Statistical Analysis Plan

Protocol Title:	A Multicenter, Randomized, Double blinded Study Evaluating the Pharmacokinetics, Efficacy and Safety of Multiple Switches Between Ustekinumab and ABP 654 Compared With Continued Use of Ustekinumab in Subjects with Moderate to Severe Plaque Psoriasis
Short Protocol Title:	A Study to Investigate Interchangeability of ABP 654 for the Treatment of Subjects with Moderate to Severe Plaque Psoriasis
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Version Number	Date (DDMMMYYYY)	Summary of Changes, including rationale for changes
Original (v2.0)	17 June 2021	Compared to v1.0, 18Dec2020: • Updated similarity margin and associated sample size to follow FDA's suggestion • Added PK and ADA assessment samples at Week 4 per protocol amendment • Changed missing data handling from LOCF to MI to follow FDA's suggestion • Added footnote for clarification that laboratory parameters will only be included at the visits where it is scheduled for assessment in the output tables. • Added clarification that actual treatment is to be used for RTS • Added COVID 19 related analyses and analysis tables. • Added additional analysis for sPGA combined score of 4/5 to follow FDA's suggestion • Added Medical History by System Organ Class and Preferred Term for not resolved findings for the Run-in Period in SAP • Updated the descriptive summary of Tmax such that only median, min and max will be presented to align with standard shell • Changed the figure for $C_{trough,ss}$ from Mean +/- SD plot using RTS to box plots using RTS • Added analysis of TEAE Leading to Dose delayed / not administered of IP

Version Number	Date (DDMMMYYYY)	Summary of Changes, including rationale for changes
		by PT for the Post-randomization Period • Added ECG analyses to align with protocol amendment • The Category of EOI query (SOC, SMQ / Amgen query) for the EOI Reversible posterior leukoencephalopathy syndrome is updated to Reversible posterior leukoencephalopathy syndrome (Amgen query) from Posterior reversible encephalopathy syndrome/reversible posterior leukoencephalopathy syndrome (Amgen query) • Serious depression including suicidality EOI scope is updated to broad. • Additional minor wording clarifications or corrections were made throughout the document.
v3.0	15 Feb 2023	Compared to v2.0, 17June2021: • Added ECG summary tables by visit and treatment arm and an ECG shift table of the worst post randomization ECG results (normal, abnormal & non clinically significant (NCS), and abnormal & clinically significant (CS)) relative to randomization at Week 28 for the Post randomization Period per Protocol Amendment 2.0 section 9.5.3. • Added ECG visits to the Study Analysis Visit table. • Added a footnote to clarify the upper bound for analysis window of Week 28 for Efficacy, Vital, Safety Lab, ADA & PK in the Study Analysis Visit table. • In TEAE summary, “TEAE leading to dose delayed / not administered” is changed to “TEAE leading to dose delayed” for being consistent with the CRF.

Version Number	Date (DDMMMYYYY)	Summary of Changes, including rationale for changes
		• Changed the method for estimating the point estimate and 90% CI of the risk difference in PASI 75 response rate and PASI 100 response rate at Week 64 and sPGA response at Week 64 from generalized linear model with an identity link to the stratified Newcombe confidence limits in Section 9.6.2.1. This change addresses the potential non-convergence issue from the generalized linear model. • Updated the definition of the PK Concentration Analysis Set in Section 6.3 to clarify that PK samples on or after randomization date should be included. • Added PK summary statistic reporting precision in Section 9.1. • Removed four categorical parameters (glucose, bilirubin, blood, and protein) from urinalysis in Section 9.7.2. That level of detail for urinalysis results is not critical in this program/study and any clinically relevant abnormal finding was also captured as Adverse Event. • Added the PK trough concentration at Week 28 as a covariate to the ANCOVA models for AUC_{tau}, C_{max} and $C_{trough,ss}$ (at Week 40 and Week 52) in Sections 9.5.1.1 and 9.5.2 to adjust for the baseline PK trough concentration. • Changed the denominator for calculating “Developing antibody incidence during the Post-randomization Period” to “the number of subjects in the Safety Analysis Set who have antibody negative or no result prior to the first dose of post-randomization IP” in Section 9.7.6, in order to exclude subjects with antibody positive at baseline or developing antibody during the Run-in Period from the denominator.

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List of Abbreviations and Definition of Terms

Abbreviation	Explanation
ADA	antidrug antibody
ADaM	Analysis Data Model
AE	adverse event
ALT	alanine aminotransferase
ANCOVA	analysis of covariance
AST	aspartate aminotransferase
AUC	area under the curve
AUC_{tau}	area under the curve from time 0 over the dosing interval
$AUC_{tau\ extrap}$	area under the curve from time 0 over the dosing interval extrapolated
BMI	body mass index
BSA	body surface area
CDISC	Clinical Data Interchange Standards Consortium
CI	confidence interval
C_{max}	maximum concentration
CRF	case report form
CS	Clinically significant
CSR	clinical study report
CTCAE	Common Terminology Criteria for Adverse Events
$C_{trough,ss}$	trough concentration at steady state
DMC	Data Monitoring Committee
EOI	events of interest
EOS	end-of-study
FAS	Full Analysis Set
GMR	geometric mean ratio
IP	investigational product
IXRS	Interactive Web/Voice Response System
LLOQ	lower limit of quantification
MedDRA	Medical Dictionary for Regulatory Activities
MI	multiple imputation
NCS	Non Clinically Significant
NRI	non responder imputation
PASI	Psoriasis Area and Severity Index
PK	pharmacokinetic(s)

PT	preferred term
Q1	25th percentile
Q3	75th percentile
RTS	Run-in Treated Set
SAP	statistical analysis plan
SDTM	Standard Data Tabulation Model
sPGA	Static Physician's Global Assessment
SAS	Safety Analyses Set
SOC	system organ class
TEAE	treatment-emergent adverse events
TFL	table, figure, listing
t_{max}	time of maximum concentration
$t_{1/2}$	terminal elimination half life
WBC	white blood cell
λ_z	terminal elimination rate constant

1. Introduction

The purpose of this Statistical Analysis Plan (SAP) is to provide details of the statistical analyses that have been outlined within the protocol for study 20200417, ABP 654, 02 June 2021 V2.0. The scope of this plan includes the final analysis that is planned and will be executed by Parexel International, the designated contract research organization.

2. Objectives, Endpoints and Hypotheses

2.1 Objectives and Endpoints

Objectives	Endpoints
Primary	
To demonstrate pharmacokinetic similarity in subjects with multiple switches between ustekinumab and ABP 654 compared to subjects receiving continued use of ustekinumab	Primary pharmacokinetic parameters: • AUC_{tau} between Week 52 and Week 64 • C_{max} between Week 52 and Week 64
Secondary	
To assess the efficacy, safety and immunogenicity in subjects with multiple switches between ABP 654 and ustekinumab compared with subjects receiving continued use of ustekinumab	Secondary pharmacokinetic parameters: • t_{max} between Week 52 and Week 64 • $C_{trough,ss}$ between Week 28 and Week 52 Efficacy related parameters: • Psoriasis Area and Severity Index (PASI) percent improvement from baseline (day 1) at Week 64 • PASI 75 response at Week 64 • PASI 100 response at Week 64 Safety related parameters: • Treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs), post randomization • Treatment-emergent events of interest (EOIs), post randomization Immunogenicity-related Endpoints: • Incidence of antidrug antibodies, post randomization

2.2 Hypotheses and/or Estimations

The analyses of the primary pharmacokinetic(s) (PK) endpoints will test the following hypotheses for each endpoint:

Null Hypothesis (H_0): The geometric means ratio (GMR) between ABP 654 and ustekinumab is outside a similarity margin of (0.8, 1.25),

versus

Alternative Hypothesis (H_a): The GMR between ABP 654 and ustekinumab is within a similarity margin of (0.8, 1.25).

To establish interchangeability, both 90% confidence intervals (CIs) of GMR of ABP 654 versus ustekinumab for AUC_{tau} and C_{max} from the primary analysis must fall within the above similarity margin.

3. Study Overview

3.1 Study Design

This is a randomized, double-blinded, phase 3 study in adult subjects with moderate to severe plaque psoriasis. This study is planned to be conducted globally at study centers including but not limited to North America and Europe.

The total duration of study participation for each subject will be 68 weeks, with up to 4 weeks for screening and 64 weeks after the first investigational product administration.

Subjects will receive an initial 3 doses of ustekinumab on day 1 (Week 0), Week 4 and Week 16. From Week 28, subjects in the continued use group will stay on ustekinumab and subjects in the switching group will switch between ABP 654 and ustekinumab every 12 weeks.

At Week 28, efficacy assessments will be conducted including evaluation of PASI.

Subjects who do not achieve a PASI 50 response or better improvement at Week 28 are considered as run-in failures and will not be randomized at Week 28; these subjects will complete End of Study (EOS) procedures at Week 28. The Run-in Period will occur from day 1 until prior to randomization at Week 28. Those unable to complete the Week 28 visit or did not have a PASI assessment completed at Week 28 will be discontinued from the study. All enrolled subjects not randomized at Week 28 will be considered run-in failures and the run-in failure reason will be documented.

3.2 Sample Size

Approximately 480 subjects will be enrolled to receive ustekinumab during the Run-in Period. Subjects with prior biologic use for psoriasis will be capped at 50% of the total enrolled subjects. This sample size will ensure approximately 310 subjects will be randomized at Week 28 after the Run-in Period, considering 35% run-in failures, in a 1:1 ratio to the continued use group or the switching group. The randomization will be stratified by prior biologic use for psoriasis (yes versus no) at baseline (Week 0), geographic region, and body weight group at baseline (Week 0). The number of subjects enrolled may be adjusted during the study with the actual run-in failure rate seen to ensure approximately 310 subjects will be randomized at Week 28. Subjects already enrolled will be allowed to be randomized at Week 28. The sample size of 310 enrolled subjects will provide 90% power to demonstrate similarity of the primary PK endpoints based on the Two One-Sided Tests at a 0.05 significance level, assuming a between-subject variability (as measured by coefficient of variation) of 55% for ABP 654 and ustekinumab, a true GMR of 1 between ABP 654 and ustekinumab, and a similarity margin of (0.8, 1.25), and 25% drop outs after randomization through Week 64 (including subjects who discontinue the study prior to Week 52 and those reaching Week 52 but do not have evaluable primary PK endpoints between weeks 52 and 64).

3.3 Adaptive Design

None.

4. Covariates and Subgroups

4.1 Planned Covariates

Unless stated otherwise, stratification factors (prior biologic use for psoriasis at baseline, geographic region, and body weight group at baseline) will be included as covariates in models for PK and efficacy endpoints. For continuous efficacy endpoints (e.g. PASI percent improvement from baseline, Body Surface Area (BSA) change from baseline), the relevant baseline scores will also be included as covariates in models.

Covariate values may be discordant if collected via case report form (CRF) and Interactive Web/Voice Response System (IXRS). Analyses that are intended to evaluate the treatment effect and include stratification variables as covariates in the model will be based on the CRF stratification values, regardless of the subject's IXRS stratification values, to provide unbiased estimates of the effects of treatment and stratification variables without loss of efficiency (Ke et al, 2017). **Analyses using the stratified Cochran-Mantel-Haenszel method will be based on the IXRS stratification values.**

4.2 Subgroups

Subgroup analyses will be conducted for the primary PK parameter endpoints for the binding antidrug antibody (ADA) negative subgroup (see definition in Section 5.1).

5. Definitions

5.1 General

Actual Treatment Received During Run-in Period

If a subject received any dose of ABP 654 during the Run-in Period, the actual treatment for the subject is defined as ABP 654. Otherwise, the actual treatment for the subject is defined as ustekinumab.

Actual Treatment Received During Post-randomization Period

For subjects randomized to switching group or continued use group and received all assigned treatments, the actual treatment received is defined as the switching group or the continued use group. Otherwise, the actual treatment received by a subject is defined as the actual treatment sequence (including missed doses, if any) received by the subject.

Baseline

Unless stated otherwise, the baseline of the study is defined as the last non-missing assessment taken prior to the first dose of investigational product (IP) a subject received (see definition of first dose date). In cases where baseline assessments are taken on the same day as the first dose of IP, and either no times are reported or the IP and assessment times are the same, it will be assumed that these assessments are taken prior to IP being administered.

Binding ADA Negative Subgroup

Defined as subjects in the subset of Safety Analysis Set (SAS) who have never tested positive (i.e. tested negative or no results) prior to the first dose of post-randomization IP, have at least one ADA result post randomization, and all available post-randomization ADA results are negative.

Change from Baseline

Change from baseline is defined as (value at post-baseline visit – value at baseline).

Concomitant and Prior Medication

Prior medications are defined as medications with a stop date prior to first dose of IP the subject received (see definition of first dose date). Concomitant medications are defined as any medications ongoing at the start of IP treatment for the subject or with a start date on or after the first dose date, **through end of study date**.

End of Study (EOS) Date

The EOS date is the date recorded on the End of Study page of the CRF.

First Dose Date

It is defined as the date the subject received the first dose of IP.

Last Dose Date

It is defined as the date the subject received the last dose of IP.

First Post-randomization Dose Date

It is defined as the date the subject received the first post-randomization dose of IP.

Multiple Imputation (MI)

A method of imputation which takes into consideration the uncertainty of the missing data by creating several different plausible imputed data sets and appropriately combining analysis results obtained from each of the imputed datasets.

Non-Responder Imputation (NRI)

A method of imputation where a subject with missing post-baseline binary response data will be imputed as a non-responder, regardless of the reasons for missing data.

Study Analysis Visit

If more than one actual visit (including the unscheduled visits) falls within the same defined window, the visit closest to the target day with non-missing data will be considered for analysis. If two actual visit dates are at the same distance from the target day, the later visit with non-missing data will be considered for analysis.

For Efficacy, Vital, Safety Lab and PK

Study Analysis Visit	Target Day	Study Day	Interval (days)	Endpoint				
				Efficacy[b][c]	Vital Sign[bc]	Safety Lab[abc]	PK[b][c]	**ECG[bc]**
Baseline	1	<=1	NA	X	X	X	X	**X**

Study Analysis Visit	Target Day	Study Day	Interval (days)	Endpoint				
				Efficacy[b c]	Vital Sign[bc]	Safety Lab[abc]	PK[b c]	**ECG[bc]**
Week 4	29	2-70	69		X		X	
Week 16	113	71-154	84		X		X	**X**
Week 28	197	155-238	84	X	X	X	X	**X**
Week 40	281	239-322	84	X	X		X	**X**
Week 52	365	323-406	84	X	X	X	X	**X**
Week 64	449	>=407	NA	X	X	X	X	

a. Laboratory parameters will only be included at the visits where it is scheduled for assessment in the output tables.

b. If only assessment dates of efficacy, vital, safety laboratory, and PK are available and the assessment date is on the same day of first dose of IP at week 0 or week 28 respectively, the measurement is treated as baseline or pre the first IP dose post-randomization assessment.

c. If both assessment date and time are available for efficacy, vital sign, safety laboratory, PK or ECG measurements, the measurements either (1) are on the same day as the first dose date at Week 0 or Week 28, but the assessment time is after the first dose of IP at Week 0 or Week 28, respectively, or (2) fall within the Week 28 window and are after the first post-randomization IP, the measurements

will not be defined as baseline or Week 28, but will be included in consideration for the next visit, Week 4 or Week 40 measurements, respectively.

PK concentrations between Week 52 – Week 64 are summarized by nominal study visit per the following table:

Tolerance Windows for Pharmacokinetic Endpoint Sample Collection

Study Visit	**Tolerance Windows[a]**
Week 52 predose	Within **1 hour** prior to Week 52 investigational product administration
2 days post Week 52 dose	±5 hours
7 days post Week 52 dose	±5 hours
10 days post Week 52 dose	**±24 hours**
2 weeks post Week 52 dose	**±24 hours**
4 weeks post Week 52 dose	**±48 hours**
8 weeks post Week 52 dose	**±72 hours**
12 weeks post Week 52 dose (End of Study Visit)	**±72 hours**

[a]The Week 52 visit should be performed 52 weeks from day 1, with a window of ± 5 days. Subsequent visits are done in relation to the actual Week 52 investigational product dose date (e.g., for the 2 days post Week 52 dose timepoint, the pharmacokinetic sample should be collected 2 days after the actual Week 52 dose, with a collection window of ± 5 hours).

For ADA

Study Analysis Visit	Target Day	Study Day
Baseline[ab]	1	<=1
By Week 4	29	<=70
By Week 16	113	<=154
By Week 28[ab]	197	<=238
By Week 40	281	<=322
By Week 52	365	<=406
By Week 64	449	<=EOS Visit Date

a. If a subject has ADA measurements on the same day as the first dose date at Week 0 or Week 28 but the administered time is after the first dose of IP at Week 0 or Week 28, respectively, the ADA measurements will not be defined as baseline or Week 28, but will be included in consideration for Week 4 or Week 40 measurements, respectively.

b. If only an assessment date of ADA is available and the assessment date is on the same day of first dose of IP at Week 0 or Week 28, respectively, the measurement is treated as baseline or pre first IP dose post-randomization assessment.

Study Day

Study day is defined as the number of days from Study Day 1.

Before Study Day 1: Study Day = (Date of assessment – Date of Study Day 1)

On or After Study Day 1: Study Day = (Date of assessment – Date of Study Day 1) +1

Therefore, the day prior to Study Day 1 is -1.

Study Day 1

Study day 1 is defined as the first day of IP the subject received (see definition of first dose date).

Study Period

The following definitions will be used for PK and safety analyses.

Run-in Period

It is defined as the time period from the first dose of IP the subject received (see definition of first dose date for the subject) to prior to first post-randomization dose for subjects who are randomized and treated post-randomization, or to the EOS visit for subjects not randomized or for subjects who were randomized but not treated post-randomization.

Post-randomization Period

For subjects who are randomized and treated post-randomization, it is defined as the time period from the first post-randomization dose to the EOS visit.

Study Randomization

Study randomization is defined as when subject receives a random treatment allocation via the IXRS system.

Total IP Exposure Duration

The total IP exposure duration for a subject (in **weeks**) for each study period (Run-in Period and Post-randomization Period) will be derived as: (the period end date – the period start date +1)**/7. The Run-in Period end date for the subjects who are**

randomized and treated post-randomization is the date of the first IP post randomization -1.

5.2 Pharmacokinetic

Pharmacokinetic parameters will be calculated from the serum concentration-time data using noncompartmental methods (Phoenix WinNonlin®, version 8.2 or higher, Pharsight Corp, St. Louis, MO) and actual sampling times. The following PK parameters will be reported:

Variable	Definition
AUC_{tau}	area under the curve from time 0 (Week 52) over the dosing interval up to Week 64 using the observed values
C_{max}	Maximum observed serum concentration obtained directly from the experimental observations. If multiple maxima occur at equal concentrations, the first temporal value will be taken.
t_{max}	Time at which the maximum serum concentration was observed obtained directly from the experimental observations
$C_{trough,ss}$	trough concentration at steady state obtained directly from the experimental observations

If data allows, the following PK parameters will also be derived:

Variable	Definition
λ_z	Terminal elimination rate constant
$t_{1/2}$	Terminal elimination half-life; calculated as $\ln(2)/\lambda_z$
$AUC_{tau\ extrap}$	area under the curve from time 0 (Week 52) over the dosing interval extrapolated to Week 64

The AUC_{tau} is the sum of areas up to the time tau and will be calculated using the linear trapezoidal rule. Actual time post dose for the observed value between weeks 52 and 64 will be used as time for AUC_{tau} and no extrapolation will be applied. In the event of below the lower limit of quantification (LLOQ) at the end of the profile, the time of the last quantifiable sample will be used. Individual AUC_{tau} will be flagged and excluded from

summary statistics and statistical testing if less than 2 post t_{max} concentration values are reported or above LLOQ.

The λ_z will be estimated by linear regression of concentration versus time data presented in a log-linear scale. Only those data points that are judged to describe the terminal log-linear decline will be used in the regression. A minimum number of three data points in the terminal phase will be used in calculating λ_z with the line of regression starting at any post t_{max} data point (C_{max} will not be part of the regression slope).

The interval used to determine λ_z should be equal or greater than 2-fold the estimated $t_{1/2}$. Otherwise, the derived λ_z and $t_{1/2}$ will be flagged.

For the estimation of $AUC_{tau\ extrap}$, extrapolation will be considered acceptable if the following conditions are satisfied:

- Extrapolation is <20% of the total area
- λ_z and $t_{1/2}$ are correctly estimated based on above criteria
- Terminal phase regression R^2 adjusted > 0.8

Any individual $AUC_{tau\ extrap}$ not meeting the above criteria will be flagged.

The derived PK parameters (i.e. λ_z, $t_{1/2}$ and $AUC_{tau\ extrap}$) will be included in the listing of individual PK parameters. No summaries statistics and statistical testing will be conducted for these derived parameters.

5.3 Efficacy

Body Surface Area (BSA) affected by psoriasis

The percent of BSA affected by psoriasis (%BSA) is estimated by assuming that the subject's palm, excluding the fingers and thumb, represents roughly 1% of the body's surface (Chandran, 2009). At any given visit, BSA should be performed by the same assessor performing PASI assessment. Because of interobserver variability in estimated BSA, all assessments for a given subject should be made by the same observer whenever possible.

PASI

The PASI is a measure of the average redness (erythema), thickness (induration), and scaliness (scaling; each graded on a 0–4 scale of the lesions, weighted by the area of involvement (Feldman and Krueger, 2005). PASI combines the assessment of the

severity of lesions and the area affected into a single score in the range 0 (no disease) to 72 (maximal disease).

PASI Percent Improvement from Baseline

PASI percent improvement from baseline is defined as 100 × (value at baseline – value at post-baseline visit) / value at baseline. A percent improvement will not be calculated if the baseline value is missing. A positive value will be considered PASI improvement. Hence, PASI percent improvement will be in a positive direction while PASI percent worsening will be in a negative direction.

PASI Response

PASI Response is defined as a subject meeting or surpassing a pre-specified threshold for percent improvement in PASI score compared to the baseline PASI score. An improvement of at least 75% qualifies a subject as being a PASI 75 responder, and an improvement of 100% qualifies a subject as being a PASI 100 responder.

Static Physician's Global Assessment (sPGA)

The sPGA is a 6-point scale (0-5) used to measure the severity of disease (induration, scaling, and erythema). The sPGA should be completed by the same assessor performing the PASI assessments. All assessments for a given subject should be made by the same observer whenever possible.

sPGA Response

An sPGA response is defined as a subject meeting sPGA assessment values of 0 (Clear) or 1 (Almost Clear).

5.4 Safety

Adverse Events Leading to Discontinuation from IP/Study

AEs leading to discontinuation from IP/study are those with an action taken with IP indicating "drug withdrawn" or Other action taken of "study discontinued".

Event of Interest (EOI)

An EOI is defined as a noteworthy event for a particular product or class of products that a sponsor may wish to monitor carefully. It could be serious or non-serious and could include events that might be potential precursors or prodromes for more serious medical conditions in susceptible individuals (Council for International Organizations of Medical Sciences [CIOMS] VI, 2005). The EOIs for this study will include:

- Serious systemic hypersensitivity reactions
- Facial palsy
- Pustular psoriasis
- Erythrodermic psoriasis
- Serious infections (including mycobacterial and salmonella infections)
- Malignancy
- Cardiovascular events
- Reversible posterior leukoencephalopathy syndrome
- Serious depression including suicidality
- Venous thromboembolism

The detailed search strategies for the EOIs are included in Appendix A.

Treatment-emergent Adverse Event

Treatment emergent adverse events (TEAEs) during the Run-in Period are defined as adverse events that start on or after the first dose of IP and prior to the first dose post randomization for randomized and treated subjects, or EOS for run-in failures or for subjects who were randomized but not treated post-randomization.

TEAEs during the post randomization period are defined as adverse events that start on or after the first dose of IP post-randomization and prior to the EOS.

If the adverse event starts on the same day as the first dose of IP, then the flag indicating whether the adverse event started prior to the first dose on the adverse event CRF page will be used to determine whether this is a TEAE during the Run-in Period. For randomized and treated subjects, an adverse event that starts on the same day as the first post-randomization dose will be considered as a TEAE post-randomization.

6. Analysis Sets

6.1 Full Analysis Set

The Full Analysis Set (FAS) consists of all randomized subjects. This analysis set will be used for sensitivity analyses of efficacy endpoints and will be analyzed according to randomized treatment group.

6.2 Safety Analysis Set

The Safety Analysis Set (SAS) consists of all randomized subjects who received at least 1 dose of IP post randomization. This analysis set will be used for analyses of the safety endpoints during the post randomization period according to actual treatment received.

6.3 PK Analysis Sets

PK Concentration Analysis Set

The PK Concentration Analysis Set will include all randomized subjects who received at least 1 dose of IP post randomization and have at least 1 reported serum concentration of ABP 654 or ustekinumab on or after the day of randomization. This analysis set will be used for analyses of PK concentrations during the post randomization period according to actual treatment received.

PK Parameter Analysis Set

The PK Parameter Analysis Set will include all randomized subjects who receive all 3 doses of the assigned IP between weeks 28 and 52 and who have an evaluable ABP 654 or ustekinumab serum concentration time profile between weeks 52 and 64. This analysis set will be used for the primary analysis of the primary and secondary PK endpoints and will be analyzed according to actual treatment received.

Per-protocol PK Parameter Analysis Set

The Per-protocol PK Parameter Analysis Set will include all subjects in the PK Parameter Analysis Set who do not have an important protocol deviation during the study that could affect the primary PK endpoints. This analysis set will be used for a sensitivity analysis of the primary PK endpoints and will be analyzed according to actual treatment received.

6.4 Health-related Quality-of-Life or Health Economics Analyses Set(s)

None.

6.5 Per-protocol Efficacy Analysis Set

The Per-protocol Efficacy Analysis Set consists of all subjects who are randomized and receive all 3 doses of the assigned IP between weeks 28 and 52 and who have not experienced an important protocol deviation during the study that may affect the evaluation of the efficacy endpoints. This analysis set will be used for primary analysis of the secondary efficacy endpoints and will be analyzed according to actual treatment received.

6.6 Interim Analyses Set(s)

None.

6.7 Study-specific Analysis Set

Run-in Treated Set

The Run-in Treated Set (RTS) consists of all enrolled subjects treated with at least 1 dose of IP during the Run-in Period. This analysis set will be used for all analyses for the Run-in Period based on actual treatment.

7. Planned Analyses

7.1 Interim Analysis and Early Stopping Guidelines

None.

7.2 Primary Analysis

None.

7.3 Final Analysis

The final analysis for the study will be performed after all subjects reach Week 64 or terminate early.

8. Data Screening and Acceptance

8.1 General Principles

The objective of the data screening is to assess the quantity, quality, and statistical characteristics of the data relative to the requirements of the planned analyses.

Data screening process will be documented in a data management plan by Parexel and agreed by Amgen. In addition to the data screening built into the Parexel Data Management Plan, the programming of analysis datasets, tables, figures and listings (TFL) provides additional data screening.

When the database has been declared to be complete and accurate, the database will be locked. Database lock will follow the standard operating procedure(s) at Parexel.

8.2 Data Handling and Electronic Transfer of Data

Clinical data will be entered in RAVE database and exported as SAS® version 9.4 or higher datasets. Converted datasets will be created using SAS® and following standard Clinical Data Interchange Standards Consortium Standard Data Tabulation Model (CDISC SDTM, version 1.4, Implementation Guide version v3.2) conventions. Analysis datasets will be created using SAS® and following CDISC Analysis Data Model (ADaM, version 2.1, Implementation Guide 1.1) standards.

Medical history and AEs will be coded using the current version of Medical Dictionary for Regulatory Activities (MedDRA) at the time of the final analysis to assign a system organ class (SOC) and preferred term (PT) to each event. Adverse events and abnormal laboratory results considered as AEs are assigned a toxicity grade according to National Cancer Institute (NCI-US) Common Terminology Criteria for Adverse Events (CTCAE) version 4.03. Prior and concomitant medications will be coded using the current version of the World Health Organization Drug Dictionary (WHO-DD) at the time of the final analysis.

8.3 Handling of Missing, Below LLOQ and Incomplete Data

Missing PK concentration data and endpoints will not be imputed.

For the purpose of calculating AUC_{tau}, concentrations that are below the LLOQ after t_{max} will be excluded; values less than the LLOQ that are encountered prior to t_{max} will be set to zero and included. Individual AUC_{tau} will be flagged if less than 2 post t_{max} concentration values are reported or if less than 2 post t_{max} concentration values are above LLOQ.

For summary statistics and linear plots for the PK concentrations, concentration values < LLOQ will be set to zero. For log-linear plots, concentration values below LLOQ will not be displayed.

The handling of missing values for efficacy endpoints are detailed in Section 9.6.

Missing safety and ADA endpoints will not be imputed.

Imputation for Partial or Missing Dates

If dates are missing or incomplete for an AE (including deaths) or concomitant medication, the following algorithm will be used for imputation:

Start Date		Stop Date						
		Complete: yyyymmdd		Partial: yyyymm		Partial: yyyy		Missing
		<1st dose	≥1st dose	<1st dose yyyymm	≥1st dose yyyymm	<1st dose yyyy	≥1st dose yyyy	
Partial: yyyymm	= 1st dose yyyymm	2	1	n/a	1	n/a	1	1
	≠ 1st dose yyyymm		2	2	2	2	2	2
Partial: yyyy	= 1st dose yyyy	3	1	3	1	n/a	1	1

	≠ 1st dose yyyy		3		3	3	3	3
Missing		4	1	4	1	4	1	1

1 = Impute as the date of first dose

2 = Impute as the first of the month

3 = Impute as January 1 of the year

4 = Impute as January 1 of the stop year

Note: If the start date imputation leads to a start date that is after the stop date, then there is a data error and do not impute the start date.

Imputation rules for partial or missing stop dates:

1. Initial imputation
    a. For partial stop date “mmyyyy”, impute the last of the month.
    b. For partial stop date “yyyy”, impute December 31 of the year.
    c. For completely missing stop date, do not impute.
2. If the stop date imputation leads to a stop date that is after the death date, then impute the stop date as the death date.
3. If the stop date imputation leads to a stop date that is before the start date, then there is a data error and do not impute the stop date.

Imputation rules for partial or missing death dates:

1. If death year and month are available but day is missing:
    a. If “mmyyyy” for last contact date = “mmyyyy” for death date, set death date to the day after the last contact date.
    b. If “mmyyyy” for last contact date < “mmyyyy” for death date, set death date to the first day of the death month.
    c. If “mmyyyy” for last contact date > “mmyyyy” for death date, data error and do not impute.
2. If both month and day are missing for death date or a death date is totally missing, set death date to the day after the last contact date.

The imputed dates will be used to assess whether AEs should be considered as treatment-emergent and if medications should be included in the safety summaries as prior or concomitant, however the original, partial dates will be included in data listings.

8.4 Detection of Bias

None.

8.5 Outliers

Individual ABP 654 and ustekinumab serum concentration-time points, if considered anomalous, may be excluded from the analysis if due to a protocol deviation at the

discretion of the pharmacokineticist following a review of the available documentation (bioanalytical report, clinical report, etc.). Any such exclusion will be documented and clearly outlined in the clinical study report (CSR).

Entire individual PK profile for a subject may be excluded following review of the available documentation. Any such exclusion will be clearly listed in the CSR along with justification for exclusion.

8.6 Distributional Characteristics

None.

8.7 Validation of Statistical Analyses

All report outputs will be produced/all statistical analyses will be performed using SAS® version 9.4 or a higher version in a secure and validated environment.

Programs will be developed and maintained and output will be verified in accordance with current standard operating procedures at Parexel. The validation process is repeated any time TFLs are re-delivered with different data. Execution of this validation process is documented throughout the study. The entire set of TFLs will be checked for completeness, accuracy prior to its delivery to Amgen.

9. Statistical Methods of Analysis

9.1 General Considerations

All statistical analyses will be performed using SAS® (Version 9.4 or higher).

Unless otherwise specified, descriptive data summaries will be tabulated by treatment for all endpoints. Categorical data will be summarized using number of subjects, frequency and percentages of subjects falling into each category, with the denominator for percentages being the number of subjects in the analysis sets for each treatment group, unless otherwise noted. Percentages will be rounded to one decimal place except for 100%, which will have no decimal place.

All continuous variables will be summarized using mean, standard deviation, median, minimum, maximum, 25th percentile (Q1), 75th percentile (Q3), and number of subjects with observations. The mean, **geometric mean**, median, Q1, and Q3 will be presented to one decimal place greater than the original data, standard deviation will be two decimal places greater than the original data, and the minimum and maximum will have the same number of decimal places as the original data.

For PK endpoints, additional precision rules are as follow:

Pharmacokinetic serum concentrations will be reported in ng/ml and will follow the general conventions for summary statistics.

Pharmacokinetic parameters with units of ng/ml or h*ng/ml will be converted to ug/ml or h*ug/ml with 1 decimal place.

Summary Statistics	Reporting Precision
CV%/geometric CV%	1 d.p.
Geometric LS mean	2 d.p.
Geometric LS mean ratios	4 d.p.
CI	Same number of decimal places as the associated statistic

d.p.= decimal place(s)

Confidence intervals may also be provided (when specified).

For any of the summaries that are to be done by visit, the derived analysis study visit as defined in Section 5.1 will be used for analysis unless otherwise noted.

9.2 Subject Accountability

The following information will be summarized for subject disposition and accountability for each of the analysis sets defined in Section 6, unless stated otherwise:

- Number of subjects enrolled in the RTS and number of subjects randomized in the FAS by region, country, and site
- Subject disposition including
    - Number of subjects in the RTS who discontinued treatment with reason of discontinuation, discontinued treatment with reason of discontinuation related to COVID-19, completed the Run-in Period and who failed the Run-in Period (i.e., run-in failures) with reason for run-in failures and reason for run-in failures related to COVID-19 for the Run-in Period;
    - Number of subjects who were randomized, who were treated with IP, completed treatment, discontinued treatment with reason of discontinuation, discontinued treatment with reason of discontinuation related to COVID-19, completed study, and discontinued study with reason of discontinuation and discontinued study with reason related to COVID-19 for the Post-randomization Period

- Summary of analysis sets with reasons for exclusion from each analysis set (for all screened subjects)
- Randomization list for the FAS
- List of discontinued subjects from IP and/or study in the RTS for the Run-in Period and in the FAS for the Post-randomization Period

9.3 Important Protocol Deviations and COVID-19 Related Protocol Deviations

Important Protocol Deviations (IPDs) data will be identified and recorded. The study team will conduct on-going reviews of the IPD data throughout the study and the resulting set of subjects to be included in the Per-protocol (PP) PK and efficacy analysis sets. The PP analysis sets must be finalized prior to database lock of the final analysis.

For the Post-randomization Period, a summary of incidence of IPDs will be based on FAS and tabulated using number and percentage of subjects by deviation type (including COVID-19 related) and randomized treatment group. A listing of subjects with IPDs will be provided (with a flag indicating whether the deviation leads to exclusion from the PP PK or efficacy analysis sets and a flag indicating whether an IPD is COVID-19 related) based on FAS.

For the Run-in Period, a summary of incidence of IPDs will be based on RTS and tabulated using number and percentage of subjects by deviation type (including COVID-19 related). A listing of subjects with IPDs (with a flag indicating whether an IPD is COVID-19 related) will be provided based on RTS.

All COVID-19 related protocol deviations (PDs) will be summarized by COVID-19 related deviation type for the FAS for the Post-randomization Period and RTS for Run-in Period. A listing of subjects with COVID-19 related PDs will be provided for the FAS for the Post-randomization Period and RTS for Run-in Period.

9.4 Demographic and Baseline Characteristics

The following demographics and baseline characteristics will be summarized descriptively by treatment group for each of the analysis sets defined in Section 6.

- age (in years, at time of signing informed consent)
- race

- sex
- ethnicity
- height
- weight
- body mass index (BMI)
- prior biologic use for psoriasis
- geographic region
- prior topical steroid use 6 months prior to the baseline
- disease duration (< 1 year vs. ≥ 1 year)
- baseline PASI
- baseline sPGA (in addition to the original scale, extra section for combined scale 4 and 5 will also be added)
- baseline BSA

Medical history by SOC and PT for not resolved findings will be summarized descriptively for RTS.

9.5 PK Analyses

9.5.1 Analyses of Primary PK Endpoint(s)

9.5.1.1 Primary Analysis

The primary analysis of the primary PK endpoints, AUC_{tau} and C_{max}, between weeks 52 and 64 will be performed based on the PK Parameter Analysis Set according to the actual treatment groups (switching group versus continued use group).

The point estimates and 90% CIs for the GMRs between ABP 654 and ustekinumab for AUC_{tau} and C_{max} between weeks 52 and 64 will be estimated using an analysis of covariance (ANCOVA) model adjusting for stratification factors **and PK trough concentration at Week 28**. Prior to statistical testing, the PK parameters will be logarithmically transformed (natural log). Point estimates and 90% CIs for the mean difference in logarithmic PK parameters will be estimated using the ANCOVA model, which will then be transformed back to the original scale to obtain the point estimates and 90% CIs for GMR. To establish interchangeability, the 90% CIs of GMR of ABP 654 vs ustekinumab for AUC_{tau} and C_{max} from the primary analysis should fall within the prespecified similarity margin (0.8, 1.25).

9.5.1.2 Secondary Analyses

AUC_{tau} and C_{max} of ABP 654 and ustekinumab between weeks 52 and 64 will be listed by subject and summarized descriptively by treatment group using PK Parameter Analysis Set.

To assess the robustness of the primary analysis result, the ANCOVA analysis described above will be repeated using the Per-protocol PK Parameter Analysis Set.

9.5.2 Analyses of Secondary PK Endpoints

The analyses of the secondary PK endpoints of t_{max} between weeks 52 and 64 and $C_{trough,ss}$ between weeks 28 and 52 will be based on the PK Parameter Analysis Set according to the actual treatment groups. The median, min and max of t_{max} will be summarized descriptively by the treatment group. $C_{trough,ss}$ between weeks 28 and 52 will be summarized descriptively by visit and treatment group. The point estimates and 90% CIs for GMR for $C_{trough,ss}$ **at Week 28** between the two treatment groups will be estimated using an ANCOVA model adjusting for stratification factors. **The point estimates and 90% CIs for GMR for $C_{trough,ss}$ at Week 40 and Week 52 between the two treatment groups will be estimated using an ANCOVA model adjusting for stratification factors and PK trough concentration at Week 28.**

In addition, $C_{trough,ss}$ between weeks 28 and 52 will be summarized descriptively by visit and treatment group in the PK Concentration Analysis Set. Boxplots of $C_{trough,ss}$ between weeks 28 and 52 will also be generated for the PK Concentration Analysis Set by actual treatment group.

9.5.3 Analyses of Other PK Endpoint(s)

PK concentrations during the Run-in Period will be summarized descriptively by visit based on the RTS. Boxplots for trough concentrations during Run-in Period will be presented using the RTS.

PK concentrations between weeks 52 and 64 will be summarized descriptively by nominal visit and actual treatment group based on the PK Concentration Analysis Set. Individual and mean (+/- STD) serum concentration time-profiles between weeks 52 and 64 by actual treatment group will be presented graphically on semi-logarithmic and linear scales using the PK Concentration Analysis Set.

9.5.4 Subgroup Analyses

The primary PK endpoints will be summarized and compared within the binding ADA negative subgroup in the PK Parameter Analysis Set using similar methods described in Section 9.5.1.

9.6 Efficacy Analyses

9.6.1 Analyses of Primary Efficacy Endpoint(s)

None.

9.6.2 Analyses of Secondary Efficacy Endpoint(s)

9.6.2.1 Primary Analysis

The primary analysis for PASI percent improvement from day 1 at Week 64 will be performed based on the Per-protocol Efficacy Analysis Set according to the actual treatment groups with missing PASI score at post-baseline visits including Week 64 imputed by MI. The MI method will use the treatment allocation, the stratification factors and PASI assessment collected in previous visits to inform the plausible values to be imputed for missing Week 64 PASI values and will involve the following 3 or 4 steps, depending on the actual missing pattern observed in the data.

(1) If the missing pattern for PASI scores at weeks 40, 52 and 64 is not monotone, PROC MI with the MCMC option for imputing missing data will be used to impute data with sporadic missing values to create 20 data sets having monotone missing pattern. A sample code for this step is provided below:

PROC MI data=dataset seed=xxxx out =Datastep1

NIMPUTE = 20 MINIMUM = 0 MAXIMUM =72;

MCMC CHAIN= MULTIPLE IMPUTE=MONOTONE;

VAR treatment <stratification variables> PASIbase PASIw40 PASIw52 PASIw64;

RUN;

This sample code requires the treatment and the stratification variables to be binary and to be coded using numeric values. The data should also have no missing values for treatment variable, stratification variables and PASI baseline assessment.

(2) For each data set with monotone missing pattern generated in the step 1, PROC MI with regression option will be used to generate 20 complete data sets, providing 400 complete data sets. A sample code for this step is provided below:

PROC MI data=Datastep1 seed = xxxxx out=yyyy

NIMPUTE =20 MINIMUM =0 MAXIMUM=72;

CLASS treatment <stratification variables>;

MONOTONE METHOD = REG;

VAR treatment <stratification variables> PASIbase PASIw40 PASIw52 PASIw64;

BY imputedsetinstep1;

RUN;

If there is no sporadic missing PASI scores, i.e., the actual PASI data for weeks 40, 52 and 64 has monotone missing pattern, step (1) is skipped. In this case 50 complete data sets will be created using regression method.

(3) For each imputed data set, the PASI percent improvement from day 1 at Week 64 will be derived and the mean difference between the treatment groups in PASI percent improvement from day 1 at Week 64 will be estimated from an ANCOVA model adjusting for the baseline PASI value and the stratification factors.

(4) Results of these ANCOVA analysis from all the imputed data sets are combined using PROC MIANALYZE, generating an overall mean treatment difference estimate and associated standard error and 90% CI.

For the primary analysis of PASI 75 and PASI 100, missing PASI scores at Week 64 will be imputed by NRI. Using this imputation method, the point estimate and 90% CI of the risk difference in PASI 75 response rate and PASI 100 response rate at Week 64 will be estimated from the Mantel-Haenszel method for the point estimate, and the stratified Newcombe confidence limits for the 90% CI, adjusting for the IXRS stratification factors. These methods deviated from the method indicated in the protocol version 2.0, in order to resolve the possible convergent issue met when using generalized linear model with identify link function.

9.6.2.2 Secondary Analyses

These endpoints will also be summarized descriptively by actual treatment group based on Per-protocol Efficacy Analysis Set using observed data.

Additional sensitivity analysis will be conducted for PASI percent improvement from day 1 at week 64 by fitting the same ANCOVA model (i.e., adjusting for the baseline PASI

value and the stratification factors) using observed data for the FAS and according to randomized treatment groups and for the Per-protocol Efficacy Analysis Set according to the actual treatment groups.

9.6.3 Analyses of Other Efficacy Endpoint(s)

The analyses of the other efficacy endpoints in this section will be based on the Per-protocol Efficacy Analysis Set by actual treatment group.

The PASI percent improvement from day 1 at weeks 28, 40, and 52 and the PASI 75 and PASI 100 response rates at weeks 28, 40, and 52 will be summarized descriptively by treatment group based on observed data.

BSA absolute values and changes from baseline will be summarized descriptively by visit (at weeks 28, 40, 52, and 64) and treatment group using observed data. In addition, the adjusted mean difference in change from baseline in BSA at Week 64 will be estimated from an ANCOVA model adjusting for the baseline BSA value and the stratification factors after applying MI as described in Section 9.6.2.1.

sPGA scores will be summarized descriptively by visit (at weeks 28, 40, 52, and 64) and treatment group. sPGA response (0/1) will also be summarized descriptively by visit and treatment group using observed data. The point estimate and 90% CI of the risk difference in sPGA response (0/1) response rate at Week 64 will use same analysis method to PASI 75 response described in Section 9.6.2.1.

9.7 Safety Analyses

Safety analyses of the safety endpoints during the post randomization period and the Run-in Period will be performed based on the SAS and RTS, respectively, according to actual treatment received.

9.7.1 Adverse Events

For summary of AEs, the following summaries, (a) through (n), will be provided for the post randomization period. In addition, summaries (a), (e), (f), (k) without risk difference, (m), and (n) will be provided for the Run-in Period.

(a) overall summary of TEAEs

(b) TEAEs by PT

(c) TEAEs by SOC and PT

(d) TEAEs by SOC, PT, and maximum severity grade

(e) treatment-emergent SAEs by PT

(f) treatment-emergent SAEs by SOC and PT

(g) grade 3 or higher TEAEs by PT

(h) TEAEs leading to discontinuation from IP/study by PT

(i) fatal TEAEs by PT

(j) treatment-emergent EOIs by PT

(k) overall summary of treatment-emergent EOIs with risk difference

(l) **TEAEs leading to dose delayed of IP** by PT

(m) Treatment Emergent COVID-19 Adverse Events by Preferred Term

(n) Treatment Emergent SAEs occurring on or after presumed start date of COVID-19 infection by PT

Counting of AEs will be by subject, and subjects will be counted only once within each SOC or PT by study period. For tables categorized by severity, subjects with multiple events within a particular SOC or preferred term will be counted under the category of their most severe event with that SOC or preferred term.

AEs tabulated by preferred term will be presented in descending order of frequency of the switching group for the post Randomization period or the ustekinumab subjects for the Run-in Period.

The risk difference and 95% CI of each EOI in post randomization period will be calculated on the SAS using Wald asymptotic confidence limits or exact confidence limits **(Farrington-Manning score)** if the number of subjects for any treatment group is less than 25.

A listing of treatment-emergent SAEs and treatment-emergent SAEs occurring on or after presumed start date of COVID-19 infection will be provided for the post randomization period and the Run-in Period separately.

9.7.2 Laboratory Test Results

Laboratory data (hematology, serum chemistry, and urinalysis) will be converted to Système International units for reporting and processing purposes.

For the Post-randomization Period, absolute values and changes from baseline by visit will be presented descriptively. In addition, shift tables of the maximum post randomization laboratory toxicity based on CTCAE grading relative to randomization at Week 28 will be presented. The shift tables will consider all post-randomization (schedule and unscheduled) laboratory results in the determination of the maximum post randomization laboratory toxicity. Furthermore,

subject incidence tables of grade ≥ 3 laboratory toxicities will be provided. Standard ranges will be used for the laboratory analysis.

For the Run-in Period, absolute values and changes from baseline by visit will be presented descriptively.

Lab assessments will be grouped for summary as follows:

Hematology: hemoglobin, hematocrit, red blood cells, platelets, total white blood cell (WBC) count, differential WBC count, and absolute neutrophil count.

Biochemistry: **albumin, alkaline phosphatase, alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine, gamma-glutamyl transferase, glucose(random), potassium, sodium, total protein, blood urea nitrogen and total bilirubin.**

Urinalysis: **pH, specific gravity, and creatinine.**

9.7.3 Vital Signs

Observed and change from baseline for each vital sign parameter will be summarized descriptively by visit for the Post-randomization Period.

9.7.4 Physical Measurements

None.

9.7.5 Electrocardiogram

For the Run-in Period, for patients in the Run-in Treated Set, their ECG assessments will be summarized by visit and treatment arm. The by visit summary will include the number and percentage of patients that have an assessment value of normal, abnormal & non clinically significant (NCS), and abnormal & clinically significant (CS).

Similarly, for the Post-randomization Period, for patients in the Safety Analysis Set, ECG assessment will be summarized by visit and treatment arm.

In addition, for patients in the Safety Analysis Set, shift tables of the worst post randomization ECG results (normal, abnormal & non clinically significant (NCS), abnormal & clinically significant (CS) and missing) relative to randomization at Week 28 will be presented. The shift tables will consider all post-randomization (schedule and unscheduled) ECG results in the determination of the worst post randomization assessment.

9.7.6 Antibody Formation

The number and percent of subjects developing binding or neutralizing ADA will be tabulated descriptively by treatment group and visit in the SAS for the post randomization period and in the RTS for the Run-in Period.

Developing antibody incidence during the Post-randomization Period is defined as the number of subjects in the SAS who have a positive result post randomization and have never tested positive (i.e., negative or no results) prior to the first dose of post randomization IP divided by **the number of subjects in the SAS who have antibody negative or no result prior to the first dose of post-randomization IP.**

Developing antibody incidence during the Run-in Period is defined as the number of subjects in the RTS with a negative or no antibody result at baseline and a positive antibody result during the Run-in Period divided by the number of subjects in the RTS with at least one post baseline result during the Run-in Period.

The incidence of transient antibody will also be summarized for each study period. A transient antibody result is defined as a positive result during a study period with a negative result at the subject's last visit tested within the respective study period.

9.7.7 Exposure to Investigational Product

Exposure to ABP 654/ustekinumab will be summarized descriptively by actual treatment group for the RTS for the Run-in Period and for the SAS for the Post-randomization Period, respectively. Summary statistics will be provided for the total number of doses administered, total dose received, subjects with at least one dose delay/not administered and reasons (including whether or not it is due to COVID-19 related reasons), subjects with at least one dose of IP missed due to COVID-19 related reasons, and total duration of IP exposure.

A subject listing of each administered lot number(s) for IP and a listing of unique manufacturing lot numbers used in the study will be provided.

9.7.8 Exposure to Non-investigational Product

None.

9.7.9 Exposure to Other Protocol-required Therapy

None.

9.7.10 Exposure to Concomitant Medication

Prior and concomitant medications will be coded using the latest available World Health Organization Drug Dictionary as of the time of the final analysis.

For the Run-in Period, concomitant medication use by PT is summarized descriptively for the RTS and for the SAS by actual treatment group.

For the Post-randomization Period, concomitant medication use by PT is summarized descriptively by actual treatment group based on SAS.

10. Changes From Protocol-specified Analyses

The protocol specifies EOI of posterior reversible encephalopathy syndrome in Section 2.2. The SMQ / AMQ search term for this EOI is reversible posterior leukoencephalopathy syndrome (RPLS). To keep consistent with the search term, the term RPLS is used in this SAP and will be used in the outputs to describe this EOI.

The method for estimating the risk difference in PASI 75 response rate and PASI 100 response rate at Week 64 has been changed from the protocol. The Mantel-Haenszel method will be used for the point estimate, and the stratified Newcombe confidence limits will be used for the 90% CI, adjusting for the IXRS stratification factors. These methods deviated from the method indicated in the protocol version 2.0, in order to resolve the possible convergent issue met when using generalized linear model with identify link function.

11. Literature Citations / References

Ke C, Wang J, Zhang C, Jiang Q, Snapinn S. On errors in stratified randomization. Statistics in Biopharmaceutical Research. 2017 Apr 3;9(2):225-33.

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Feldman SR, Krueger GG. Psoriasis assessment tools in clinical trials. Annals of the rheumatic diseases. 2005 Mar 1;64(suppl 2):ii65-8.

12. Prioritization of Analyses

None.

13. Data Not Covered by This Plan

None.

14. Appendices

Appendix A. List of Events of Interest and the Associated SMQ and EOI Searching Strategies

Event of Interest	Category of EOI query (SOC, SMQ / Amgen query)	Search Strategy
Serious systemic hypersensitivity reactions	Hypersensitivity (SMQ)	Broad – CTCAE grade >=3 or the serious TEAE terms with cut-off period up to 2 days after IP administration
Facial palsy	Facial paralysis	PT
Pustular psoriasis	Pustular psoriasis	PT
Erythrodermic psoriasis	Erythrodermic psoriasis	PT
Serious infections (including mycobacterial and salmonella infections)	Infections and Infestations (SOC)	CTCAE grade >=3 or the serious TEAE terms
Malignancy	Malignancies (SMQ)	Narrow
Cardiovascular events	Cardiac disorders (SOC)	SOC
Reversible posterior leukoencephalopathy syndrome	Reversible posterior leukoencephalopathy syndrome (Amgen query)	Narrow
Serious depression including suicidality	Depression and suicide/self- injury (SMQ)	CTCAE grade >=3 or the serious TEAE terms (broad)
Venous thromboembolism	Embolic and thrombotic events, venous (SMQ)	Narrow