.2.1	IGA-BP: Tabulation - FAS	FAS	IA	TL

14.2.1.2.2.2	Proportion of Participants Who Achieved IGA-BP Score of 0 While off OCS Therapy for at Least 8 Weeks at Week 36: Cochran-Mantel-Haenszel - FAS	FAS	IA	TL
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9. APPENDICES

9.1 MAIN INTERCURRENT EVENTS (ICE)

9.1.1 Immunosuppressants or dapsone at therapeutic doses for at least 4 weeks in total in the last 12 weeks before Week 36

- Azathioprine, at least 1 mg/kg/day
- Mycophenolate mofetil, at least 2 g/day
- Mycophenolate mofetil hydrochloride, at least 2 g/day
- Mycophenolic acid, at least 1000 mg/day
- Cyclophosphamide, at least 1 mg/kg/day, or IV pulse 500 mg/month
- Methotrexate (sodium), at least 5 mg/week (in Japan), whereas 10 mg/week in Europe
- Ciclosporine, at least 3 mg/kg/day
- Dapsone, at least 1 mg/kg/day
- Hydroxychloroquine sulfate, at least 400mg/day
- Thalidomide, at least 50mg/day

For NCOD, time-to-event analyses and endpoints that consider the period 'through Week 36' any episode of at least 4 weeks in total is to be considered as an ICE, even if not in the last 12 weeks before Week 36. For these analyses, use the end of the 4 weeks as start date of the ICE. For endpoints 'at Week 36', use the end of 4 weeks that fully fall in the last 12 weeks before Week 36 as start date of the ICE.

9.1.2 *IVIg/SCIg at immunomodulating dose (≥1 g/kg/month) at any moment before Week 36*

- 'Immunoglobulins NOS' or 'Immunoglobulin G Human' or 'Immunoglobulins' or 'Immunoglobulin Human Normal' or 'Anti-D Immunoglobulin' and cmroute='INTRAVENOUS' or 'SUBCUTANEOUS'.

9.1.3 *Immunoadsorption or plasma exchange (at least 1 procedure) at any moment before Week 36*

- 'Plasmapheresis' or 'Immunoadsorption therapy' as PRDECOD, at least one cycle

9.1.4 *Rituximab or other anti-CD20 biologics (at least 1 infusion) at any moment before Week 36*

- Rituximab (PVVR, ARRX, ABBS), at least one cycle of 1 g or 375 mg/m^2
- Obinutuzumab
- Ofatumumab
- Ocrelizumab
- Ibritumomab tiuxetan
- Veltuzumab
- Tocilizumab

9.1.5 *IV or IM corticosteroids*

- administered (at least 1 administration, any dose) during the period from Week 28 to Week 36 (i.e, during the 8 week period required in the protocol to confirm the CRoff status)

  or administered at any moment before Week 28 in any of the three following situations:

  a) more than 60 mg/day of prednisone equivalent for 3 consecutive days (prednisone equivalent dose)

  b) more than 40 mg/day of prednisone equivalent for 4 consecutive days (prednisone equivalent dose)

  c) more than 7 days in total

- medications with ATC level2 ='CORTICOSTEROIDS FOR SYSTEMIC USE' and cmroute='INTRAVENOUS' or 'INTRAMUSCULAR'

For NCOD, time-to-event analyses and endpoints that consider the period 'through Week 36' any administration of this type of medication is to be considered as an ICE, even if not during the period from Week 28 to Week 36. For these analyses, use the first day of the medication as start date of the ICE. For endpoints 'at Week 36', use the end of the 3, 4 or 8 (more than 7) days as start date of the ICE for situations a), b) and c) respectively.

9.1.6 Tetracyclines administered at least 100 mg/day for at least 2 weeks in total in the last 10 weeks before Week 36

- medications with ATC level4 = 'TETRACYCLINES'

For NCOD, time-to-event analyses and endpoints that consider the period 'through Week 36' any episode of at least 2 weeks in total is to be considered as an ICE, even if not in the last 10 weeks before Week 36. For these analyses, use the end of the 2 weeks as start date of the ICE. For endpoints 'at Week 36', use the end of 2 weeks that fully fall in the last 10 weeks before Week 36 as start date of the ICE.

9.1.7 Any interventional study drug under development for BP given at any moment before Week 36

- medications will be evaluated during the course of the study

9.1.8 Very potent TCS for 7 consecutive days or 14 days in total given at any moment before Week 36

- medications with ATC level4 = 'CORTICOSTEROIDS, VERY POTENT (GROUP IV)' and cmroute = 'TOPICAL'

Use the end of the 7 or 14 days as start date of the ICE.

9.2 GTI: DERIVATION OF CWS AND AIS

9.2.1 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).

9.2.1.1 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

9.2.1.2 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.

9.2.1.3 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

9.2.1.4 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

9.2.1.5 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

9.2.1.6 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)

9.2.1.8 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)

9.2.1.9 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 W12 and again at W26 and the subjects may be assigned a score of 93 for the worsening from W12 to W26 if the investigator has collected 'Infection' at W26.

9.2.2 CWS and AIS calculation

9.2.2.1 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 post-baseline, 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 W12, at W26 and at W36 as the sum of the worsening items in all post-baseline timepoints up to that timepoint respectively. The overall CWS at the last assessment is the sum of all worsening items over all post-baseline timepoints.

9.2.2.2 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 W12, at W26 and at W36 as the sum of the items in all post-baseline timepoints up to that timepoint respectively. The overall AIS at the last assessment is the sum over all post-baseline timepoints.

9.3 SAS CODE

9.3.1 [redacted]

[redacted]

9.3.2 [redacted]

[redacted]

9.3.3 [redacted]

[redacted]

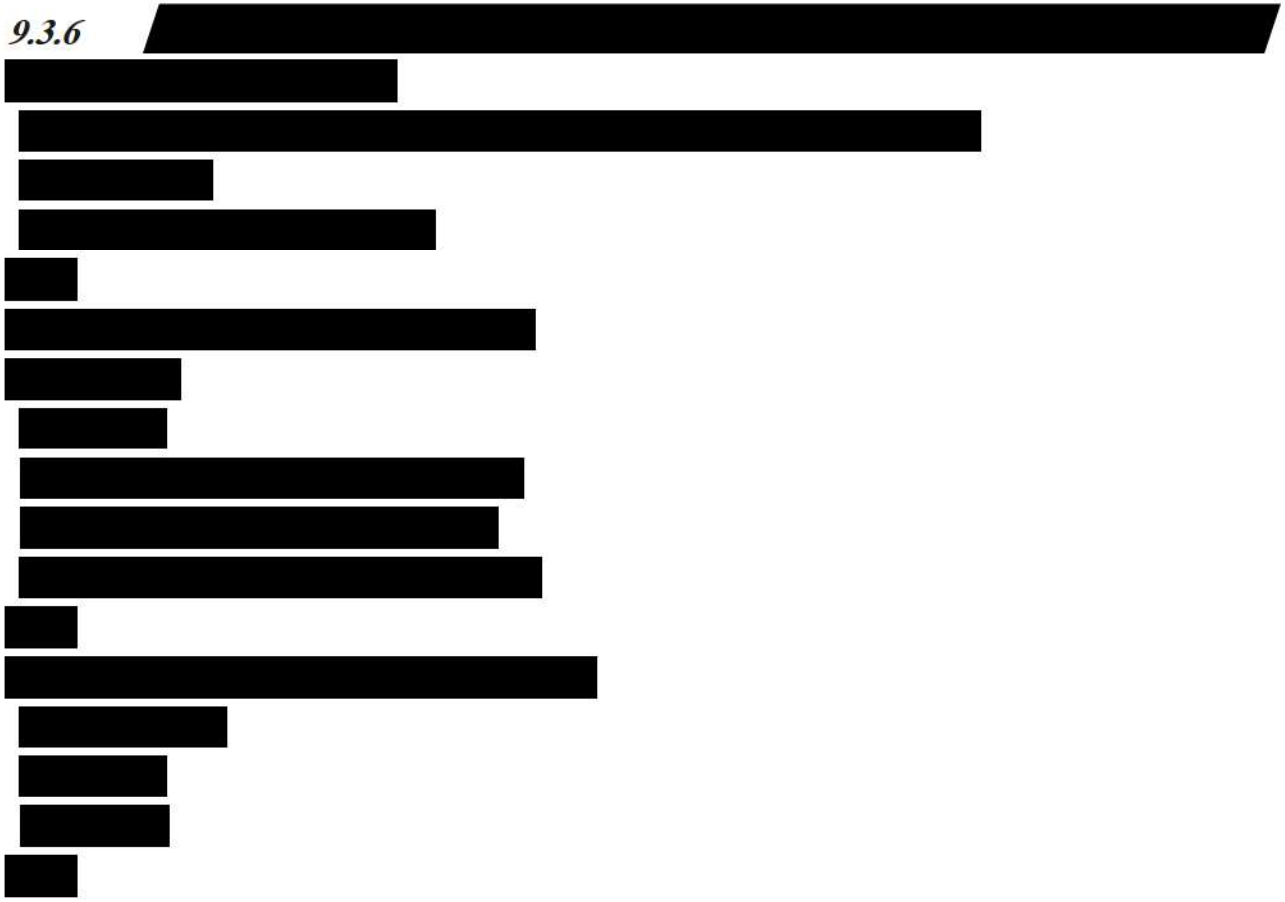
9.3.4 [redacted]

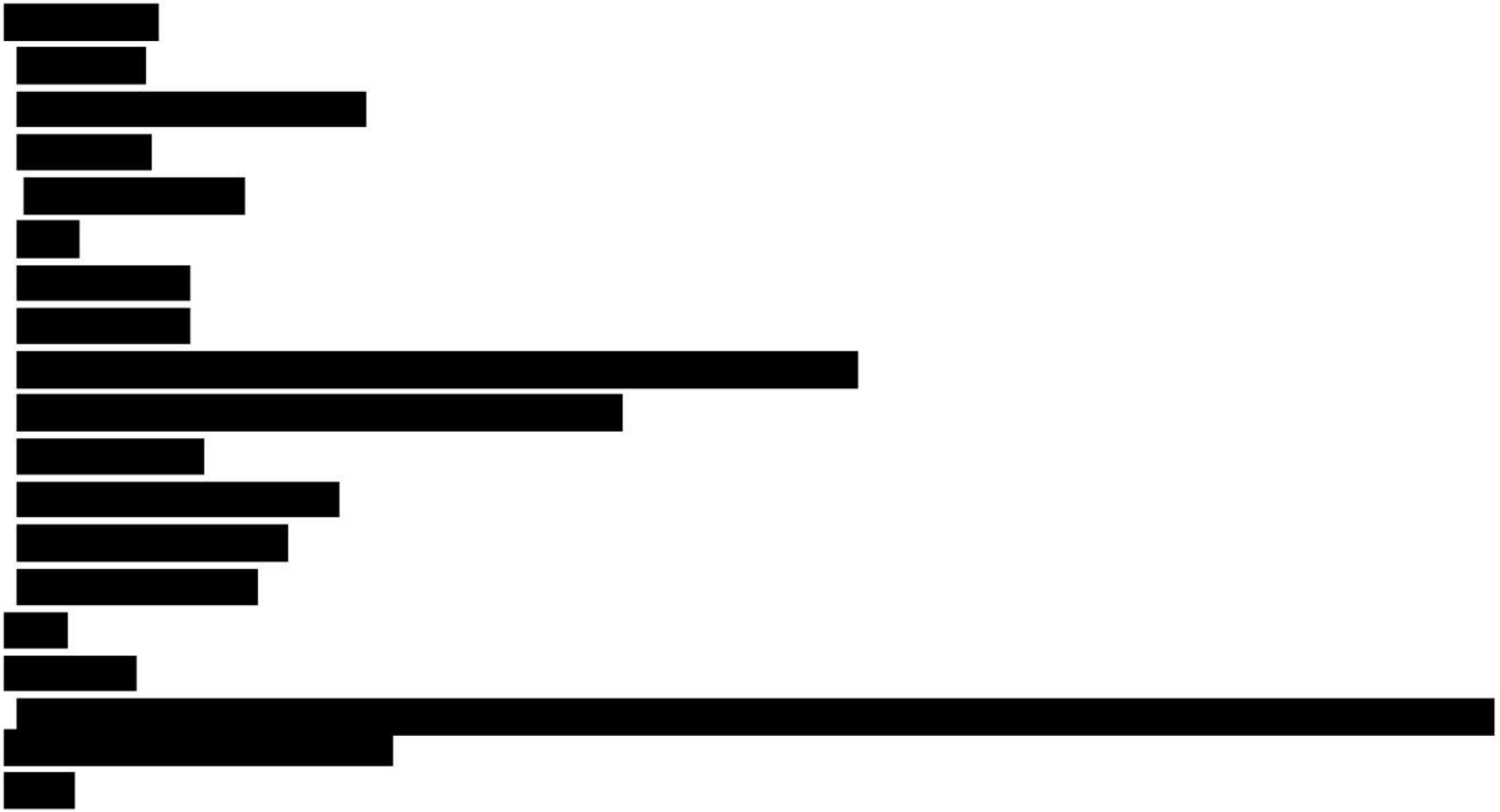
[redacted]

9.3.5 [redacted]

[redacted]

9.3.6 [redacted]





[redacted]

9.3.7 [redacted]

[redacted]

9.3.8 [redacted]

[redacted]

9.3.9 [redacted]

First create a horizontal dataset with CRoff response at each visit in separate variables. Intermittent missing values of CRoff as well as missing values after Week 32 will be imputed via Last Observation Carried Forward (LOCF) approach. For participants who take rescue therapy or died, the CRoff response at all visits after the start of rescue therapy or death will be set to non-response.

[redacted]

9.3.10 [redacted]

[redacted]

9.4 TOXICITY GRADES (CTCAE, V5.0)

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

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

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	mmol/L	>ULN-7.75	>7.75-10.34	>10.34-12.92	>12.92
	mg/dL	>ULN-300	>300-400	>400-500	>500
Creatine kinase		>1.0-2.5 *ULN	>2.5-5.0 *ULN	>5.0-10.0 *ULN	>10.0 *ULN
Creatinine		>1.0-1.5 *ULN	>1.5-3.0 *ULN	>3.0-6.0 *ULN	>6.0 *ULN
Gamma-glutamyl transferase		>1.0-2.5 *ULN	>2.5-5.0 *ULN	>5.0-20.0 *ULN	>20.0 *ULN
Glucose (fasting) low [1]	mmol/L	<LLN-3.0	<3.0-2.2	<2.2-1.7	<1.7
	mg/dL	<LLN-55	<55-40	<40-30	<30
Lipase		>1.0-1.5 *ULN	>1.5-2.0 *ULN	>2.0-5.0 *ULN	>5.0 *ULN
Magnesium low	mmol/L	<LLN-0.5	<0.5-0.4	<0.4-0.3	<0.3
	mg/dL	<LLN-1.2	<1.2-0.9	<0.9-0.7	<0.7
Magnesium high	mmol/L	>ULN-1.23	-	>1.23-3.30	>3.30
	mg/dL	>ULN-3.0	-	>3.0-8.0	>8.0
Potassium low	mmol/L	-	<LLN-3.0	<3.0-2.5	<2.5
	mEq/L	-	<LLN-3.0	<3.0-2.5	<2.5
Potassium high	mmol/L	>ULN-5.5	>5.5-6.0	>6.0-7.0	>7.0
	mEq/L	>ULN-5.5	>5.5-6.0	>6.0-7.0	>7.0
Sodium low	mmol/L	<LLN-130	-	<130-120	<120

PARAMETER	Unit	GRADE 1	GRADE 2	GRADE 3	GRADE 4
	mEq/L	<LLN-130	-	<130-120	<120
Sodium high	mmol/L	>ULN-150	>150-155	>155-160	>160
	mEq/L	>ULN-150	>150-155	>155-160	>160
Triglycerides	mmol/L	1.71-3.42	>3.42-5.70	>5.70-11.4	>11.4
	mg/dL	150-300	>300-500	>500-1000	>1000
Partial thromboplastin time (activated or not specified		>1.0-1.5 *ULN	>1.5-2.5 *ULN	>2.5 *ULN	-
CD4 count	giga/L	<LLN-0.50	<0.50-0.20	<0.20-0.05	<0.05
	counts/mm^3	<LLN-500	<500-200	<200-50	<50
Fibrinogen		<1.00-0.75 *LLN	<0.75-0.50 *LLN	<0.50-0.25 *LLN	<0.25 *LLN
International normalized ratio		>1.2-1.5 *ULN	>1.5-2.5 *ULN	>2.5 *ULN	-
Lymphocytes (absolute count) low	giga/L	<LLN-0.80	<0.80-0.50	<0.50-0.20	<0.20
	counts/mm^3	<LLN-800	<800-500	<500-200	<200
Lymphocytes (absolute count) high	giga/L	-	>4-20	>20	-
	counts/mm^3	-	>4000-20000	>20000	-
Neutrophils (absolute count)	giga/L	<LLN-1.5	<1.5-1.0	<1.0-0.5	<0.5
	counts/mm^3	<LLN-1500	<1500-1000	<1000-500	<500
Platelets	giga/L	<LLN-75	<75-50	<50-25	<25

PARAMETER	Unit	GRADE 1	GRADE 2	GRADE 3	GRADE 4
	counts/mm^3	<LLN-75000	<75000-50000	<50000-25000	<25000
White blood cells	giga/L	<LLN-3	<3-2	<2-1	<1
	counts/mm^3	<LLN-3000	<3000-2000	<2000-1000	<1000

[1] Grade definition will also be applied when the fasting conditions into which the sample was drawn have not been declared.

Note: In case ULN/LLN is higher/lower than the upper/lower limit of grade 1 (or even higher grades), ULN/LLN will be ignored and only the fixed values of CTCAE will be considered. 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.

9.5 SCHEDULE OF ASSESSMENTS

Study Period	Screening Period[a]	Treatment Period[b]															Follow-up Period[c]		Other Visits		
Visit Type	SCR	BL	Mandatory On-site Visits													Other Weekly Visits	EoTP	F1	F2	ETD[d]	ESD[e]	UNS[f]
Visit Week		0	1	(D10)	2	3	4	8	12	16	20	24	26	28	32	–	36	39	43	ETD	ESD	
Visit Day	-14 to -1	1	8	10	15	22	29	57	85	113	141	169	183	197	225		253					
Visit Window (±days)	+7	–	±2	±1	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±3	±3	–	–	–
Informed consent[g]	X																					
Inclusion / exclusion criteria	X	X																				
Randomization		X																				
Demography	X																					
Medical and surgical history	X																					
Histopathology/DIF[h]	X																					
Karnofsky performance index score	X																					
QoL questionnaires (EQ-5D-5L, DLQI, ABQoL)		X							X				X				X			X	X	

Study Period	Screening Period[a]	Treatment Period[b]															Follow-up Period[c]		Other Visits		
Visit Type	SCR	BL	Mandatory On-site Visits													Other Weekly Visits	EoTP	F1	F2	ETD[d]	ESD[e]	UNS[f]
Visit Week		0	1	(D10)	2	3	4	8	12	16	20	24	26	28	32	–	36	39	43	ETD	ESD	
Visit Day	-14 to -1	1	8	10	15	22	29	57	85	113	141	169	183	197	225		253					
Visit Window (±days)	+7	–	±2	±1	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±3	±3	–	–	–
Concomitant therapies/procedures[i]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Height	X																					
Weight	X	X	X		X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	
Physical examination and vital signs (blood pressure, HR, body temperature)	X	X	X		X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X
ECG	X												X				X			X	X	
Urinalysis	X	X					X	X	X	X	X	X		X	X		X	X	X	X	X	X
Active viral infection tests (HBV, HCV, HIV)	X																					
SARS-CoV-2 nasopharyngeal swab	X																					
QuantiFERON TB-test	X																					
Serum pregnancy *or* serum FSH test[j]	X																					
Urine pregnancy test (local laboratory)[k]		X					X	X	X	X	X	X		X	X		X	X	X	X	X	X

Study Period	Screening Period[a]	Treatment Period[b]															Follow-up Period[c]		Other Visits		
Visit Type	SCR	BL	Mandatory On-site Visits													Other Weekly Visits	EoTP	F1	F2	ETD[d]	ESD[e]	UNS[f]
Visit Week		0	1	(D10)	2	3	4	8	12	16	20	24	26	28	32	–	36	39	43	ETD	ESD	
Visit Day	-14 to -1	1	8	10	15	22	29	57	85	113	141	169	183	197	225		253					
Visit Window (±days)	+7	–	±2	±1	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±3	±3	–	–	–
Clinical chemistry and hematology	X[l]	X	X		X		X	X	X	X	X	X	X	X	X		X	X	X	X	X	X
Specialty laboratory tests (Section 8.3.6.1)		X							X													
Pharmacokinetics (Section 8.5)		X	X	X[m]	X		X	X	X	X	X	X	X	X	X		X	X	X	X	X	X
Immunogenicity (Section 8.9)	X	X			X		X	X	X	X	X	X	X	X	X		X	X	X	X	X	X
Pharmacodynamics (total IgG serum levels; anti-BP180 and anti-BP230 antibodies; [redacted] serum levels) (Section 8.6)	X	X	X		X		X	X	X	X	X	X	X	X	X		X	X	X	X	X	X
Substudy (selected sites): historical protective antibody titers (serum) (Section 8.3.6.2)		X					X															
Substudy (selected sites): vaccination antibody titers (serum) (Section 8.3.6.2)		Before vaccination; first available on-site visits at +4 weeks, +12 weeks, and +24 weeks postvaccination																	(x)		(x)	

Study Period	Screening Period[a]	Treatment Period[b]															Follow-up Period[c]		Other Visits		
Visit Type	SCR	BL	Mandatory On-site Visits													Other Weekly Visits	EoTP	F1	F2	ETD[d]	ESD[e]	UNS[f]
Visit Week		0	1	(D10)	2	3	4	8	12	16	20	24	26	28	32	–	36	39	43	ETD	ESD	
Visit Day	-14 to -1	1	8	10	15	22	29	57	85	113	141	169	183	197	225		253					
Visit Window (±days)	+7	–	±2	±1	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±3	±3	–	–	–
Substudy (selected sites): vaccination cellular responses (PBMCs) (Section 8.3.6.2)		Before vaccination; first available on-site visits at +12 weeks and +24 weeks postvaccination																	(x)		(x)	
IGA-BP (Section 8.2.1.2)	X	X	X		X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X
BPDAI (Section 8.2.1.3)	X	X	X		X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X
Itch NRS (Section 8.2.1.4)		X	X		X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X
BP disease status[n]		X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concurrent OCS dose monitoring[o]		X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Investigator telephone calls[p]																Xp						
Substudy (selected sites): photography of BP lesions (Section 8.10)		The sponsor suggests that photos be taken at BL and when CDA, CR, and relapse occur. Photos may also be taken at intermediate timepoints per investigator discretion.															The sponsor suggests that photos be taken at BL and when CDA, CR, and relapse occur. Photos may also be taken at intermediate timepoints per investigator discretion.					
GTI (including C-GTI & GTI-SL)		X							X				X				X			X	X	
AEs	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Study Period	Screening Period[a]	Treatment Period[b]															Follow-up Period[c]		Other Visits		
Visit Type	SCR	BL	Mandatory On-site Visits													Other Weekly Visits	EoTP	F1	F2	ETD[d]	ESD[e]	UNS[f]
Visit Week		0	1	(D10)	2	3	4	8	12	16	20	24	26	28	32	–	36	39	43	ETD	ESD	
Visit Day	-14 to -1	1	8	10	15	22	29	57	85	113	141	169	183	197	225		253					
Visit Window (±days)	+7	–	±2	±1	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±2	±3	±3	–	–	–
IMP administration[g]		X	X		X	X	X	X	X	X	X	X	X	X	X	X						
IMP (self-) administration training (Section 6.4)					X	X	X	X	X	X	X	X	X	X	X							
Rescue therapy evaluation / initiation (Section 6.8.3)																				X		

ABQoL=Autoimmune Bullous Disease Quality of Life questionnaire; AE=adverse event; aPTT=activated partial thromboplastin time; BL=baseline; BP=bullous pemphigoid; BPDAI=Bullous Pemphigoid Disease Area Index; CDA=control of disease activity; C-GTI=composite Glucocorticoid Toxicity Index; DIF=direct immunofluorescence; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; EFG=efgartigimod; EFG PH20 SC=efgartigimod coformulated with rHuPH20 for subcutaneous injection (dosing formulation); EoTP=end of treatment period; EQ-5D-5L=EuroQoL 5-Dimension 5-Level; ESD=early study discontinuation; ETD=early treatment discontinuation; FSH=follicle-stimulating hormone; F1 and F2=follow-up visits 1 and 2; GTI=Glucocorticoid Toxicity Index; GTI-SL=Glucocorticoid Toxicity Index Specific List; HBV=hepatitis B virus; HCV=hepatitis C virus; HR=heart rate; IGA-BP=Investigator Global Assessment of Bullous Pemphigoid; [redacted] IgG=immunoglobulin type-G; IMP=investigational medicinal product; INR=international normalized ratio; Itch NRS=Itch Numerical Rating Scale; OCS=oral corticosteroid(s); OLE=open-label extension (study); PBMCs=peripheral blood mononuclear cells; PBO PH20 SC=placebo coformulated with rHuPH20 for subcutaneous injection (dosing formulation); PK=pharmacokinetic; QoL=quality of life; rHuPh20=recombinant human hyaluronidase PH20; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; SCR=screening; TB=tuberculosis; UNS=unscheduled; WOCBP=women of childbearing potential.

[a] The screening period may be extended by a maximum of 7 days for logistical or administrative reasons (eg, receipt of laboratory results). Additional details are provided in Section 8.1.2.

[b] The treatment period consists of weekly visits, starting with the BL visit and ending with the EoTP visit. Mandatory on-site visits must be performed as indicated. Weekly visits that are not designated as mandatory on-site visits may be performed at home if the participant has achieved CDA. During home visits, IMP will be administered by a home nurse. Additional details are provided in Section 8.1.3.

[c] Follow-up visits are only applicable for participants who choose not to roll over to the OLE study ARGX-113-2010. Additional details are provided in Section 8.1.3.

[d] The ETD visit must be performed when IMP is discontinued before the EoTP visit; the study site should make every effort to perform this visit within 7 days of the participant's last IMP dose. Participants will remain in the study (provided that they have not withdrawn consent) and will continue to participate in study visits as scheduled, only without IMP administration. Rescue therapy may be initiated at this visit. Additional details are provided in Section 7.1.

[e] The ESD visit must be performed when the participant either withdraws consent or is permanently discontinued from the study (refer to Section see Section 7.2 for examples of study discontinuation criteria). The study site must make every effort to perform this visit within 7 days of the participant's last IMP dose.
[f] An unscheduled visit should be performed if the participant has (or suspects they have) new BP lesions, has new AEs, or has other issues requiring site staff intervention.
[g] No study-related activities can be performed before the participant has provided signed informed consent.
[h] Histopathology/DIF are performed only if positive test results are not available as part of the participant's medical history.
[i] All vaccinations received prior to the study should be recorded as part of the participant's prior medication history, while all vaccinations received during the study should be recorded as concomitant medications.
[j] WOCBP must have a negative serum pregnancy test and must be performed in WOCBP. Alternatively, postmenopausal female participants must have a serum FSH test to confirm postmenopausal status.
[k] Urine pregnancy tests will be performed at the specified visits for WOCBP only.
[l] In addition to the standard clinical chemistry and hematology parameters (Section 10.2), the screening assessment also includes INR and aPTT.
[m] The day 10 PK blood sample will only be collected during part A of the study. The sample should be collected no earlier than day 9, and no later than day 11.
[n] BP disease assessment (Section 8.2.1.1) must be performed according to the definitions presented in Section 4.1.3.
[o] The participant's concurrent prednisone (or alternate OCS of equivalent dose strength) dosage will be monitored throughout the study (Section 8.2.1.1) and will be adjusted based on the procedures described in Section 6.8.1.3.
[p] For study visits that occur at home (in between mandatory on-site visits), the investigator will call the participant once weekly to assess BP disease status and review/adjust the participant's concurrent prednisone dosage.
[q] At BL (week 0 [day 1]) and week 1 (day 8), 2000 mg of IMP (EFG PH20 SC or PBO PH20 SC) will be administered via 2 SC injections (Table 5). At weeks 2 through 35, 1000 mg of IMP (EFG PH20 SC or PBO PH20 SC) will be administered via a single SC injection (Table 5). To monitor for possible injection-related reactions, the participant will remain at the study site for at least 1 hour after receiving their first dose of IMP at BL (week 0 [day 1]), at least 30 minutes after receiving their IMP doses at weeks 1-4, and at least 15 minutes after receiving their IMP doses at subsequent visits. Following completion of these monitoring periods, participants will be released after site staff confirm stable clinical status.