Janssen Research & Development

Statistical Analysis Plan

A Phase 2, Multicenter, Randomized, Placebo-Controlled, Double-Blind, Proof-of-Concept Study to Evaluate Guselkumab for the Treatment of Subjects with Moderate to Severe Hidradenitis Suppurativa

Protocol CNTO1959HDS2001; Phase 2

CNTO1959 (Guselkumab)

Status: Approved
Date: 31 May 2019
Prepared by: Janssen Research & Development, LLC
Document No.: EDMS-ERI-168719194

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

TABLE OF CONTENTS

ABBREVIATIONS

ADA	anti-drug antibody
AE	adverse event
ALT/SGPT	alanine aminotransferase
ANCOVA	analysis of covariance
AST/SGOT	aspartate aminotransferase
ATC	anatomic and therapeutic Class
AUC	area under the curve
BMI	body mass index
BSA	body surface area
CI	confidence interval
CL	total systemic clearance
Cmax	maximum concentration
CRF	case report form
CSR	Clinical Study Report
CMH	Cochran-Mantel-Haenszel
CV	coefficient of variation
DBL	Database Lock
DLQI	Dermatology Life Quality Index
DMC	Data Monitoring Committee
DPS	Data Presentation Specifications
ECG	electrocardiogram
eCRF	electronic case report form
FAS	full analysis set
FCS	Full Conditional Specification
FDA	Food and Drug Administration
HADS	Hospital Anxiety and Depression Scale
HiSCR	Hidradenitis Suppurativa Clinical Response
HS	Hidradenitis Suppurativa
HS-IGA	Hidradenitis Suppurativa Investigator's Global Assessment
HSSD	Hidradenitis Suppurativa Symptom Diary
ICH	International Conference on Harmonization
IQ	interquartile
IWRS	interactive web response system
LLOQ	lower limit of quantification
LOCF	last observation carried forward
LS means	Least square means
MAR	missing at random
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	Mixed-Effect Model Repeated Measure
NAb	neutralizing antibodies
NCI-CTCAE	National Cancer Institute - Common Terminology Criteria for Adverse Events
PD	pharmacodynamic
PGIC	Patient's Global Impression of Change
PK	pharmacokinetic(s)
PP	per protocol
q4w	every 4 weeks
q8w	every 8 weeks
SAE	serious adverse event
SAP	Statistical Analysis Plan
SC	subcutaneous
SD	standard deviation
TEAE	treatment-emergent adverse event
WHO	World Health Organization
WHO-DD	World Health Organization Drug Dictionary

1. INTRODUCTION

This statistical analysis plan (SAP) contains definitions of analysis sets, derived variables, and statistical methods for the analysis of efficacy, safety, pharmacokinetics (PK), pharmacodynamics (PD), Immunogenicity and health-related quality of life in the CNTO1959HDS2001 study.

1.1. Trial Objectives

Primary Objective

The primary objective of this study is to evaluate the initial efficacy, safety, and tolerability of guselkumab in adult participants with moderate to severe hidradenitis suppurativa (HS).

Secondary Objectives

The secondary objectives of this study are:

- To evaluate the efficacy of guselkumab in adult participants with moderate to severe HS during the maintenance phase.
- To evaluate the effect of guselkumab on the dermatologic health-related quality of life in adult participants with moderate to severe HS.
- To evaluate the pharmacokinetics (PK), immunogenicity, and pharmacodynamics (PD) of guselkumab therapy in adult participants with moderate to severe HS.

1.2. Trial Design

This is a Phase 2, multicenter, randomized, placebo-controlled, double-blind, proof-of-concept (POC) study evaluating the efficacy, safety, PK, and immunogenicity of SC and IV administered guselkumab for the treatment of moderate to severe HS in adult participants. The participant population will comprise men and women who have had moderate to severe HS for at least 1 year.

A diagram of the study design (Figure 1) is provided below and as depicted in Figure 1, approximately 180 participants who satisfy all inclusion and exclusion criteria will be randomized in a 1:1:1 ratio to 1 of 3 groups:

Group 1: Guselkumab Regimen 1 (1200 mg IV q4w x 3 → 200 mg SC q4w)

Participants will receive guselkumab 1200 mg IV at Week 0, Week 4, and Week 8 (ie, a total of 3 IV guselkumab doses and 3 SC placebo doses). At Week 12, participants will continue treatment with guselkumab 200 mg SC q4w through Week 36.

Group 2: Guselkumab Regimen 2 (200 mg SC q4w x 3 → 200 mg SC q4w)

Participants will receive guselkumab 200 mg SC at Week 0, Week 4, and Week 8 (ie, a total of 3 SC guselkumab doses and 3 IV placebo doses). At Week 12, participants will switch treatment to guselkumab 200 mg SC q4w through Week 36.

Group 3: Placebo

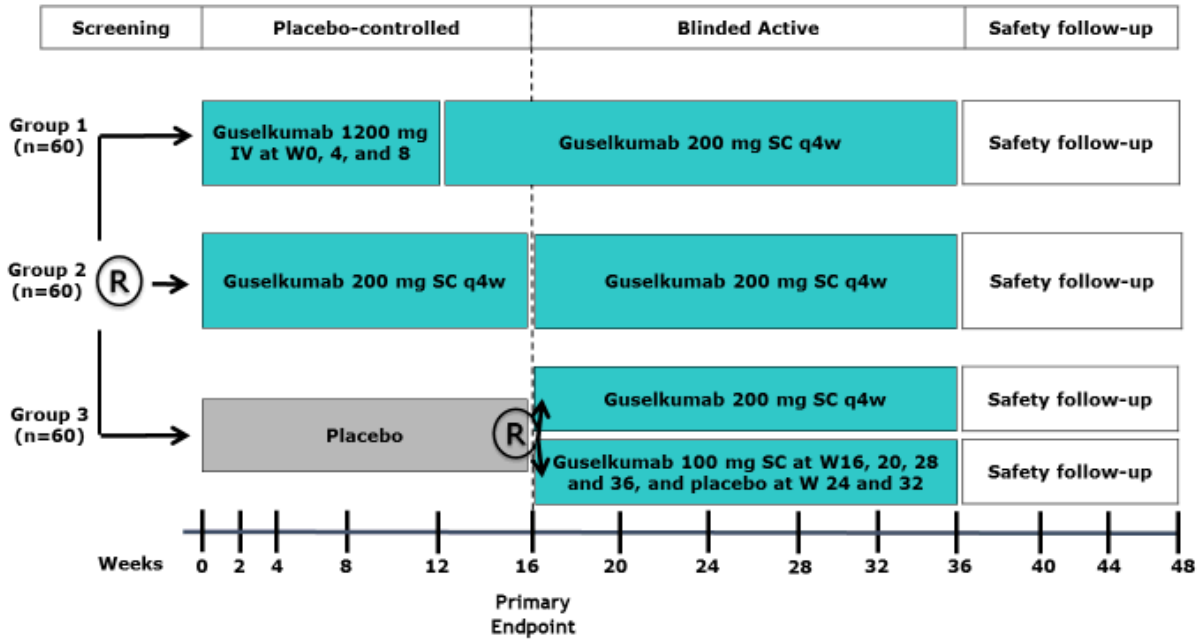
Participants will receive placebo IV and SC at Week 0, Week 4, and Week 8 (ie, a total of 3 IV and 3 SC placebo doses) and an additional SC placebo dose at Week 12. At Week 16, participants will be rerandomized in a 1:1 ratio to either guselkumab 200 mg SC q4w through Week 36 or guselkumab 100 mg SC at Weeks 16, 20, 28, and 36, and placebo at Weeks 24 and 32.

A screening period will take approximately 4 weeks. All participants will enter safety follow-up after Week 36 through Week 48. Two planned database locks (DBLs) will occur, at Week 16 and at Week 48.

Efficacy assessments (HS-IGA, lesion counts, Hurley staging, Hidradenitis Suppurativa Symptom Diary [HSSD], Dermatology Life Quality Index [DLQI], Hospital Anxiety and Depression Scale [HADS], and Patient's Global Impression of Change [PGIC] will be performed according to the Schedules of Activities. Serum samples for PK, immunogenicity, and biomarker analyses will be collected at the timepoints shown in the Schedules of Activities (Section 1.3 of the protocol).

An interim analysis is planned. A sponsor's committee, otherwise not involved in the study conduct, will be responsible for reviewing the results of this interim analysis. In addition, a separate, external independent DMC will be commissioned for this study for safety evaluation. Refer to Section 9.5 of the protocol (Interim Analysis) and Section 9.6 of the protocol (Data Monitoring Committee) for details.

Figure 1: Schematic Overview of CNTO1959HDS2001



1.3. Statistical Hypotheses for Trial Objectives

The primary hypothesis is that guselkumab treatment is superior to placebo as assessed by the proportion of participants achieving Hidradenitis Suppurativa Clinical Response (HiSCR) at Week 16.

- HiSCR is defined as at least 50% reduction in total abscess and inflammatory nodule count (AN count) with no increase in abscess count and no increase in draining fistula count relative to baseline.

The major secondary hypotheses are that guselkumab treatment is:

- Superior to placebo as assessed by the change from baseline in AN count at Week 16.
- Superior to placebo as assessed by the improvement in patient-reported outcomes (PRO) as measured by:
  - The change from baseline in DLQI score at Week 16.
  - The change from baseline in HS-related pain in the past 24 hours based on HSSD at Week 16.

1.4. Sample Size Justification

This study is designed to enroll approximately 180 participants in order to have sufficient power to detect a difference between the guselkumab groups and the placebo group for the primary efficacy endpoint. The rationale for the study sample size is based on the hypothesis tests for the primary efficacy endpoint.

Two adalimumab (Humira®) Phase 3 clinical studies have been conducted to evaluate the safety and efficacy of adalimumab in the treatment of adult participants with moderate to severe HS. The response rates observed in Study M11-313 (PIONEER I) and M11-810 (PIONEER II) for HiSCR at Week 12 were 42% vs 26% and 59% vs 28% in the adalimumab weekly group and placebo group, respectively.

Therefore, based on the data from these studies, various assumptions to calculate sample size and power are shown in Table 1.

Based on these assumptions, with 60 participants in each of the guselkumab treatment group and 60 participants in the placebo group, there will be more than 80% power to detect a treatment difference with a 2-sided significance level of 0.05.

Table 1:	**Statistical Power for the HiSCR Response Rate Comparing to Placebo at Week 16**				
	Treatment group	**Sample size**	**HiSCR**	**Δ (difference)**	**Power**
1	Placebo	60	20%	25%	85%
	Guselkumab	60	45%		
2	Placebo	60	20%	30%	94%
	Guselkumab	60	50%		
3	Placebo	60	20%	35%	98%
	Guselkumab	60	55%		
4	Placebo	60	25%	25%	82%
	Guselkumab	60	50%		
5	Placebo	60	25%	30%	93%
	Guselkumab	60	55%		
6	Placebo	60	25%	35%	98%
	Guselkumab	60	60%		
HiSCR=Hidradenitis Suppurativa Clinical Response					

1.5. Randomization and Blinding

1.5.1. Procedures for Randomization and Stratification

Central randomization will be implemented in this study. Participants will be randomly assigned to 1 of 3 intervention groups based on a computer-generated randomization schedule prepared under the supervision of the sponsor. Permuted block randomization with stratification by baseline weight (≤ 95 kg, > 95 kg) and baseline Hurley stage (I, II, and III) will be used. The number of participants in Hurley stage I should be limited to approximately 30% of the total planned number of participants. Additionally, the number of participants in Hurley stage III should be limited to approximately 50% of the total planned number of participants. The interactive web response system (IWRS) will assign a unique intervention code, which will dictate the intervention assignment and matching study intervention kits for the participant. The requestor must use his or her own user identification and personal identification number when contacting the IWRS, and will then be given the relevant participant details to uniquely identify the participant.

At Week 16, participants randomized to placebo at Week 0 will be rerandomized using the IWRS either to guselkumab 200 mg SC q4w or guselkumab 100 mg SC at Weeks 16, 20, and q8w thereafter (participants will receive placebo SC at Weeks 24 and 32) in a 1:1 ratio using permuted block randomization and the randomization and will be stratified by baseline weight (≤95 kg, >95 kg) and baseline Hurley stage (I, II, and III).

1.5.2. Maintenance of Blind

The study blind will be maintained for the duration of the study, until after the Final (Week 48) DBL.

To maintain the study blind, the study intervention container will have a label containing the study name, study intervention number, and reference number. The blinded label will not identify the specific study intervention in the container (ie, guselkumab or placebo). However, if it is necessary for a participant's safety, the study blind may be broken and the identity of the study intervention ascertained. The study intervention number will be entered in the eCRF when the study intervention is administered. The guselkumab and placebo will be identical in appearance and will be packaged in identical containers.

The investigator will not be provided with randomization codes. The codes will be maintained within the IWRS, which has the functionality to allow the investigator to break the blind for an individual participant.

Data that may potentially unblind the intervention assignment (ie, study intervention serum concentrations, anti-guselkumab antibodies, and intervention allocation) will be handled with special care to ensure that the integrity of the blind is maintained and the potential for bias is minimized. This can include making special provisions, such as segregating the data in question from view by the investigators, clinical team, or others as appropriate until the time of DBL and unblinding.

Under normal circumstances, the blind should not be broken until all participants have completed the study and the database is finalized. However, selected sponsor personnel will be unblinded for analysis after the Week 16 DBL has occurred. All site personnel and participants will remain blinded to the treatment assignments until the last participant completes Week 48 evaluations and the database has been locked. The investigator may, in an emergency, determine the identity of the intervention by contacting the IWRS. While the responsibility to break the intervention code in emergency situations resides solely with the investigator, it is recommended that the investigator contact the sponsor or its designee if possible to discuss the particular situation, before breaking the blind. Telephone contact with the sponsor or its designee will be available 24 hours per day, 7 days per week. In the event the blind is broken, the sponsor must be informed as soon as possible. The date and reason for unblinding must be documented in the appropriate section of the eCRF, and in the source document. The documentation received from the IWRS indicating the code break must be retained with the participant's source documents in a secure manner.

Participants who have had their intervention assignment unblinded by the investigator will not be eligible to receive further study intervention, but should continue to complete evaluations specified in the Schedule of Activities (Section 1.3 of the protocol).

An independent, external DMC will monitor the safety of the study in an unblinded fashion on a regular basis and whenever deemed necessary. In addition, the Sponsor Medical Monitor will review safety data in a blinded manner as the study is ongoing. The DMC's roles and responsibilities, the safety data for DMC review, and other related information (such as, the general procedures, communications, etc.) are defined and documented in the DMC charter.

In addition, an internal Sponsor Interim Analysis Committee and the statistical supporting group (SSG) otherwise not involved in the study conduct will have access to the unblinded data when approximately 30% of the participants have completed their Week 16 visit or have terminated their study participation before Week 16

For the planned interim analyses and the DMC review, the randomization codes and the translation of randomization codes into intervention and control groups will be disclosed to those authorized.

2. GENERAL ANALYSIS DEFINITIONS

This analysis plan provides the general analysis definitions and describes the planned subject information, efficacy, safety, pharmacokinetics, and antibody analyses for the two planned DBLs.

2.1. Imputation Rules for Partial or Missing AE Dates

Partial AE onset dates will be imputed as follows:

- If the onset date of an adverse event is missing day only, it will be set to:
  - First day of the month that the AE occurred, if month/year of the onset of AE is different than the month/year of the study agent start
  - The day of study agent start, if the month/year of the onset of AE is the same as month/year of the study agent start date and month/year of the AE resolution date is different
  - The day of study agent start or day of AE resolution date, whichever is the earliest, if month/year of the onset of AE and month/year of the study agent start date and month/year of the AE resolution date are same
- If the onset date of an adverse event is missing both day and month, it will be set to the earliest of:
  - January 1 of the year of onset, as long as this date is on or after the study agent start date
  - Month and day of the study agent start date, if this date is in the same year that the AE occurred
  - Last day of the year if the year of the AE onset is prior to the year of the study agent start date,
  - The AE resolution date.
- Completely missing onset dates will not be imputed.

Partial AE resolution dates not marked as ongoing will be imputed as follows:

- If the resolution date of an adverse event is missing day only, it will be set to the earliest of the last day of the month of occurrence of resolution or the date of death, if the death occurred in that month.
- If the resolution date of an adverse event is missing both day and month, it will be set to the earliest of December 31 of the year or the day and month of the date of death, if the death occurred in that year.
- Completely missing resolution dates will not be imputed.

2.2. Visit Windows

Nominal visits will be used for all by-visit analyses in the study. The study visits scheduled post randomization should occur at the times delineated in the Schedule of Activities. The study visits through Week 36 should occur within ± 7 days of the scheduled visit. The sponsor must be contacted for any significant deviation in the scheduling of a visit outside the appropriate window and determine how the subject should resume his/her normal dosing schedule relative to the baseline visit (Week 0).

2.3. Pooling Algorithm for Analysis Centers

Unless otherwise specified, data from all investigational centers/sites will be pooled for analyses.

2.4. Analysis Sets

There will be at least two database locks at Weeks 16 and 48 respectively, but additional locks may be performed.

Week 16 database lock

Week 16 database lock will include all data through Week 16 for all randomized participants. In addition, the available data through Week 48 by the time the last participant completes Week 16 visit will also be included. The additional data will be primarily used to assess the maintenance of clinical response through week 48 in planning for future clinical development in HS; selected efficacy, safety, and PK/PD analyses (Section 5.5, 6.1, and 7.1.1) with the data through Week 48 will be included in Week 16 database lock.

Week 48 database lock

Week 48 DBL would include all data through Week 48 for all randomized participants.

2.4.1. Efficacy Analysis Set(s)

2.4.1.1. Full Analysis Set

The full analysis set (FAS) includes all randomized participants who received at least 1 dose (complete or partial) of study agent. This analysis set will be used for the efficacy analyses of the endpoints through Week 48, ***unless otherwise specified***.

In the efficacy analyses, participants will be analyzed according to the randomized treatment groups they were assigned to, regardless of the treatments they actually received.

2.4.1.2. Per Protocol Analysis Set

The primary endpoint will also be analyzed using the per-protocol population, which includes participants who are generally compliant with the protocol.

Specifically, the per protocol population includes participants in FAS except those

- who did not meet the inclusion criteria 6 in the protocol as listed below:
  - Have a total abscess and inflammatory nodule (AN) count of ≥3 at the screening and baseline.
- who met the exclusion criteria 2 in the protocol as listed below:
  - Has a draining fistula count of >20 at the baseline visit.
- who did not complete the specified exposure to study agent as outline below
  - participants randomized to placebo at Week 0 who received guselkumab prior to Week 16.
  - participants randomized to guselkumab 1200 mg at Week 0 but did not receive all scheduled guselkumab administrations prior to Week 16.
  - participants randomized to guselkumab 200 mg at Week 0 but did not receive all scheduled guselkumab administrations prior to Week 16.

However, for those who did not complete the specified exposure to study agent as outline above, participants who discontinued the study agent due to unsatisfactory therapeutic effect (lack of efficacy) or an adverse event (AE) of worsening of HS, or participants who started prohibited medications and continued receiving study agents prior to the specified timepoint for the endpoints will be included in the per protocol analysis and the treatment failure rules specified in Section 5.2.3.2 will apply.

Participants who were excluded from the per protocol analyses will also be summarized.

2.4.2. Safety Analysis Set

The safety analysis set includes all randomized participants who received at least 1 (partial or complete) dose of study agent, i.e., the treated population.

In the safety analyses, participants will be analyzed according to the treatment they actually received, regardless of the treatments they are randomized to.

2.4.3. Pharmacokinetics Analysis Set

The pharmacokinetic (PK) analysis set includes all participants who received at least 1 complete dose of guselkumab and had at least 1 valid blood sample drawn for PK analysis after their first dose of guselkumab.

In the PK analyses, participants will be analyzed according to the treatment they actually received, regardless of the treatments they are randomized to.

2.4.4. Immunogenicity Analysis Set

The immunogenicity analysis set includes all participants who received at least 1 (partial or complete) dose of guselkumab and who have at least 1 sample obtained after their first dose of guselkumab for the detection of antibodies to guselkumab.

In the immunogenicity analyses, participants will be analyzed according to the treatment they actually received, regardless of the treatments they are randomized to.

2.5. Definition of Subgroups

To evaluate the consistency in the primary efficacy endpoint (proportion of participants who achieve HiSCR at Week 16) over demographics, baseline characteristics, prior and baseline medication use, subgroup analyses will be performed when sample sizes are permitted. The subgroups include, but are not limited to, the following:

Baseline demographics:

- Sex (male, female)
- Race
- Baseline Age (<40 years, 40 to <65 years, ≥65 years)
- Baseline weight (≤95 kg, >95 kg)
- BMI (Normal [<25], Overweight [25 -<30], Obese [≥ 30])

Baseline disease characteristics:

- Baseline Hurley stage status (I, II, and III)
- Age at diagnosis (years) (< median, ≥ median)
- HS disease duration (years) (< median, ≥ median)
- Baseline high-sensitivity C-reactive protein (hs-CRP) (< median, ≥ median)
- Baseline AN count category (3 to 5, 6 to 10, ≥11)
- Baseline AN count (< median, ≥ median)
- Baseline HS-IGA (<3, 3, 4)

HS medication and surgery history:

- Systemic immunomodulatory biologics (adalimumab, infliximab, other-anti-TNF inhibitors, ustekinumab)
  - Never used
  - Ever Used

- Hidradenitis Suppurativa related surgery (Deroofing Surgery, Laser Surgery, Excision Surgery)
  - Never had
  - Ever had

2.6. Study Day and Relative Day

Study day is defined as the number of days from the study reference date to the event/visit date. It will be calculated as follows:

- If the event/assessment occurs on or after the reference date, then study day = event/assessment date – reference date + 1.
- If the event/assessment occurs before the reference date, then study day = event/assessment date – reference date.

Hence, the day of reference date is Study Day 1; the previous day is Study Day -1.

2.7. Baseline and Endpoint

In general, 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.

3. INTERIM ANALYSIS AND DATA MONITORING COMMITTEE REVIEW

3.1. Interim Analysis

Before the first DBL at Week 16, an interim analysis will be conducted when a subset of the participants who received at least one administration of study agent (including a partial dose) have completed their Week 16 visit or have terminated their study participation before Week 16. Details of the plan for the interim analysis will be specified in a separate IAC charter and interim analysis plan document before the interim analysis is performed. The interim analysis will be used to determine whether the efficacy of guselkumab 1200 mg IV and guselkumab 200 mg SC doses, as measured by the primary endpoint, is sufficiently low to consider terminating the study based on prespecified guidelines from the data accrued up to the interim analysis. Interim analysis results will not be disseminated to investigators or individuals involved with the conduct of the study.

An interim analysis committee otherwise not involved in the study conduct will be responsible for reviewing the results of this interim analysis. Detail of the organization and roles and responsibilities of the committee, interim analysis procedure, analysis methods, possible recommendations or requests, and the communication following this review will be specified in interim analysis committee charter and analysis plan document.

3.2. Data Monitoring Committee

An independent, external DMC has been established to monitor data on an ongoing basis to ensure the continuing safety of the participants enrolled in this study. The DMC consists of 3 members who are independent of the sponsor. None of the members is participating as an investigator in the current study.

The major function of the DMC is to monitor the safety of the study agent by reviewing the serious adverse events (SAEs) each month and by reviewing the study safety data approximately every 3/4 months. The content of the safety summaries for this study are defined and documented in the DMC SAP developed by the sponsor. No hypothesis testing will be conducted. An independent statistical supporting group, provided by COVANCE (Chiltern), supports the DMC and is the liaison between sponsor and the DMC.

After each review, the DMC is to make recommendations regarding the continuation of the study as planned or, in the event that any unanticipated concerning safety events or issues occur, placing the study on hold or stopping the study. In addition, the DMC roles and responsibilities, and the general procedures (including communications) are defined and documented in the Data Monitoring Committee charter developed by the sponsor detailing the safety data monitoring to be conducted by the DMC.

4. SUBJECT INFORMATION

Unless specified otherwise, FAS will be used for the subject information analyses and participants will be analyzed according to the treatment group to which they were randomized at Week 0, regardless of the treatment they actually received. The number of participants in FAS will be summarized by treatment group and overall.

Simple descriptive statistics, such as mean, median, standard deviation, interquartile range, maximum, and minimum for continuous variables, and counts and percentages for discrete variables will be used to summarize most data and no formal hypothesis testing for treatment comparisons will be performed. In addition, subject listings will also be used to present the data.

4.1. Demographics and Baseline Characteristics

The full analysis set will be used for all tabulations. Participants' demographic data and baseline disease characteristics will be summarized by treatment group. In addition, summaries of participants' medical history and current diagnoses, alcohol intake, and smoking status will be provided by treatment group. If imbalances are found at baseline, then additional analyses may be performed adjusting for baseline differences.

4.1.1. Demographic

Table 2 presents a list of the demographic variables that will be summarized by treatment group, and overall for the FAS.

Table 2: 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)	
Categorical Variables:	
Age (<40 years, 40 to <65 years, and ≥65 years)	Frequency distribution with the number and percentage of participants in each category.
Sex (male, female)	
Weight (kg) (≤ 95 kg, > 95 kg)	
Race (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander, White, Multiple)	
Ethnicity (Hispanic or Latino, Not Hispanic or Latino)	
BMI (Normal [<25], Overweight [25 -<30], Obese [≥30])	

4.1.2. Baseline Disease Characteristics and Medical History

Baseline disease characteristics (e.g., duration of HS disease, baseline Hurley stage status, baseline AN count, inflammatory nodule count, abscess count, and draining fistula, HS-IGA, and PRO related measurements) will be summarized by treatment group. In addition, summaries of participants' medical history and current diagnoses, alcohol intake, and smoking status will be provided by treatment group and the distribution of participants by Hurley stage status (I, II, and III) and weight category (≤95 kg, >95 kg) will also be provided.

4.2. Disposition Information

Disposition data will be summarized through the study periods that include the following:

- Through Week 16
- Through Week 48

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

- Participants randomized
- Participants who received study agent
- Participants who discontinued study agent
- Reasons for discontinuation of study agent

- Participants who completed the study
- Participants who terminated study prematurely
- Reasons for termination of study

Listings of participants will be provided for the following categories:

- Participants who discontinued study agent
- Participants who terminated study prematurely
- Participants who were unblinded during the study period
- Participants who were randomized yet did not receive study agent
- In addition, screened participants will be summarized overall.

4.3. Treatment Compliance

Study agent compliance will be summarized descriptively through Week 36 for the FAS. Number of participants by randomized treatment versus actual treatment will be presented in a summary table. Number of the participants receiving each scheduled treatment will be summarized. In addition, treatment compliance will also be assessed by protocol deviations related to study agent administration (i.e., incorrect study agent or dose received).

4.4. Extent of Exposure

The exposure data through Week 16 and through Week 36 will be summarized. The number and percentage of participants who receive study agent will be summarized by treatment group for the safety analysis set. Descriptive statistics will be presented for the following parameters:

- Number of administrations
- Cumulative total dose

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.

4.5. 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 trial. Participants with major protocol deviations will be identified prior to database lock and will be summarized by category by treatment group through Week 48 for the FAS.

- Entered but did not satisfy criteria
- Developed withdrawal criteria but not withdrawn

- Received a disallowed concomitant treatment
- Received wrong treatment or incorrect dose
- Other: to be defined in the major protocol deviation criteria document

In addition, a listing of participants with major protocol deviations and a listing of participants who missed scheduled study agent administrations (including SC injections and/or IV infusions) will also be provided by randomized treatment group.

4.6. Prior and Concomitant Medications/Surgeries

Prior and concomitant medications will be summarized by treatment group. Prior medications are defined as any therapy used before the day of first dose (partial or complete) of study agent. Concomitant medications are defined as any therapy used on or after the same day as the first dose of study agent, including those that started before and continue on after the first dose of study agent.

Prior HS treatment received (including prior HS related surgery) and the reasons for which participants discontinued these treatments will be summarized by randomized treatment group for the FAS. In addition, a summary of concomitant analgesic therapy for HS, a list of participants who received a protocol-prohibited concomitant treatment meeting the definition of a treatment failure and a listing of participants who received concomitant analgesic therapy meeting the definition of a treatment failure of pain related endpoints will also be provided.

Participants who received concomitant systemic corticosteroids for indications other than HS and participants with concomitant prophylactic treatments for latent TB infection will be listed.

5. EFFICACY

5.1. General Method of Analysis

Unless specified otherwise, efficacy data summaries will be provided by treatment group for the FAS. Statistical comparisons will be made between each of the guselkumab treatment groups (1200 mg IV, 200 mg SC q4w) and the placebo treatment group.

In general, for response efficacy endpoints, treatment comparisons will be performed using a Cochran-Mantel-Haenszel (CMH) test stratified by the baseline weight (≤95 kg, >95 kg) and baseline Hurley stage (I, II, and III). For continuous efficacy endpoints, treatment comparisons will be performed using either a Mixed-Effect Model Repeated Measure (MMRM) model or an analysis of covariance (ANCOVA) model. All of the models will have treatment group, baseline weight (≤95 kg, >95 kg), baseline Hurley stage (I, II, and III), and baseline value as explanatory factors. The MMRM model will also include visit, treatment group by visit interaction, and baseline value by visit interaction as additional explanatory factors. In addition, treatment differences and their associated 95% confidence intervals will be presented.

If the total number of participants that are Hurley stage I at baseline is less than 18, participants that are Hurley stage I will be pooled with the participants that are Hurley stage II, when analyses are adjusted by Hurley stage. Descriptive statistics, such as mean, median, standard

deviation, minimum and maximum, interquartile range for continuous variables, and counts and percentages for categorical variables will be used to summarize the data. Graphical data displays and subject listings may also be used to summarize the data.

5.2. Analysis Specifications

5.2.1. Level of Significance

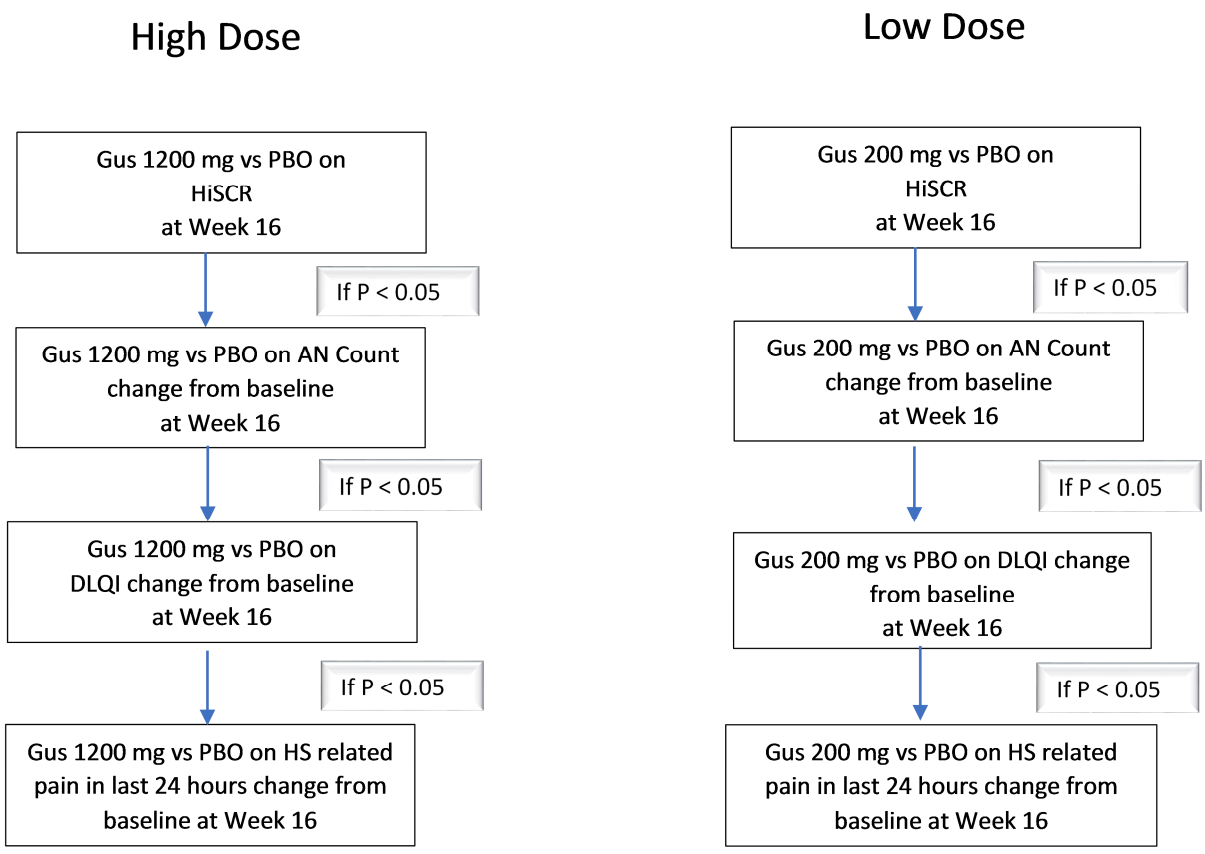
Unless otherwise specified, all statistical testing procedures will be performed at a 2-sided significance level of 0.05. This study is designed to maintain an overall Type I error of 0.1 or less for the primary analysis and major secondary analyses. Nominal p-values will be reported for other secondary analyses.

5.2.1.1. Multiplicity Adjustment for Testing Procedures

This study has 1 primary endpoint (proportion of participants who achieved Hidradenitis Suppurativa Clinical Response (HiSCR) at Week 16) and 3 major secondary endpoints. With 2 treatment comparisons for each of these endpoints, there are a total of 8 hypotheses to be tested.

The primary and major secondary hypotheses will be tested in the specified order and the order and procedure are shown in Figure 2.

Figure 2: Diagram for Multiple Testing Procedure for Primary and Secondary Hypotheses



With the sequential analyses specified above within each dose group vs placebo, each of the hypotheses will be tested at a 2-sided α-level of 0.05 provided that the significance is achieved for the preceding hypothesis test in the specified order shown in Figure 2. If a given comparison is not significant at the 2-sided α-level of 0.05, nominal p values will be provided for the subsequent treatment group comparisons within each dose group vs placebo and these comparisons will be considered as supportive.

5.2.2. Definition of the Efficacy Endpoints and Calculation of the Efficacy Instruments

5.2.2.1. Hidradenitis Suppurativa Clinical Response (HiSCR)

HiSCR responder status is defined as at least a 50% reduction from baseline in the total abscess and inflammatory nodule count, with no increase in abscess or draining fistula count.

5.2.2.2. Lesion Counts

Lesion counts are defined as the number of abscesses, inflammatory nodules, non-inflammatory nodules, draining fistulas, and non-draining fistulas. Lesions will be counted during each visit.

AN Count

- AN count is defined as total abscess and inflammatory nodule count.
- AN50 is defined as at least a 50% reduction in AN count relative to baseline.
- AN75 is defined as at least a 75% reduction in AN count relative to baseline.
- AN90 is defined as at least a 90% reduction in AN count relative to baseline.
- AN100 is defined as a 100% reduction in AN count relative to baseline (ie, AN count = 0).

5.2.2.3. Hurley Staging

Hurley staging consists of 3 stages of disease:

- Stage I: Abscess formation, single or multiple, without sinus tracts and scarring
- Stage II: One or more widely separated recurrent abscesses with tract formation and scarring
- Stage III: Multiple interconnected tracts and abscesses across the entire area, with diffuse or near diffuse involvement

5.2.2.4. Hidradenitis Suppurativa Investigator's Global Assessment

The HS-IGA documents the investigator's assessment of the participant's HS at a given timepoint. The anatomic region with the most severe HS activity at baseline visit should be evaluated for erythema, drainage, and pain and/or tenderness to palpation for each participant. For each participant, the same anatomic site selected for evaluation at baseline visit should then be evaluated at each subsequent visit.

The participant's HS-IGA is assessed as inactive (0), almost inactive (1), mild activity (2), moderate activity (3), or severe activity (4). A higher score indicates more severe disease.

The participant's HS-IGA of erythema is assessed as no erythema, hypopigmentation or hyperpigmentation may be present (0), faint, barely perceptible erythema (1), light red color (2), moderate red color (3), or bright red coloration (4). A higher score indicates more severe disease.

The participant's HS-IGA of drainage is assessed as no drainage, areas are dry following palpation (0), slight pain and/or tenderness with palpation (1), mild pain and/or tenderness with palpation (2), moderate amount of spontaneous drainage (3), or severe spontaneous drainage occurring over broad area(s) (4). A higher score indicates more severe disease.

The participant's HS-IGA of pain and/or tenderness to palpation is assessed as no pain and/or tenderness with palpation (0), slight pain and/or tenderness with palpation (1), mild pain and/or tenderness with palpation (2), moderate pain and/or tenderness with palpation, participant winces (3), or severe pain and/or tenderness with palpation, participant winces and attempts to withdraw (4). A higher score indicates more severe disease.

5.2.2.5. Patients Reported Outcomes

5.2.2.5.1. Hidradenitis Suppurativa Symptom Diary

The HSSD (Section 10.11 of the protocol [Appendix 11]) is a 7-item patient self-reported questionnaire that assesses 5 HS-related symptoms including pain, tenderness, hot skin feeling, odor, and itchiness. The participants are asked to rate the severity of each symptom on a 0 to 10 numerical rating scale, with 0 indicating no symptom experience and 10 indicating the worst possible symptom experience. All 5 symptoms have a recall period of the past 7 days, except for 2 additional questions on pain which evaluate current pain and pain in the past 24 hours. Each individual symptom scale score, ranging from 0-10, will be summarized. A total symptom score, which will also range from 0-10, will be derived by averaging the 5 individual scale scores that utilize the past 7-day recall period.

5.2.2.5.2. Dermatology Life Quality Index

The DLQI is a dermatology-specific quality of life instrument designed to assess the impact of the disease on a subject's quality of life. It is a 10-item questionnaire that, in addition to evaluating overall quality of life, can be used to assess 6 different aspects that may affect quality of life: symptoms and feelings, daily activities, leisure, work or school performance, personal relationships, and treatment. The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. A higher score indicates more severe disease. A score of ≤ 1 indicates no effect at all of disease on subject's health related quality of life, and a reduction of 5 points or more in total DLQI score is considered clinically meaningful improvement.

For a partially answered questionnaire (eg, not all 10 answers in the DLQI questionnaire were available):

- If one question's answer is not available, this question will be scored 0. The total score will then be calculated.
- If two or more questions' answers are unavailable, the questionnaire is not scored. Hence, the total score and each of the 6 component scores will be set to missing.
- If one question from one of the 6 component scores is missing, the affected component score will be set to be missing.

5.2.2.6. Hospital Anxiety and Depression

The Hospital Anxiety and Depression Scale (HADS), a self-assessment scale, was developed to detect states of depression, anxiety and emotional distress amongst patients who were being treated for a variety of clinical problems. The HADS consists of 2 subscales, one measuring Anxiety (A-scale) and one measuring Depression (D scale), which are scored separately.

The HADS is a 14-item questionnaire. Seven of the items relate to anxiety and seven relate to depression. Each item on the questionnaire is scored from 0-3 resulting in a score between 0 and 21 for either anxiety or depression.

If one or more of the items within each domain are left unanswered, that HADS component score will be considered missing.

5.2.3. Data Handling Rules

The following treatment failure rules and data handling rules will be applied to the efficacy analyses in this study.

5.2.3.1. Treatment Failure Criteria

Participants who discontinue study intervention due to lack of efficacy or an AE of worsening of HS, or who started a protocol-prohibited medication or therapy during the study that could improve HS, are considered treatment failures.

The particular protocol-prohibited medications/therapies include:

Systemic Therapies:

- Any immunodulatory biologic therapy
- Any conventional systemic immunosuppressive therapy
- Any systemic corticosteroid for HS
- Any systemic antibiotic therapy for HS or any indications other than infection
- Any systemic retinoid

- Investigational Agents for HS
- Analgesic therapy for HS (Section 5.2.3.2.1)
- Phototherapy (PUVA and/or UVB) for any indications and other phototherapies for indication of HS

5.2.3.2. Treatment Failure Rules

A participant who meets one or more of the treatment failure criteria specified in Section 5.2.3.1 will be considered a treatment failure from that point onward. The baseline values will be used for all directly measured endpoints regardless of the actual measurements. Zero will be assigned to improvement, and non-responder status will be assigned to binary response variables. However, treatment failure rules for the HSSD pain related endpoints will be handle differently and are specified in Section 5.2.3.2.1.

Treatment failure is assumed to have occurred at the earlier of the following dates:

- Date of discontinuation of study treatment due to lack of efficacy or an AE of worsening of HS or
- Date of initiation of a protocol-prohibited medication/therapy during the study that could improve HS.

In addition, lesions that received intervention as rescue therapy will be counted as present after the visit of intervention.

5.2.3.2.1. Treatment Failure Rule for HSSD Pain Related Endpoints

Participants who received analgesic therapy for HS within 1 day of a scheduled visit, will be considered a treatment failure for the HSSD past 24 hours pain and current pain endpoints at that visit. Treatment failure rules will not be applied throughout the study for analyses of the HSSD 7 days recall pain component.

5.2.3.3. Missing Data Imputation

For the following binary and continuous composite endpoints, participants with missing data on component(s) but not all components, a last observation carried forward (LOCF) imputation will be performed for the missing component(s) and response status or change from baseline will then be determined.

- HiSCR (abscess, inflammatory nodule, and draining fistula counts)
- Endpoints related to total AN count (abscess and inflammatory nodule counts)
- Endpoints related to total inflammatory and non-inflammatory nodule counts
- HSSD total symptom score (pain, tenderness, hot skin feeling, odor, and itchiness)

After the treatment failure rules are applied, the remaining missing data will be handled as follows for all of the efficacy analyses including the analyses at key visit Week 16 and over time ***unless otherwise specified***.

5.2.3.3.1. Missing Data Binary Endpoints

For binary efficacy endpoints, participants with missing response status will be considered non-responders for all of the efficacy analyses at key visit of Week 16 and over time summaries.

5.2.3.3.2. Missing Data Remain as Missing for Continuous Endpoints

For continuous endpoints for which longitudinal data were collected prior to the analysis visits, efficacy analyses or over time summaries are performed using a Mixed-Effect Model Repeated Measures (MMRM) model and all available data from the 3 treatment groups through Week 16 or from Week 16 through Week 48 will be included. Missing data will not be imputed after treatment failure rules are applied. Under the assumption of MAR, the missing data will be accounted for through correlation of repeated measures in the model.

For the MMRM model, an unstructured covariance matrix for repeated measure within a subject will be used. In case that convergence cannot be achieved, first order Autoregressive Moving Average will be used.

In addition, for the continuous endpoints with no post baseline data scheduled to be collected prior to the analysis visit (eg, change from baseline in DLQI at Week 16), under the assumption of missing at random (MAR), multivariate response modeling approach will be performed with SAS Proc Mixed. With this approach, baseline and post-baseline AN count data that potentially can be predictive of missingness will be included in the model and marginal means of change from baseline will be compared between the treatment groups.

In addition, no imputation will be done with missing data for efficacy analyses and over time summaries for other continuous endpoints.

5.2.4. Estimand

The same population, ie, all participants with moderate to severe HS for at least one year and meet inclusion/exclusion criteria will be used for all estimands defined below. The FAS (Section 2.4.1.1) will be used to analyze the data.

5.2.4.1. Composite Strategy

The Composite Strategy assesses the treatment effects not only based on the variable measurements, but also based on intercurrent event defined in TF criteria. If a participant meets TF criteria, participant will be a non-responder for binary response variables and no improvement will be assigned for continuous variables.

- **Composite Estimand (Continuous)**

  Variables: The endpoint is defined as change for baseline score. No improvement (zero change) will be assigned after a subject meets one or more treatment failure criteria.

  Intercurrent Events: the intercurrent events are captured through variable definition.

Population level summary: difference in mean changes from baseline between a guselkumab group and placebo group.

- **Composite Estimand (Binary)**

  Variables: The endpoint (e.g. HiSCR) is defined as the proportion of participants achieving a response. No responder status will be assigned after a subject meets one or more TF criteria.

  Intercurrent Events: the intercurrent events are captured through variable definition.

  Population level summary: difference in proportion of responders between a guselkumab group and placebo group.

The composite strategy will be used for analyzing all efficacy endpoints.

5.2.5. Treatment Groups

In the efficacy analyses, full analysis set will be used and the participants will be analyzed according to the randomized treatment groups they were assigned to, regardless of the treatments they actually received. Unless otherwise specified, efficacy analyses during each of study periods below are in general displayed as follows:

- Analysis through Week 16
  - Efficacy analyses for placebo comparison at Week 16 or through Week 16 will be summarized by randomized treatment group at Week 0:
    - **Placebo**: Participants randomized to placebo group at Week 0.
    - **Guselkumab 200 mg SC**: Participants randomized to guselkumab 200 mg SC group at Week 0.
    - **Guselkumab 1200 mg IV**: Participants randomized to guselkumab 1200 mg IV group at Week 0.
  - Efficacy data from Week 16 through Week 48 will be summarized by the following treatment groups:
    - **Placebo → Guselkumab 100 mg SC**: Participants randomized to placebo group at week 0 and re-randomized at Week 16 to receive guselkumab SC 100 mg.
      - Only placebo participants who were re-randomized to guselkumab 100 mg SC and received guselkumab 100 mg at Week 16 will be included in the summary for the visits after Week 16.
    - **Placebo → Guselkumab 200 mg SC**: Participants randomized to placebo group at week 0 and re-randomized at Week 16 to receive guselkumab SC 200 mg.
      - Only placebo participants who were re-randomized to guselkumab 200 mg SC and received guselkumab 200 mg at Week 16 will be included in the summary for the visits after Week 16.

- **Guselkumab 200 mg SC**: Participants randomized to guselkumab 200 mg SC group at Week 0.
- **Guselkumab 1200 mg IV**: Participants randomized to guselkumab 1200 mg IV at Week 0.

These presentations allow assessment of efficacy over time between treatment groups.

5.3. Primary Efficacy Endpoint(s)

5.3.1. Definition

The primary efficacy endpoint is the proportion of patients achieve a HiSCR at Week 16. Refer to Section 5.2.2.1 for the definition of a HiSCR responder.

5.3.2. Analysis Methods

The primary endpoint will be compared between the each guselkumab group and the placebo group. The primary endpoint will be analyzed at Week 16 based on the composite estimand (Section 5.2.4.1) and the data from all participants in FAS (Section 2.4.1.1) will be analyzed according to randomized treatment group regardless of the treatment actually received.

Participants who meet treatment failure criteria prior to Week 16 will be considered nonresponders for the primary endpoint at Week 16. In addition, participants who do not return for evaluation at Week 16 will be considered nonresponders at Week 16.

In this primary analysis, the number and proportion of participants who achieve a HiSCR at Week 16 will be summarized for each treatment group. To address the primary objective, a CMH chi-square statistic stratified by baseline weight (≤95 kg, >95 kg) and baseline Hurley stage status at an alpha level of 0.05 will be used for each of the following hypotheses:

1. Guselkumab 1200 mg IV versus placebo in HiSCR at Week 16.
2. Guselkumab 200 mg SC versus placebo in HiSCR at Week 16.

The study is considered positive if at least one of the hypotheses is tested as significant.

5.3.3. Data Handling

The data handling rules specified in Section 5.2.3.3 and 5.2.3.3.1 will be applied to the primary analysis. In the case of participants with missing components (abscess, inflammatory nodule, or draining fistula counts) at Week 16, LOCF will be applied for the missing lesion count(s). This partial component missing data imputation rule will be applied to all the following analyses related to the primary endpoint.

Participants who meet treatment failure criteria specified in Section 5.2.3.2 prior to Week 16 will be considered not achieving HiSCR at Week 16. In addition, for participants who do not return for evaluation at Week 16 will be considered as non-responders.

5.3.4. Sensitivity Analysis

Sensitivity Analysis 1

For participants who do not return for evaluation at Week 16, the analysis will be performed using observed data after applying treatment failure rules (as defined in Section 5.2.3.2).

Sensitivity Analysis 2

A second sensitivity analysis will be performed by using multiple imputations (MI) by treatment group based HiSCR responses respectively. The fully conditional specification (FCS) method will be used to impute the missing data after applying treatment failure for the HiSCR response at Week 16.

More specifically, the missing HiSCR response status will be imputed using FCS method with 50 imputed data sets with seed = 1231 to fill in the missing HiSCR responses through Week 16 in each of the 50 copies of datasets. The proportion difference of HiSCR at Week 16 adjusted for baseline weight (≤95 kg, >95 kg) and baseline Hurley stage using Mantel-Haenszel weight between the guselkumab groups and the placebo group and its 95% CI combining multiple datasets will be provided. In addition, the p-value for testing the treatment difference will be obtained from SAS PROC MIANALYZE based on these combined Mantel-Haenszel estimates from the multiple imputation datasets.

5.3.5. Subgroup Analysis

For each of the subgroups defined in Section 2.5, the difference between each of the guselkumab treatment group and placebo group in the proportion of participants achieving HiSCR at Week 16 and its 95% continuity adjusted confidence interval (when the number of participants permits) will be calculated. Subgroup analyses will not be stratified by baseline weight (≤95 kg, >95 kg) and baseline Hurley stage status.

In addition, the proportion of participants achieving HiSCR at Week 16 by investigator site/region will be summarized.

5.3.6. Per-protocol Analysis

The primary analyses for primary endpoint will also be performed on per-protocol analysis set (Section 2.4.1.2). Similar treatment failure rules and data handling rules specified in Section 5.2.3 will apply.

5.4. Major Secondary Endpoints

There are 3 major secondary endpoints with 6 corresponding major secondary analyses. They will be performed in the order listed in Figure 2.

- The change from baseline in total AN count at Week 16.
- The change from baseline in DLQI at Week 16.

- The change from baseline in HS-related skin pain in the past 24 hours based on HSSD at Week 16.

This section outlines the definition and analyses of these major secondary endpoints. Data from all participants in FAS (Section 2.4.1.1) will be included and analyzed according to the randomized treatment groups.

5.4.1. Definition

Refer to Section 5.2.2 for the definition of the major secondary endpoints

5.4.2. Analysis Methods

5.4.2.1. The Change from Baseline in Total AN Count at Week 16

For the change from baseline in AN count at Week 16, treatment comparisons will be performed using a Mixed-Effect Model Repeated Measures (MMRM) Model. The MMRM model will include baseline weight (≤95 kg, >95 kg), baseline Hurley stage status baseline values, visit, treatment group by visit interaction, and baseline value by visit interaction as explanatory factors.

The model will be performed based on all available data from the 3 treatment groups through Week 16. The treatment difference between a guselkumab group and the placebo group will be estimated by the difference in the least squares means (LSmeans). The 95% CIs for the differences in LSmeans and p-values will be calculated.

5.4.2.2. The Change from Baseline in DLQI at Week 16

The change from baseline in DLQI at Week 16 will be analyzed based on a mixed model (Section 5.2.3.3.2). under the assumption of missing at random (MAR). Marginal mean model will account for treatment group, baseline weight (≤95 kg, >95 kg), baseline Hurley stage status, baseline DLQI score, and AN count at each visit up to Week 16 through correlations among these variables. Marginal means will be compared between each of the guselknumab groups and placebo.

In addition, treatment differences and their associated 95% confidence intervals will be presented.

5.4.2.3. The Change from Baseline in HS-related Skin Pain in the Past 24 Hours Based on HSSD at Week 16.

The change from baseline in HS-related skin pain in the past 24 hours based on HSSD at Week 16 will be analyzed based on the analysis approach as specified in Section 5.4.2.1.

5.4.3. Data Handling

Unless otherwise specified, data handling rules specified in Sections 5.2.3.3, 5.2.3.3.2, will be applied to the major secondary analyses.

5.5. Other Efficacy Variable(s)

In addition to the primary and major secondary analyses, the analyses for other efficacy endpoints will be performed and nominal p-values will be provided. Other efficacy endpoints include the endpoints related to

- HiSCR
- Lesion Count
- HS-IGA
- Patient-reported Outcomes
  - HSSD
  - DLQI
  - HADS
  - Patient's Global Impression of Change (PGIC) of Hidradenitis Suppurativa Severity

The other secondary efficacy analyses outlined in the following sections in general will be carried out at key endpoint (Week 16) and over time.

5.5.1. Definition

Refer to Section 5.2.2 for the definitions of the secondary endpoints described in the following sections.

5.5.2. Analysis Methods

Most of the secondary efficacy analyses described in sections below will be based on FAS. For participants randomized to placebo, only participants who crossed over to receive guselkumab at Week 16 will be included in the efficacy summaries for the visits after Week 16. All statistical testing will be performed at the 2-sided 0.05 significance level. Nominal p-values will be presented.

5.5.2.1. At Week 16

For continuous endpoints related to lesion count and HSSD; where longitudinal data were collected prior to the analysis visits; treatment comparisons will be performed using Mixed-Effect Model Repeated Measure (MMRM) model as specified in Section 5.1 and Section 5.2.3.3.2. For the other continuous endpoints (DLQI components and HADS) with no post baseline data is scheduled to be collected prior to the analysis visit, treatment comparisons will be performed using analysis specified in Section 5.4.2.2.

For binary response endpoints treatment comparisons will be performed using a Cochran-Mantel-Haenszel (CMH) test stratified by the baseline weight (≤95 kg, >95 kg) and baseline Hurley stage status with missing data imputed with Non-Responder Imputation (NRI) defined in Section 5.1.

5.5.2.2. Over Time Summaries

In general, all endpoints with over time analyses will be descriptively summarized by treatment groups using descriptive statistics, such as mean, median, standard deviation, interquartile range, minimum and maximum for continuous variables, and counts and percentages for categorical variables.

Through Week 16

For selected continuous endpoints (change from baseline in AN count, abscess, inflammatory nodule, and draining fistula), Mixed-Effect Model Repeated Measure (MMRM) model will be used and Least Square means (LS means), LS means differences and their corresponding 95% confidence interval will be provided overtime through Week 16 by visit and treatment group in addition to the descriptive summary statistics based on observed data after treatment failures.

From Week 16 through Week 48

For selected continuous endpoints (change from baseline in AN count, abscess, inflammatory nodule, and draining fistula), Mixed-Effect Model Repeated Measure (MMRM) model will be used, Least Square means (LS means) and the corresponding 95% confidence intervals will be provided over time from Week 16 through Week 48 by visit and treatment group in addition to the descriptive summary statistics based on observed data after treatment failures.

Furthermore, for the over time summaries in proportion of participants achieving HiSCR and HS-IGA score of 0 or 1, the corresponding 95% CIs will also be provided for each treatment group at Week 40.

Additionally, the following overtime analyses will be performed at Week 16 DBL with the data available at the time of Week 16 database lock. These analyses will be performed based on the observed data without applying treatment failure rules.

- The proportion of participants who achieved HiSCR from Week 16 through Week 48.
- The change from baseline in total AN count from Week 16 through Week 48.
- The proportion of participants with HS-IGA score of inactive (0), HS-IGA score of inactive (0) or almost inactive (1), and the proportion of participants achieving HS-IGA score of mild activity or better (≤2) from Week 16 through Week 48.
- The change from baseline for the past 24 hours pain from Week 16 through Week 48.

5.5.3. Data Handling Rule

Unless otherwise specified, data handling rules specified in Section 5.2.3.3 will be applied to these secondary analyses. Over time summaries for continuous endpoints will be based on the observed data after treatment failure rules. For binary endpoints, participants with missing response status after applying treatment failures rules will be considered non-responders for the over time analyses.

5.5.4. Analysis Related to HiSCR

- The proportion of participants who achieved HiSCR, the proportion of participants who achieved HiSCR by baseline weight (≤95 kg, >95 kg), and the proportion of participants who achieved HiSCR by baseline Hurley stage status will be summarized by treatment group over time.

The proportion of participants who achieved HiSCR will also be summarized over time by treatment groups using observed data after applying treatment failure rules and observed data without considering treatment failure rules respectively as sensitivity analyses.

In addition, the HiSCR will be summarized over time from Week 20 through Week 48 with Week 16 as baseline for the placebo participants who are re-randomized to either guselkumab 100 mg q8w or guselkumab 200 mg q4w group.

5.5.5. Analysis Related to Lesion Count

AN Count

- The change from baseline in total AN count, the change from baseline in total AN count by weight, and the change from baseline in total AN count by Hurley stage status will be summarized by treatment groups over time.
- The proportion of participants achieving at least 50%, 75%, 90%, and 100% reduction in total AN count at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The proportion of participants achieving at least 50%, 75%, 90%, and 100% reduction in total AN count will be summarized by treatment group over time.
- The proportion of participants achieving AN count of 0, 0/1, and 0/1/2 respectively at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The proportion of participants achieving AN count of 0, 0/1, and 0/1/2, respectively will be summarized by treatment group over time.
- The proportion of participants who experience at least one flare (defined as at least a 25% increase in AN count with a minimum increase of 2 AN relative to baseline) over 16 weeks will be compared between each of the guselkumab groups and the placebo group at Week 16. Furthermore, the proportion of participants who experience at least one flare over 48 weeks will be summarized at Week 48 by treatment groups.

In addition, the change from baseline in AN count by prespecified anatomic region and treatment group will be summarized at Week 16 and Week 40.

Abscess

- The proportion of participants who achieved complete elimination of abscesses at Week 16 will be compared between each of the guselkumab groups and the placebo group among participants who had any abscess at baseline.
- The change from baseline in number of abscesses at Week 16 will be compared between each of the guselkumab groups and the placebo group.

- The change from baseline in number of abscesses will be summarized by treatment group over time.

Fistulas

- The proportion of participants who achieved complete elimination of draining fistulas at Week 16 will be compared between each of the guselkumab groups and the placebo group among those with draining fistulas at baseline.
- The change from baseline in number of draining fistulas at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The change from baseline in number of draining fistulas will be summarized by treatment group over time.

Inflammatory and non-inflammatory Nodules

- The proportion of participants who achieved complete elimination of inflammatory nodules at Week 16 will be compared between each of the guselkumab groups and the placebo group among those with inflammatory nodules at baseline.
- The change from baseline in number of inflammatory nodules at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The change from baseline in number of inflammatory nodules will be summarized by treatment group over time.
- The change from baseline in number of non-inflammatory nodules at Week 16 will be compared between each of the guselkumab groups and the placebo group among pts with non-inflammatory nodules at baseline.
- The change from baseline in number of non-inflammatory nodules will be summarized by treatment group over time.

5.5.6. Analysis Related to HS-IGA

- The proportion of participants with HS-IGA score of inactive (0), HS-IGA score of inactive (0) or almost inactive (1), and the proportion of participants achieving HS-IGA score of mild activity or better (≤2) and with at least 2-grade improvement relative to baseline at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The proportion of participants with HS-IGA score of inactive (0), HS-IGA score of inactive (0) or almost inactive (1), and the proportion of participants achieving HS-IGA score of mild activity or better (≤2) will be summarized by treatment groups over time. In addition, the proportion of participants with 1 -grade and 2-grade improvement in HS-IGA scores from baseline will be summarized over time respectively.
- The proportion of participants with HS-IGA score of inactive (0), almost inactive (1) at Week 16 among participants with HS-IGA score of moderate activity (3) or severe activity (4) at baseline will be compared between each of the guselkumab groups and the placebo group and will also be summarized by treatment groups over time.

- The proportion of participants with HS-IGA erythema score of (0), erythema score of (0) or (1), and the proportion of participants with HS-IGA erythema score of light red color or better (≤2) at Week 16 will be compared between each of the guselkumab groups and the placebo group and will also be summarized by treatment groups over time.
- The proportion of participants with HS-IGA erythema score of 0, erythema score of 0 or 1, and the proportion of participants with HS-IGA erythema score of light red color or better (≤2) will be summarized by treatment groups over time.
- The proportion of participants with HS-IGA drainage score of 0, drainage score of 0 or 1, and the proportion of participants with HS-IGA drainage score of mild spontaneous drainage or better (≤2) at Week 16 will be compared between each of the guselkumab groups and the placebo group and will also be summarized by treatment groups over time.
- The proportion of participants with HS-IGA drainage score of 0, drainage score of 0 or 1, and the proportion of participants with HS-IGA drainage score of mild spontaneous drainage or better (≤2) will be summarized by treatment groups over time.
- The proportion of participants with HS-IGA pain and/or tenderness to gentile palpation (excluding scarring area) score of 0, score of 0 or 1, and the proportion of participants with HS-IGA pain and/or tenderness to gentile palpation (excluding scarring area) score of mild pain and/or tenderness with palpation or better (≤2) at Week 16 will be compared between each of the guselkumab groups and the placebo group and will also be summarized by treatment groups over time.
- The proportion of participants with HS-IGA pain and/or tenderness to gentile palpation (excluding scarring area) score of 0, score of 0 or 1, and the proportion of participants with HS-IGA pain and/or tenderness to gentile palpation (excluding scarring area) score of mild pain and/or tenderness with palpation or better (≤2) will be summarized by treatment groups over time.

In addition, an IGA score derived from the evaluation for erythema, drainage, and pain and/or tenderness to palpation will be summarized over time.

5.5.7. Analysis Related to Patient Reported Outcome

5.5.7.1. DLQI

- The proportions of participants with DLQI score of 0 and 1 at Week 16 for the participants with baseline DLQI score >1 and the proportion of participants with a reduction of 5 or more points in DLQI score for the participants with baseline DLQI score ≥ 5 at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The change from baseline in DLQI component scores at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The proportions of participants with DLQI score of 0 and 1 at Week 40 for the participants with baseline DLQI score >1 and the proportion of participants with a reduction of 5 or more points in DLQI score at Week 40 for the participants with baseline DLQI score ≥ 5 will be summarized.

5.5.7.2. Hidradenitis Suppurativa Symptoms Diary (HSSD)

- The change from baseline in each HSSD symptom scale score (7 days recall) and the change from baseline in current pain at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The change from baseline in HSSD total symptom score at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- Number of participants with a reduction of ½ SD or more from baseline in HSSD total symptom score at week 16 will be compared between each of the guselkumab groups and the placebo group.
- The change from baseline in each HSSD symptom scale score (7 days recall), the change from baseline for the past 24 hours pain and current pain, and the change from baseline in HSSD total symptom score will be summarized over time.

5.5.7.3. Other Patients Reported Outcomes

Hospital Anxiety and Depression

- The change from baseline in Hospital Anxiety and Depression scale (HADs) at Week 16 will be compared between each of the guselkumab groups and the placebo group.
- The change from baseline in Hospital Anxiety and Depression scale will be summarized at Week 16 and Week 40.
- The proportion of participants with hospital anxiety scale <8 and depression scale <8 at Week 16 will be compared between each of the guselkumab groups and placebo groups, among participants with a baseline hospital anxiety scale and depression scale >=8.
- Hospital anxiety scale and depression scale shift from baseline to Week 16 and Week 40 with respect to the hospital anxiety and depression scale category (<8, >=8) will be summarized.

Patient's Global Impression of Change (PGIC) of Hidradenitis Suppurativa Severity

- The distribution of the PGIC at Week 16 will be compared between each of the guselkumab groups and the placebo group.

5.5.8. Other

In addition to the above efficacy analyses, the follow efficacy analyses and summaries will be explored by using the observed data without considering treatment failure rules:

- The change from baseline in high-sensitivity-C-reactive protein (hs-CRP) at Week 4, Week 16, and Week 40 will be summarized by treatment groups.
- Hurley stage status shift from baseline to Week 16 and Week 40 will be summarized respectively.

6. SAFETY

Safety will be assessed by summarizing the incidence and type of AEs and examining changes in laboratory parameters (hematology and chemistry), vital signs, and suicidal ideation and behavior as measured by the C-SSRS (Columbia-Suicide Severity Rating Scale).

In all the safety analysis, randomized participants who received at least 1 (partial or complete) dose of study agent administration will be included and analyzed according to the treatment they actually received, regardless of the treatments they are randomized to. No formal statistical comparison is planned.

Depending on the safety data categories, the cumulative safety data will be analyzed through different study periods through Week 16 and Week 48. Unless otherwise specified, tabular summaries of safety events for key study periods are in general presented as following:

Summaries through Week 16 (placebo controlled):

Safety data through Week 16 will be summarized by treatment groups

1. Placebo
2. Guselkumab 200 mg SC
3. Guselkumab 1200 mg IV
4. Combined Guselkumab

This allows between-group comparisons of safety between the guselkumab regimens and the placebo group based on similar follow-up period in each group.

Summaries through Week 48

Safety data through Week 48 will be summarized by treatment groups including

1. Placebo → guselkumab 100 mg SC
2. Placebo → guselkumab 200 mg SC
3. Guselkumab 200 mg SC
4. Guselkumab 1200 mg IV
5. Combined Guselkumab

This allows safety comparisons between each guselkumab regimen through Week 48 based on the similar follow-up time in each group.

The list of actual treatment groups for safety analyses and inclusions of participants and safety events/measurements in each group are defined as follows:

1. **Placebo:** all participants who were randomized to placebo at Week 0 and received treatment with placebo only or received treatment with placebo prior to receiving treatment with guselkumab. For participants who started treatment with placebo but later received

guselkumab, the safety events/measurements on and after the first dose of guselkumab will be excluded from this group. Only the safety events/measurements that occurred while the participants had been receiving placebo only will be included in this group.

2. **Placebo → guselkumab 100 mg SC:** all participants who were randomized to placebo at Week 0 started treatment with placebo only and later randomized to treatment with guselkumab 100 mg SC q8w. Only the safety events/measurements from these participants that occurred on and after their first administration of guselkumab will be included in this group.

3. **Placebo → guselkumab 200 mg SC:** all participants who were randomized to placebo at Week 0 started treatment with placebo only and later randomized to treatment with guselkumab 200 mg SC q4w. Only the safety events/measurements from these participants that occurred on and after their first administration of guselkumab will be included in this group.

4. **Guselkumab 200 mg SC:** all participants who were randomized to guselkumab 200 mg SC q4w at Week 0 and received guselkumab. All the safety events/measurements from these participants that occurred from Week 0 will be included in this group.

5. **Guselkumab 1200 mg IV:** all participants who were randomized to guselkumab 1200 mg IV q4w at Week 0 and received guselkumab. All the safety events/measurements from these participants that occurred from Week 0 will be included in this group.

6.1. 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 starting at or after the initial administration of study agent through the end of the trial is considered to be treatment emergent. If the event occurs on the day of the initial administration of study agent, 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 agent based on partial onset date or resolution date. All reported treatment-emergent adverse events will be included in the analysis.

Infusion Reactions

A comprehensive clinical review of all AEs that occurred on the same day of infusion, with a start time during infusion or ≤ 60 minutes after the end of IV infusion of study agent (AEs temporally related to infusion), with the exception of laboratory abnormalities, will be performed to identify the occurrence of potential infusion reactions. Specifically, the reported AEs temporally related to infusion will be reviewed to identify participants with a contemporaneous constellation of AE terms that are consistent with the signs or symptoms that typically occur during hypersensitivity reactions or cytokine release syndromes (eg, anaphylaxis, fever, chills, rigors, hypotension,

hypertension, bronchospasm, laryngospasm, wheezing, dyspnea, syncope, pre-syncope, urticaria, angioedema, generalized pruritus, flushing, rash, and nausea), to identify all participants with potential infusion reactions.

Injection-site Reactions

A study intervention injection-site reaction is any adverse reaction at an SC study intervention injection-site. The injection sites will be evaluated for reactions and any injection-site reactions will be recorded as an AE.

Any unfavorable or unintended sign that occurs at the injection (infusion) site is an injection site reaction and will be recorded as an injection site reaction by the investigator on the eCRF

Infection

An infection is defined as any AE that was recorded as an infection by the investigator on the eCRF.

The following analyses will also be used to assess the safety of participants in the study:

- The incidence and type of AEs.
- The incidence and type of SAEs.
- The incidence and type of infections.
- The incidence and type of reasonably related AEs.
- The incidence and type of AEs temporally associated with infusion (defined as an AE that occurred on the same day of infusion, with a start time during infusion or ≤ 60 minutes after the end of infusion).
- The incidence and type of injection-site reactions.

These summary tables will provide the count and percentage of participants with 1 or more of the specified AEs by treatment group. In addition to the summary tables, listings will be provided for participants who:

- Had SAEs.
- Had AEs leading to discontinuation of study agent administration.
- Had AEs of severe intensity.
- Had treatment-emergent adverse events temporally associated with infusion.
- Had anaphylactic or serum sickness-like reactions.

Since safety should be assessed relative to exposure and follow-up, most AE summary tables will include average weeks of follow-up and average number of study agent administrations, infusions and injections for each treatment group. A listing of participants who died will be provided.

6.2. Clinical Laboratory Tests

All clinical laboratory reports will be displayed for the participants included in the safety analysis set. The clinical laboratory parameters to be evaluated by the central laboratory include but are not limited to:

- **Hematology**: hemoglobin, hematocrit, lymphocytes, neutrophils, platelets, red blood cell (RBC) count and white blood cell (WBC) count.
- **Chemistry**: albumin, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, total bilirubin, blood urea nitrogen/urea, calcium, chloride, creatinine, glucose, potassium, total protein, sodium.

Box plots of laboratory measurements and change from baseline will be provided for the selected laboratory measurement.

Applicable laboratory results will be graded according to National Cancer Institute's Common Terminology Criteria for Adverse Events (NCI-CTCAE version 5.0). The worst NCI-CTCAE will be summarized by treatment group.

For non-fasting glucose, the screening measurement will be used as the baseline measurement. A listing of participants with 1 or more NCI-CTCAE toxicity grade ≥2 in hematology and clinical chemistry laboratory measurements will be provided

6.3. Vital Signs and Physical Examination Findings

Vital signs variables including heart rate and blood pressure (systolic and diastolic) will be measured at visits as per the schedule of activities in the protocol. Descriptive statistics of the observed value and change from baseline of the vital signs will be summarized by treatment group.

Physical exam findings will not be analyzed. When physical exam findings are captured as AEs, those will be included in the analyses of AEs.

6.4. Other Safety Parameters

Weight and Waist Circumference

Descriptive statistics of changes from baseline will be summarized at selected scheduled time points.

6.5. Columbia-Suicide Severity Rating Scale (C-SSRS)

The Columbia-Suicide Severity Rating Scale (C-SSRS) will be used as a screening tool to prospectively evaluate the potential of guselkumab to induce suicidal ideation and behavior. The C-SSRS defines five subtypes of suicidal ideation and behavior in addition to self-injurious behavior with no suicidal intent and is a fully-structured subject self-report questionnaire, including standardized questions, follow-up prompts, error handling routines, and scoring conventions. The Screening version of the C-SSRS will be conducted at Screening followed by the Since Last Visit version of the C-SSRS at all other visits through the end of study.

The C-SSRS will be performed during each evaluation visit according to the assessment schedule. The C-SSRS will be performed at screening after signing informed consent, and before study agent administration, and as the first assessment for all post-baseline visits. The baseline is defined as the most severe/maximum C-SSRS score at either screening or Week 0.

In addition, potential suicide related adverse events including suicidal ideation, suicidal behavior excluding completed suicide, and completed suicide will be identified by the investigators and collected in the eCRF.

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 48.

The maximum score assigned for each subject 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 48 will be presented, where the baseline category is based on C-SSRS score and the post baseline is based on C-SSRS and/or AE data.

7. PHARMACOKINETICS/PHARMACODYNAMICS

7.1. Pharmacokinetics

All PK analyses will be based on the PK analysis set (Section 2.4.3). Unless otherwise specified, tabular summaries of PK for key study periods are in general presented as following:

Summaries through Week 16:

PK data through Week 16 will be summarized by treatment groups

- Guselkumab 200 mg SC
- Guselkumab 1200 mg IV

Summaries through Week 48:

PK data through Week 48 will be summarized by treatment groups including

- Placebo → 100 mg SC
- Placebo → 200 mg SC
- Guselkumab 200 mg SC
- Guselkumab 1200 mg IV

7.1.1. Serum Guselkumab Concentrations

Blood samples for measuring serum guselkumab concentrations will be collected from all participants at the specified visits as shown in the schedule of activities in the protocol. Serum samples will also be collected at the final visit from participants who terminate study participation early. Samples must be collected before study agent administration at visits when a study agent administration is scheduled. In addition, for IV infusion-related visits (i.e., Weeks 0, 4, and 8), another blood draw should be taken approximately 60 minutes after completion of the infusion for serum concentration of guselkumab.

Serum guselkumab concentrations will be summarized using descriptive statistics, including n, arithmetic mean, SD, coefficient of variation (%CV), median, interquartile range, range (minimum and maximum), by treatment group at each PK sampling time where appropriate. PK data may be displayed graphically. The following analyses will be performed as appropriate:

- Summary of serum guselkumab concentrations at each visit by treatment group
- Proportion of participants without detectable serum guselkumab concentration (below the lower limit of quantification) at each visit by treatment group
- Summary of serum guselkumab concentrations at each visit by treatment group and baseline body weight (quartiles). Other covariates may also be applied, e.g. Diabetes or BMI status (normal, overweight, obese).

- Summary of serum guselkumab concentrations at each visit by treatment group and baseline Hurley stage status
- Summary of serum guselkumab concentrations by baseline AN count category (3 to 5, 6 to 10, ≥11)
- Plot of median serum guselkumab concentrations over time by treatment group
- Plot of median serum guselkumab concentrations over time by treatment group by baseline body weight (≤ median, > median)

7.1.1.1. Data Handling Rules

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

- Participants will be analyzed according to the treatment groups that they actually received.
- 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 the lower limit of quantification) 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 subject who meets 1 of the following dosing deviation criteria will be excluded from the by-visit data analyses from that point onwards:
- Discontinue guselkumab administrations.
- Skipped a guselkumab administration.
- Received an incomplete/ incorrect dose.
- Received an incorrect study agent.
- Received an additional guselkumab dose.

In addition, if a subject has an administration outside of dosing windows (Table 3), the concentration data collected at and after that visit will be excluded from the by-visit data analyses. Additional exclusions for incongruous PK data to be implemented based on Janssen SOP-07948. All participants and samples excluded from the analysis will be clearly documented in the Clinical Study Report.

Table 3: Dosing Window

Visit	Window
Week 0 through Week 36	± 7 days from scheduled visit day
Final Safety and Efficacy Follow-up visits	± 14 days from scheduled visit day

7.1.2. PK vs Efficacy/Safety

The relationship between serum guselkumab concentrations and safety or efficacy endpoints may be explored, e.g.:

- The relationship between serum guselkumab concentrations (quartiles) and proportion of participants achieving HiSCR and change from baseline in AN count at Week 16, and Week 40 will be explored. Summaries by baseline body weight (≤ median, > median) or baseline Hurley stage status may also be provided.

7.1.3. Population PK Analysis

When appropriate, population PK analysis will be performed using serum guselkumab concentration-time data in all randomized participants with the nonlinear mixed-effects modeling (NONMEM) approach. Details will be provided in a separate technical report.

7.2. Immunogenicity

Immunogenicity analyses will be based on the Immunogenicity Analysis Set (Section 2.4.4). Participants will be analyzed according to the treatment groups that they actually received. No imputation for missing concentration data will be performed.

Unless otherwise specified, tabular summaries of immunogenicity for key study periods are in general presented as following:

Summaries through Week 16:

PK data through Week 16 will be summarized by treatment groups

- Guselkumab 200 mg SC
- Guselkumab 1200 mg IV
- Combined Guselkumab

Summaries through Week 48:

PK data through Week 48 will be summarized by treatment groups including

- Placebo → 100 mg SC
- Placebo → 200 mg SC
- Guselkumab 200 mg SC
- Guselkumab 1200 mg IV
- Combined Guselkumab

7.2.1. Antibodies to Guselkumab

Blood samples will be collected to examine the formation of antibodies to guselkumab at the specified visits as shown in the schedule of activities in the protocol. Serum samples will also be collected at the final visit from participants who terminate study participation early.

The antibodies to guselkumab status (positive at any time, negative) and titers will be summarized by treatment group for participants who receive at least one dose of guselkumab and have appropriate samples for detection of antibodies to guselkumab. The maximum titers of antibodies to guselkumab will be provided for participants who are positive for antibodies to guselkumab.

A listing of participants who are positive for antibodies to guselkumab will be provided. This listing will provide information regarding dose administered, injection-site/infusion reactions, guselkumab serum concentration, and antibody status for all visits.

7.2.2. Neutralized Antibodies to Guselkumab

The incidence of neutralizing antibodies (NAbs) to guselkumab will be summarized for participants who are positive for antibodies to guselkumab and have samples evaluable for NAbs to guselkumab.

7.2.3. Antibody vs PK/Efficacy/Safety

To explore the relationship between antibodies to guselkumab status and serum guselkumab concentrations, efficacy and safety, the following analysis may be performed if sufficient numbers of participants are positive for antibodies:

- Summary of serum guselkumab concentrations by antibodies to guselkumab status
- Plots of median trough serum guselkumab concentrations over time by antibodies to guselkumab status
- Summary of clinical response status (e.g., proportion of participants achieving HiSCR and change from baseline in AN count) at Week 16 and/or Week 40 by antibodies to guselkumab status
- Summary of injection-site reactions by antibodies to guselkumab status
- List of antibodies to guselkumab status in participants who discontinued study agent early

7.3. Pharmacokinetic vs Efficacy Relationships

If data permit, the relationships between serum guselkumab concentration and efficacy may be analyzed graphically. If any visual trend is observed, a suitable population PK/PD model may be developed to describe the exposure-response relationship. Details will be given in a population PK/PD analysis plan and results of the population PK/PD analysis will be presented in a separate technical report.

7.4. Biomarkers

Biomarker assessments will include the evaluation of relevant markers in serum for all participants. The samples will be used to better understand the biology of HS in some or all of the following ways: to provide mechanistic assessment of the pharmacodynamic response of participants to treatment with guselkumab, to analyze differences between responders and nonresponders, and to determine if the markers might be used to classify participants as potential responders prior to treatment.

Serum samples will be analyzed for circulating factors such as cytokines and other inflammatory markers (eg, IL-17A, IL-17F, IL-23, TNFα, IL-6, IL-22), and other categories of biomarkers potentially associated with the development and progression of HS or related to the guselkumab mechanism of action. These analyses are considered exploratory and will be summarized in a separate biomarker technical report.