Janssen Research & Development

Statistical Analysis Plan

A Proof-of-Concept Study of Guselkumab in the Treatment of Subjects with New-onset or Relapsing Giant Cell Arteritis

Protocol CNTO1959GCA2001; Phase 2

CNTO1959 (Guselkumab)

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Compliance: The study described in this report was performed according to the principles of Good Clinical Practice (GCP).

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1. INTRODUCTION

This Statistical Analysis Plan (SAP) contains definitions of analysis sets, derived variables, and addresses the statistical methods for all planned analyses of efficacy, safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD) and immunogenicity of guselkumab. This SAP incorporates all analyses through the Week 28 database lock (DBL), through the Week 60 DBL for the main study, and a final DBL when the last participant completes last visit in the long-term extension (LTE) period for the CNTO1959GCA2001 study.

1.1. Objectives and Endpoints

Objectives	Endpoints
Primary	
To evaluate the efficacy of guselkumab compared to placebo, in combination with a 26-week GC taper regimen, in adult participants with new-onset or relapsing GCA.	The proportion of participants achieving GC-free remission at Week 28
Secondary	
To evaluate the efficacy of guselkumab compared to placebo, in combination with a 26-week GC taper regimen, in adult participants with new-onset or relapsing GCA as measured by alternative definitions of GC free remission, GC-sparing effects, and prevention of disease flares.	The proportion of participants achieving GC-free remission from Week 28 by visit through Week 52 The proportion of participants achieving GC-free remission and normalization of erythrocyte sedimentation rate (ESR) at Week 28 and by visit through Week 52 The proportion of participants achieving GC-free remission and normalization of C-reactive protein (CRP) at Week 28 and by visit through Week 52 The proportion of participants achieving GC-free remission and normalization of both ESR and CRP at Week 28 and by visit through Week 52 The cumulative GC dose through Week 28 and through Week 52 The time to first GCA disease flare or discontinuation of study intervention due to AE of worsening of GCA through Week 28 and through Week 52

Objectives	Endpoints
	The number of GCA disease flares or discontinuation of study intervention due to AE of worsening of GCA through Week 28 and through Week 52
To evaluate the safety of guselkumab, in combination with a 26-week GC taper regimen, in adult participants with new- onset or relapsing GCA.	Number/proportion of participants with treatment- emergent adverse events (TEAEs) through Week 60 Number/proportion of participants with TEAEs by system organ class with a frequency threshold of 5% or more through Week 60 Number/proportion of participants with treatment- emergent serious adverse events (SAEs) through Week 60 Number/proportion of participants with clinically significant abnormalities in vital signs, laboratory safety tests through Week 60
To evaluate the PK and immunogenicity of guselkumab, in combination with a 26-week GC taper regimen, in adult participants with new-onset or relapsing GCA.	Mean (standard deviation [SD]) serum concentrations of guselkumab through Week 52 in participants receiving active study intervention. Number/proportion of participants with antibodies to guselkumab in participants receiving active study intervention.
Exploratory	
To explore the longer-term efficacy of guselkumab compared to placebo, in combination with a 26-week GC taper regimen, in adult participants with new-onset or relapsing GCA.	Proportion of participants in sustained remission through Week 52
To evaluate the changes in immune- markers to guselkumab compared to placebo, in combination with a 26-week GC taper regimen, in adult participants with new-onset or relapsing GCA.	Change from baseline in CRP through Week 52 Change from baseline in ESR through Week 52
To explore the changes in pharmacodynamic (PD) markers and arterial vessel wall inflammation following administration of guselkumab in adult participants with new-onset or relapsing GCA.	Assessment of IL-23 pathway related and disease related biomarkers in serum, whole blood and peripheral blood mononuclear cell (PBMC) through Week 52.

Objectives	Endpoints
	Large-Vessel Imaging (fluorodeoxyglucose positron emission tomography/computed tomography [FDG-PET/CT]) changes from baseline at Week 52 (or flare)
To explore changes in participant reported Clinical Outcome Assessments, pain and fatigue, and physician reported outcomes	Change from baseline on electronic patient-reported outcome (ePRO): Patient's Global Assessment of Disease Activity (PGA), Pain Assessment, Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue and short form-36 (SF-36) by visit through Week 52 Change from baseline on clinician reported outcome: Physician's Global Assessment of Disease Activity (PhGA) by visit through Week 52
To explore digital health parameters following administration of guselkumab in adult participants with new-onset or relapsing GCA.	Change from baseline in Actigraphy Watch collected continuous data on physical activity, mobility, and sleep by visit through Week 52
Exploratory Objectives for the Long-Term Extension (LTE) period	
To evaluate long-term efficacy of guselkumab in adult participants with new-onset or relapsing GCA	The proportion of participants achieving GC-free remission from Week 52 (LTE Week 0) through Week 104 by visit (LTE Week 52) The time to first GCA disease flare from Week 52 (LTE week 0) through Week 104 (LTE Week 52).
To evaluate the continued safety of guselkumab in adult participants with new-onset or relapsing GCA.	Number/proportion of participants with TEAEs or SAEs from Week 52 (LTE Week 0) through Week 112 (LTE Week 60) Number/proportion of participants with clinically significant abnormalities in vital signs and laboratory safety tests from Week 52 (LTE Week 0) through Week 112 (LTE Week 60)
To evaluate the PK and immunogenicity of guselkumab, in adult participants with new-onset or relapsing GCA.	Mean (SD) serum concentrations of guselkumab from Week 52 through Week 104 (LTE Week 52) in participants receiving active study intervention. Number/proportion of participants with antibodies to guselkumab in participants receiving active study intervention

Objectives	Endpoints
To explore the changes in PD markers and arterial vessel wall inflammation following administration of guselkumab in adult participants with new-onset or relapsing GCA in the LTE period.	Assessment of IL-23 pathway related and disease related biomarkers in serum and whole blood at Week 104 (LTE Week 52) Large-Vessel Imaging (FDG-PET/CT) changes from baseline and Week 52 at Week 104 (LTE Week 52) or flare
To explore changes in participant reported Clinical Outcome Assessments, pain and fatigue, and physician reported outcomes following administration of guselkumab in adult participants with new-onset or relapsing GCA in the LTE period.	Change from baseline on electronic patient-reported outcome (ePRO): Patient's Global Assessment of Disease Activity (PGA), Pain Assessment, Functional Assessment of Chronic Illness Therapy (FACIT)-fatigue and short form-36 (SF-36) at Week 76 (LTE Week 24), Week 104 (LTE week 52) and or Flare visit. Change from baseline on clinician reported outcome: Physician's Global Assessment of Disease Activity (PhGA) at Week 76 (LTE Week 24) week 104 (LTE Week 52) and or Flare visit.

1.2. Study Design

CNTO1959GCA2001 is a randomized, double-blind, placebo-controlled, parallel, multicenter, interventional Phase 2 Proof-of-Concept study evaluating the efficacy, safety, PK, and immunogenicity of guselkumab for the treatment of active new-onset or relapsing GCA in adult participants.

Main Study Treatment Period (Through up to Week 60)

A target of approximately 51 participants will be enrolled in this study. Participants will be randomly assigned into 2 study intervention groups with a 2:1 ratio for guselkumab versus placebo.

- **Group 1: Guselkumab (200 mg SC every 4 weeks)**

  Participants will receive guselkumab 200 mg SC every 4 weeks at Week 0 through Week 48 in the Main study.

- **Group 2: Placebo**

  Participants will receive placebo SC every 4 weeks at Week 0 through Week 48.

Participant randomization will be stratified by baseline disease status (new-onset and relapsing GCA; relapsing preferentially limited to 70% to ensure some enrollment of new-onset GCA but may be increased depending on the rate of enrollment of relapsing versus new-onset GCA), and by baseline GC dose (≤30 mg/day or >30 mg/day).

The placebo comparator (in addition to standard-of-care background therapy of GCs) will be used in this study through Week 48 of the Main study to allow for blinded, placebo-controlled evaluation of the long-term efficacy and safety of guselkumab in participants with GCA. Participants on placebo that continue into the LTE will continue to receive placebo until the participant reaches Week 100 (LTE Week 48) or experiences a GCA flare, or until unblinding of the study due to completion of the main study, whichever occurs first.

The total duration of the study is up to 66 weeks of the main study: a screening period of ≤6 week, a 48-week main study treatment period, and a 12-week safety follow-up period after the last dose (a final efficacy visit 4 weeks after the last dose and a safety follow-up visit 12 weeks after the last dose). Participants that continue in the LTE period may continue in the study for a total duration of 112 weeks.).

Participants who develop a GCA flare should stop the protocol-defined GC taper and be given rescue therapy with GCs at the discretion of the investigator.

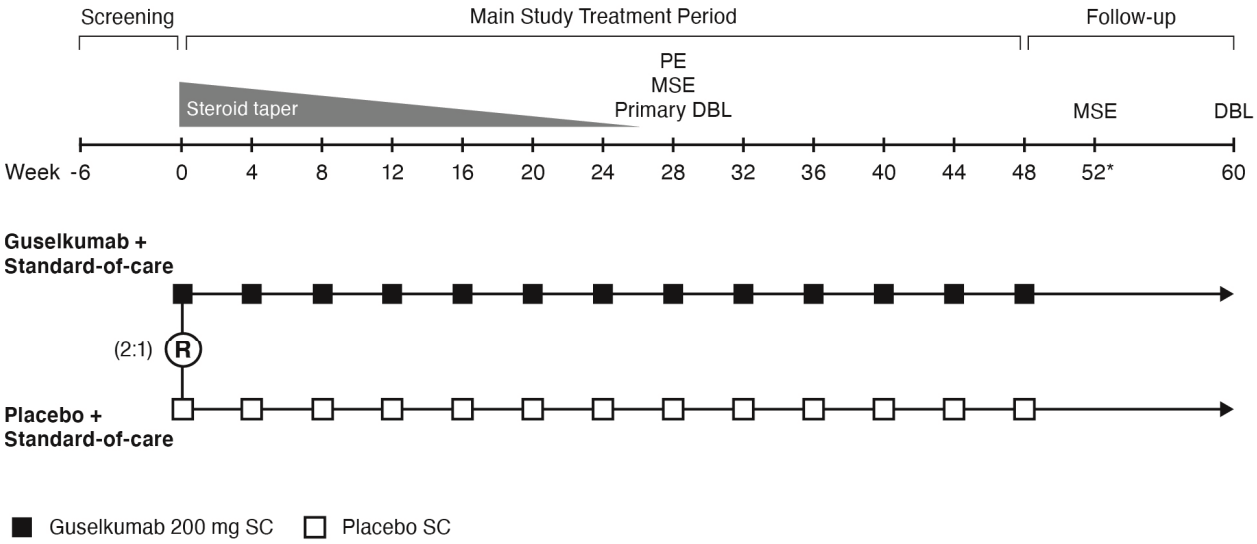
Efficacy, safety, PK, immunogenicity, and biomarkers will be assessed according to the Schedule of Activities of the protocol. An optional pharmacogenomic blood sample will be collected from participants who consent to the collection of these samples (where local regulations permit).

The primary efficacy analysis will be performed after all participants have completed Week 28 efficacy assessments (or discontinued). Additional secondary endpoints will be completed at Week 28 and Week 52. Three planned database locks (DBLs) will occur, at Week 28 and at Week 60 for the main study and a final DBL lock when the last participant completes last visit in the LTE period. The study will be double-blind until all participants have completed the main study and associated Week 60 DBL has occurred.

Participants who complete the Week 52 visit and are assessed to be in GC-free remission, may have the option to participate in a long-term extension (LTE) study. Participants not entering LTE will be followed to Week 60 and are deemed having completed the main study.

An overview of the main study design is presented in Figure 1.

Figure 1: Schematic Overview of the Study



Abbreviations: DBL = database lock; MSE = major secondary endpoint; N = number of participants; PE = primary endpoint; R = randomization; SC = subcutaneous.

* Participants who are eligible and want to participate in the LTE study will continue with study activities according to the LTE schedule after completing Week 52 assessments of the main study.

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Long-term Extension Treatment Period (Week 52 to Week 112; optional for eligible participants)

Participants who complete the Week 52 visit and are assessed to be in GC-free remission, may have the option to participate in the LTE period of the study.

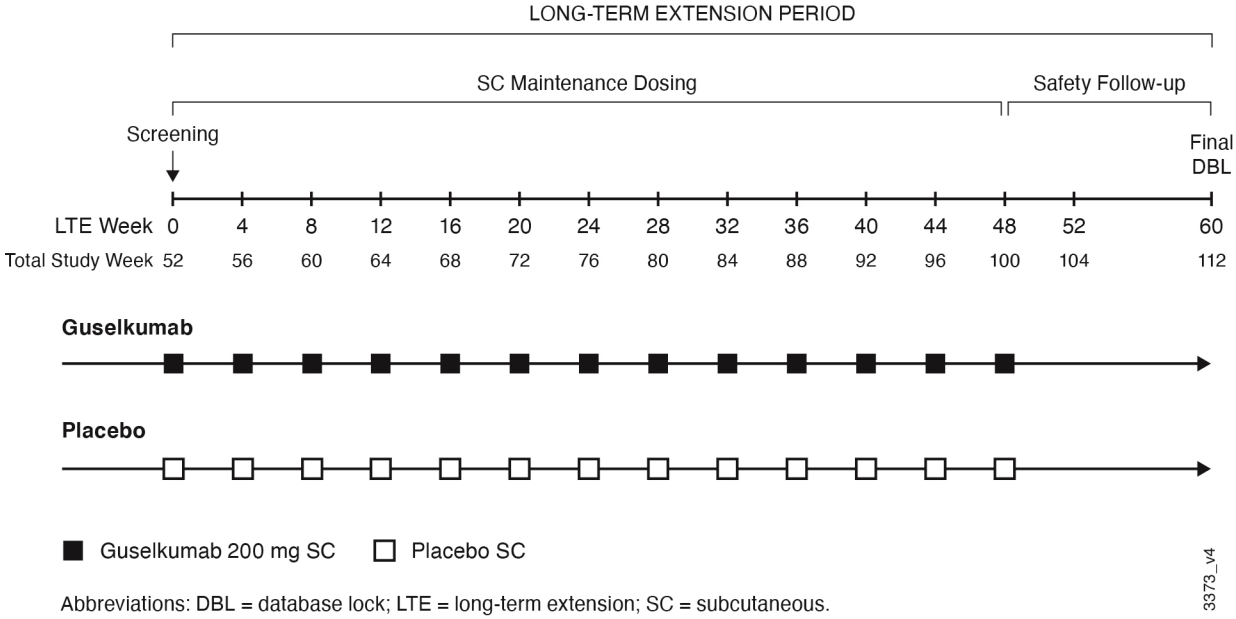
If a participant is in GC-free remission at Week 48, the participant will be informed of the possibility to participate in the LTE period and continue to receive study intervention. Study intervention will continue to be blinded, meaning that a participant will continue to receive the treatment that had been allocated to that participant (placebo or guselkumab) in the main study. After the Week 52 evaluations, if the participant is eligible and has consented for the LTE, the participants will continue to receive SC study intervention every 4 weeks starting at Week 52 (LTE Week 0) under this protocol's study extension until participants reach Week 100 (LTE Week 48) or until a participant experiences a GCA flare requiring GC rescue medication, or the participants discontinue study intervention due to unblinding after the Week 60 DBL for the Main study, or until the Sponsor makes a decision not to continue this study, whichever occurs first. Participants who continue treatment as part of the study extension will be intermittently evaluated per the protocol for efficacy, PK, and safety. The LTE treatment period is followed by a 12-week safety follow-up period after the last dose (a final efficacy visit 4 weeks after the last dose and a safety follow-up visit 12 weeks after the last dose). Participants that experience a flare should have a Flare visit with assessments performed according to the SoA of the protocol preferably within 1 week of having the flare and an early termination visit approximately 12 weeks after the last dose. In case a participant is diagnosed as having a flare during a study visit or shortly before a planned study visit, the Flare visit and regular visit can be combined. Overlapping procedures and

assessments need only be performed once. The FDG-PET/CT scan can be scheduled separately from other assessments.

After the Week 60 DBL, the study will be unblinded to treatment. Any participants in the LTE that are on placebo will be informed and administration of study intervention will be discontinued. The participants may still continue in the study until Week 112 or until the end of the safety follow-up period in case they experienced a GCA flare.

An overview of the long-term extension (LTE) period is presented in Figure 2.

Figure 2: Schematic Overview of the Long-Term Extension (LTE) Period



Abbreviations: DBL = database lock; LTE = long-term extension; SC = subcutaneous.

2. STATISTICAL HYPOTHESES

The primary hypothesis is that guselkumab treatment with a 26-week GC taper is superior to placebo with a 26-week GC taper in participants with new-onset or relapsing GCA as assessed by the proportion of participants achieving GC-free remission at Week 28.

3. SAMPLE SIZE DETERMINATION

Approximately 51 participants are planned to be randomized into the study. The assumptions for the sample size and power calculation were based on the data from the Actemra Phase 3 GCA study. In the Actemra Phase 3 study, the proportions of participants in GC-free remission at Week 28 were estimated to be approximately 38% and 74% for placebo (+26-week GC taper) and Actemra qw (+26-week GC-taper), respectively, for a treatment difference of 36%.

Based on the data above, the GC-free remission rates at Week 28 are assumed to be 40% for placebo and 80% for guselkumab treatment arm. Based on these assumptions, 51 participants are planned to be randomized in a 2:1 ratio to either the guselkumab group (N=34) or the placebo

group (N=17). These sample sizes provide the study with 82% power to detect a difference in the primary endpoint between the 2 study intervention groups.

Table 1 shows the power to detect a difference in proportions of participants in GC-free remission between the guselkumab and placebo intervention groups at Week 28 under various assumptions.

Table 1: Power to Detect Difference in Proportions of Participants Achieving Glucocorticoid-free Remission between the Guselkumab and Placebo Intervention Groups at Week 28

Placebo (n = 17)	Guselkumab (n = 34)	Power (%)
35%	70%	68
	75%	81
	80%	90
40%	75%	69
	80%	**82**
	85%	91

Notes:
- The power calculation is based on two-sample Z test with continuity correction (pooled variance) under the normal distribution approximation.
- Power calculation is based on a 2-sided significance level of 0.10.
- Total sample size is 60.

4. POPULATIONS (ANALYSIS SETS) FOR ANALYSIS

For purposes of analysis, the following populations are defined:

Analysis Sets	Description
Enrolled Analysis Set	All participants who signed the ICF
Randomized Analysis Set	The randomized analysis set includes all participants who were randomized in the study.
Full Analysis Set (FAS)	The full analysis set (FAS) includes all randomized participants who received at least 1 administration of study intervention.
Per Protocol (PP)	The per protocol analysis set (PP) includes a subset of participants in the full analysis set (FAS) who were in general compliance with the protocol. General compliance is defined as having no major protocol deviations that could have an impact on the efficacy assessment per clinical judgement. This analysis will be used for the primary endpoint. Participants will be excluded from this analysis as below: • who did not meet the inclusion criteria 3, 4, 6, 8 in the protocol; • who met the exclusion criteria 1, 6, 22, 24 in the protocol;

Analysis Sets	Description
	• who discontinued study intervention for reasons other than lack of efficacy or an AE of worsening of GCA, or missed at least two scheduled study agent administrations prior to Week 28. Participants who did not completed all scheduled study intervention administration due to intercurrent events (discontinued the study intervention due to lack of efficacy or an AE of worsening of GCA, or participants who started prohibited medications or therapy during the study that could improve GCA, or received a rescue medication for a GCA flare) will be included in the per protocol analysis and the data handling rules for these intercurrent events specified in Section 5.3.2 and Section 5.3.3 will be applied.
Safety Analysis Set	The safety analysis set includes all participants who received at least 1 dose of study intervention.
Pharmacokinetics Analysis Set	All participants who received at least 1 administration of guselkumab and have at least one valid post-dose blood sample drawn for PK analysis.
Immunogenicity Analysis Set	All participants who received at least 1 administration of guselkumab and have at least one post-dose sample collection.
Pharmacodynamic Analysis Set	All participants who received at least 1 administration of study intervention and have at least one post-dose sample collection.
Full Analysis Set with Subjects Participating in the Long-Term Extension	All participants who were in the FAS and received at least 1 injection at or beyond Week 52.
Safety Analysis Set with Subjects Participating in the Long-Term Extension	All participants who were in the safety analysis set and received at least 1 injection at or beyond Week 52.

5. STATISTICAL ANALYSES

5.1. General Considerations

Unless specified otherwise, efficacy data summaries will be provided by intervention group for the FAS. Data primarily will be summarized using descriptive statistics. Continuous variables will be summarized using the number of observations, mean, SD, median, interquartile range, minimum and maximum, as appropriate. Categorical values will be summarized using the number of observations and percentages as appropriate. Median time will be reported for time to event variables. In addition, graphical data displays (eg, line plots) and participant listings may also be used to summarize/present the data. Statistical comparisons will be made between the guselkumab intervention group and the placebo intervention group.

In general, all statistical tests will be performed at a 2-sided significance level of α=0.10. No multiplicity adjustment will be made for the secondary endpoints being tested and nominal p-values will be reported.

The baseline measurement is defined as the closest measurement taken prior to or at the time of the first study agent administration date unless otherwise specified.

5.1.1. Visit Windows

Unless otherwise specified, nominal visits will be used for all by visit analyses. The study visits scheduled after randomization should occur at the time delineated in the Schedule of Activities of the protocol.

5.1.2. Pooling Algorithm for Analysis Centers

No pooling algorithm will be performed.

5.1.3. Reference Date, Study Day and Relative Day

The Reference Date is the date of the first study agent administration. If the date of the first study agent administration is missing or the first study agent administration is not done, then the Reference Date equals the corresponding visit date (eg, Week 0 visit date). If the corresponding visit date is also missing, then the Reference Date equals the randomization date.

Study Day 1 or Day 1 refers to the reference date (there is no Study Day 0). All efficacy and safety assessments at all visits will be assigned a day relative to this date.

5.2. Participant Dispositions

Screened participants and reason for screen failures will be summarized overall.

The number of participants in the following disposition categories will be summarized throughout the study by intervention group and overall:

- Participants randomized
- Participants who received study intervention
- Participants who completed the study
- Participants who enrolled in LTE
- Participants who discontinued study intervention
  - Reasons for discontinuation of study intervention, including those due to COVID-19 related events
- Participants who terminated study prematurely, including those due to COVID-19 related events
  - Reasons for termination of study

The above categories will include summaries through Week 28 and through Week 60 for the main study, and from Week 52 through Week 112 for participants in the LTE period excluding the summary of participants randomized.

A listing of participants will be provided for the following categories:

- Participants who discontinued study intervention
- Participants who terminated study prematurely
- Participants who were unblinded during the study period
- Participants who were randomized yet did not receive study intervention

5.3. Primary Endpoint Analysis

The primary endpoint is the proportion of participants achieving GC-free remission at Week 28 (ie, meeting remission definition and not on GC for GCA at Week 28).

5.3.1. Definition of Endpoint

GC-free remission response at Week 28 is defined as:

1. No signs or symptoms of active GCA at Week 28

   AND

2. Absence of GCA flare from first dose of the study agent through Week 28,

   AND

3. Adherence to the protocol specified 26-week GC taper

Definition of GCA Flare: GCA flare is defined as the recurrence of signs and symptoms of active GCA, with or without elevation of inflammatory markers, and with the necessity for an increase in GC dose for GCA.

Having CRP/ESR elevations in isolation without clinical signs and symptoms attributable to GCA, does not qualify as flare, unless the investigator decided to increase the GC dose.

Definition of GC Taper Adherence. The protocol specified 26-Week open-label GC tapering schedule is provided in Section 10.8 of the protocol. Adherence to this schedule is required. Participants will remain on the GC dose they were on at baseline for one week (Week 0). The taper is starting at Week 1 and continues down to GC-free in Week 26, as per the schedule. Participant should adhere to the tapering schedule through Week 26 unless they require use of rescue GC therapy for GCA disease flare.

A participant will be considered as not adherent to the protocol-defined 26-week GC taper, if the compliance of GC intake (any oral GC intake) is greater than 120% cumulative prednisone (or equivalent) dose, between first and last planned dose of GC taper. Patients not adhering to the GC

taper will be considered as non-responders in the primary analysis. Participants receiving less than the planned amount of prednisone (or equivalent) will not be considered as non-responders.

Compliance of GC intake will be calculated as follows:

Compliance (%) = (actual GC dose taken/total GC dose supposed to be taken) x100.

If a participant receives GC other than prednisone or prednisolone, the amount of GC dosage equivalent to prednisone recorded on Concomitant Therapy page in the eCRFs will be converted to a prednisone-equivalent dose using the following table.

GC	Conversion factor from alternative GC to prednisone equivalent dose (mg)
Cortisone acetate	0.2
Hydrocortisone	0.25
Deflazacort	0.67
Prednisone	1
Prednisolone	1
Triamcinolone	1.25
Methylprednisolone	1.25
Dexamethasone	6.67
Betamethasone	6.67

The following rules will be used to assess a GC-free remission at Week 28:

A participant will not be considered to be in GC-free remission at Week 28, if a participant meets one of the following criteria; otherwise the participant will be considered as a GC-free remission at Week 28:

- If an investigator answers the question "What is the participant's disease status at the time of the visit?" at Week 28 as "Participant has stable active disease, not requiring increase in GC dose." on the Clinical Assessment of GCA – Signs and Symptoms eCRF page.
- If an investigator answers the question "What is the participant's disease status at the time of the visit?" from first dose of the study agent through Week 28, inclusive as "GCA Flare or has experienced a GCA flare since last visit." on the Clinical Assessment of GCA – Signs and Symptoms eCRF page including both scheduled and flare visits.
- The participant cannot adhere to the protocol specified 26-week GC taper.

5.3.2. Estimand

Primary Trial Objective: To evaluate the efficacy of guselkumab compared to placebo, in combination with a 26-week glucocorticoid (GC) taper regimen, in adult participants with new-onset or relapsing giant cell arteritis (GCA).

Clinical Question of Interest: For a patient with new-onset or relapsing GCA, what would the expected effect of being assigned guselkumab together with the protocol allowed background 26-week GC-taper medication on the likelihood of experiencing a treatment response at Week 28?

5.3.2.1. Primary Estimand

The primary estimand, based on the above primary objective, is defined by the following 5 components which assess the treatment effects not only based on the variable measurements, but also based on intercurrent events:

- **Study intervention:**
  - Guselkumab in addition to 26-week GC-taper (including participants who received 400 mg IV induction doses followed by 200 mg SC dosing from Week 12 onwards and participants that received 200 mg SC dosing only)
  - Placebo in addition to 26-week GC-taper
- **Population:** adult participants 50 years or older with active new-onset or relapsing GCA (defined by American College of Rheumatology criteria).
- **Variable:** Binary response variable, where a responder is defined as a participant achieving GC-free remission at Week 28. A participant with an intercurrent event in categories 1-3 defined below will be considered as a non-responder.
- **Summary Measure (Population-level summary**): difference in the proportions of GC-free remission at Week 28 between the guselkumab group and the placebo group.
- **Intercurrent Events:**

Intercurrent Events (ICEs)	**Strategy for Addressing Intercurrent Events and Its Description**
1. Discontinuation (DC) of study intervention due to lack of efficacy or an AE of worsening of GCA. 2. Initiation of a protocol-prohibited medication during the study that could improve GCA. 3. Initiation of GC rescue therapy.	**Composite Strategy:** A participant with this intercurrent event is considered as a non-responder after this event. The occurrence of this intercurrent event is captured in the variable definition.
4. Discontinuation of study intervention other than ICEs #1	**Treatment Policy:** Use observed data regardless of whether or not this intercurrent event had occurred

Note: For participants experiencing multiple ICEs, an ICE in categories 2 or 3 will override an ICE in category 4.

5.3.2.2. Supplementary Estimand

5.3.2.2.1. Supplementary Estimand 1 (Hypothetical Strategy Estimand)

In this supplementary estimand, the only component that changes from the definition of the primary estimand is that the hypothetical strategy will be used for addressing ICEs 1-4.

Hypothetical strategy: assess the treatment effect as if the intercurrent event would not have occurred. Under the hypothetical strategy, data collected after ICEs 1-4 will not be used in analysis and will be imputed using a MAR multiple imputation method.

5.3.2.2.2. Supplementary Estimand 2 (Treatment Policy Estimand)

Treatment policy estimand has the same components as the primary estimand, except for the strategies used for the intercurrent events 1-4:

Treatment policy strategy: assess the treatment effect regardless of whether or not intercurrent events had occurred. Under the treatment policy strategy, the observed data after the intercurrent event will be used in analysis.

5.3.3. Analysis Methods for the Primary Estimand

The primary endpoint will be compared between the guselkumab group and the placebo group at Week 28 based on the primary estimand (Section 5.3.2.1) and the data from all participants in FAS (Section 4) will include data from all randomized participants who received at least one administration of study intervention based on their assigned intervention group, regardless of the actual intervention received.

The primary endpoint will be analyzed using the primary estimand. Participants with ICEs 1-3 before Week 28 will be considered as GC-free remission non-responders at Week 28. Participants with ICE 4, observed data after this ICE will be utilized in the analysis. For participants experiencing multiple ICEs, an ICEs 2 or 3 will override an ICE in category 4.

After accounting for the ICEs for the primary estimand, the remaining missing data of the primary endpoint at Week 28 will be considered as a non-responder.

In this primary analysis, the proportion of participants who achieve GC-free remission at Week 28 will be summarized for each intervention group. To address the primary objective, Cochran-Mantel-Haenszel chi-square statistic stratified by baseline disease status (new-onset and relapsing GCA), and the baseline GC dose (≤30 mg/day or >30 mg/day) at a 2-sided significance level of 0.10 will be used. Difference in response rates between the guselkumab group and the placebo group at Week 28 adjusted for baseline disease status (new-onset and relapsing GCA), and the baseline GC dose (≤30 mg/day or >30 mg/day) using Mantel-Haenszel weight and the corresponding 90% CI will be presented. Baseline disease status (new-onset and relapsing GCA), and the baseline GC dose (≤30 mg/day or >30 mg/day) entered into IWRS are to be used. Similar analyses using the observed baseline disease status (new-onset and relapsing GCA), and the observed baseline GC dose (≤30 mg/day or >30 mg/day) will be performed as sensitivity analyses.

5.3.4. Supplementary Estimand Analyses

5.3.4.1. Supplementary Analysis 1 (Supplementary Estimand 1, Hypothetical Strategy Estimand)

The primary endpoint will be analyzed using the Hypothetical Estimand for ICEs 1-4 (see Section 5.3.2.2.1). Under this estimand, data after an ICE will be set as missing and missing data will be imputed using multiple imputations by fully conditional specification (FCS).

More specifically, the missing GC-free remission response status at Week 28 will be imputed using the FCS logistic regression including intervention group, the baseline disease status (new-onset and relapsing GCA), the baseline GC dose (≤30 mg/day or >30 mg/day), and remission response status as defined in Section 5.5.1.3 starting from Week 4 in the model with seed = 1231 and 500 imputations.

The proportion difference of GC-free remission at Week 28 adjusted for the baseline disease status (new-onset and relapsing GCA), and the baseline GC dose (≤30 mg/day or >30 mg/day) using Mantel-Haenszel weight between the guselkumab group and the placebo group and its 90% CI combining multiple datasets will be provided. Each imputed dataset will be analyzed by CMH test stratified by baseline disease status (new-onset and relapsing GCA), and the baseline GC dose (≤30 mg/day or >30 mg/day).

The values of the general association test statistics from the CMH test for each imputed dataset will be transformed using the Wilson-Hilferty transformation to create a more normal distributed statistic:

$$Z = \frac{(CMH)^{(1/3)} - 7/9}{(2/9)^{(1/2)}}.$$

The resulting transformed values will be combined using SAS PROC MIANALYZE and obtain overall p-value for the CMH test.

5.3.4.2. Supplementary Analysis 2 (Supplementary Estimand 2, Treatment Policy Estimand)

The primary endpoint will be analyzed utilizing the Treatment Policy (de Facto) Estimand. For participants who experience an intercurrent event through Week 28, the analysis will be performed using observed data regardless of intercurrent events. Missing data will not be imputed. The Cochran-Mantel-Haenszel chi-square statistic stratified by baseline disease status (new-onset and relapsing GCA), and the baseline GC dose (≤30 mg/day or >30 mg/day) at a 2-sided significance level of 0.10 will be used. Difference in response rates between the 2 study intervention groups at Week 28 adjusted for baseline disease status (new-onset and relapsing GCA), and the baseline GC dose (≤30 mg/day or >30 mg/day) using Mantel-Haenszel weight and the corresponding 90% CI will be presented.

5.3.4.3. Supplementary Analysis 3 (Supplementary Estimand 2, Treatment Policy Estimand [Sensitivity Analysis])

The primary endpoint will be analyzed utilizing the Treatment Policy Estimand. For participants who experience an intercurrent event through Week 28, the analysis will be performed using observed data regardless of intercurrent events.

The same missing data handling rules and analysis methods specified in Section 5.3.4.1 for Supplementary Analysis 1 (Hypothetical Strategy Estimand) will be applied.

5.3.4.4. Supplementary Analysis 4 (Supplementary Estimand 2, Treatment Policy Estimand)

A generalized linear model with logit link for binary repeated measurement data will be performed on the primary endpoint after applying the Treatment Policy to ICEs. The model will include the intervention group, baseline disease status (new-onset and relapsing GCA), and the baseline GC dose (≤30 mg/day or >30 mg/day), visit, and intervention and visit interaction in the model. The derived odds ratio on GC-free remission at Week 28 and its 2-sided 90% CI will be provided. In addition, the proportion difference of GC-free remission response at Week 28 between the guselkumab and the placebo group and its 2-sided 90% CI will also be provided. Missing data will not be imputed and will be handled by the model under missing at random assumption.

5.3.5. Per Protocol Analysis

The primary analyses for primary endpoint will also be performed on per protocol analysis set (Section 4). The same data handling rules specified in Section 5.3.2 and Section 5.3.3 will be applied.

5.4. Secondary Endpoints Analysis

5.4.1. Secondary Endpoints

Objective: To evaluate the efficacy of guselkumab with a comparison to placebo, in combination with a 26-week GC taper regimen, in adult participants with new-onset or relapsing GCA for the following secondary endpoints:

1. The proportion of participants achieving GC-free remission from Week 28 through Week 52 by visit
2. The proportion of participants achieving GC-free remission and normalization of ESR at Week 28 and from Week 28 through Week 52 by visit
3. The proportion of participants achieving GC-free remission and normalization of CRP at Week 28 and from Week 28 through Week 52 by visit
4. The proportion of participants achieving GC-free remission and normalization of both ESR and CRP at Week 28 and from Week 28 through Week 52 by visit
5. The cumulative GC dose through Week 28 and through Week 52

6. The time to first GCA disease flare or discontinuation of study intervention due to AE of worsening of GCA through Week 28 and through Week 52
7. The number of GCA disease flares or discontinuation of study intervention due to AE of worsening of GCA through Week 28and through Week 52

5.4.1.1. Definition of Endpoints

5.4.1.1.1. GC-free Remission at Each Timepoint from Week 28 through Week 52

1. No signs or symptoms of active GCA at timepoint Week X

   AND

2. Absence of GCA flare from first dose of the study agent through Week X

   AND

3. Adherence to the protocol specified 26-week GC taper

5.4.1.1.2. GC-free Remission and Normalization of ESR at Week 28 and from Week 28 through Week 52 by Visit

1. No signs or symptoms of active GCA at timepoint Week X

   AND

2. Absence of GCA flare from first dose of the study agent through Week X, inclusive,

   AND

3. Adherence to the protocol specified 26-week GC taper

   AND

4. Normalization of ESR is defined as ESR <30 mm/hr at Week X.

5.4.1.1.3. GC-free Remission and Normalization of CRP at Week 28 and from Week 28 through Week 52 by Visit

1. No signs or symptoms of active GCA at timepoint Week X

   AND

2. Absence of GCA flare from first dose of the study agent through Week X, inclusive,

   AND

3. Adherence to the protocol specified 26-week GC taper,

   AND

4. Normalization of CRP is defined as CRP <10 mg/L or <1 mg/dL.

5.4.1.1.4. Cumulative GC Dose

The total cumulative GC dose administered will include GCA taper, GC rescue therapy as well as for all other indications (any oral GC) from first dose of the study agent to Week 28 or Week 52.

5.4.1.1.5. Time to First GCA Disease Flare or Discontinuation of Study Intervention due to AE of Worsening of GCA

Time to occurrence of GCA disease flare is defined as the time from first dose of the study agent to the occurrence of the first observation of GCA disease flare or discontinuation due to AE of worsening of GCA.

The definition of GCA disease flare is defined in Section 5.3.1.

5.4.1.1.6. Number of GCA Disease Flares or Discontinuation of Study Intervention due to AE of Worsening of GCA

The number of GCA disease flares or discontinuation of study intervention due to AE of worsening of GCA is the total number of flares or discontinuation of study intervention due to AE of worsening of GCA participants experience from first dose of the study agent through Week 28 or through Week 52.

The definition of GCA disease flare is defined in Section 5.3.1.

5.4.1.2. Estimands

The study intervention and population are the same as the primary estimand. The following table provides the list of variables, summary measure (population-level summary) and intercurrent event for secondary endpoints.

Table 2: List of Secondary Endpoints and Estimands

Estimands	Variable	Summary Measure (Population-level summary)	Intercurrent Events
Sec 1	Binary response variable, where a responder is defined as a participant achieving GC-free remission from Week 28 through Week 52 by visit	Difference in the proportions of achieving GC-free remission between the guselkumab groups and the placebo group	Using the same analysis strategies as the primary estimand.
Sec 2	Binary responder variable, where a responder is defined as a participant achieving GC-free remission and normalization of ESR at Week 28 and from Week 28 through Week 52 by visit	Difference in the proportions of achieving GC-free remission and normalization of ESR between the guselkumab group and the placebo group	1. The analysis strategies for the Week 28 endpoint will be the same as those for the primary estimand. 2. The analysis strategies for summary over time by visit from Week 28 through Week 52 are the same as those in #1 in this table.

Estimands	Variable	Summary Measure (Population-level summary)	Intercurrent Events
Sec 3	Binary response variable, where a responder is defined as a participant achieving GC-free remission and normalization of CRP at Week 28 and from Week 28 through Week 52 by visit	Difference in the proportions of achieving GC-free remission and normalization of CSR between the guselkumab group and the placebo group	1. The analysis strategies for the Week 28 endpoint will be the same as those for the primary estimand. 2. The analysis strategies for summary over time are the same as those in #1 in this table.
Sec 4	Binary response variable, where a responder is defined as a participant achieving GC-free remission and normalization of both ESR and CRP at Week 28 and from Week 28 through Week 52 by visit	Difference in the proportion of achieving GC-free remission and normalization of both ESR and CRP between the guselkumab group and the placebo group	1. The analysis strategies for the Week 28 endpoint will be the same as those for the primary estimand. 2. The analysis strategies for summary over time by visit from Week 28 through Week 52 are the same as those in #1 in this table.
Sec 5	Cumulative GC dose through Week 28 and through Week 52	Descriptive statistics for the guselkumab group and the placebo group	Treatment Policy strategy will be used regardless of ICEs.
Sec 6	Time to first GCA disease flare or discontinuation of study intervention due to AE of worsening of GCA through Week 28 and through Week 52	Hazard ratio of the guselkumab group vs. the placebo group	Treatment Policy strategy will be used regardless of the ICEs.
Sec 7	Number of GCA disease flares or discontinuation of study intervention due to AE of worsening of GCA through Week 28and through Week 52	Descriptive statistics for the guselkumab group and the placebo group	Treatment Policy strategy will be used regardless of the ICEs.

5.4.1.3. Analysis Methods

Unless otherwise specified, the analysis population will be the FAS defined in Section 4. The endpoints will be summarized by intervention group.

Simple descriptive statistics, such as n, mean, SD, median, IQ range, minimum and maximum for continuous variables and counts and percentages for discrete variables will be used to summarize most data, if appropriate.

5.4.1.3.1. Binary Endpoints (Secondary Endpoints 1 - 4)

Analyses for binary secondary endpoints (proportion of responders) at Week 28 will be the same as the primary endpoint.

For secondary binary endpoints at Week 28, Cochran-Mantel-Haenszel chi-square statistic stratified by baseline disease status (new-onset and relapsing GCA), and the baseline GC dose (≤30 mg/day or >30 mg/day) at a 2-sided significance level of 0.10 will be used to compare between the guselkumab and the placebo groups. Difference in response rates between the 2 intervention groups at Week 28 adjusted for baseline disease status (new-onset and relapsing GCA), and the baseline GC dose (≤30 mg/day or >30 mg/day) using Mantel-Haenszel weight and the corresponding 90% CI will be presented.

For the summary over time by visit, after accounting for the ICEs for the primary estimand, any missing data for an endpoint will be imputed as not achieving the associated binary endpoints at Week X.

5.4.1.3.2. Continuous Endpoint (Secondary Endpoints 5, 7)

Analyses for continuous endpoints will be based upon the Treatment Policy estimand. If a participant experiences an intercurrent event, the intercurrent event does not affect the outcome, and the data collected at and after the event will be used for analysis. Missing data will not be imputed.

The total cumulative glucocorticoid dose will be compared between the guselkumab and the placebo groups using van Elteren test stratified by baseline disease status (new-onset and relapsing GCA) and baseline GC dose (≤30 mg/day or >30 mg/day) at Week 28.

5.4.1.3.3. Time to First Event Endpoint

For time to first event data, the hazard ratio will be estimated using the Cox proportional hazards model, adjusting for the baseline disease status (new-onset or relapsing GCA), and the baseline GC dose (≤30 mg/day or >30 mg/day), and its associated 90% confidence interval will be presented. The proportional hazards assumption will be verified with appropriate methods (e.g. log-minus-log plots) as part of the analysis. The reported p-value for time to first flare analysis will be derived from a log-rank test. The survival curves will be estimated using Kaplan-Meier estimates.

Efficacy data through Week 28 and through Week 52 will be summarized and displayed by the following intervention groups:

1. Placebo
2. Guselkumab

5.5. Exploratory Endpoints Analysis for the Main Study

Objective: To evaluate the efficacy of guselkumab with a compared to placebo, in combination with a 26-week GC taper regimen, in adult participants with new-onset or relapsing GCA for the following exploratory endpoints:

Other Efficacy Endpoints

- Summary of signs, symptoms, and elevated CRP and/or ESR due to GCA disease flares
- Proportion of participants who experience at least one GCA disease flare or discontinuation of study intervention due to AE of worsening of GCA through week 28 and from Week 28 through Week 52 by visit
- Proportion of participants in sustained remission through Week 52 following remission at Week 8
- Proportion of participants in sustained remission through Week 52 following remission at Week 12
- Proportion of participants in sustained remission through Week 52 following remission at Week 16
- Proportion of participants in sustained remission from Week 28 through Week 52 by visit following remission at Week 8
- Proportion of participants in sustained remission from Week 28 through Week 52 by visit following remission at Week 12
- Proportion of participants in sustained remission from Week 28 through Week 52 by visit following remission at Week 16
- Cumulative GC dose through Week 28 and through Week 52 by baseline disease status (new-onset or relapsing GCA)
- Cumulative GC dose through Week 28 and through Week 52 by baseline GC dose (≤30 mg/day or >30 mg/day)
- Change from baseline in ESR through Week 28 and from Week 28 through Week 52 by visit
- Proportion of participants with normalization of ESR through Week 28 and from Week 28 through Week 52 by visit
- Change from baseline in CRP through Week 28 and from Week 28 through Week 52 by visit
- Proportion of participants with normalization of CRP through Week 28 and from Week 28 through Week 52 by visit

Sustained remission through Week 52 is defined as: No signs and symptoms of GCA through Week 52, and completion of the protocol defined GC taper, and not having required GC rescue therapy at any time by Week 52.

Efficacy data through Week 28 and through Week 52 will be summarized and displayed by the following intervention groups:

1. Placebo
2. Guselkumab

Clinical Outcome Assessments (COAs)

In this study, patient-reported outcome measures include patient's global assessment of their GCA disease activity (PGA), pain severity assessment, SF-36 health survey, Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-fatigue) and a clinician-reported outcome, the Physician's Global Assessment of Disease Activity (PhGA). The following analyses will be performed by treatment group. This section outlines the definitions and analyses for the following PRO and ClinRO endpoints.

Other efficacy endpoints related to COAs include:

Patient-reported Outcomes

- Change from baseline in PGA at Week 28 and at Week 52.
- Change from baseline in Pain Severity Assessment at Week 28 and at Week 52.
- Change from baseline SF-36 PCS (physical component summary) score and MCS (mental component summary) score at Week 28 and at Week 52.
- Change from baseline in SF-36 individual domains at Week 28 and at Week 52.
- Change from baseline in FACIT-fatigue scale score (raw score) at Week 28 and Week 52.
- Proportions of participants with FACIT-fatigue scale score ≥40 (mean=40, SD=10) at Week 0, 28, and 52.
- Proportions of participants with ≥ 4-points improvement in FACIT-fatigue scale score (raw score) at Week 28 and 52.

Physician-reported Outcomes

- Change from baseline in PhGA at Week 28 and Week 52.

COAs data at Week 28 and Week 52 will be summarized and displayed by the following intervention groups:

1. Placebo
2. Guselkumab

5.5.1. Definition of Endpoints

5.5.1.1. Sustained Remission through Week 52 Following Induction of Remission at Week 8

1. Remission at Week 8

   AND

2. No signs or symptoms of active GCA from Week 8 through Week 52, inclusive

   AND

3. Adherence to the protocol specified 26-week GC taper

   AND

4. Absence of GCA flare from first dose through Week 52

Similar definitions for sustained remission through Week 52 following induction of remission at Week 12 and following induction of remission at Week 16.

5.5.1.2. Sustained Remission from Week 28 through Week 52 by Visit Following Induction of Remission at Week 8

1. Remission at Week 8

   AND

2. No signs or symptoms of active GCA from Week 8 through Week X, inclusive

   AND

3. Adherence to the protocol specified 26-week GC taper

   AND

4. Absence of GCA flare from first dose through Week X

Similar definitions for sustained remission through Week X following induction of remission at Week 12 and following induction of remission at Week 16.

5.5.1.3. Normalization of CRP and ESR

The normalization of CRP is defined as CRP<10 mg/L or <1 mg/dL and the normalization of ESR is defined as ESR<30 mm/hr.

5.5.1.4. Patient's Global Assessment of Disease Activity (PGA)

The patient's global assessment of their GCA disease activity is recorded on a 10-cm VAS with verbal anchors on how their GCA feels today are "very poor" on the far-left side of the scale and "very well" on the far right of the scale. For this endpoint, a positive change from baseline reflects an improvement, and a negative change from baseline reflects a worsening.

The baseline measurement for the PGA is defined as the closest measurement taken prior to the initiation of the Week 0 administration.

5.5.1.5. Pain Severity Assessment

Participants will be asked to rate the severity of their average pain now on 10-cm VAS with anchors ranging from 0, "no pain" to 10, "worst pain imaginable". For this endpoint, a negative change from baseline reflects an improvement, and a positive change from baseline reflects a worsening.

The baseline measurement for the pain assessment is defined as the closest measurement taken prior to the initiation of the Week 0 administration.

5.5.1.6. SF-36

The Medical Outcome Study health measure entitled the 36-item Short-Form Version 2 acute (SF-36v2 acute) health survey questionnaire was developed as part of the Rand Health Insurance Experiment and consists of 8 multi-item scales.

- Limitations in physical functioning due to health problems.
- Limitations in usual role activities due to physical health problems.
- Bodily pain.
- General mental health (psychological distress and well-being).
- Limitations in usual role activities due to personal or emotional problems.
- Limitations in social functioning due to physical or mental health problems.
- Vitality (energy and fatigue).
- General health perception.

These scales will be scored following two approaches: Based on transformed raw scores that range from 0 to 100 with higher scores indicating better health, and standardized scores using a *T*-score transformation to compare to the US general population normative values (mean=50, SD=10) or other populations of interest.

Another algorithm yields 2 summary scores, the Physical Component Score (PCS) and Mental Component Score (MCS). These summary scores are also scaled with higher scores indicating better health. The concepts measured by the SF-36 are not specific to any age, disease, or intervention group, allowing comparison of relative burden of different diseases and the relative benefit of different treatments).

Change from baseline in SF-36 score measures the change in health-related quality of life, where a positive change indicates an improvement, and a negative change indicates a worsening.

Missing data will be handled following the Full Missing Score Estimation (Full MSE) method, which assumes that the missing item responses in a given scale are the same as the response to the scale's answered item. The final item response values are assigned accordingly. This approach should not be used in the Physical Functioning (PF) domain scale, but the PF can be estimated using item response theory (IRT), which is performed by the QualityMetric Health Outcomes™ Scoring Software 5.0.

5.5.1.7. FACIT-fatigue

The FACIT-fatigue version 4.0 is a 13-item questionnaire formatted for self-administration that assesses patient-reported fatigue and its impact upon daily activities and function over the past 7 days. Participants will be asked to answer each question using a 5-point Likert-type scale (0=Not at all; 1=A little bit; 2=Somewhat; 3=Quite a bit; and 4=Very much). Questions 1-6 and 9-13 are scored in reverse order. If 7 or more questions are answered, then the score can be calculated and is adjusted by the number of available questions. The interpretation of FACIT-fatigue scores is such that a higher score indicates less fatigue, with a range of possible scores of 0-52, with 0 being the worst possible score and 52 the best.

Change from baseline in FACIT-fatigue scores measures the change in fatigue where a positive change indicates an improvement, and a negative change indicates a worsening.

Missing data will be handled by calculating a total score that is prorated from the score of the answered items as long as more than 50% of the items (i.e., at least 7 of 13) were answered.

5.5.1.8. Physician's Global Assessment of Disease Activity (PhGA)

The physician's global assessment independent of participants' assessment of the patients GCA activity is recorded on a 10-cm visual analog scale (VAS) with verbal anchors "No GCA" on the far-left side of the scale and "Very severe GCA" on the far right of the scale. For this endpoint, a negative change from baseline reflects an improvement, and a positive change from baseline reflects a worsening.

The baseline measurement for the PhGA is defined as the closest measurement taken prior to the initiation of the Week 0 administration.

5.5.1.9. Analysis Methods

Unless otherwise specified, the analysis population will be the FAS defined in Section 4. The endpoints will be summarized by intervention group as specified in Section 5.6.

Analyses for binary endpoints (proportion of responders) over time will be the same as the analyses for the above secondary endpoints 1-4 in Table 2 based upon the primary estimand only.

Unless otherwise specified, the analyses for continuous endpoints at Week 28 and Week 52 will be based on the following strategies to handle ICEs and missing data:

- ICEs in categories 1-3 in the primary estimand (definitions in Section 5.3.2) will be handled with the Composite Strategy. Participants experiencing ICEs 1-3 will have a zero change (or zero improvement) from baseline assigned from that point onward.
- ICE in category 4 in the primary estimand will be handled by the Treatment Policy strategy. The analysis will be performed using observed data regardless of intercurrent events. For participants experiencing multiple ICEs, an ICE in categories 2 or 3 of the primary estimand will override an ICE in category 4.
- Missing data will not be imputed after applying the rules for intercurrent events.

Simple descriptive statistics, such as n, mean, SD, median, IQ range, minimum and maximum for these continuous variables.

5.6. Exploratory Endpoints Analysis for the LTE Period

- Proportion of participants achieving GC-free remission from Week 52 (LTE Week 0) through Week 104 (LTE Week 52) by visit
- Time to first GCA disease flare discontinuation of study intervention due to AE of worsening of GCA from Week 52 (LTE Week 0) through Week 104 (LTE Week 52)
- The number of GCA disease flares or discontinuation of study intervention due to AE of worsening of GCA from Week 52 (LTE Week 0) through Week 104 (LTE Week 60) by visit
- Change from baseline in ESR from Week 52 (LTE Week 0) through Week 104 (LTE Week 52) by visit
- Proportion of participants with normalization of ESR from Week 52 (LTE Week 0) through Week 104 (LTE Week 52) by visit
- Change from baseline in CRP from Week 52 (LTE Week 0) through Week 104 (LTE Week 52) by visit
- Proportion of participants with normalization of CRP from Week 52 (LTE Week 0) through Week 104 (LTE Week 52) by visit

<u>Patient-reported Outcomes by visit at Weeks 52, 76, and 104</u>

- Change from baseline in PGA.
- Change from baseline in Pain Severity Assessment.
- Change from baseline SF-36 PCS (physical component summary) score and MCS (mental component summary) score.
- Change from baseline in SF-36 individual domains.
- Change from baseline in FACIT-fatigue scale score (raw score).
- Proportions of participants with FACIT-fatigue scale score ≥40 (mean= 40, SD=10).

- Proportions of participants with ≥ 4-points improvement in FACIT-fatigue scale score (raw score).

Physician-reported Outcomes

- Change from baseline in PhGA.

5.6.1. Definition of Endpoints

5.6.1.1. GC-free Remission at Each Timepoint from Week 52 through Week 104

1. No signs or symptoms of active GCA at timepoint Week X

   AND

2. Absence of GCA flare from first dose of the study agent from Week 52 through Week X

5.6.2. Analysis Methods

The analysis population will be participants who enter into the Long-Term Extension. The endpoints will be summarized by intervention group.

The Treatment Policy strategy will be applied to the binary exploratory secondary endpoints (proportion of responders). For participants who experience an intercurrent event from Week 52 through Week 104, the analysis will be performed using observed data regardless of intercurrent events. Missing data will not be imputed.

The survival curves will be estimated using Kaplan-Meier estimates for time to first GCA disease flare or discontinuation of study intervention due to AE of worsening of GCA from Week 52 through Week 104.

Simple descriptive statistics, such as n, mean, SD, median, IQ range, minimum and maximum for the continuous variables over time. The remaining missing data will not be imputed.

The efficacy data during the LTE period will be summarized and displayed by the following intervention groups:

1. Placebo
2. Guselkumab

5.7. Safety Analyses

All safety analyses for the main study will be based on the safety analysis set based on actual intervention received, unless otherwise specified. Safety analyses for the long-term extension will include participants who complete the Week 52 visits and are assessed to be in GC-free remission with at least one SC injection at Week 52 or later.

For all continuous safety variables, descriptive statistics by intervention group will include the N, mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized by intervention group using frequency counts and percentages.

Depending on the safety data, the cumulative safety data will be analyzed through different study periods which include but are not limited to through Week 28 and through Week 60 for the main study. The safety analyses through Week 60 for the main study will include safety data through Week 60 for participants not entering the LTE and safety data through Week 52 for participants continuing onto the LTE. Safety analyses from Week 52 (LTE Week 0) through Week 112 (LTE Week 60) will be performed for participants in the LTE period.

5.7.1. Extent of Exposure

The number and percentage of participants who receive study intervention will be summarized. The cumulative dose and number of administrations of study intervention received will be summarized by treatment group for the safety analysis.

Study agent lots received by treatment, including matching placebo for active treatment will be summarized.

In addition, the average exposure (number of administrations) and average duration of follow-up (weeks) will also be summarized by treatment group in the safety tables through different study time periods.

For IV and SC study intervention:

Descriptive statistics will be presented for the following parameters:

- Number of administrations
- Cumulative total dose

Compliance to randomized intervention versus actual intervention will be presented in a summary table.

5.7.2. Adverse Events

The verbatim terms used in the CRF by investigators to identify adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). Any AE occurring at or after the initial administration of study intervention is considered to be treatment emergent. If the event occurs on the day of the initial administration of study intervention, and either event time or time of administration are missing, then the event will be assumed to be treatment emergent. If the event date is recorded as partial or completely missing, then the event will be considered to be treatment emergent unless it is known to be prior to the first administration of study intervention based on partial onset date or resolution date. All reported treatment-emergent adverse events will be included in the analysis. For each adverse event, the number and percentage of participants who experience at least 1 occurrence of the given event will be summarized by intervention group.

Safety data will be summarized and displayed by the following intervention groups:

- through Week 28
    1. Placebo
    2. Guselkumab

    In addition, overall AEs will be also summarized and displayed by the following intervention groups:

        a. Placebo IV: participants receiving placebo during the study.
        b. Placebo SC: participants receiving placebo during the study.
        c. Guselkumab ─ Receiving 400 mg IV Induction Doses: participants receiving at least one administration of guselkumab 400 mg IV at Week 0, 4 and 8
        d. Guselkumab ─ Receiving 200 mg SC Induction Doses: participants receiving at least one administration of guselkumab 200 mg SC at Week 0, 4, and 8.
- through Week 60

1. Placebo
2. Guselkumab

- during the LTE period

1. Placebo
2. Guselkumab

The following summary tables will be provided for treatment-emergent adverse events:

- AEs
- AEs with a frequency threshold of 5% or more
- Serious AEs (SAEs)
- AEs leading to discontinuation of study intervention
- AEs by severity
- AEs by relationship to each study agent within a study intervention
- AEs temporally associated with an IV infusion
- Injection-site reactions

In addition to the summary tables, listings will be provided for participants who:

- Had SAEs
- Had AEs leading to discontinuation of study intervention
- Had AEs of severity
- Had temporally associated with infusion

- Had VTEs
- Had arterial thromboembolic AEs
- Had anaphylactic reactions and serum sickness reactions
- Had suicidal ideation or suicidal behavior
- Had COVID-19 related AEs
- Had died

5.7.3. Additional Safety Assessments

5.7.3.1. Clinical Laboratory Tests

Clinical laboratory tests will be displayed for the participants included in the safety analysis set.

Descriptive statistics and graphical displays will be presented for selected chemistry and hematology laboratory tests at scheduled time points.

Change from baseline through Week 28 and through Week 60 for the main study, and from Week 52 (LTE Week 0) through Week 112 (LTE Week 60) will be summarized for chemistry and hematology tests and displayed by intervention group. A box plot of change from baseline through Week 28 and through Week 60 for the main study, and from Week 52 (LTE Week 0) through Week 112 (LTE Week 60) will be provided.

- **Hematology assessments** will include but are not limited to the following: hemoglobin, hematocrit, lymphocytes, neutrophils, platelet count, total and differential White Blood Cell (WBC) count.
- **Blood chemistry assessments** will include but are not limited to the following: chemistry panel (total and direct bilirubin, ALT, AST, alkaline phosphatase, albumin, total protein, calcium, phosphate, sodium, potassium, chloride, blood urea nitrogen/urea, and creatinine).

The National Cancer Institute's Common Terminology Criteria for Adverse Events will be used in the summary of laboratory data (Grade 0-4). The proportion of participants with post-baseline values by maximum toxicity grade for clinical laboratory tests will be summarized by study intervention group. Shift tables will be provided summarizing the shift in laboratory values from baseline to the end of the reporting period with respect to NCI-CTCAE grades. Participants with toxicity grades ≥ 2 will be listed.

For ALT and AST, highest postbaseline elevated liver function tests will be summarized by intervention group. In addition to the summary table, listings will be provided for participants with highest postbaseline elevated liver function tests ALT ≥3, ≥5, ≥8xULN, AST ≥3, ≥5, ≥8xULN, and participants meeting combined criteria (total bilirubin ≥2xULN, and either AST or ALT ≥3x ULN), respectively.

5.7.3.2. Vital Signs and Physical Examination Findings

Continuous vital sign parameters including temperature, respiratory rate, weight, pulse, blood pressure (systolic and diastolic), and Body Mass Index (BMI) will be summarized at each assessment time point. Body Mass Index will be calculated as weight (kg)/(height (m))^2, at each time point that body weight is measured. The height measurement collected at screening will be used in the calculation. Change from baseline will be summarized through Week 28 and from Week 28 through Week 60 for the main study, and from Week 52 through Week 112 for participants in the LTE period. Descriptive statistics (mean, standard deviation, median, minimum and maximum) will be presented.

Incidence of treatment-emergent clinically important abnormal vital signs during intervention, as defined in Table 3, will be summarized for participants who had a baseline assessment and at least 1 postbaseline assessment for that vital sign. A listing of participants with treatment-emergent clinically important abnormality in vital signs will be presented.

Table 3: Clinically Important Abnormal Limits for Vital Signs

Vital Sign	Criteria
Pulse	>115 bpm and with >30 bpm increase from baseline
	<50 bpm and with >20 bpm decrease from baseline
Systolic blood pressure	>150 mm Hg and with >40 mm Hg increase from baseline
	<90 mm Hg and with >30 mm Hg decrease from baseline
Diastolic blood pressure	>95 mm Hg and with >30 mm Hg increase from baseline
	<50 mm Hg and with >20 mm Hg decrease from baseline
Interarm blood pressure	interarm blood pressure absolute difference ≥15 mmHg in systolic blood pressure at 3 consecutive visits
Temperature	>38.4°C and with ≥1°C increase from baseline
Weight	increase 10% from baseline
	decrease 10% from baseline
Respiratory rate	>20 breaths per minute

5.7.3.3. Columbia-Suicide Severity Rating Scale

The C-SSRS will be used as a screening tool to prospectively evaluate suicidal ideation and behavior among study participants. The C-SSRS measures 5 possible levels of suicidal ideation and 4 possible suicidal behaviors, as well as non-suicidal self-injurious behavior. The assessment is a fully-structured, participant self-report C-SSRS questionnaire, including standardized questions, follow-up prompts, error handling routines, and scoring conventions. Two versions of the C-SSRS will be used in this study, the *Lifetime* version and the *Since Last Contact* version. The *Lifetime* version will be conducted during the screening visit and the *Since Last Contact* version will be conducted at all other visits.

At the screening visit, the C-SSRS should be completed as the first assessment after signing informed consent and before any other tests, procedures, or other consultations. For subsequent visits, the C-SSRS should be completed after all PROs and before any other tests, procedures, or other consultations. Participants will be interviewed by the investigator or trained study site personnel in a private, quiet place.

The following are C-SSRS categories and have binary responses (yes/no). A "yes" response to any C-SSRS category will be assigned a score as below:

Suicidal Ideation (1-5)

1 = Wish to be Dead

2 = Non-specific Active Suicidal Thoughts

3 = Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act

4 = Active Suicidal Ideation with Some Intent to Act, without Specific Plan

5 = Active Suicidal Ideation with Specific Plan and Intent

Suicidal Behavior (6-10)

6 = Preparatory Acts or Behavior

7 = Aborted Attempt

8 = Interrupted Attempt

9 = Actual Attempt (non-fatal)

10 = Completed Suicide

If no events qualify for a score of 1 to 10, a score of 0 will be assigned (0="Negative result [no suicidal ideation or behavior]"). Higher scores indicate greater severity.

The summary for suicidal ideation and behavior will be based on the safety analysis set. Suicidal ideation and behavior will be summarized based on the most severe/maximum post baseline C-SSRS outcome or AE of suicidal ideation, suicidal behavior excluding completed suicide, or completed suicide through Week 28 or through Week 60 for the main study, and from Week 52 through Week 112 for participants in the LTE period. The baseline is defined as the most severe/maximum C-SSRS score at either screening or Week 0.

The maximum score assigned for each participant will also be summarized into one of three broad categories: No suicidal ideation or behavior, suicidal ideation, suicidal behavior. A shift table for change in C-SSRS categories of no suicidal ideation or behavior, suicidal ideation, and suicidal behavior from baseline through Week 28 and through 60 for the main study, and from Week 52

through Week 112 for participants in the LTE period will be presented, where the baseline category is based on C-SSRS score and the post baseline is based on C-SSRS or AE data.

5.8. Other Analyses

5.8.1. Pharmacokinetics

Pharmacokinetics (PK) samples for measuring serum guselkumab concentrations will be collected from all participants at the specified visits as shown in the Schedule of Activities. All PK evaluations will be performed on the PK analysis set for the main study, defined as participants who have received at least 1 administration of guselkumab and have at least one post-dose sample collection. The PK analyses for LTE period will include all participants who participate LTE period.

Descriptive statistics (N, mean, SD, median, range, coefficient of variation (%CV) and IQ range) will be used to summarize guselkumab serum concentrations at each sampling time point. PK data may be displayed graphically, such as median +/- IQ range PK concentrations over time. The following analyses will be performed as appropriate:

- Summary of serum guselkumab concentrations at each visit
- Summary of serum guselkumab concentrations at each visit by baseline body weight quartiles
- Summary of participants with serum guselkumab concentrations below the lowest level of quantification x minimum required dilution (LLOQxMRD) at each visit
- Plot of median +/- IQ range serum guselkumab concentrations over time

If sufficient data are available, then population PK analysis using serum guselkumab concentration-time data will be performed using nonlinear mixed-effects modeling to estimate total systemic clearance and volume of distribution. Details will be given in a population PK analysis plan and the results of the analysis will be presented in a separate report.

The relationship between serum guselkumab concentrations (quartiles) at Week 28 and the proportion of participants achieving GC-free remission at Week 28 and Week 52 will be performed. The relationship between serum guselkumab concentrations and key secondary endpoints (e.g. GC-free remission through Week 52, time to first flare, and cumulative GC dose through Week 28 and Week 52) may also performed. In addition, summary of change from baseline in CRP concentration (mg/L), ESR at Week 28 by serum guselkumab concentration quartiles at Week 28 will be perform when appropriate.

5.8.1.1. Data Handling Guidelines

Unless otherwise specified, the following data handling guideline will apply to PK analyses:

- All serum concentration summaries for a particular timepoint will include data obtained from treated participants at the timepoint of interest without imputing any missing data
- A concentration not quantifiable (below LLOQ) will be treated as 0 in the summary statistics and shown as the lower limit of quantification (<LLOQ) in the data listings

- The data from a participant who meets one of the following dosing deviation criteria will be excluded from the by-visit data analyses and from that point onwards:
  - Discontinue guselkumab administrations
  - Skipped a guselkumab administration
  - Received incomplete/incorrect dose
  - Received incorrect study agent
  - Received additional dose

Of note, serum guselkumab concentrations prior to the first of such events will be included in the summaries. In addition, if a participant has an administration outside of dosing window, the concentration data collected at and after that will be excluded from the by-visit data analyses. Additional exclusions for PK data to be implemented based on TV-GDL-00362. All participants and samples excluded from analysis will be documented in the Clinical Study Report.

5.8.2. Immunogenicity

Blood samples will be collected to examine the formation of antibodies to guselkumab at the specified visits as shown in the Schedule of Activities of the protocol.

"Sample ADA status" and sample titer as well as the cumulative "subject ADA status" and peak titer through the visit will be coded and provided by the bioanalytical group.

5.8.2.1. Participant ADA Classifications

Participants evaluable for immunogenicity are defined as having at least one post-dose ADA time point collected for antibodies to guselkumab detection.

1. Participants with **treatment-emergent** antibodies to guselkumab include participants with treatment-induced antibodies to guselkumab and treatment-boosted antibodies to guselkumab.
2. Participants with **treatment-induced** antibodies to guselkumab have antibodies to guselkumab negative sample prior to guselkumab administration and at least one antibody to guselkumab positive sample after guselkumab.
3. Participants with **treatment-boosted** antibodies to guselkumab have antibodies to guselkumab positive sample prior to guselkumab administration and at least one antibody to guselkumab positive sample after guselkumab with a 2-fold increase in titer over baseline.

If titer remains the same after intervention or if ADA titer reduces or ADA disappears, the participant is classified as "treatment-emergent ADA negative". Participants that are unevaluable for treatment-emergent ADA following intervention will be classified as "participants with baseline samples only", ie, no appropriate sample is available after intervention.

5.8.2.2. Immunogenicity Analyses

The summary and evaluation of antibodies to guselkumab will be based on the observed data; therefore, no imputation of missing data will be performed. Note: participant status is through each visit, thus, participant status and peak titers may change as the study progresses over time. Therefore, the 'subject ADA status' at a visit represents the cumulative ADA status through that visit. For example, if a study has a lock at Week 28, datasets through Week 28 will have participant level status (eg, negative) but at Week 40, they may have developed ADA and the participant status becomes "treatment-emergent ADA positive" from the primary to the final DBL. Peak titers can also change (increase) if a higher titer occurs after an initial DBL.

The summary of participants with baseline positive samples is taken from the sample status at baseline. There is no participant level status at baseline.

The data analysis of antibodies to guselkumab includes the following when appropriate:

1. Incidence of antibody (evaluable, treatment-emergent ADA positive, treatment-emergent ADA negative) status and neutralizing antibodies (NAb) to gueslkumab will be summarized.

2. Descriptive statistics (N, mean, SD, median, range, and IQ range) and incidence (N, %) of the relationship between treatment-emergent antibodies to guselkumab status (positive or negative) and PK concentration will be assessed.

3. Participants in response (N, %) for treatment-emergent antibodies to guselkumab status (positive or negative) and efficacy endpoints may be assessed:

   - Participants evaluable for immunogenicity
   - Efficacy endpoints repeated for different levels of response (eg, GC-free remission)
     - Number of participants (N)
     - Participants in response (N, %)

4. Incidence (N, %) between treatment-emergent antibodies to guselkumab status (positive or negative) and infusion-related reactions may be assessed:

   - Participants evaluable for immunogenicity
   - Participants with infusion-related reaction
   - Participants with severe infusion-related reaction
   - Participants with serious infusion-related reaction
   - Participants with infusion-related reaction leading to discontinuation
   - Guselkumab infusions with infusion-related reactions (out of total number of guselkumab infusions)
   - Placebo infusions with infusion-related reactions (out of total number of placebo infusions).

5. Incidence (N, %) between treatment-emergent antibodies to guselkumab status (positive or negative) and injection site reactions may be assessed:

   – Participants evaluable for immunogenicity
   – Participants with injection site reaction
   – Participants with severe injection site reaction
   – Participants with serious injection site reaction
   – Participants with injection site reaction leading to discontinuation
   – Guselkumab injections with injection site reactions (out of total number of guselkumab injections)
   – Placebo injections with injection site reactions (out of total number of placebo injections).

In addition, listings of participants with baseline positive ADA samples, participants who are classified as positive for treatment-emergent antibodies to guselkumab and participants who discontinue the study by antibodies to guselkumab status as well as graphical representation of median serum concentration by antibody status may be presented.

5.8.3. Pharmacokinetic/Pharmacodynamic Relationships

Exploratory PK-PD analyses, including graphical exploration of PK-PD data, may be performed.

For binary PD/efficacy endpoints, percent responders within each quartile of PK concentration may be presented, if data permits.

If deemed feasible and necessary, exposure-response analyses may be performed. The analysis methods may be summarized in a separate analysis plan. Results of such analyses may be presented in a separate technical report.

5.8.4. Biomarkers

Biomarker analyses will be used to examine the biologic response to treatment and to identify biomarkers which are relevant to guselkumab treatment, GCs, and GCA. These biomarker analyses are exploratory and will include characterization of the molecular effects of guselkumab treatment, assessment of GCA pathogenesis, and determination if these markers can predict response to guselkumab. Exploratory changes in serum analytes and RNA levels in whole blood may be summarized by intervention group, in separate technical reports. Additionally, single cells from PBMC and leukocyte subset counts and frequencies in PBMCs over time may be assessed from PBMC collections and summarized in separate technical reports. Associations between baseline levels and changes from baseline in select markers and clinical response on primary and major secondary endpoints in Section 9.4.2 and Section 9.4.3 of the protocol will be explored and summarized in separate technical reports. Planned biomarker analyses may be deferred if emerging study data show no likelihood of providing useful scientific information. Any biomarker samples received by the contract vendor or sponsor after the cutoff date will not be analyzed, and therefore, excluded from the biomarker analysis.

5.8.5. Pharmacogenomic Analyses

Genetic (DNA) analyses will be conducted only in participants who sign the consent form to participate in the pharmacogenomic substudy. DNA samples will be used for research related to Guselkumab, GCs, or GCA. Pharmacogenomic research may consist of the analysis of one or more candidate genes or of the analysis of genetic markers throughout the genome (as appropriate) in relation to Guselkumab, GCs or GCA clinical endpoints. These analyses are considered exploratory and will be summarized in a separate technical report.

5.8.6. Exploratory FDG-PET/CT Imaging Analyses

FDG-PET/CT scans will be qualitatively assessed for FDG uptake in 9 arterial territories (carotid arteries, subclavian arteries, brachiocephalic artery, ascending aorta, aortic arch, descending thoracic aorta, and the abdominal aorta). The degree of arterial uptake will be visually assessed relative to liver uptake as: 0 = no uptake; 1 = less than liver; 2 = same as liver; 3 = greater than liver. To assess the qualitative inflammatory burden by arterial FDG uptake across multiple arterial regions, a summary score (hereafter termed PET Vascular Activity Score [PETVAS]) will be created by adding the qualitative scores in specific arterial territories.

A separate analysis plan for FDG-PET/CT imaging analyses will describe how the data will be analyzed including a detailed description of the data summarization methods and modeling approach. These analyses are considered exploratory and will be summarized in a separate technical report.

5.8.7. Digital Health - Actigraphy Analyses

A separate digital biomarker analysis plan will describe how actigraphy data will be analyzed including a detailed description of the data summarization methods and modeling approach. Results of the actigraphy analysis will be presented in a separate digital biomarker technical report.

5.8.8. Definition of Subgroups

To evaluate the consistency of the primary efficacy endpoint (proportion of participants who achieve GC-free remission at Week 28), subgroup analyses may be performed when the number of participants in the subset permits (at least 5 participants for each intervention group within a subset).

The subgroups for subgroup analysis may include, but are not limited to, the following:

1. Demographic subgroups

Subgroup	Variant	Definition
Region	1	• North America • Europe • Asian
Sex	1	• Male • Female
Race	1	• White • Black or African American • Asian • Other
Age Group	1	• ≥50 to ≤64 • ≥65
Body Weight Group	1	• ≤70 kg • >70 kg
BMI	1	• normal <25 kg/m^2 • overweight 25-<30 kg/m^2 • obese ≥30 kg/m^2

2. Disease Characteristics subgroups

Subgroup	Variant	Definition
Age at diagnosis	1	• ≤ Median • > Median
GCA disease duration	1	• ≤ Median • > Median
Baseline GC dose	1	• ≤30 mg/day • >30 mg/day
Baseline disease status	1	• New-onset GCA • Relapsing GCA
Baseline ESR	1	• ≥30 mm/hr • <30 mm/hr
Baseline CRP	1	• ≥10 mg/L • <10 mg/L
Participant was in remission (No signs or symptoms of GCA) at baseline	1	• Yes • No

3. Prior medication subgroups

Subgroup	Variant	Definition
IV glucocorticoids	1	• Yes/No
Tocilizumab	1	• Yes/No
Other biologic therapy	1	• Yes/No
Methotrexate	1	• Yes/No
Other non-biologic immunosuppressant (other than methotrexate)	1	• Yes/No

4. Baseline medication subgroups

Subgroup	Variant	Definition
Methotrexate	1	• Yes/No

5.9. Interim Analyses

No formal interim analysis is planned. However, a Data Monitoring Committee (DMC) will monitor the safety for this study.

5.9.1. Data Monitoring Committee (DMC) or Other Review Board

An independent DMC will monitor data on an ongoing basis to ensure the continuing safety of the participants enrolled in the study. The committee will meet periodically to review interim safety data. After the review, the DMC will make recommendations regarding the continuation of the study. If there is any safety concern, the GMS Therapeutic Area Head should call Safety Management Team (SMT) to discuss concerns of safety within the clinical study.

The DMC will consist of one external and one internal clinical physician with relevant therapeutic expertise (rheumatology), the internal GMS Therapeutic Area Safety Head, and one internal statistician. An additional internal statistical modeling expert would be involved in Week 28 IA and is optional in participating in the other DMC safety reviews. No DMC member is directly involved with the study conduct.

The major function of the DMC is to monitor the safety of the study agent and to provide recommendations for placing the study on hold or stopping the study in the event of serious safety concerns. The content of the safety summaries, the DMC roles and responsibilities and the general procedures (including communication plan) and their possible recommendations on study conduct will be defined and documented in the DMC Charter prior to the first DMC review.

In addition, during the study, the sponsor's study responsible physician (or designee) will regularly review blinded safety data from the sites and notify the DMC and appropriate sponsor personnel of any issues.

6. SUPPORTING DOCUMENTATION

6.1. Appendix 1 List of Abbreviations

ADA	anti-drug antibody
AE	adverse event
ALT/SGPT	alanine aminotransferase
AST/SGOT	aspartate aminotransferase
ATC	anatomic and therapeutic class
BMI	body mass index
CI	confidence interval
CRF	case report form
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
CV	coefficient of variation
DMC	Data Monitoring Committee
DPS	Data Presentation Specifications
eCRF	electronic case report form
FAS	full analysis set
GCA	giant cell arteritis
GMS	Global Medical Safety
hr	hour
IQ	interquartile
IWRS	interactive web response system
LLOQ	lower limit of quantification
MedDRA	Medical Dictionary for Regulatory Activities
MRD	minimum required dilution
NAb	neutralizing antibodies
PD	pharmacodynamic(s)
PK	pharmacokinetic(s)
PP	per protocol
SAE	serious adverse event
SAP	Statistical Analysis Plan
SD	standard deviation
SMT	Safety Management Team
SoA	Schedule of Activities
TEAE	treatment-emergent adverse event
US NCI	United States National Cancer Institute
VTE	Venous Thromboembolic adverse events
WHO	World Health Organization
WHO-DD	World Health Organization Drug Dictionary

6.2. Appendix 2 Demographics and Baseline Characteristics

The number of participants in full analysis set will be summarized and listed by intervention group, and overall. In addition, the distribution of participants by region, country, and site ID will be presented unless otherwise noted.

Table 4 presents a list of the demographic variables that will be summarized by intervention group, and overall for the full analysis set.

Table 4: Demographic Variables

Continuous Variables:	**Summary Type**
Age (years)	Descriptive statistics (N, mean, standard deviation [SD], median and range [minimum and maximum], and IQ range).
Weight (kg)	
Height (cm)	
Body Mass Index (BMI) (kg/m^2)	
Categorical Variables	
Age 50−64 years, and ≥65 years)	Frequency distribution with the number and percentage of participants in each category.
Sex (male, female)	
Race[a] (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander, White, Not reported, Unknown, Multiple)	
Ethnicity (Hispanic or Latino, Not Hispanic or Latino, Not reported, Unknown)	
BMI (normal <25 kg/m^2, overweight ≥25-<30 kg/m^2, obese ≥30 kg/m^2)	

[a] If multiple race categories are indicated, the Race is recorded as 'Multiple'

Table 5 presents a list of the screening or baseline disease characteristics that will be summarized by intervention group and overall for the Full Analysis Set.

Table 5: Screening or Baseline Disease Characteristics

Continuous Variables:	**Categories**	**Summary Type**
GCA disease duration (weeks)		Descriptive statistics (N, mean, standard deviation [SD], median and range [minimum and maximum], and IQ range).
Age at diagnosis (years)		
Total criteria score		
GC dose at baseline (mg/day)		Descriptive statistics (N, mean, standard deviation [SD], median and range [minimum and maximum], and IQ range).
Baseline erythrocyte sedimentation rate (ESR)		
Baseline C-reactive protein (CRP)		
Physician's Global Assessment of Disease Activity (PhGA)		
Patient's Global Assessment of Disease Activity (PGA)		
Pain assessment		
FACIT-fatigue scale score (raw score)		

Continuous Variables:	**Categories**	**Summary Type**
Categorical Variables		Frequency distribution with the number and percentage of participants in each category.
GCA diagnosis at screening	Disease type • New-onset • Relapsing	
Baseline GC use	• ≤30 mg/day • >30 mg/day	
Remission status at baseline	Participant was in remission (No signs or symptoms of GCA)	
GCA disease assessment at baseline	• Symptoms of GCA • Signs of GCA	
Acute-phase reactants and renders at screening	• ESR ≥ 30 mm/hr • CRP ≥ 10 mg/L	
Acute-phase reactants and renders at baseline	• ESR ≥ 30 mm/hr • CRP ≥ 10 mg/L	

6.3. Appendix 3 Protocol Deviations

In general, the following list of major protocol deviations may have the potential to impact participants' rights, safety or well-being, or the integrity and/or result of the clinical study. Participants with major protocol deviations will be identified prior to database lock and the participants with major protocol deviations will be summarized by category.

- Developed withdrawal criteria but not withdrawn
- Entered but did not satisfy criteria
- Received a disallowed concomitant treatment
- Received wrong treatment or incorrect dose
- Other
  - due to COVID-19

In addition to the summary tables, the following listings will be provided:

- List of participants with major protocol deviations

6.4. Appendix 4 Prior and Concomitant Medications

Prior and Concomitant medications will be coded using the World Health Organization Drug Dictionary (WHO-DD). Prior medications are defined as any therapy used before the day of first dose (partial or complete) of study intervention. Concomitant medications are defined as any therapy used on or after the same day as the first dose of study intervention, including those that started before and continue on after the first dose of study intervention.

Summaries of concomitant medications with non-rescue therapies for GCA will be presented by ATC term and intervention group for non-rescue therapy.

6.5. Appendix 5 Medical History of Interest

Medical history of interest will be summarized by intervention group.

6.6. Appendix 6 Laboratory Toxicity Grading

The grading scale use for lab assessments is based on the latest version of 'Common Terminology Criteria for Adverse Events (CTCAE).

Pre-baseline measurements will use the same grading ranges as applied to baseline measurements. In case a test has two sets of ranges – one for baseline normal and one for baseline abnormal, the one for baseline normal will be applied for all measurements taken pre-baseline and on baseline.

Text in gray italic in the table is present in the grading scale but is not applied by Janssen when grading lab data.

6.7. Appendix 7 COVID-19 Related Summaries

Participant disposition as related to COVID-19 will be summarized by intervention group. This includes the following COVID-19 related disposition events:

- Termination of study due to COVID-19
- Discontinuation of stud agent due to COVID-19
- Death related to COVID-19

Participants discontinuing treatment or terminating study participation due to COVID-19 and/or reason(s) will be listed.

Protocol deviations (major and minor) as related to COVID-19 will be summarized and listed.

Adverse events related to COVID-19 will be identified and coded using the MedDRA coding guidance for COVID-19, and summary tables will be provided for COVID-19 related TEAEs. The following will be listed by participant:

- TEAEs related to COVID-19
- Serious TEAEs related to COVID-19

6.8. Appendix 8 Protocol-prohibited Concomitant Medications/Therapies

The prohibited medications/therapies for GCA disease include the below concomitant medications/therapies with the answer "Yes" to the question "Is this a prohibited medication?" on eCRFs Concomitant Therapy page:

- Immunomodulatory biologic agent
- Other biologic therapy
- Methotrexate
- Other non-biologic immunomodulator
- Investigational agent
- Other

In addition to the above, the below glucocorticoid will also be considered as protocol-prohibited concomitant medications.

- Any oral glucocorticoid for indications other than GCA
- Any intramuscular, intra-articular, intrabursal, epidural, intra-lesional, or IV GCs