NCT #: NCT05216224

STATISTICAL ANALYSIS PLAN

Study Title:	A Phase 2a, Randomized, Double-blind, Placebo-controlled Study to Investigate the Efficacy, Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of ATI-450 vs Placebo in Patients with Moderate to Severe Hidradenitis Suppurativa (HS)
Phase:	2a
Protocol No.:	ATI-450-HS-201
Protocol Date(s):	Original Protocol, Version 1.0, 08SEP2021 Amendment 1,Version 2.0, 01NOV2021 Amendment 2,Version 3.0, 02NOV2021 Amendment 3,Version 4.0, 03FEB2022 Amendment 4,Version 5.0, 04AUG2022
Analysis Plan Version and Date:	Version 3.0 Final, 16FEB2023
Sponsor:	Aclaris Therapeutics, Inc. 640 Lee Rd Suite 200 Wayne, PA 19087

CONFIDENTIAL AND PROPRIETARY INFORMATION

STATISTICAL ANALYSIS PLAN REVIEW AND APPROVAL

This Statistical Analysis Plan has been prepared in accordance with team reviewers' specifications.

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Aclaris Therapeutics, Inc.

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GLOSSARY OF ABBREVIATIONS

Abbreviation	Term
AE	Adverse Event
AESI	Adverse event of special interest
ALT	Alanine aminotransferase
AN	abscess and inflammatory nodule
Anti-CCP	Anti-cyclic citrullinated protein
AST	Aspartate aminotransferase
BID	Twice daily
BMI	Body mass index
BLQ	Below the limit of quantification
CI	Confidence Interval
CK	Creatine kinase
CTCAE	Common Terminology Criteria for Adverse Event
DLQI	Dermatology Quality of Life Index
DSMB	Data Safety Monitoring Board
ECG	Electrocardiogram
eCRF	Electronic case report form
EOS	End of Study
EOT	End of Treatment
ET	Early Termination
FAS	Full analysis set population
FSH	Follicle-stimulating hormone
HiCSR	Hidradenitis Suppurativa Clinical Response
HIV	Human immunodeficiency virus
HS	Hidradenitis suppurativa
HS-PGA	Physician Global Assessment Scale
hsCRP	High sensitivity C-reactive protein
ICH	International Council for Harmonisation
IHS-4	International Hidradenitis Suppurativa Severity Score System
IxRS	Interactive Voice/Web Response System
LOCF	Last observation carried forward
LS Means	Least squares mean
mRNA	Messenger RNA
MMRM	Mixed effect for repeated measures
PD	Pharmacodynamics
PE	Physical examination
PGA-SP	Patient's Global Assessment of Skin Pain
PK	Pharmacokinetics
PP	Per-protocol
PT	Preferred term
QTcF	Fredericia-corrected QT interval

RT-PCR	Reverse transcription polymerase chain reaction
SAE	Serious adverse event
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SI	Système International
SOC	System organ class
TE	Treatment emergent
TEAE	Treatment-emergent adverse event
TB	Tuberculosis
ULN	Upper limit of normal
WOCBP	Women of childbearing potential

1. INTRODUCTION

This document describes the statistical methods and data presentations to be used in the summary and analysis of data from Protocol ATI-450-HS-201. Background information is provided for the overall study design and objectives. The reader is referred to the study protocol and case report forms (eCRFs) for details of study conduct and data collection.

The scope of this document excludes the analysis of biomarker data and exploratory endpoints.

1.1. STUDY OVERVIEW

This is a Phase 2a, randomized, double-blind, placebo-controlled study to investigate the efficacy, safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of ATI-450 50 mg twice daily (BID) versus placebo in patients with moderate to severe HS.

The study will consist of an up to 28-day Screening Period, a 12-week treatment period, and a 30-day follow-up period. The total duration of the study for patients remaining until their final follow-up assessment will be up to 21 weeks. Patients will attend clinic visits on Days 1, 8, 15, 29, 43, 57, and 85 for safety, efficacy, PK, and PD assessments of the 12-week treatment period. A safety follow-up visit will be conducted 30 days after the last dose of study treatment for patients who completed the treatment period, as well as those who discontinue early.

Approximately 20 study centers in the United States are expected to participate in this study. Patients confirmed eligible at Baseline will be randomized in a 1:1 ratio to receive either ATI-450 tablets (50 mg BID) or matching placebo tablets BID. It is planned to randomize approximately 90 patients to obtain 45 patients per arm.

Study drug will be administered orally BID for 12 weeks. On clinic visit days, the morning dose of study treatment will be administered in the clinic.

The total duration of the study for patients remaining until their final follow-up assessment will be up to 21 weeks.

1.2. SCHEDULE OF ASSESSMENTS

Study Period[8]	**Screening Period**	**Treatment Period**							**Follow-up Period**
Visit Number (Visit Name)	**Visit 1**	**Baseline Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visit 8**	**Visit 9**
Visit Day (Visit Week)	**Day -28 to Day -1**	**Day 1**[j]	**Day 8**[j]	**Day 15**	**Day 29**	**Day 43**	**Day 57**	**Day 85 (Week 12/ET)**	**30 Days After Last Dose**
Visit Window	**NA**	**NA**	**± 1 Day**						**+ 7 Days**
Assessment[i]									
Informed Consent	X								
Eligibility Review	X	X							
Randomization		X							
Demographics	X								
Medical History; HS and Other Current Medical Conditions	X								
Lesion Count including AN and draining fistula (tunnels) count	X	X	X	X	X	X	X	X	X
NRS30 - Patient's Global Assessment Skin Pain (PGA-SP)		X	X	X	X	X	X	X	
DLQI Scale		X			X		X	X	
Hurley Stage Assessment	X	X	X	X	X	X	X	X	X
HS-PGA Scale	X	X	X	X	X	X	X	X	X
12-lead ECG[a]	X	X	X	X	X	X	X	X	
Vital Signs[b]	X	X	X	X	X	X	X	X	X
Body Weight, BMI (derived)	X							X	

Study Period[8]	**Screening Period**	**Treatment Period**							**Follow-up Period**
Visit Number (Visit Name)	**Visit 1**	**Baseline Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visit 8**	**Visit 9**
Visit Day (Visit Week)	**Day -28 to Day -1**	**Day 1**[j]	**Day 8**[j]	**Day 15**	**Day 29**	**Day 43**	**Day 57**	**Day 85 (Week 12/ET)**	**30 Days After Last Dose**
Visit Window	**NA**	**NA**	**± 1 Day**						**+ 7 Days**
Assessment									
Full Physical Exam Including Height	X								
Targeted Physical Exam		X	X	X	X	X	X	X	X
Lesion Photography (optional)		X			X			X	
Laboratory Assessments: Hematology, Coagulation, Chemistry, Lipids, Urinalysis	X	X	X	X	X	X	X	X	X
hsCRP	X	X	X	X	X	X	X	X	X
HIV and Hepatitis B & C Screen	X								
SARS-CoV-2 Testing	X	X							
QuantiFERON Gold Test for TB	X								
Serum Pregnancy Test (WOCBP Only)	X								
Urine Pregnancy Test (WOCBP Only)		X	X	X	X	X	X	X	X
Blood Sampling for PK		X[c]	X[c]	X[c]	X[d]	X[d]	X[d]	X[c]	
[redacted]									
Dispense Study Drug		X	X	X	X	X	X		
Administration of Morning Dose of Study Drug in Clinic		X	X	X	X	X	X	X[g]	

Study Period[8]	Screening Period	Treatment Period							Follow-up Period
Visit Number (Visit Name)	Visit 1	Baseline Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9 (EoS)
Visit Day (Visit Week)	Day -28 to Day -1	Day 1[j]	Day 8[j]	Day 15	Day 29	Day 43	Day 57	Day 85 (Week 12/ET)	30 Days After Last Dose
Visit Window	NA	NA	± 1 Day						+ 7 Days
Assessment									
Study Treatment Accountability			X	X	X	X	X	X	
Adverse Events[h]	X	X	X	X	X	X	X	X	X
Prior and Concomitant Medications	X	X	X	X	X	X	X	X	X

AE=adverse event; AN=abscess and inflammatory nodule count; BMI=body mass index; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; ET=early termination; HIV=human immunodeficiency virus; HS=hidradenitis suppurativa; hsCRP=high sensitivity C-reactive protein; HS-PGA=Physician Global Assessment Scale; mRNA=messenger RNA; NRS30= 30% reduction in Numerical Rating Scale for Patient's Global Assessment of Skin Pain (PGA-SP); PD=pharmacodynamic; PK=pharmacokinetic; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; TB=tuberculosis; WOCBP=women of childbearing potential.

a. Triplicate 12-lead ECGs will be performed at least 30 seconds apart, in a supine position, after resting for at least 10 minutes (without external stimulation, e.g., talking, TV, noise) and submitted for central reading. Screening ECGs will be collected prior vital signs and blood samples. On Day 1 and 8, ECGs will be taken pre-dose and 2 hours post dose. Patients not fasting on Day 1 and 8 will have an additional 4 hr post dose ECG. On Days 15, 29, 43, 57, and 85, ECGs will be performed as the last assessment in the clinic (as close to Cmax). See Protocol Section 8.2.3 for additional details on collection parameters.

b. Vital signs are to be taken before blood collection for laboratory tests. See Protocol Section 8.2.2 for additional details on collection parameters.

c. PK blood sampling times on Days 1, 8, and 85 will occur pre dose and 2 hours after the morning dose. Patients not fasting on Days 1 and 8 will have an additional PK sample collected at 4 hours post dose. If the patient objects to both blood draws at the 2hr and 4hr timepoint, the 4hr PK sample is more important to collect. Patients must remain in the clinic until 30 minutes after the morning post dose PK blood sampling is completed. See Section 8.5 for additional details on collection parameters.

d. PK blood sampling will occur prior to the morning dose on Days 15, 29, 43, and 57. See Protocol Section 8.5 for additional details on collection parameters.

[redacted]

g. The last dose of study treatment will be administered in the clinic on Day 85. The second dose of study treatment is not to be administered on Day 85.

h. Serious AE reporting will start at the time of consent. Any AE that occurs between the time of consent and prior to dosing on Day 1 will be recorded as medical history. Treatment-emergent AEs will be collected following the first dose of study treatment on Day 1 through the Follow-up Visit (30 days after the last administration of study treatment) (Protocol Section 5.5).
i. Unscheduled visits are allowed, as deemed necessary by the Investigator, if assessments need to be repeated (eg, lab draws), safety follow-up needs to be conducted, or additional dispensing activities need to occur.
j. Patient should be fasted for visits on Days 1 and 8, defined as 8 hours since last food. A snack is permitted 2 hours after the morning dose.

2. OBJECTIVES

Primary Objective:

The primary objective of this study is to assess the efficacy of ATI-450 in patients with moderate to severe HS

Secondary Objective:

The secondary objectives are as follows:

- To assess the efficacy and safety of ATI-450 in patients with moderate to severe HS
- To assess the PK of ATI-450 in patients with moderate to severe HS

Exploratory Objectives: To assess the PD of ATI-450 in patients with moderate to severe HS

3. GENERAL STATISTICAL CONSIDERATIONS

3.1. SAMPLE SIZE AND POWER

Approximately 90 patients will be randomized (approximately 45 per treatment group) to provide 90.3% power to demonstrate the superiority of ATI-450 to placebo in the reduction in inflammatory nodules and abscesses at Week 12. This power computation assumes that the reduction in the placebo arm will be on average 2.5 nodules/abscesses and the ATI-450 reduction will be on average 4.75 nodules/abscesses. A standard deviation of 3.6 was assumed for the number of nodules/abscesses. These sample size assumptions were based on the values observed in the adalimumab PIONEER I and PIONEER II Phase 3 trials (Frew et al, 2020, see Protocol Section 10.0).

3.2. RANDOMIZATION AND MASKING

Patients will be randomized to study treatment in a 1:1 ratio to ATI-450 50 mg BID or placebo. All patients will be centrally assigned to randomized study treatment using an Interactive Voice/Web Response System (IxRS). Before the study is initiated, access instructions and directions for the IxRS will be provided to each study center.

This is a double-blind study with limited access to the randomization code. The ATI-450 and placebo tablets will be identical in physical appearance. The treatment each patient will receive will not be disclosed to the Investigator, study center staff, patient, or Sponsor. The treatment codes will be available to a limited number of third-party vendor personnel (IxRS administrative personnel, Clinical Supplies Management personnel, and unblinded Biostatistician) and Data Safety Monitoring Board (DSMB) members, as necessary, for them to support their functions on the study.

The IxRS will be programmed with blind-breaking instructions. In case of an emergency, the

Investigator has the sole responsibility for determining if unblinding of a patient's treatment assignment is warranted. Patient safety must always be the first consideration in making such a determination. If the Investigator decides that unblinding is warranted, the Investigator should make every effort to contact the study Medical Monitor prior to unblinding a patient's treatment assignment unless this could delay emergency treatment of the patient. If a patient's treatment assignment is unblinded, the study Medical Monitor must be notified within 24 hours after breaking the blind. The date and reason that the blind was broken must be recorded in the source documentation and eCRF, as applicable.

3.3. HANDLING OF DATA

3.3.1. Strata and Covariates

There are no planned adjustments for strata.

3.3.2. Examination of Subject Subsets

The following subject subsets are of interest.

- Baseline Hurley stage (mild, moderate, severe),
- Sex, and
- Baseline BMI category (underweight/normal [<25 kg/m2], overweight [25 to <30 kg/m2], and obese [≥ 30 kg/m2].

The categorization of patients into a baseline Hurley stage will be based on the worst stage from the locations evaluated at the baseline assessment.

3.3.3. Multiple Testing and Comparisons

There are no planned adjustments for multiple comparisons.

3.3.4. Missing Data and Outliers

Analysis visit windows will be applied as indicated in Section 3.3.7. If an efficacy assessment is not available in an analysis visit window, then last observation carried forward (LOCF) will be applied to obtain a value for that analysis visit window for analyses conducted on the full analysis set population. For categorical efficacy endpoints, an additional sensitivity analysis will be conducted using non-responder imputation for cases where an efficacy assessment is not available in an analysis visit window. Missing data will not be imputed for safety summaries or efficacy summaries on the per protocol population.

There are multiple reasons that an assessment may not be available within an analysis visit windows:

- Clinic visits out of window or missed visits

- Data excluded from use in analysis due to confounding intercurrent event (see Section 5.4.1.5)

For the latter reason, any assessments that occur after a confounding intercurrent event will be considered missing for purpose of analyses.

For analysis visit windows without an assessment, regardless of the reason, the last non-missing value prior to the start of the analysis visit window will replace the missing values. The baseline assessment can be carried forward.

If an AE has missing relationship to the study drug or severity, then that AE will be considered as 'related' to the study drug and the severity will be considered as 'Severe' in the table summaries, but the AE will be displayed as having a missing relationship or severity in the listings

3.3.5. Imputation of Incomplete Dates

A missing date is one in which the day, month or year are all unknown. For adverse events, if a date is missing entirely then the date will be set to equal Day 1.

An incomplete date is any date for which either the day, month or year is unknown, but all three fields are not unknown. An incomplete date occurs when the exact date an event occurred or ended cannot be obtained from a subject. For many of the analyses, a complete date is necessary to determine if the event should be included in the analysis (i.e., if the event is treatment-emergent). In such cases, incomplete dates will be imputed.

To minimize bias, the project statistician will impute dates in a systematic, but reasonable manner. If the month/year is the same as the Day 1 month/year, then the date will be set to the date of Day 1. In other cases, missing days will be imputed as the day component of Day 1; missing months/years will be imputed as the month/year of Day 1. For nonexistent dates occurring at the end of a month created by this imputation method, the first date of the next month will be used (e.g. Day 1 = 31JAN2017, incomplete date = XXFEB2017 -> imputed date = 01MAR2017).

3.3.6. Imputation of Alphanumeric Data

Should there be instances where a clinical laboratory parameter is reported with imbedded non-numeric characters, as for example, "<0.1" or ">10", the data will be imputed for the purpose of quantitative summaries. The actual values as reported in the database will be presented in data listings.

For incorporation in quantitative summaries, the following imputation rules will be employed:

The lower limit of quantification will be replaced with ½ the value of the lower limit. For example, "< 0.1" will be imputed as "0.05".

The upper limit of quantitation will be increased by one level of precision that precedes the value. For example, ">0.1" will be imputed as "0.11", and ">10" will be imputed as "10.1".

Results reported as "≥X" and "≤X" will be imputed as "X".

3.3.7. [redacted]

[redacted]

3.3.8. Definitions and Terminology

Duration of HS (years)
(Date of informed consent minus the start date of the HS +1)/365.25.

The start date of the HS is collected as part of Medical History and based on the Medical Dictionary for Regulatory Activities (MedDRA) coded preferred term of 'Hidradenitis suppurativa'.

Baseline Value
For purpose of analysis, the baseline value is defined as the last non-missing value obtained prior to initiation of study drug. For assessments occurring on the date of first administration of study drug, if time of collection is reported, the time will be used to determine if the assessment occurred prior to initiation of study drug. If collection time is not reported, then the assessment will be assumed to be prior to initiation of study drug.

Study Day
Study Day is defined relative to Day 1, where Day 1 is the day of date of first dose as reported on the Dosing Diary eCRF. Thus, the study day of an event is calculated as:

Study Day = ((event date – date of Day 1) + 1) for dates on or after Day 1

Study Day = (event date – date of Day 1) for dates prior to Day 1

Last Dose of Study Drug
Last Dose of Study Drug is defined as the date of last dose taken as recorded on eDiary page of the eCRF.

Study Drug Exposure (days)
Study drug exposure is defined as: ((date of last dose of study drug – date of Day 1) + 1).

Dose Interruptions
Dose interruption is defined as ≥ 2 consecutive days where the subject missed both doses of the study drug as determined by the date and time fields on the eDiary page of the eCRF.

Study drug compliance (%) based on number of doses

Compliance (%) = (number of doses taken / number of doses that should have been taken) x100.

- The number of doses taken is calculated as: [day 1 dose + sum of number of doses taken as indicated on the eDiary CRF].
- The number of doses that should have been taken is calculated as: (2 * study drug exposure days).

Prior Medications

Prior medications are those medications taken prior to the initiation of study medication, regardless of whether it continues into the blinded treatment period.

Concomitant Medications

Concomitant medications are those medications taken on or after the initiation of study medication through the end of treatment date minus 1. This definition includes medications started prior to the initiation of study medication but continued concomitantly with the study medication.

Change from Baseline

Change from Baseline for a given endpoint is defined as the value at the analysis visit minus the baseline value.

Percent Change from Baseline

Percent Change from Baseline for a given endpoint is defined as the value at the analysis visit minus the baseline value, quantity divided by the baseline value.

Hidradenitis Suppurativa Clinical Response (HiSCR50) Achiever

To meet the HiSCR50 criteria for achiever, the patient must have ≥ 50% reduction from baseline in the total abscess and inflammatory nodule (AN) count, have no increase in the number of abscesses from baseline, and have no increase in the number of draining fistula counts. A patient is considered an achiever only if all 3 criteria are fulfilled.

[redacted]

NRS30 Achiever

To meet the NRS30 criteria for achiever, the patient must have ≥30% reduction from baseline in PGA-SP and at least 1 unit reduction from baseline in the PGA-SP. This is assessed in patients with Baseline PGA-SP ≥3.

[redacted]

International Hidradenitis Suppurativa Severity Score System (IHS-4)
The IHS-4 score (points) = (number of nodules multiplied by 1) + (number of abscesses multiplied by 2) + [number of draining tunnels (fistulas/sinuses) multiplied by 4].

Interpretation of the IHS-4 is as follows: mild HS is a score of 3 or less, moderate HS is a score of 4-10, and severe HS is a score of 11 or higher.

Dermatology Life Quality Index (DLQI)
The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired. If one question is unanswered, this is allocated a score of 0 for the purpose of summing to the DLQI score. If two or more questions are unanswered, the questionnaire is not scored.

Each question is answered on a Likert scale: Very much=scored 3, A lot=scored 2, A little= scored 1, Not at all= scored 0, Not relevant=scored 0, Question Not Answered=0. Question 7 is asked in two parts. The first part asks if the skin disease has 'prevented you from working or studying'. If skin disease has prevented working or studying, then Question 7 is scored 3. If working or studying are not relevant, the response is Not relevant and scored 0. If the answer is No, then Question 7 is scored based on the second part of the question as to 'How much has your skin been a problem at work or studying': 'A lot'(scored 2), 'A little' (scored 1) or 'Not at all' (scored 0).

Treatment-Emergent Adverse Event (TEAE)
TEAEs are defined as AEs with an onset date on or after the date of first administration of study drug and before the date of last administration of study drug + 30 days.

Treatment-Emergent Laboratory Abnormalities
A treatment-emergent laboratory abnormality is defined as a result in which the baseline value is within normal laboratory limits and the post-baseline value is outside normal laboratory limits. If the relevant baseline assessment is missing, then any post-baseline value outside normal laboratory limits will be considered a treatment-emergent value.

Treatment-emergent Laboratory Toxicity
A treatment-emergent laboratory toxicity is defined as an increase of at least one toxicity grade from the baseline assessment at any post baseline visit. If the relevant baseline assessment is missing, then any graded abnormality (i.e., at least Grade 1) is considered to be treatment-emergent.

3.3.9. Presentations by Study Visit

Scheduled and unscheduled assessments collected from Visit 1 through Visit 8 for all efficacy assessments and safety assessments (labs, vital signs, and ECG) will be assigned to an analysis visit window using the study day ranges described in Table 1 and Table 2. All study days up to and

including Day 1 are in the baseline-eligible analysis visit window. The last non-missing assessment in the baseline-eligible analysis visit window will be used in any summaries that present the baseline results with the exception of ECG interpretation where the best result from the triplicate values will be chosen. Day 1 post-dose ECG, PK and vital signs assessments will be analyzed as collected. Day 8 ECG assessments, Day 8 and 85 PK assessments, and Day 8, 15, 29, 43, 57 and 85 vital sign assessments will be windowed per Table 2, then each time point will be analyzed as collected. For all other assessments, for post-baseline analysis windows, if multiple assessments occur within a given analysis visit window, the result closest to the target study day, regardless of whether scheduled or unscheduled, will be used for summary presentations. If two measurements have the same distance to the target study day, the first assessment will be used in the summary presentations with the exception of ECG interpretation where the worst result from the triplicate values for the given visit and timepoint will be used. All assessments will be presented in the listings. In addition to the analysis visits indicated in Table 1 and Table 2, for patients who prematurely discontinue the study, data collected during the withdrawal visit will be used as an EOS assessment for these patients. The EOS assessment will be included in safety analyses.

Table 1: Visit Windows for DLQI

CRF Visit	***Target Study Day***	***Analysis Visit***	***Study Day Range***
Visit 2	1	Baseline	≤1
Visit 5	29	Week 4	[2 – 42]
Visit 7	57	Week 8	[43 – 70]
Visit 8(EoT/ET)	85	Week 12	[71 – 98]

Table 2: Visit Windows Assessments Other than DLQI

CRF Visit	***Target Study Day***	***Analysis Visit***	***Study Day Range***
Visit 1	-28 to -1	Baseline	<1 or Day 1 pre-dose
Visit 2	1		
Visit 3	8	Week 1	[2 – 11]
Visit 4	15	Week 2	[12 – 21]
Visit 5	29	Week 4	[22 – 35]
Visit 6	43	Week 6	[36 – 49]
Visit 7	57	Week 8	[50 – 70]
Visit 8(EoT/ET)	85	Week 12	[71 – 98]
Visit 9(EoS)	30 days after last dose	EOS	Latest assessment after the EoT/ET

3.4. TIMING OF ANALYSES

When all patients have completed study ATI-450-HS-201 or terminated early from the study and the database has been locked, the analyses will be performed according to this SAP. No interim analysis is planned for this study.

4. ANALYSIS POPULATIONS

The populations for analysis will include the full analysis set population (FAS), the per-protocol (PP) population, the safety population and the PK Population.

4.1. FULL ANALYSIS SET (FAS) POPULATION

All patients who have been randomized and administered at least 1 dose of study treatment. The efficacy analyses will be conducted on the FAS population as randomized.

4.2. PER PROTOCOL (PP) POPULATION

All randomized patients who remain on study drug and complete their assessments for the Day 85 visit and do not have major protocol deviations that could impact efficacy.

Patients are considered to have completed their Day 85 assessments if the AN count is recorded in the Week 12 analysis visit window. Protocol deviations and violations will be tracked as part of clinical monitoring and clinically evaluated by the sponsor as major or minor. Determination of protocol deviations that could impact efficacy will be conducted in a blinded manner by the sponsor prior to database lock.

4.3. SAFETY POPULATION

All patients randomly assigned to study treatment and who take at least 1 dose of study treatment. Patients will be analyzed according to the treatment they received.

4.4. PHARMACOKINETIC (PK) POPULATION

All patients randomly assigned to study treatment, take at least 1 dose of study treatment and have at least 1 evaluable PK assay will be included in the PK population, even if the results are below the limit of quantification (BLQ).

5. STATISTICAL METHODS

Descriptive statistical methods will be used to summarize the data from this study, with hypothesis testing performed for the primary and secondary efficacy endpoints. Unless stated otherwise, the term “descriptive statistics” refers to number of patients, mean, median, standard deviation, minimum, and maximum for continuous data, and frequencies and percentages for categorical data. For categorical variables, the denominator of percentages will be the number of patients with a

non-missing value at the visit and/or the scheduled time point. If a different denominator is used, this will be identified in the summary table.

All data collected during the study will be included in data listings. Unless otherwise noted, the data will be sorted first by treatment group, subject number, and then by date within each subject number. Assessments indicated as 'Not Done' will not be included in the listings.

The term 'treatment group' refers to all patients on the same dosing regimen. There will be two treatment groups in this study: Placebo BID and ATI-450 50mg BID.

All statistical testing will be one-sided and will be performed using a significance (alpha) level of 0.05 unless otherwise stated. P-values will be presented to three decimal places. For the efficacy endpoints, the ATI-450 treatment group will be tested versus Placebo via statistical inference.

The statistical analyses will be conducted with the SAS® software package version 9.4 or higher. All analyses will be subject to formal verification procedures. Specifically, results will be independently verified by a second programmer or statistician prior to issuance of the draft statistical report. All documents will be reviewed by the lead statistician to ensure accuracy and consistency.

5.1. SUBJECT DISPOSITION, DEMOGRAPHIC AND BASELINE CHARACTERISTICS

Subject disposition will be presented for all patients in the FAS. The number of patients who completed the study or discontinued the study early will be provided. The reasons for early discontinuation from the study will be presented by treatment group. Similarly, descriptive statistics for end of treatment status (completed or discontinued) and the reasons for early discontinuation of study treatment will be presented.

Demographic and baseline characteristics will be summarized using the FAS population.

Demographic data reported by treatment group will include age, sex (at birth), race, ethnicity, and baseline body mass index (BMI) (kg/m^2). This information will be reviewed for baseline differences, but no statistical testing will be performed.

To allow evaluation of baseline HS disease characteristics, descriptive statistics for the duration of HS disease (years) and the following continuous measures of baseline abscesses and inflammatory nodule count, baseline HS-PGA, and baseline PGA-SP rating will be summarized by treatment group. Additionally, the number and percentage of patients in each of the Hurley stages will be provided with patients categorized based on the worst grade from all anatomical locations.

Medical history conditions/events will be summarized using the system organ class and preferred terms coded with MedDRA version 24.0.

Findings from the screening physical examination (PE) will be summarized using the pre-specified body system categories and include reporting of abnormal not clinically significant and abnormal clinically significant.

The results of special labs collected at screening only (TB, Anti-CCP antibody, hepatitis B core antibody, hepatitis C antibody, HIV-12 AB, and SARS-CoV-2 virus) will be presented in listings.

5.2. PRIOR AND CONCOMITANT MEDICATIONS

All medication (including vaccines, over-the-counter or prescription medicines, vitamins, and/or herbal supplements) taken from 14 days before start of screening until the end of the follow-up period will be recorded in the appropriate section of the eCRF.

Prior and concomitant medications will be coded using the WHO Drug Dictionary (version WHODrug - B3 Global March 2021) for the entire period of the study.

A summary by treatment for prior medications and a summary by treatment of concomitant medication will be provided for the FAS population. Each summary table will report the number (%) of patients by ATC classification using ATC level 2 and medication preferred term. Patients will be counted only once within each ATC and preferred term.

All prior and concomitant medications will be included in a subject data listing. Listings will distinguish medications as prior and/or concomitant.

5.3. STUDY DRUG EXPOSURE

Study drug exposure and compliance will be summarized by treatment for the Safety population. The study drug treatment duration along with summaries of dose interruptions and treatment compliance will be reported.

The study drug dosing data collected in the subject diary will be provided in a data listing. Likewise, full accounting of the study drug dispensing, collection, and tablet counts will be provided in a data listing.

5.4. EFFICACY ANALYSIS

All efficacy summaries will be conducted per SAP on both the FAS and PP Populations; analyses per the PP Population will be considered supportive.

All efficacy data will be presented in data listings.

5.4.1. Primary Efficacy Endpoint

The primary efficacy variable will be the change from baseline in abscess and inflammatory nodule (AN) count at Week 12 in the FAS population.

5.4.1.1. Statement of Estimand

The primary objective of this study is to assess the efficacy of ATI-450 50mg BID versus placebo in patients with moderate to severe HS. This efficacy assessment is intended to test the hypothesis that the ATI-450 treatment group is superior to placebo for the treatment of HS based upon the 12-week change from Baseline in inflammatory nodules and abscesses versus the null hypothesis of no difference. The following estimands (International Council for Harmonization [ICH] E9- R1) are defined to adequately achieve the intended primary objective for this study.

5.4.1.2. Treatment

The treatment condition of interest for this study is the fixed 12-week BID dosing of 50 mg of ATI-450 versus placebo. The administration of Protocol Excluded Medications/Treatments listed in the Protocol Appendix 5 for the purpose of rescue or as standard care following the discontinuation of study medication is strictly outside the treatment condition of interest for this study since they could confound or prohibit the determination of an optimal dose for ATI-450. Treatment durations less than 12-weeks based on the analysis visit windows, while providing supportive information, are, for the purpose of the primary estimand, outside the treatment condition of interest.

5.4.1.3. Population

The population of patients targeted by the clinical question of interest for this study includes patients with moderate to severe HS as defined by the inclusion and exclusion criteria who are randomized in the study and administered at least 1 dose of study drug.

5.4.1.4. Variable

The abscess and inflammatory nodule count at Week 12 was chosen as the variable (or endpoint) of our primary estimand because it is a well-established measure of the improvement in the signs and symptoms of HS. If the data to compute the primary endpoint is not collected, the endpoint will be imputed using the LOCF. Additionally, data collected after the occurrence of a confounding event (see Section 5.4.1.5) will not be used to calculate the primary endpoint. Instead, the endpoint will be imputed using the LOCF prior to the intercurrent event.

5.4.1.5. Intercurrent Event Strategy

Prior to week 12 lesion counts, the following are confounding intercurrent events that are likely to occur in some patients during conduct of the trial: 1) discontinuation of study treatment for any reason, 2) the administration of protocol prohibited medications listed in Appendix 5 of the

Protocol that could impact efficacy for any reason, and 3) surgical intervention. Determination of prohibited medications that could impact efficacy will be conducted in a blinded manner prior to database lock. Assessments that occur after a confounding event will be excluded from the analysis and imputed using the last observed assessment prior to the intercurrent event. The date/time of the confounding event and the start date/time of imputation will be determined based upon the last dose of study medication, the start date of any relevant prohibited medications, and the start date of any surgical procedures.

5.4.1.6. Population-Level Summary

The population-level summary for this study will be the model-based treatment difference and corresponding p-value for the change from baseline in inflammatory abscesses and nodules. The statistical model will be a mixed effect for repeated measures (MMRM) model that includes fixed factors for treatment group, visit, treatment by visit interaction, and baseline abscess and inflammatory nodule count. Patient identifier will be included in the model in a manner that allows observations within a given patient over time to be treated as repeated measures. The ATI-450 treatment group will be compared with placebo; the model-based estimate for the difference in least squares mean (LS Means), 90% confidence intervals (CIs), and one-sided p-value will be calculated.

5.4.2. Primary Efficacy Analysis

Descriptive statistics for the count and change from baseline in the inflammatory abscesses and nodules will be presented for each scheduled analysis visit. This primary analysis will utilize the count with imputation for LOCF and will be based on the FAS population. Change from baseline in count of inflammatory abscesses and nodules up to Week 12 will be analyzed using a MMRM model. The model will include fixed effect terms for treatment, study visit, treatment by visit interaction and baseline count of inflammatory abscesses and nodules. Patient identifier will be included in the model in a manner that allows observations within a given patient over time to be treated as repeated measures. Within-subject variability will be modeled using a compound symmetry covariance structure. The LS Mean change from baseline in the count at each visit, estimated from the MMRM model, with the estimated standard error and 90% CI, will be presented in tabular and graphic format. The difference in the adjusted means between treatment groups and the associated 90% CI of the difference will be provided.

The model results from Week 12 are the primary efficacy analysis.

5.4.3. Supportive Analysis of Primary Efficacy Endpoint

The statistical methods with LOCF for the main analysis will be repeated using the PP population.

A one-sided Mood's median test will be used to compare the treatment groups for the primary endpoint of change from baseline in AN count with LOCF. This test will be conducted at each

analysis visit separately. Only the one-sided p-values and associated medians for each group will be presented for this non-parametric test (no confidence intervals).

For each of the subsets defined in Section 3.3.2, the primary efficacy MMRM analysis will be performed. If there are not enough patients in a subset to perform the MMRM, then descriptive statistics only will be presented for that subset.

5.4.4. Secondary Efficacy Endpoints

The secondary efficacy endpoints include:

- Percentage of patients achieving HiSCR50 at each analysis visit.
- Percentage of patients achieving [redacted] at each analysis visit.
- Percentage of patients achieving NRS30 at Week 12 among patients with Baseline PGA-SP ≥3.
- Percentage of patients meeting [redacted] criteria at Week 12.
- Change from baseline in IHS-4 at scheduled timepoints in 12-week treatment period
- Change from baseline in Hidradenitis Suppurativa-Physician Global Assessment (HS-PGA) at scheduled timepoints during the 12-week treatment period
- Change from baseline in DLQI at scheduled timepoints for the 12-week treatment period

The HiSCR50, [redacted], NRS30, [redacted], IHS-4, and DLQI will all be derived per the algorithms indicated in Section 3.3.8, as part of the statistical analysis. All analyses will be based on the analysis visit windows defined in Section 3.3.9. Endpoints will only be presented for those analysis visit windows at which the endpoint was scheduled for collection.

5.4.5. Secondary Efficacy Analysis

MMRM Analyses

For continuous efficacy measures IHS-4, HS-PGA, and DLQI, the descriptive statistics for the calculated scores and the change from baseline in the scores will be reported for each analysis visit at which the assessment was planned for collection.

The change from baseline in the IHS-4, the change from baseline in DLQI, and change from baseline in HS-PGA will be analyzed for inferential results using the methods planned for the primary efficacy analysis with LOCF.

Logistic Analyses

For each treatment group, the observed achiever/responder rate for HiSCR50, [redacted], NRS30 and [redacted] will be reported along with the 90% CI for the response rate using the normal approximation. The difference in observed response rates will also be presented.

The percentage of patients achieving HiSCR50, [redacted], NRS30, and [redacted] at Week 12 and each scheduled analysis visit will be assessed using a Firth's penalized likelihood logistic regression model with fixed effect for treatment and an applicable baseline as a covariate. For HiSCR50, [redacted], and [redacted], the baseline covariate will be the count of inflammatory abscesses and nodules. For NRS30, the covariate will be the baseline PGA-SP. The analysis on the FAS population will use LOCF for missing values. An additional sensitivity analysis will be conducted for all of these responder endpoints except [redacted] where missing will be imputed as non-response.

Inferential results will include model-based responder estimates and associated 90% CIs, differences in estimates and associated 90% CIs for the active group versus placebo, and p-values testing for significance in the difference.

All efficacy data will be presented in data listings.

5.4.6. Graphical Displays

For change in inflammatory nodules and abscesses and change in HS-PGA, the LS Mean (90% CI) will be plotted over time. For the binary efficacy endpoints of proportion of patients achieving HiSCR50, NRS30, and [redacted] the responder rate (percentage) and 90% CI will be plotted over time by treatment group.

5.5. SAFETY

All safety analyses will be performed on the Safety Population. Values for all safety variables will be listed by subject and visit (as applicable).

5.5.1. Adverse Events

Adverse events (AE) will be mapped to a PT and system organ classification (SOC) using MedDRA version 24.0.

An overall summary will be presented which includes the number of TEAEs and the number and percentage of patients who experienced at least one TEAE. This summary will also include:

- Any TEAE
- Any Serious TEAE
- Any Mild TEAEs
- Any Moderate TEAEs
- Any Severe TEAEs
- Any Related TEAEs (defined as Probably or Possibly Related)
- Any TEAEs leading to discontinuation of study drug
- Any Related TEAEs leading to discontinuation of study drug

- Commonly occurring TEAEs (defined as those AEs occurring in >=10% of ATI-450 patients)

Adverse events of special interest (AESI) are captured on the AE eCRF page and include the following events: mouth ulceration, severe skin reaction which is considered to be related to the study drug, confirmed creatine kinase (CK) > 5X ULN without benign explanation, absolute neutrophil count < 1000 cells/mm3, and QTcF > 500 msec or change from baseline QTcF > 60 msec.

Additional summaries of TEAEs will be provided showing the number and percentage of patients who experienced at least one TEAE. These summaries will be presented by SOC and PT. If a participant reports the same PT multiple times within the same SOC, that PT will only be counted once within that SOC for that participant. As with the PT, if a participant reports multiple conditions within the same SOC, that SOC will only be counted once for that participant. In the summary, SOC will be listed in ascending alphabetical order; PTs will be listed in order of descending frequency for all participants within each SOC.

The occurrence of TEAEs related to study medication, TEAEs leading to discontinuation of study drug, study drug related TEAEs leading to discontinuation, AESIs, and serious adverse events (SAEs) will be tabulated by SOC and PT. An additional summary of TEAEs will be provided by SOC, PT and maximum severity. Most frequent TEAEs, defined as AEs occurring in 10% of ATI-450 patients, will be summarized by PT.

All AEs reported will be listed by individual subject, showing both verbatim and PT. All AEs reported with a start date prior to the initiation of study medication will be excluded from the TEAE tables but will be included in the listings.

Missing onset dates will be imputed as previously outlined in Section 3.3.5 as required to determine TEAEs.

5.5.2. Clinical Laboratory Assessments and Vital Signs

Laboratory data (hematology, serum chemistry, coagulation, FSH and urinalysis) will be converted to Système International (SI) units for reporting and processing purposes. Descriptive summaries of absolute values of quantitative clinical laboratory results and their change from baseline values will be presented by analysis visit and treatment group. Observed values of categorical urinalysis data will be displayed with frequencies and percentages. All laboratory data will be listed for individual patients.

Treatment-emergent abnormal laboratory assessments will be based on the lab provided normal ranges. If the baseline laboratory assessment is normal and shifts to Low or High post-baseline, then the laboratory value is considered a TE abnormal laboratory value. If the baseline laboratory assessment is Low and shifts to High post-baseline or the baseline laboratory assessment is High and shifts to Low post-baseline, then the laboratory value is considered a TE abnormal laboratory

value. For each protocol specified lab test, the number and percent of patients reporting a TE abnormal lab will be reported.

For CK, Absolute Neutrophils, ALT, AST, and Bilirubin, laboratory abnormalities will be graded via the Common Terminology Criteria for Adverse Event (CTCAE) version 5.0. A summary of treatment-emergent laboratory toxicities for the indicated laboratory results by maximum CTCAE toxicity grades will be reported.

All laboratory summaries will be limited to the tests specified in the protocol.

Descriptive summaries of vital signs, weight, and BMI and their change from baseline will be presented by study visit and treatment group and all vital signs will be listed.

5.5.3. Other Safety Analyses

ECG measurements will include heart rate, QT interval, Fredericia-corrected QT interval (QTcF), PR interval, and QRS interval. Triplicate ECG values will be obtained at each time point. Summary tables will present the average of the triplicate ECG results. ECG results and their change from baseline values will be summarized descriptively by treatment group at each scheduled evaluation and all ECG data will be listed. Proportion of patients with abnormal ECG interpretations will be summarized at each study visit and by treatment group for both investigator and central interpretation. Proportion of patients who meet each of the following criteria based on triplicate averages from International Conference on Harmonization Guideline E14 “Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs” (October 2005) for QT and corrected QT intervals will be summarized across treatment groups:

- QTcF >450 msec
- QTcF >480 msec
- QTcF >500 msec
- QTcF increases from baseline by >30 msec
- QTcF increases from baseline by >60 msec

The above summaries will be repeated for QT.

5.5.4. Safety Graphs

Plots of QTcF and laboratory values over time will be prepared for tests as specified by the DSMB. The laboratory tests include: CK, Absolute Neutrophils, ALT, AST, and Bilirubin.

5.6. PHARMAKOKINETICS

All PK analyses will be performed using the PK Population. Plasma concentrations of ATI-450 and its primary circulating metabolite, CDD-2164, will be summarized by day. Concentration versus time since dose (Days 1, 8, 15, 29, 43, 57, and 85) will be displayed by linear scale.

The PK blood sample collection dates and times for each nominal day and time point will be reported in a data listing. The listing will also include the actual elapsed time calculated relative to the time of dosing for each nominal time point and the ATI-450 plasma concentration value.

6. CHANGES IN THE PROTOCOL-SPECIFIED ANALYSES

[redacted]

Should any deviations from the analyses specified in the authorized statistical analysis plan arise, such deviations will be documented in the final clinical study report.

7. REVISION HISTORY

Date	Revision	Rationale
18OCT2022	Updated sample size Schedule of assessments updated for PGA-SP [redacted]	Changes in protocol amendment
	Added details for imputation of alphanumeric data [redacted] Specified how missing AE relationship and severity will be handled in the summary tables Added definition of treatment-emergent	Clarification

Date	Revision	Rationale
	laboratory toxicity and specified that CK, absolute neutrophils, ALT, AST and Bilirubin will be summarized by maximum toxicity grade Specified the criteria for AESI Specified that coagulation will be included in hematology tables and listings Specified that triplicate averages will be summarized and used to determine if patients meeting noteworthy QT/QTcF criteria Separate out QT and QTcF noteworthy tables [redacted] Specified how to choose ECG interpretation results amongst the triplicate values Specified that both investigator and central ECG interpretation will be summarized	
	Added PK figures to list of proposed figures	Consistency with text
	Removed PD analyses and outputs	Data will be presented in a separate report
	Updated numbering for some tables, listings, and figures	Consistency with ICH guidelines
16FEB2023	Limited the prohibited medications considered to cause an intercurrent event to those that would impact efficacy. Specified that these medications would be determined prior to database lock in a blinded manner	Imputation of data following prohibited medication administration that would not impact efficacy is not appropriate.
	[redacted]	[redacted]
	[redacted]	[redacted]
	Added a one-sided Mood's median test to assess the impact of outliers, non-normality, and skewness of the data on the primary analysis.	To provide a sensitivity analysis of the impact of outliers, non-normality, and skewness of the data on the primary analysis.

Date	Revision	Rationale
	[redacted]	[redacted]
	Updated HiSCR to HiSCR50	Distinguish between HiSCR50 and the added endpoints [redacted]

8. PROGRAMMING CONVENTIONS

- Page orientation, margins, and fonts: Summary tables, listings, and figures will appear in landscape orientation. There should be a minimum of a 1" boundary on the upper (bound) edge, and a minimum of a 1.0" boundary on the remaining three edges. Output should be printed in Courier New with a point size of 8.
- Identification of analysis population: Every summary table and figure should clearly specify the analysis population being summarized. Listings will be prepared for all patients.
- Group headers: In the summary tables, the group headers will identify the summary group and the sample size for the indicated analysis population.
- Suppression of percentages corresponding to null categories: When count data are presented as category frequencies and corresponding percentages, the percent should be suppressed when the count is zero in order to draw attention to the non-zero counts.
- Presentation of sample sizes: Summary modules should indicate, in one way or another, the number of patients contributing to the summary statistics presented in any given summary module. As mentioned above, this may be less than the number of patients in the analysis population due to missing data.
    - In the quantitative modules describing continuous variables (and thus presenting sample size, means, and standard deviations), the sample size should be the number of non-missing observations.
    - For categorical variables that are presented in frequency tables, the module should present the total count in addition to the count in each category. Percentages should be calculated using this total as the denominator, and the percentage corresponding to the sum itself (that is, 100%) should be presented to indicate clearly to a reviewer the method of calculation.
- Sorting: Listings will be sorted by treatment group, subject number and date, if applicable. Lab listings may be sorted by subject, parameter, and date.
- General formatting rules: Rounding for all variables will occur only as the last step, immediately prior to presentation in listings, tables, and figures. No intermediate rounding will be performed on derived variables. The standard rounding practice of rounding numbers ending in 0-4 down and numbers ending in 5-9 up will be employed.
- Numerical Values: The presentation of numerical values will adhere to the following guidelines:
    - Raw measurements will be reported to the number of significant digits as captured electronically or on the eCRFs.
    - Standard deviations will be reported to two decimal places beyond the number of decimal places the original parameter is presented.

- Means will be reported to one decimal place beyond the number of significant digits as the parameter.
- Calculated percentages will be reported to one decimal place.

- Dates will be formatted as DDMMMYYYY. Partial dates will be presented on data listings as recorded on eCRFs.
  - Time will be presented according to the 24-hour clock (HH:MM).

9. PROPOSED TABLES, LISTINGS, AND FIGURES

Tables

Section 14.1 Accountability and Baseline Characteristics

Table 14.1.1.1 Study Disposition and Reasons for Early Termination from Study FAS Population

Table 14.1.1.2 Treatment Disposition and Reasons for Discontinuation of Study Medication FAS Population

Table 14.1.1.3 Analysis Populations FAS Population

Table 14.1.1.4 Protocol Violations and Deviations FAS Population

Table 14.1.2.1 Demographics FAS Population

Table 14.1.2.2 Baseline Disease Characteristics FAS Population

Table 14.1.2.3 Medical History FAS Population

Table 14.1.2.4 Complete Physical Examination at Screening FAS Population

Table 14.1.3 Study Drug Exposure and Compliance Safety Population

Table 14.1.4.1 Prior Medications FAS Population

Table 14.1.4.2 Concomitant Medications FAS Population

Section 14.2 Efficacy

Table 14.2.1.1 Summary of Abscess and Inflammatory Nodule Count Change from Baseline by Analysis Visit FAS Population

Table 14.2.1.2 Summary of Abscess and Inflammatory Nodule Count Change from Baseline by Analysis Visit, PP Population

Table 14.2.1.3 Analysis of Change from Baseline in Abscess and Inflammatory Nodule Count by Analysis Visit FAS Population

Table 14.2.1.4 Analysis of Change from Baseline in Abscess and Inflammatory Nodule Count by Analysis Visit, PP Population

Table 14.2.1.5 Analysis of Median Change from Baseline in Abscess and Inflammatory Nodule Count by Analysis Visit, FAS Population

Table 14.2.1.6.1 Analysis of Change from Baseline in Abscess and Inflammatory Nodule Count by Analysis Visit FAS Population – Baseline Hurley Stage: Mild (I)

Table 14.2.1.6.2 Analysis of Change from Baseline in Abscess and Inflammatory Nodule Count by Analysis Visit FAS Population – Baseline Hurley Stage: Moderate (II)

Table 14.2.1.6.3 Analysis of Change from Baseline in Abscess and Inflammatory Nodule Count by Analysis Visit FAS Population – Baseline Hurley Stage: Severe (III)

Table 14.2.1.6.4 Analysis of Change from Baseline in Abscess and Inflammatory Nodule Count by Analysis Visit FAS Population – Sex: Male

Table 14.2.1.6.5 Analysis of Change from Baseline in Abscess and Inflammatory Nodule Count by Analysis Visit FAS Population – Sex: Female

Table 14.2.1.6.6 Analysis of Change from Baseline in Abscess and Inflammatory Nodule Count by Analysis Visit FAS Population – Baseline BMI: Underweight/normal [<25 kg/m2]

Table 14.2.1.6.7 Analysis of Change from Baseline in Abscess and Inflammatory Nodule Count by Analysis Visit FAS Population – Baseline BMI: Overweight [25 to <30 kg/m2]

Table 14.2.1.6.8 Analysis of Change from Baseline in Abscess and Inflammatory Nodule Count by Analysis Visit FAS Population – Baseline BMI: and Obese [≥ 30 kg/m2]

Table 14.2.2.1 Percentage of Patients Achieving Hidradenitis Suppurativa Clinical Response (HiSCR50) by Analysis Visit FAS Population, Missing Imputed as LOCF

Table 14.2.2.2 Percentage of Patients Achieving Hidradenitis Suppurativa Clinical Response (HiSCR50) by Analysis Visit FAS Population, Missing Imputed as Non-Response

Table 14.2.2.3 Percentage of Patients Achieving Hidradenitis Suppurativa Clinical Response (HiSCR50) by Analysis Visit, PP Population

Table 14.2.3 Percentage of Patients Achieving Hidradenitis Suppurativa Clinical Response [redacted] by Analysis Visit FAS Population, Missing Imputed as LOCF

Table 14.2.4 Percentage of Patients Achieving Hidradenitis Suppurativa Clinical Response [redacted] by Analysis Visit FAS Population, Missing Imputed as LOCF

Table 14.2.5.1 Percentage of Patients Achieving NRS30 among Patients with Baseline PGA of Skin Pain ≥ 3 by Analysis Visit, FAS Population, Missing Imputed as LOCF

Table 14.2.5.2 Percentage of Patients Achieving NRS30 among Patients with Baseline PGA of Skin Pain ≥ 3 by Analysis Visit, FAS Population, Missing Imputed as Non-Response

Table 14.2.5.3 Percentage of Patients Achieving NRS30 among Patients with Baseline PGA of Skin Pain ≥ 3 by Analysis Visit, PP Population

Table 14.2.6.1 Percentage of Patients Meeting [redacted] Criteria by Analysis Visit, FAS Population, Missing Imputed as LOCF

Table 14.2.6.2 Percentage of Patients Meeting [redacted] Criteria by Analysis Visit, FAS Population, Missing Imputed as Non-Response

Table 14.2.6.3 Percentage of Patients Meeting [redacted] Criteria by Analysis Visit, PP Population

Table 14.2.7.1 Summary of IHS-4 Score and Change from Baseline by Analysis Visit, FAS Population

Table 14.2.7.2 Summary of IHS-4 Score and Change from Baseline by Analysis Visit, PP Population

Table 14.2.7.3 Analysis of Change from Baseline in IHS-4 by Analysis Visit, FAS Population

Table 14.2.7.4 Analysis of Change from Baseline in IHS-4 by Analysis Visit, PP Population

Table 14.2.8.1 Summary of HS-Physician's Global Assessment (HS-PGA) and Change from Baseline by Analysis Visit, FAS Population

Table 14.2.8.2 Summary of HS-Physician's Global Assessment (HS-PGA) and Change from Baseline by Analysis Visit, PP Population

Table 14.2.8.3 Analysis of Change from Baseline in HS-PGA by Analysis Visit, FAS Population

Table 14.2.8.4 Analysis of Change from Baseline in HS-PGA by Analysis Visit, PP Population

Table 14.2.9.1 Summary of DLQI Score and Change from Baseline by Analysis Visit, FAS Population

Table 14.2.9.2 Summary of DLQI Score and Change from Baseline by Analysis Visit, PP Population

Table 14.2.9.3 Analysis of Change from Baseline in DLQI Score by Analysis Visit, FAS Population

Table 14.2.9.4 Analysis of Change from Baseline in DLQI Score by Analysis Visit, PP Population

Section 14.3 Safety

Table 14.3.1.1 Overall Summary of Adverse Events, Safety Population

Table 14.3.1.2 Treatment-Emergent Adverse Events by System Organ Classification, Preferred Term and Greatest Severity, Safety Population

Table 14.3.1.3 Treatment-Emergent Adverse Events by System Organ Classification and Preferred Term, Safety Population

Table 14.3.1.4 Treatment-Emergent Serious Adverse Events by SOC and PT, Safety Population

Table 14.3.1.5 Treatment-Emergent Adverse Events Related to Study Drug by SOC and PT, Safety Population

Table 14.3.1.6 Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by SOC and PT, Safety Population

Table 14.3.1.7 Study Drug Related Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by SOC and PT, Safety Population

Table 14.3.1.8 Adverse Events of Special Interest (AESI) by SOC and PT, Safety Population

Table 14.3.1.9 Summary of Most Frequent Treatment Emergent Adverse Events by Preferred Term, Safety Population

Table 14.3.4.1.1 Summary of Hematology and Coagulation Results and Change from Baseline by Analysis Visit, Safety Population

Table 14.3.4.1.2 Summary of Serum Chemistry Results and Change from Baseline by Analysis Visit, Safety Population

Table 14.3.4.1.3 Summary of Urinalysis Results and Change from Baseline by Analysis Visit, Safety Population

Table 14.3.4.2.1 Summary of Treatment-Emergent Abnormal Hematology and Coagulation by Analysis Visit Safety Population

Table 14.3.4.2.2 Summary of Treatment-Emergent Abnormal Serum Chemistry by Analysis Visit, Safety Population

Table 14.3.4.2.3 Summary of Treatment-Emergent Abnormal Urinalysis by Analysis Visit, Safety Population

Table 14.3.4.4 Summary of Laboratory Results by CTCAE Toxicity Grades for CK, Absolute Neutrophils, ALT, AST, and Bilirubin, Safety Population

Table 14.3.5.1 Summary of Vital Signs and Change from Baseline by Analysis Visit, Safety Population

Table 14.3.5.2.1 Summary of ECG Results and Change from Baseline by Analysis Visit, Safety Population

Table 14.3.5.2.2.1 Proportion of Patients with Abnormal Investigator ECG Interpretations by Analysis Visit, Safety Population

Table 14.3.5.2.2.2 Proportion of Patients with Abnormal Central ECG Interpretations by Analysis Visit, Safety Population

Table 14.3.5.2.3 Proportion of Patients with Noteworthy QT Changes by Analysis Visit, Safety Population

Table 14.3.5.2.4 Proportion of Patients with Noteworthy QTcF Changes by Analysis Visit, Safety Population

Section 14.4 Other

Table 14.3.5.3 Summary of ATI-450 and Metabolite Concentrations, PK Population

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Listing 16.2.1 Subject Disposition and Reasons for Early Termination FAS Population

Listing 16.2.2 Protocol Violations FAS Population

Listing 16.2.3 Study Populations FAS Population

Listing 16.2.4.1 Demographics FAS Population

Listing 16.2.4.2 Medical History FAS Population

Listing 16.2.5.1.1 Dosing Diary Safety Population

Listing 16.2.5.1.2 Study Drug Accountability Safety Population

Listing 16.2.5.2 Prior and Concomitant Medications FAS Population

Listing 16.2.5.3 Pharmacokinetics at Scheduled Collection Times, PK Population

Listing 16.2.6.1 Lesion Count, Hurley Stage, HiSCR Responder, and HIS-4 Score, FAS Population

Listing 16.2.6.2 Patient's Global Assessment of Skin Pain (PGA-SP), FAS Population

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Listing 16.2.6.4 Dermatology Life Quality Index (DLQI), FAS Population

Listing 16.2.7.1 Adverse Events Safety Population

Listing 16.2.7.2 Related Adverse Events, Safety Population

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Listing 16.2.7.4 Adverse Events Leading to Discontinuation, Safety Population

Listing 16.2.7.5 Adverse Events of Special Interest, Safety Population

Listing 16.2.8.1.1 Laboratory Tests – Serum Chemistry FAS Population

Listing 16.2.8.1.2 Laboratory Tests – Hematology and Coagulation, Safety Population

Listing 16.2.8.1.3 Laboratory Tests – Urinalysis, Safety Population

Listing 16.2.8.1.4 Laboratory Abnormalities, Safety Population

Listing 16.2.8.1.5 Laboratory Tests – Serum and Urine Pregnancy Test Results, Safety Population

Listing 16.2.8.1.6 Laboratory Tests – Other Tests, Safety Population

Listing 16.2.8.2 Vital Signs, Safety Population

Listing 16.2.8.3 Physical Examination, Population

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Figures

Figure 14.2.1 LS Mean Change from Baseline (90% CI) in Abscess and Inflammatory Nodule Count Over Time by Treatment Group (LOCF), FAS Population

Figure 14.2.2 Responder Rate (90% CI) for HiSCR50 Over Time by Treatment Group (LOCF), FAS Population

Figure 14.2.5 Responder Rate (90% CI) for NRS30 Over Time by Treatment Group (LOCF), FAS Population

Figure 14.2.6 Responder Rate (90% CI) for [redacted] Over Time by Treatment Group (LOCF), FAS Population

Figure 14.2.8 LS Mean Change from Baseline (90% CI) in HS-PGA Over Time by Treatment Group, FAS Population

Figure 14.3.4.3.X Mean (+/- SE) Laboratory Parameters Over Time by Treatment Group for CK, Absolute Neutrophils, ALT, AST, and Bilirubin, Safety Population

Figure 14.3.5.2 Mean (+/- SE) QTcF Values Over Time by Treatment Group, Safety Population

Figure 14.3.5.3 Mean Plasma Concentration (+/- SD) of ATI-450 Over Time by Treatment Group, PK Population

Figure 14.3.5.4 Mean Plasma Concentration (+/- SD) of CDD-2164 Over Time by Treatment Group, PK Population