US Specific Statistical Analysis Plan

Protocol Title:	A Phase 3, Multicenter, Randomized, Double-Blind Study Evaluating the Efficacy and Safety of ABP 654 Compared with Ustekinumab in Subjects With Moderate to Severe Plaque Psoriasis
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Table of Contents

List of Table

List of Figures

List of Abbreviations and Definition of Terms

Abbreviation or Term	Definition/Explanation
ADA	Anti-drug Antibody
ADaM	Analysis Data Model
AE	Adverse Event
ALT	Alanine Aminotransferase
ANCOVA	Analysis of Covariance
AST	Aspartate Aminotransferase
BMI	Body Mass Index
BSA	Body Surface Area
BUN	Blood Urea Nitrogen
BW	Body Weight
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CIOMS	Council for International Organizations of Medical Sciences
CRF	Case Report Form
CRO	Contract Research Organization
CTCAE	Common Terminology Criteria for Adverse Events
DMC	Data Monitoring Committee
EDC	Electronic Data Capture
EOI	Event of Interest
EOS	End of Study
FA	Final Analysis
FAS	Full Analysis Set
FDA	Food and Drug Administration
ICF	Informed Consent Form
ICH	International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
IP	Investigational Product
IPD	Important Protocol Deviation
IXRS	Interactive Web/Voice Response System
LOCF	Last Observation Carried Forward
MAR	Missing at Random
MCAR	Missing Completely at Random
MedDRA	Medical Dictionary for Regulatory Activities
NCI	National Cancer Institute
NRI	Non-Responder Imputation

PA	Primary Analysis
PASI	Psoriasis Area Severity Index
PK	Pharmacokinetic(s)
PP	Per Protocol
PT	Preferred Term
Q1	25th percentile
Q3	75th percentile
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Safety Analysis Set
SDTM	Standard Data Tabulation Model
sPGA	Static Physician's Global Assessment
TEAE	Treatment-Emergent Adverse Event
TFL	Tables, Figures and Listings
WBC	White Blood Cell
WHO-DD	World Health Organization Drug Dictionary

1. Introduction

The purpose of this US-specific Statistical Analysis Plan (SAP) is to provide details of the statistical analyses that are outlined within the protocol for ABP 654 study 20190232 (Final, dated 6 August 2020) and the additional analyses to support the BLA submission in the US. The scope of this plan includes the primary analysis (PA) and the final analysis (FA) that are planned and will be executed by the designated contract research organization (CRO), Parexel International. There is a separate Global SAP to support the marketing application for other countries.

2. Objectives, Endpoints and Hypotheses

2.1 Objectives and Endpoints

Objectives	Endpoints
Primary	***Primary efficacy endpoint***
To compare the efficacy of ABP 654 with ustekinumab in subjects with moderate to severe plaque psoriasis.	Psoriasis area severity index (PASI) percent improvement from baseline to week 12
	Secondary efficacy endpoints
	• PASI percent improvement at other timepoints • PASI 75 response throughout the study • PASI 100 response throughout the study • Static Physician's Global Assessment (sPGA) responses (0/1) at week 12 and week 52 • Body surface area (BSA) change from baseline at week 12 and week 52
Secondary	
To assess the safety and immunogenicity of ABP 654 compared to ustekinumab.	• Treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) • Events of interest (EOI) • Incidence of anti-drug antibodies

2.2 Hypotheses and/or Estimations

The study will assess the hypothesis that there are no clinically meaningful differences between ABP 654 and ustekinumab treatment arms in the primary efficacy endpoint: PASI percent improvement from baseline to week 12. Per the global SAP, this primary efficacy endpoint will be evaluated by comparing the 2-sided 95% Confidence Interval

(CI) of the mean difference of PASI percent improvement from baseline to week 12 between ABP 654 and ustekinumab arms with an equivalence margin of (-15, +15). For the US BLA, this primary efficacy endpoint will be evaluated by comparing the 2-sided 90% CI of the mean difference of PASI percent improvement from baseline to week 12 between ABP 654 and ustekinumab arms with an equivalence margin of (-10, +10).

3. Study Overview

3.1 Study Design

This is a randomized, double-blind, active-controlled phase 3 study in adult subjects with moderate to severe plaque psoriasis. This study is planned to be conducted globally at sites in North America and Europe.

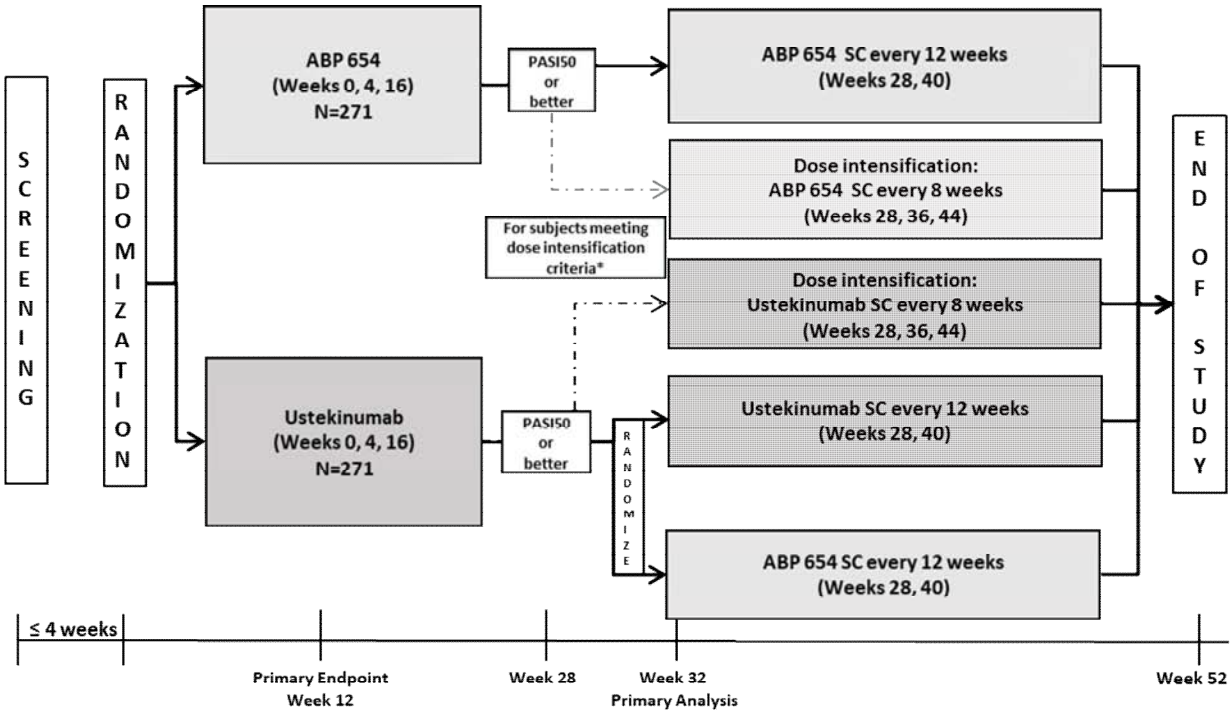
Approximately 542 adult subjects will be randomized (approximately 271 in the ABP 654 group and approximately 271 in the ustekinumab group). See Section 3.2 for sample size determination. Randomization will be stratified based on prior biologic use for psoriasis (yes versus [vs] no (no more than 50% of the overall study population will have prior biologic use for psoriasis), baseline body weight (BW) (≤ 100 kg vs > 100 kg), and geographic region. Subjects will be randomized (1:1) to Treatment Group A (ABP 654) or Treatment Group B (ustekinumab). Subjects will receive ABP 654 or ustekinumab at a dose of 45 mg (baseline BW ≤ 100 kg) or 90 mg (baseline BW > 100 kg) administered subcutaneously (SC) on day 1 (week 0), week 4, and week 16. The primary endpoint (PASI percent improvement from baseline to week 12) will be evaluated at week 12.

At week 28, subjects who do not achieve a PASI 50 response or better improvement will be considered to have completed the study and will complete end of study procedures (i.e., week 52 procedures), and those unable to complete the week 28 visit, or do not have a PASI assessment completed, will be discontinued from the study (see Figure 1). Subjects with a PASI 75 response or better improvement will continue on the study and will be re-randomized in a blinded fashion such that subjects initially randomized to Group A (ABP 654) will continue to receive ABP 654 and those in Group B (ustekinumab) will re-randomized, using the same stratification factors as the original randomization, 1:1 to either continue on ustekinumab (Treatment Group B1) or switch to ABP 654 (Treatment Group B2). Subjects will receive investigational product at week 28 and the last dose of investigational product at week 40. For subjects with PASI 50 response or better but less than PASI 75 response at week 28, based on the Investigator's discretion, the dose frequency may be increased to Q8W. Subjects with baseline BW ≤ 100 kg will receive 45 mg Q8W and subjects > 100 kg at baseline will

receive 90 mg Q8W at weeks 28, 36, and 44. These subjects will continue on the originally assigned treatment with dose intensification and will not be rerandomized. Subjects that do not dose intensify will be re-randomized.

An external, independent data monitoring committee (DMC) will evaluate the safety data throughout the study. A SAP for the DMC will be prepared separately.

Figure 1 Study Schematic



- Subjects with body weight at baseline ≤100kg receive 45mg SC; >100kg receive 90 mg SC
- At week 28, non-responders (ie, subjects not achieving PASI 50 response of better) will be considered to have completed the study and will complete the end of study procedures (ie, week 52 procedures) at week 28. Subjects missing the week 28 visit or missing the PASI assessment at week 28, will be discontinued from the study.
- *For subjects with PASI 50 response or better but less than PASI 75 response at week 28, based on investigator's discretion, subjects may increase dose frequency to every 8 weeks (Q8W). Subjects with body weight at baseline ≤ 100kg will receive 45mg Q8W and subjects > 100kg at baseline will receive 90mg Q8W at weeks 28, 36, and 44. These subjects will continue on original treatment and will NOT be re-randomized.

PASI = Psoriasis Area and Severity Index; Q8W = every 8 weeks; Q12W = every 12 weeks; SC = subcutaneous

3.2 Sample Size

Approximately 542 adult subjects will be randomized in a 1:1 ratio to receive investigational product (IP) (ABP 654 or ustekinumab) stratified by prior biologic use for psoriasis, geographic region, and baseline BW. For the global primary analysis, the sample size will provide greater than 95% power to demonstrate equivalence at a significance level of 0.025 on the primary efficacy endpoint of PASI percent improvement from baseline to week 12 with an equivalence margin of (-15, +15), assuming a common standard deviation of 30.0 (Leonardi, 2008; Papp, 2008), a true mean difference of 0 in the primary efficacy endpoint between the 2 groups, and a 10% dropout rate. For the US primary analysis, the sample size will provide greater than 90% power to demonstrate equivalence at a significance level of 0.05 on the primary efficacy endpoint of PASI percent improvement from baseline to week 12 with an equivalence margin of (-10, +10), assuming a common standard deviation of 30.0, a true mean difference of 0 in the primary efficacy endpoint between the 2 groups, and a 10% dropout rate.

3.3 Randomization

Assignment to the treatment arms will be based on a computer-generated randomization schedule created before the start of the study. The randomization schedule will be generated using a permuted block design within each stratum. Interactive Voice/Web Response System (IXRS) data is integrated into the electronic data capture (EDC) system for subject enrollment.

4. Covariates and Subgroups

4.1 Planned Covariates

Unless stated otherwise, the following stratification factors will be adjusted as covariates in models or will be used to examine treatment effect in subgroups:

- Prior biologic use for psoriasis (yes vs. no)
- Baseline BW (≤ 100 kg vs. > 100 kg)
- Geographic region

For continuous endpoints (e.g. PASI percent improvement from baseline, BSA change from baseline), the relevant baseline scores will be used as covariates in models.

In addition, the following covariates may be used for further exploration in subgroups or as covariates:

- Age (< 65 years vs. ≥ 65 years)

- Race (White vs. Non-White)
- Gender
- Disease duration (< 1 year vs. ≥ 1 year)

Covariate values may be discordant if collected via the case report form (CRF) and 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).

For subgroup analyses where the subgroup factor is a stratification variable, an analysis similar to the primary analysis (except the inclusion of the subgroup factor) should be done for each subgroup defined by the CRF values of the subgroup factor.

4.2 Subgroups

Please refer to Section 4.1.

5. Definitions

5.1 General

Actual Treatment Received

Defined as the type of IP (ABP 654 or ustekinumab) received for the majority of doses administered. In the case of a tie, the actual treatment received will be assigned to ABP 654. For the Entire Study period, the actual treatment sequence for subjects who are re-randomized and treated post re-randomization will be defined based on the actual treatments received during the through week 28 and post week 28 study periods (ABP 654/ABP 654, ustekinumab/ustekinumab, or ustekinumab/ABP 654).

Baseline

Unless stated otherwise, the baseline is defined as the last non-missing assessment taken prior to or on the date of first dose of administration of IP. 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. For subjects who are randomized but not dosed after the randomization, the baseline is defined as the last non-missing assessment prior to or on the date of randomization.

Change from Baseline

Change from baseline is defined as (value at post-baseline visit – value at baseline). A change from baseline will not be calculated if the baseline value is missing.

Concomitant and Prior Medication

Prior medications are defined as medications with a stop date prior to first dose of IP. 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.

Disease Duration

The disease duration is the number of years from the date of diagnosis of psoriasis to the date of randomization, which will be derived based on the table below. No imputation will be done for disease diagnosis date, but to avoid disease duration of zero, 1 month (or 1/12 years) may be added.

Table 1: Calculation of the Duration of Psoriasis

Observed portion	Missing portion	Formula to Calculate Duration
Year, Month, Day		(Date of Randomization – Date of Psoriasis Diagnosis + 1)/365.25
Year, Month	Day	[Year(Date of Randomization) - Year(Date of Psoriasis Diagnosis)] + [Month(Date of Randomization) - Month(Date of Psoriasis Diagnosis)]/12*
Year	Month, Day	[Year(Date of Randomization) - Year(Date of Psoriasis Diagnosis)] *

*if the duration equals 0, add 1 month or 1/12 years.

Dose Intensification

A dose intensification subject is defined as a subject who has a PASI 50 response or better but less than PASI 75 response at week 28, and, based on the Investigator's discretion, increases dose frequency to Q8W. These subjects continue on original assigned treatment with dose intensification and are not re-randomized. The dose intensification assignment will be derived directly from the "Does Subject Need Dose Intensification?" field on the CRF, and will not be re-derived based on actual dose received.

End of Study (EOS) Date

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

First Dose Date

First Dose Date is defined as the date the subject receives the first dose of IP.

Last Dose Date

Last Dose Date for the subject is the date the subject receives the last dose of IP.

Last Observation Carried Forward (LOCF)

A method of imputation where missing post-baseline data will be imputed by carrying forward the last non-missing post-baseline value for that endpoint. Baseline values will not be carried forward.

Non-Responder Imputation (NRI)

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

Study Analysis Visit

Since the actual visit for a subject may not exactly coincide with their scheduled visit date, the actual visit date is mapped to the study analysis visit as follows based on the type of data.

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, PASI, sPGA, BSA:

Study Analysis Visit	Target Day	Study Day	Interval (days)
Baseline	1	≤1	NA
Week 4	29	2-57	56
Week 12	85	58-99	42
Week 16	113	100-155	56

Post week 28 Efficacy, for re-randomized subjects:

Study Analysis Visit	Target Day	Study Day	Interval (days)
Week 28	197	156-239	84
Week 40	281	240-323	84
Week 52	365	≥324	NA

Post week 28 Efficacy, for Dose Intensification subjects:

Study Analysis Visit	Target Day	Study Day	Interval (days)
Week 28	197	156-225	70
Week 36	253	226-281	56
Week 44	309	282-337	56
Week 52	365	≥338	NA

For vital signs, safety laboratory[a] (including serum chemistry, hematology, urinalysis)

Study Analysis Visit	Target Day	Study Day	Interval (days)
Baseline[b]	1	≤1	NA
Week 4	29	2-57	56
Week 12	85	58-99	42
Week 16	113	100-155	56

Post week 28 Vital signs, safety laboratory[a] for re-randomized subjects:

Study Analysis Visit	Target Day	Study Day	Interval (days)
Week 28[b]	197	156-211	56
Week 32	225	212-253	42
Week 40	281	254-323	70
Week 52	365	≥324	NA

Post week 28 Vital signs, safety laboratory[a] for Dose Intensification subjects:

Study Analysis Visit	Target Day	Study Day	Interval (days)
Week 28[b]	197	156-211	56
Week 32	225	212-239	28
Week 36	253	240-281	42
Week 44	309	282-337	56
Week 52	365	≥338	NA

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

[b] If a subject has laboratory measurements on the same day as the first dose date at week 0 or week 28 but at a time after the first dose of IP at week 0 or week 28, respectively is administered, the laboratory measurements will not be defined as baseline or week 28, but will be included in consideration for week 4 or 32 measurements, respectively.

The rules above for selecting a visit from multiple ones within the same visit window are not applicable to retest values of laboratory data. If the laboratory measurement is a retest, the retest value will be chosen.

For anti-drug antibody (ADA), all subjects:

Study Analysis Visit	Target Day	Study Day
Baseline[a]	1	≤1
by Week 4	29	≤57
by Week 12	85	≤99

Post week 28 ADA, for re-randomized subjects:

Study Analysis Visit	Target Day	Study Day
by Week 28[a]	197	≤211
by Week 32	225	≤253
by Week 40	281	≤323

by Week 52	365	NA

Post week 28 ADA, for Dose Intensification subjects:

Study Analysis Visit	Target Day	Study Day
by Week 32	225	≤239
by Week 52	365	NA

[a] If a subject has ADA samples on the same day as the first dose date at week 0 or week 28 but at a time after the first dose of IP at week 0 or week 28, respectively is administered, the ADA samples will not be defined as baseline or week 28, but will be included in consideration for week 4 or 32 samples, respectively.

For PK, all subjects:

Study Analysis Visit	Target Day	Study Day	Interval (days)
Baseline[a]	1	≤1	NA
Week 4	29	2-57	56
Week 12	85	58-99	42

Post week 28 PK, for re-randomized subjects:

Study Analysis Visit	Target Day	Study Day	Interval (days)
Week 28[a]	197	156-211	112
Week 32	225	212-253	42
Week 40	281	254-323	70
Week 52	365	≥324	NA

Post week 28 PK, for Dose Intensification subjects:

Study Analysis Visit	Target Day	Study Day	Interval (days)
Week 28[a]	197	156-211	112
Week 32	225	212-239	28
Week 52	365	≥338	NA

[a] If a subject has PK measurements on the same day as the first dose date at week 0 or week 28 but at a time after the first dose of IP at week 0 or week 28, respectively is administered, the PK measurements will not be defined as baseline or week 28, but will be included in consideration for week 4 or 32 measurements, respectively.

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 the subject receives IP. For subjects who are randomized but not dosed after randomization, Study Day 1 is defined as the date of study randomization.

Study Period

- Through week 12:

It is defined as the time period from Study Day 1 to Study Day 99 or to the EOS visit for subjects who discontinue the study prior to the week 12 visit.

- Through week 28:

It is defined as the time period from Study Day 1 to the first dose post re-randomization for re-randomized and treated subjects, or to the EOS visit for subjects not re-randomized or for subjects who are re-randomized but not treated post re-randomization, or to the first post (including) week 28 dose for subjects who dose intensify.

- Post week 28:

For subjects who are re-randomized and treated post re-randomization, it is defined as the time period from the first dose post re-randomization to the EOS visit or analysis data cutoff date, whichever is earlier. For subjects who dose intensify, it is defined as the time period from the first post (including) week 28 dose to the EOS visit or analysis cutoff date, whichever is earlier. Subjects who are re-randomized and treated post re-randomization are classified according to their full treatment sequence: ABP 654/ABP 654, ustekinumab/ustekinumab, or ustekinumab/ABP 654. Subjects who dose intensify are classified according to their post-week 28 treatment: ABP 654 or ustekinumab.

- Entire Study:

It is defined as the time period throughout the study from Study Day 1 to the EOS visit or analysis data cutoff date, whichever is earlier. Subjects are re-randomized and treated post re-randomization are classified according to their full treatment sequence: ABP 654/ABP 654, ustekinumab/ustekinumab, or ustekinumab/ABP 654. Subjects who dose intensify will not contribute to Entire Study summaries.

Study Randomization

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

Study Re-Randomization

Study re-randomization is defined as when a subject receives a second random treatment allocation at week 28 via the IXRS system. In order to maintain the blind, subjects from both treatment arms will be re-randomized in a blinded fashion such that subjects initially randomized to Group A (ABP 654) will continue to receive ABP 654 and those in Group B (ustekinumab) will be re-randomized 1:1 to either continue on ustekinumab (Treatment Group B1) or switch to ABP 654 (Treatment Group B2).

Total IP Exposure Duration

The total IP exposure duration for a subject (in weeks) for each study period (through week 12, through week 28, post week 28, and Entire Study) will be derived as: the period end date for the subject – the period start date for the subject +1.

The definitions for each study period are defined in section 5.1.

5.2 Efficacy

Body Surface Area

The percent of BSA affected (%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 50% qualifies a subject as being a PASI 50 responder, 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.

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).

5.3 Safety

AE 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 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

Additional adverse events (AE) may be identified as being of interest during the study and prior to the unblinding for the primary analysis.

The detailed search strategies for the EOIs are included in Appendix 1.

Laboratory Test Results

In general, laboratory test results will be associated with the study period in which they are taken. However, laboratory test results taken on the same day as the first dose post re-randomization or post dose intensification, and before the first dose post re-randomization or post dose intensification will be counted in the through week 28 period.

Treatment-emergent Adverse Event

Treatment-emergent adverse events (and serious TEAEs) are defined as those that occur on or after the time of first treatment up to EOS visit.

A treatment-emergent AE (TEAE) for subjects is defined for each study period, when applicable. A TEAE for a given study period is defined as an AE that begins in the respective study period (see definition of Study Period in section 5.1).

If the AE starts on the same day as the first dose of IP, then the flag indicating whether the AE started prior to the first dose on the adverse event CRF page will be used. For re-randomized or dose intensified and treated subjects, an AE that starts on the same day as the first dose post re-randomization (or post dose intensification) will be considered as a TEAE post week 28.

6. Analysis Sets

6.1 Full Analysis Set

The Full Analysis Set (FAS) will include all randomized subjects. It will be analyzed according to the treatment the subject is randomized to (regardless of actual treatment received). This analysis set will be the primary set used for analyses/summaries of the primary efficacy endpoint, as well as for all secondary efficacy endpoints.

6.2 Re-randomized Full Analysis Set

The Re-randomized FAS will be a subset of the FAS who are re-randomized. It will be analyzed according to the treatment sequence the subject is re-randomized to (regardless of actual treatment received). This analysis set will be the set used for analyses/summaries of efficacy for the Entire Study period.

6.3 Safety Analysis Set

The Safety Analysis Set (SAS) will include all randomized subjects who receive at least one dose of IP. It will be analyzed according to actual treatment received. This analysis set will be used for summaries of safety data as well as immunogenicity data and PK data.

6.4 Re-randomized Safety Analysis Set

The Re-randomized Safety Analysis Set will be a subset of the SAS and will include all SAS subjects who are re-randomized and receive at least one dose of IP after re-randomization. It will be analyzed according to actual treatment sequence received prior to and post week 28. This analysis set will be used for summaries of safety, immunogenicity, and PK data post week 28 and for the Entire Study period.

6.5 Per Protocol Set

The Per Protocol (PP) Analysis Set will include all randomized subjects in the FAS who have completed dosing at Study Day 1 and week 4 and have completed PASI assessment at week 12 without experiencing an important protocol deviation that may affect their evaluation for the primary endpoint of the study. Important protocol deviations that could affect the primary endpoint will be defined and agreed upon before unblinding for the primary and final analyses. This analysis set will be used for sensitivity analyses for the primary and key secondary efficacy endpoints. Analyses will be based on actual treatment the subject received. Note that per-visit analyses that use the PP Analysis Set will only be summarized for through week 12, which is the timepoint that the primary endpoint is evaluated at.

7. Planned Analyses

7.1 Interim Analysis and Early Stopping Guidelines

No interim analyses are planned for this study.

7.2 Primary Analysis

The PA for the study will be performed when all randomized subjects reach week 32 or terminate early, and the analysis will comprise at least 32 weeks of efficacy, safety, immunogenicity, and PK data.

All data collected by the time of data cut will be included in the PA. An independent unblinded team who are not involved in the operations of the study after PA database lock will perform the PA.

7.3 Final Analysis

The final analysis will be performed at the end of study when all randomized subjects reach the week 52 visit or terminate early from the study.

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.

The data review and cleaning 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 primary 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 primary analysis.

8.3 Handling of Missing and Incomplete Data

The analysis of the primary efficacy endpoint will be performed in the FAS with missing post-baseline PASI scores imputed using LOCF. Any missing score (other than the baseline value) will be imputed using the score from the previous post baseline visit. In addition, for the primary endpoint, a mixed model repeated measures analysis and

tipping point analyses will be performed to explore the sensitivity of the results based on different assumptions for the missing data.

Additionally, PASI 75 and PASI 100 response rates will be summarized at each scheduled timepoint via NRI in the FAS.

Similar to PASI, missing post baseline BSA assessments will be imputed using LOCF, and missing post baseline sPGA assessments will be imputed using NRI.

Missing safety, ADA and PK 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:

Table 2: Imputation Rules for Partial or Missing Start Dates

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 Validation of Statistical Analyses

All statistical report outputs will be produced 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

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, median, Q1, and Q3 will be presented to one decimal place greater than the original data, standard deviation will be to 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.

CIs 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:

- Number of subjects randomized at the initial randomization (2 treatment groups) and re-randomization (3 treatment sequences) by geographic region, country, and site.
- Subject disposition before and after re-randomization (including number of subjects who are randomized, treated with ABP 654/ustekinumab, completed the week 28 visit, not re-randomized at week 28 with reasons for not re-randomized, re-randomized at week 28, treated post week 28 re-randomization, completed study, and discontinued study with reasons for discontinuation) for each of the analysis sets defined in Section 6. Note that completed study will include PASI 50 non-responders who completed study at week 28 and subjects who completed study at week 52.
- Number of screened subjects and number of subjects in each analysis set by initial randomized treatment, and reasons for exclusion from each analysis set.
- Randomization list of subjects and their actual versus randomized and/or re-randomized treatment groups for all randomized subjects.

9.3 Important 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 PP Analysis Set. The PP Analysis Set must be finalized prior to database lock of each analysis (PA and FA).

A summary of incidence of IPDs will be tabulated using number and percentage of subjects by deviation type and initial randomized treatment through week 28 for the FAS and for the Entire Study for the Re-randomized FAS. In addition, the summary of incidence of IPDs will be generated for the subset of dose intensification subjects post week 28. A listing of subjects with IPDs will be provided (with a flag indicating whether the deviation leads to exclusion from the PP Analysis Set).

9.4 Demographic and Baseline Characteristics

The following demographics and baseline characteristics will be summarized by treatment for the FAS, PP Analysis Set, SAS, and Dose Intensified subjects, and by treatment sequence for the subjects in the Re-randomized FAS, and the Re-randomized SAS:

- age (in years, at time of signing informed consent form (ICF)) and age category (< 65 vs ≥ 65),
- race,
- sex,
- ethnicity,
- height,
- weight,
- body mass index (BMI),
- geographic region,
- prior biologic use for psoriasis
- prior topical steroid use
- disease duration (< 1 year vs. ≥ 1 year)
- baseline PASI
- baseline sPGA
- baseline BSA

9.5 Efficacy Analyses

9.5.1 Analyses of Primary Efficacy Endpoint

The primary efficacy endpoint is the PASI percent improvement from baseline to week 12.

9.5.1.1 Primary Analysis

The primary analysis will be performed using the FAS based on the randomized treatment and LOCF data.

Analysis will assess the hypothesis that there are no clinically meaningful differences between ABP 654 and ustekinumab treatment arms in PASI percent improvement from baseline to week 12.

Clinical equivalence of the primary endpoint will be evaluated by comparing the 2-sided 90% CI of the mean difference of PASI percent improvement from baseline to week 12 between ABP 654 versus ustekinumab with equivalence margin of (-10, +10). If the 2-sided 90% CI is within the pre-specified global equivalence margin (-10, +10), then it is declared that ABP 654 and ustekinumab is clinically similar. The point estimate of the mean difference in PASI percent improvement from baseline to week 12 between ABP 654 and ustekinumab and its corresponding 2-sided 90% CI will be obtained from an Analysis of Covariance (ANCOVA) model with treatment, baseline PASI value, and the stratification factors of baseline BW, prior biologic use, and region as covariates. Regions with small number of subjects in them will be combined.

9.5.1.2 Sensitivity Analyses

To assess the robustness of the primary analysis result, the ANCOVA analysis described above will be repeated using the FAS and also on the PP Analysis Set based on observed data.

In addition, a repeated-measures analysis based on the FAS will be performed as a sensitivity analysis. Besides the stratification factor of region, the baseline PASI value, visit, treatment, and treatment-by-visit interaction will be included in the model, with visit as a categorical variable. The point estimate of the mean difference in PASI percent improvement from baseline to week 12 between ABP 654 and ustekinumab and its corresponding 2-sided 90% CI will be obtained. The mixed model repeated measures analysis will be implemented using PROC MIXED and a compound symmetry covariance structure in SAS®.

Another sensitivity analysis based on the FAS will be done to explore the impact of the baseline covariates in section 9.4 on mean difference in PASI percent improvement from baseline to week 12 in addition to the stratification factors of baseline BW, prior biologic use, region and the baseline PASI value. The LOCF data will be used in this analysis. A stepwise model selection (with <0.25 p-value to enter the model and <0.1 to stay in the model) will be fit using PROC GLM and will be used to determine if any of the covariates have significant impact on the outcome variable. The final ANCOVA model will be fit using PROC GLM and will maintain treatment, the stratification factors of baseline BW,

prior biologic use, region, the baseline PASI value, and the covariates identified by the stepwise model.

In addition, the mean difference in the PASI percent improvement from baseline to week 12 between the two group will be examined in the subgroups as defined by the covariates in Section 4.1. These additional explorations will be performed on the FAS by using the ANCOVA analysis on LOCF data.

The rate of missing PASI assessments at week 12 will be tabulated with reasons, such as missing baseline, outside of the defined week 12 analysis time frame (study day 58-99) and discontinued from the study early prior to week 12. Discontinuations from the study prior to week 12 will be further broken down by reasons on the EOS CRF page.

Tipping point analyses will be performed using the FAS to explore the sensitivity of LOCF primary analysis results to violations in assumptions about the missing data (i.e., to various MCAR and missing at random (MAR) assumptions). Assumptions under which the 90% CI no longer rules out unacceptable differences in efficacy as determined by PASI percent improvement from baseline to week 12 between ABP 654 and ustekinumab will be identified.

In this analysis, all the observed data will be included as non-missing. The analysis will be performed using a general three-step approach:

(1) Multiple imputation will be done using PROC MI to generate 20 imputed datasets by imputing missing data assuming monotone missing pattern and that subjects with missing data have, on average, worse or better efficacy compared to those who have values. The mean difference between the (unobserved) missing values and observed values (refer to as shift) can vary independently for the different treatment groups.

(2) Each of these imputed datasets (which contains identical values of non-missing data, but different values imputed for missing data) is analyzed using standard SAS® procedure, e.g., PROC GLM.

(3) Results from all imputed datasets are then combined together for overall inference using PROC MIANALYZE.

For PASI percent improvement from baseline to week 12, seven equally spaced shifts (e.g., -15 to 15 by 5) for the PASI percent improvement from baseline for subjects with missing data will be explored.

Sensitivity analyses may be performed for the situation where a subject is re-randomized via IXRS based on an incorrect PASI percent improvement at week 28 calculated by the site (i.e. the improvement percentage is too low, and they are still re-randomized). Should this occur in greater than 10 subjects, the following efficacy and safety analyses that use the Re-randomized FAS and Re-randomized SAS will be regenerated only using the group of subjects that are correctly re-randomized: observed PASI percent improvement from baseline post week 28, observed PASI 75 and PASI 100 response rates post week 28, observed sPGA response rates post week 28, observed BSA change from baseline post week 28, and the overall summary of TEAEs post week 28.

9.5.1.3 Impact of COVID-19 on missing data

The COVID-19 global pandemic could have a profound impact on the amount and pattern of missing primary efficacy results for various reasons, e.g.:

- Exorbitant amount of missing endpoint data due to infection
- Extended site closures / Inability to obtain an assessment
- Lack of drug supply

These can reasonably be treated as missing completely at random (MCAR), and hence are not expected to introduce bias.

9.5.2 Analyses of Secondary Efficacy Endpoint(s)

All secondary efficacy endpoints will be analyzed descriptively.

Analyses for secondary efficacy endpoints will be provided by visit from Study Day 1 to EOS. In general, treatment comparison of interest for timepoints prior to re-randomization (week 28 included) include the comparison between treatment ABP 654 and ustekinumab; treatment comparison of interest for timepoints post re-randomization (week 28) include the comparison between treatment sequence ABP 654/ABP 654 and ustekinumab/ustekinumab and the comparison between treatment sequence ustekinumab/ABP 654 and ustekinumab/ustekinumab. For timepoints post week 28 for subjects who dose intensify, the treatment comparison is between ABP 654 and ustekinumab. Separate analyses will be presented for re-randomized subjects and subjects who dose intensify. Strata with small number of subjects in them will be combined.

9.5.2.1 PASI percent improvement from baseline at other timepoints

PASI percent improvement from baseline at other timepoints will be summarized by scheduled visit and will be analyzed based on LOCF in the FAS and Re-randomized FAS and as observed in the FAS and Re-randomized FAS and PP Analysis Sets. PASI percent improvement from baseline will only be summarized at week 4 for the PP Analysis Set. Additionally, observed PASI percent improvement from baseline post week 28 will be summarized separately for subjects who dose intensify. The LS mean differences and 90% CIs of PASI percent improvement from baseline between the treatment arms to other scheduled visits will be estimated using separate ANCOVA models similar to that used for the primary efficacy endpoint.

9.5.2.2 PASI 75 and PASI 100 response throughout the study

PASI 75 and PASI 100 response will be summarized by frequency and percentage of subjects at each scheduled timepoint via NRI in the FAS and re-randomized FAS and as observed in the FAS and re-randomized FAS and PP Analysis Sets. PASI 75 and PASI 100 response will only be summarized at weeks 4 and 12 for the PP Analysis Set. Additionally, PASI 75 and PASI 100 observed response rates post week 28 will be summarized separately for subjects who dose intensify.

Generalized linear models adjusted for the stratification factors with an identity link will be used to obtain the point estimate and 90% CI for the risk difference of PASI 75 and PASI 100 response rate at each scheduled timepoint.

9.5.2.3 sPGA responses at week 12 and week 52

sPGA response (0/1) rates will be summarized at each scheduled timepoint via NRI in the FAS and Re-randomized FAS and as observed in the FAS and Re-randomized FAS and PP Analysis Sets. sPGA response rates will only be summarized at week 12 for the PP Analysis Set. Additionally, observed sPGA response rates post week 28 will be summarized separately for subjects who dose intensify.

Separate generalized linear models adjusted for the stratification factors with an identity link will be used to obtain the point estimate and 90% CI for the risk difference of sPGA response rate at week 12 and week 52.

9.5.2.4 BSA change from baseline at week 12 and week 52

BSA change from baseline at week 12 and week 52 will be analyzed using an ANCOVA model, similar to the primary efficacy endpoint in the FAS and Re-randomized FAS and as observed in the FAS and Re-randomized FAS and PP Analysis Sets. BSA change

from baseline will only be summarized at week 12 for the PP Analysis Set. Additionally, observed BSA change from baseline post week 28 will be summarized separately for subjects who dose intensify. The point estimate of the mean difference in change from baseline in BSA at week 12 and week 52 between the treatment arms and its corresponding 2-sided 90% CI will be obtained from an ANCOVA model with treatment, baseline BSA value, and the stratification factors of baseline BW, prior biologic use, and region as covariates. Separate ANCOVA models will be fit for each timepoint.

9.6 Safety Analyses

All safety analyses will be performed on the SAS based on actual treatment received or Re-randomized SAS based on actual treatment sequence received (see definitions of actual treatment in Section 5.1).

Safety summaries will be provided separately as follows:

- Through week 12 period for the actual treatment groups: ABP 654 or ustekinumab
- Through week 28 period for the actual treatment groups: ABP 654 or ustekinumab.
- Post week 28 period for the actual treatment sequence for subjects who are re-randomized and treated post re-randomization: ABP 654/ABP 654, ustekinumab/ustekinumab, or ustekinumab/ABP 654.
- Post week 28 period for the actual treatment groups for subjects who receive intensive dosing: ABP 654 or ustekinumab.
- Entire Study period for the actual treatment sequence: ABP 654/ABP 654, ustekinumab/ustekinumab, or ustekinumab/ABP 654. Note that the safety summaries for the Entire Study period exclude subjects who dose intensify.

The definitions for each study period are provided in Section 5.1.

9.6.1 Adverse Events

All reported AEs will be coded to the appropriate SOC and PT according to the most current version of MedDRA at the time of the primary analysis, and the severity of each AE will be graded by the investigator per CTCAE v4.03 criteria.

For summary of AEs the following AE summaries, (a) through (h), will be provided by treatment for each study period of through week 12, through week 28, and post week 28.

In addition, summaries (a) and (c) will be provided for the Entire Study period, and summary (a) will be provided for post week 28 for subjects who dose intensify.

(a) overall summary of treatment-emergent AEs,

(b) treatment-emergent AEs by SOC, PT, and maximum severity grade,

(c) treatment-emergent AEs by SOC and PT,

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

(e) treatment-emergent AEs by PT,

(f) grade 3 or higher treatment-emergent AEs by PT,

(g) treatment-emergent AEs leading to discontinuation from IP/study by PT,

(h) treatment-emergent EOIs 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 in the ABP 654 arm or the ABP 654/ABP 654 arm when appropriate.

The risk difference and 90% CI of each EOI ((d) above) through week 12, through week 28 and post week 28 will be calculated on the SAS or re-randomized SAS using Wald asymptotic confidence limits or exact confidence limits if the number of subjects for any treatment is less than 25.

9.6.2 Deaths and Serious Adverse Events

Subject incidence of the following will be tabulated for study period: through week 12, through week 28, post week 28, and Entire Study period:

(i) serious treatment-emergent AEs by SOC and PT,

(j) serious treatment-emergent AEs by PT,

(k) treatment-emergent fatal AEs by PT.

Summaries will be sorted in descending order of frequency in the ABP 654 arm or ABP 654/ABP654, when applicable.

A listing of treatment-emergent serious AE for the Entire Study period will be provided.

9.6.3 Laboratory Test Results

Laboratory data (hematology, serum chemistry, and urinalysis) will be converted to Système International units for reporting and processing purposes. Absolute values and changes from baseline by visit will be presented descriptively for through week 28 and Entire Study periods (refer to study period definition in section 5.1). Shift tables of the worst on-study laboratory toxicity based on CTCAE grading relative to baseline will be presented by study period. There is no categorization for re-baseline for post week 28 analyses.

The shift tables will take into account all post-baseline (schedule and unscheduled) laboratory results in the determination of the worst on-study laboratory toxicity for parameters that have CTCAE criteria. In addition, subject incidence tables of grade ≥ 3 laboratory toxicities will be provided. Standard ranges will be used for the laboratory analysis.

Protocol-required laboratory 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), amylase, aspartate aminotransferase (AST), blood urea nitrogen (BUN), creatinine, gamma glutamyltransferase, glucose (random), potassium, sodium, total protein, and total bilirubin

Urinalysis: pH, specific gravity, creatinine, glucose, bilirubin, blood, and protein

9.6.4 Vital Signs

Observed and change from baseline for each vital sign parameter will be summarized descriptively by visit for through week 28 and the Entire Study periods (refer to study period definition in section 5.1).

9.6.5 Physical Examinations

None.

9.6.6 Immunogenicity

The number and percentage of subjects developing binding ADAs and those developing neutralizing antibodies will be tabulated by visit and actual treatment received using the SAS and actual treatment sequence received using the Re-randomized SAS.

Developing antibody incidence through week 28 and through EOS is defined as the number of subjects with a negative or no antibody result at baseline and a positive antibody result at a post-baseline visit divided by the number of subjects with at least one post baseline result within the respective study period. Treatment boosted antibody result is defined as a binding antibody positive at baseline with a > 4x increase in magnitude (reflected by S/N value) post-baseline within the respective study period. A transient antibody result is defined as a positive post-baseline result with a negative result at the subject's last visit tested within the respective study period (refer to definition of ADA study visit in section 5.1).

Developing antibody incidence in the post week 28 period is evaluated among subjects who are treated post re-randomization. It is defined as number of subjects who have a positive result post re-randomization, have never tested positive (i.e., negative or no results) prior to the first dose in post week 28 period, divided by the number of subjects who have at least a result post re-randomization in the study period. Additionally, developing antibody incidence will be summarized for subjects who dose intensify post week 28 according to actual treatment received.

9.6.7 Exposure to Investigational Product

IP exposure (ABP 654 or ustekinumab) will be tabulated separately through week 12 and through week 28 using the SAS according to the actual treatment received, and post week 28 using the Re-randomized SAS according to the actual treatment sequence received. Subjects who dose intensify will be summarized post week 28 according to actual treatment received. Summary statistics will be provided for the total number of doses administered, total dose received, and total duration of IP exposure by the different study periods specified for the safety analyses in section 9.6.1.

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 by subject.

9.6.8 Prior and Concomitant Medications

Prior and concomitant medications will be coded using the World Health Organization-Drug Dictionary (WHO-DD) and will be summarized by preferred name. The prior medications will be summarized by initial treatment the subject received. The concomitant medications will be summarized for the different study periods specified for the safety analyses in section 9.6.1 using SAS or the Re-randomized SAS.

The number and percentage of subjects using each medication will be displayed by treatment arm. Subjects taking more than one medication in the same preferred name will be counted once for the number of subjects taking that preferred name.

9.7 Other Analyses

9.7.1 Analyses of Pharmacokinetic Endpoints

Serum ABP 654 and ustekinumab concentrations from PK sampling will be summarized descriptively for each visit through week 28 for the SAS and post week 28 for both the Re-randomized SAS and the subjects who dose intensify. Boxplots for trough serum ABP 654 and ustekinumab concentrations will be generated for each visit through week 28 for the SAS and post week 28 for both the Re-randomized SAS and the subjects who dose intensify.

9.7.2 Analyses of Clinical Outcome Assessments

None.

9.7.3 Analyses of Health Economic Endpoints

None.

9.7.4 Analyses of Biomarker Endpoints

None.

10. Changes From Protocol-specified Analyses

There are no changes to the protocol-specified analyses.

11. Literature Citations / References

1. Feldman SR, Krueger GG. Psoriasis Assessment Tools in Clinical Trials. Ann Rheum Dis. 2005;64 suppl 2(Suppl2):ii65-ii68;discussion ii69-ii73. doi 10.1136/ard.2004.031237

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

3. US FDA. Guidance for Industry: Scientific considerations in demonstrating biosimilarity to a reference product. April 2015a, US FDA.

Appendix 1 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 serious TEAE terms
Malignancy	Malignancies (SMQ)	Narrow
Cardiovascular events	Cardiac disorders (SOC)	SOC
Reversible posterior leukoencephalopathy syndrome	Posterior reversible encephalopathy 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
Venous thromboembolism	Embolic and thrombotic events, venous (SMQ)	Narrow