STATISTICAL ANALYSIS PLAN

Study: PS0014

Product: Bimekizumab

A MULTICENTER, OPEN-LABEL STUDY TO ASSESS THE LONG-TERM SAFETY, TOLERABILITY, AND EFFICACY OF BIMEKIZUMAB IN ADULT SUBJECTS WITH MODERATE TO SEVERE CHRONIC PLAQUE PSORIASIS

SAP/Amendment Number	Date
Final SAP	11 OCT 2022

Confidentiality Statement

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

ACR	American College of Rheumatology
ADAb	anti-bimekizumab antibody
AE	adverse event
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AST	aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical
BMI	body mass index
BSA	body surface area
CA-ES	Cohort A Enrolled Set
CA-FAS	Cohort A Full Analysis Set
CA-OL2S	Cohort A OLE2 Period Set
CAPK-PPS	Cohort A Pharmacokinetics Per-Protocol Set
CA-SS	Cohort A Safety Set
CBEP-FAS	Cohort B Erythrodermic Psoriasis Full Analysis Set
CBEP-SS	Cohort B Erythrodermic Psoriasis Safety Set
CB-ES	Cohort B Enrolled Set
CB-FAS	Cohort B Full Analysis Set
CBGPP-FAS	Cohort B Generalized Pustular Psoriasis Full Analysis Set
CBGPP-SS	Cohort B Generalized Pustular Psoriasis Safety Set
CBPK-PPS	Cohort B Pharmacokinetics Per Protocol Set
CBPSO-FAS	Cohort B Psoriasis Full Analysis Set
CBPSO-SS	Cohort B Psoriasis Safety Set

CB-SS	Cohort B Safety Set
CGI-I	Clinical Global Impressions - Improvement
CI	confidence interval
COVID-19	Coronavirus Disease 2019
CRP	C-reactive protein
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
CV-CAC	Cardiovascular Event Adjudication Committee
DAP	Data Analysis Plan
DLQI	Dermatology Life Quality Index
DNA	deoxyribonucleic acid
EAER	exposure adjusted event rate
EAIR	exposure adjusted incidence rate
ECG	electrocardiogram
eCRF	electronic Case Report Form
eC-SSRS	electronic Columbia Suicide Severity Rating Scale
EQ-5D-3L	Euro-Quality of Life 5-Dimensions, 3 levels
EP	erythrodermic psoriasis
GGT	gamma glutamyltransferase
GPP	generalized pustular psoriasis
HAQ-DI	Health Assessment Questionnaire-Disability Index
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HIV	human immunodeficiency virus

HLT	Higher Level Term
IBD	inflammatory bowel disease
IBD-CAC	Inflammatory Bowel Disease Adjudication Committee
IDC	Infectious Disease Committee
IGA	Investigator's Global Assessment
IMP	investigational medicinal product
IRT	Interactive Response Technology
IWRS	Interactive Web Response System
JAK	janus kinase
JDA	Japanese Dermatological Association
LLN	Lower limit of normal
LLT	Lowest Level Term
LOCF	Last Observation Carried Forward
MACE	Major Adverse Cardiac Event
MCMC	Markov-Chain Monte Carlo
MCS	Mental Component Summary
MedDRA	Medical Dictionary for Regulatory Activities
MI	multiple imputation
mNRI	Modified non-responder imputation
mNAPSI	Modified Nail Psoriasis Severity Index
NAb	Neutralizing Anti-Drug Antibody
NE	non estimable
NRI	non-responder imputation
OC	Observed Case

OLE2	Open-label extension 2
PASE	Psoriatic Arthritis Screening and Evaluation
PASI	Psoriasis Area Severity Index
PCS	Physical Component Summary
PEOT	Premature End of Treatment
PGA	Patient Global Assessment
PGADA	Patient Global Assessment of Disease Activity
PhGADA	Physician's Global Assessment of Disease Activity
PHQ-9	Patient Health Questionnaire 9
PK	pharmacokinetics
PK-PPS	Pharmacokinetics Per-Protocol Set
pp-IGA	palmoplantar Investigator's Global Assessment
PsA	psoriatic arthritis
PSO	psoriasis
PT	Preferred Term
Q4W	every 4 weeks
Q8W	every 8 weeks
SAE	serious adverse event
SAP	Statistical Analysis Plan
sc	subcutaneously
SD	standard deviation
SDTM	Study Data Tabulation Model
SF-36	Short Form 36-item Health Survey
SFU	Safety Follow-Up

SIB	suicidal ideation and behavior
SMQ	Standard MedDRA® Query
SOC	System Organ Class
SOP	Standard Operating Procedure(s)
SMQ	Standardized MedDRA Query
SS	Safety Set
TEAE	treatment-emergent adverse event
TNF	tumor necrosis factor
TSQM-9	Treatment Satisfaction Questionnaire for Medication
ULN	upper limit of normal
VAS	visual analog scale
WBC	white blood cell
WHO	World Health Organization
WHO-DD	World Health Organization Drug Dictionary
WPAI-SHP	Work Productivity and Activity Impairment Questionnaire-specific health problem

1 INTRODUCTION

This Statistical Analysis Plan (SAP) defines the scope of the statistical analyses and provides a detailed description of the statistical methodology for the statistical analyses to support the Clinical Study Report (CSR). The SAP for final analysis is based upon the following protocol and amendments:

- Final Protocol, 05 Apr 2018
- Protocol Amendment 0.1 (Japan), 18 Apr 2018
- Protocol Amendment 0.2 (Japan), 25 Jun 2018
- Protocol Amendment 0.3 (Japan), 13 Sep 2018
- Protocol Amendment 0.4 (UK), 18 Oct 2018
- Protocol Amendment 1.0, 16 Jan 2019
- Protocol Amendment 1.1 (Canada), 26 Feb 2019
- Protocol Amendment 1.2 (Japan), 9 May 2019
- Protocol Amendment 2.0, 9 Jun 2020
- Protocol Amendment 2.1 (Italy), 18 Jun 2020
- Protocol Amendment 3.0, 16 Jul 2020
- Protocol Amendment 3.1 (Italy), 16 Jul 2020
- Protocol Amendment 3.2 (Japan), 21 Jul 2020
- Protocol Amendment 3.3 (USA and Canada), 12 Oct 2021
- Protocol Amendment 3.4 (Canada), 8 Dec 2021

The final analysis, which will include both Cohort A and Cohort B, will be performed after the last subject completes the open-label extension 2 period (OLE2), including the Safety follow-up 2 period (SFU2).

2 PROTOCOL SUMMARY

2.1 Study objectives

2.1.1 Primary objective

The primary objective of the study is to assess the long-term safety and tolerability of bimekizumab administered sc in adult subjects with moderate to severe chronic plaque psoriasis (PSO).

2.1.2 Secondary objectives

The secondary objectives of the study are to:

- Assess the safety of maintenance therapy bimekizumab dose regimens administered over 144 weeks as measured by serious adverse events (SAEs) and treatment-emergent adverse events (TEAEs) leading to study withdrawal
- Assess the efficacy of maintenance therapy bimekizumab dose regimens administered over 144 weeks as measured by Psoriasis Area and Severity Index (PASI) 90 (defined as a subject who achieves 90% reduction in the PASI score from the feeder study Baseline) and Investigator's Global Assessment (IGA) response (Clear or Almost Clear with at least a 2 category improvement from Baseline on a 5 point scale)

2.1.3 Other objectives

The other objectives of the study are to:

- Assess the safety of maintenance therapy bimekizumab dose regimens administered over 144 weeks
- Assess the efficacy of maintenance therapy bimekizumab dose regimens administered over 144 weeks
- Assess the impact of initiating bimekizumab therapy in subjects who received ustekinumab in PS0009
- Assess the pharmacokinetics (PK) of bimekizumab
- Assess the immunogenicity of bimekizumab
- Assess the change in psoriatic nail disease in subjects with nail disease at Baseline in the feeder studies
- Assess the change in psoriatic scalp disease over time for subjects with scalp psoriasis (PSO) at Baseline in the feeder studies
- Assess the change in palmoplantar PSO for subjects who have palmoplantar PSO at Baseline in the feeder studies
- Assess the symptoms of psoriatic arthritis (PsA) as measured by the Psoriatic Arthritis Screening and Evaluation (PASE) questionnaire
- Assess general health-related quality of life (QOL), including the change in impact of skin disease on QOL and treatment satisfaction
- Assess the safety of bimekizumab manufactured using Process 5

2.1.4 Cohort B specific other objectives

- The Japan-specific other objectives are to:
  - Assess the long-term safety and tolerability of bimekizumab in adult Japanese subjects in Cohort B
  - Assess the efficacy of bimekizumab in adult Japanese subjects with generalized pustular psoriasis (GPP) and erythrodermic psoriasis (EP)
  - Assess the pharmacokinetics of bimekizumab in adult Japanese subjects with GPP and EP.

2.2 Study variables

2.2.1 Cohort A

2.2.1.1 Primary safety variable

The primary safety variable is the incidence of TEAEs adjusted by duration of subject exposure to treatment.

2.2.1.2 Secondary variables

2.2.1.2.1 Secondary safety variables

The secondary safety variables are:

- Incidence of serious TEAEs adjusted by duration of subject exposure to treatment
- Incidence of TEAEs leading to withdrawal adjusted by duration of subject exposure to treatment

2.2.1.2.2 Secondary efficacy variables

The secondary efficacy variables are:

- PASI90 at Week 144
- IGA 0/1 response (Clear or Almost Clear with at least 2 category improvement relative to Baseline) at Week 144

2.2.1.3 Other variables

The other variables are listed below and will be evaluated according to the Schedule of study assessments in the protocol.

2.2.1.3.1 Other safety variables

Change from Baseline variables for safety will be defined relative to the Baseline entry measurement from PS0014.

The other safety variables to be assessed are:

- Severity and frequency of TEAEs
- Change from Baseline in clinical laboratory variables (chemistry and hematology)
- Change from Baseline in vital signs
- Change from Baseline in 12-lead electrocardiogram (ECG) results
- Change from Baseline in the Patient Health Questionnaire 9 (PHQ9) total score
- Safety of bimekizumab manufacturing using Process 5

Physical examination findings considered to be clinically significant changes since the physical examination at the Baseline Visit will be recorded as adverse events (AEs).

2.2.1.3.2 Other efficacy variables

Change from Baseline efficacy variables will be defined relative to the Baseline measurement from the feeder study for the other efficacy variables listed below:

- PASI75, PASI90, and PASI100 response
- Percentage of subjects with PASI ≤1, ≤2, ≤3 and ≤5
- IGA response (Clear or Almost Clear with at least 2-category improvement relative to Baseline)
- IGA response (Clear with at least 2-category improvement relative to Baseline)
- Absolute and percent change from Baseline in PASI score
- Absolute and percent change from Baseline in the body surface area (BSA) affected by PSO
- Absolute and percent change from Baseline in the product of IGA and BSA (IGAxBSA)
- Change from Baseline in Dermatology Life Quality Index (DLQI) total score
- Percentage of subjects achieving a DLQI total score of 0 or 1
- Percentage of subjects achieving a minimal clinically important difference (improvement from Baseline of 4 or more) in the DLQI total score
- Change from Baseline in Modified Nail Psoriasis Severity Index (mNAPSI) score for subjects with nail disease at Baseline
- mNAPSI75, mNAPSI90 and mNAPSI100 response
- Change from Baseline in the Patient's Global Assessment of Disease Activity (PGADA) for the arthritis visual analog scale (VAS) for subjects with PsA at Baseline
- Change from Baseline in Patient Global Assessment (PGA) of PSO
- Scalp-specific IGA (Scalp IGA) response (Clear or Almost Clear with at least 2 category improvement relative to Baseline) for subjects with scalp PSO at Baseline
- Palmoplantar Investigator's Global Assessment (pp-IGA) response (Clear or Almost Clear with at least 2 category improvement relative to Baseline) for subjects with palmoplantar PSO at Baseline
- Change from Baseline in the PASE questionnaire scores (function score, symptom score, and total score)
- Shift from Baseline in PASE score suggestive of PsA (<47 versus ≥47)
- Change from Baseline in Short Form 36-item Health Survey (SF-36) Physical Component Summary (PCS) score, Mental Component Summary (MCS) score, and domain scores
- Responses to Euro-Quality of Life 5-Dimensions, 3 levels (EQ-5D-3L)
- Changes from Baseline in EQ-5D-3L VAS scores and all dimensions
- Change from Baseline in Work Productivity and Activity Impairment Questionnaire-specific health problem (WPAI-SHP) V2.0 adapted to PSO scores

- Treatment Satisfaction Questionnaire for Medication (TSQM-9): effectiveness, convenience and global satisfaction scores

2.2.2 Cohort B

2.2.2.1 Safety variables

The safety variables for Cohort B will be the same as listed in Section 2.2.1.1, Section 2.2.1.2.1, and Section 2.2.1.3.1.

2.2.2.2 Efficacy variables

Change from Baseline efficacy variables will be defined relative to the Baseline measurement from the PS0014 study for the efficacy variables listed below. All efficacy variables below will be considered as other variables for the purpose of reporting:

- PASI75, PASI90, and PASI100 response
- Percentage of subjects with PASI ≤1, ≤2, ≤3 and ≤5
- IGA response (Clear or Almost Clear with at least 2 category improvement relative to Baseline) for subjects with plaque PSO
- IGA response (Clear with at least 2 category improvement relative to Baseline) for subjects with plaque PSO
- IGA score (Clear or Almost Clear) for subjects with GPP and EP
- IGA score (Clear) for subjects with GPP and EP
- Absolute and percent change from Baseline in PASI score
- Absolute and percent change from Baseline in the BSA affected by PSO, GPP, or EP
- Absolute and percent change from Baseline in the product of IGA and BSA (IGAxBSA)
- Change from Baseline in DLQI total score
- Percentage of subjects achieving a DLQI total score of 0 or 1
- Percentage of subjects achieving a minimal clinically important difference (improvement from Baseline of 4 or more) in the DLQI total score
- Change from Baseline in mNAPSI score for subjects with nail disease at Baseline
- mNAPSI75, mNAPSI90 and mNAPSI100 response
- Change from Baseline in the PGADA for the arthritis VAS for subjects with PSO who have PsA at Baseline
- Change from Baseline in PGA of PSO
- Scalp IGA response (Clear or Almost Clear with at least 2 category improvement relative to Baseline) for subjects with plaque PSO who have scalp PSO at Baseline
- Scalp IGA score (Clear or Almost Clear) for GPP and EP subjects with scalp PSO at Baseline

- pp-IGA response (Clear or Almost Clear with at least 2 category improvement relative to Baseline) for subjects with plaque PSO who have palmoplantar PSO at Baseline
- pp-IGA score (Clear or Almost Clear) for subjects with GPP and EP who have palmoplantar PSO at baseline
- Change from Baseline in the PASE questionnaire scores (function score, symptom score, and total score) for subjects with plaque PSO
- Shift from Baseline in PASE score suggestive of PsA (<47 versus ≥47) for subjects with plaque PSO
- Change from Baseline in SF-36 PCS score, and MCS score, and domain scores
- Responses to EQ-5D-3L
- Changes from Baseline in EQ-5D-3L VAS scores and all dimensions
- Change from Baseline in WPAI-SHP V2.0 adapted to PSO scores
- TSQM-9 scores at Week 48
- Clinical Global Impressions-Improvement (CGI-I) (for subjects with GPP and EP only)
- Global Improvement Score by Japanese Dermatological Association (JDA) severity index score (for subjects with GPP only)

2.2.3 Pharmacokinetic/pharmacodynamic variables

The PK variable is plasma concentration of bimekizumab.

2.2.4 Immunological variables

The immunological variables are anti-bimekizumab antibody (ADAb) and neutralizing anti-bimekizumab antibody (NAb) levels prior to and following investigational medicinal product (IMP) administration.

2.3 Study design and conduct

2.3.1 Study Description

PS0014 is a multicenter, open-label study to assess the long-term safety, tolerability, and efficacy of bimekizumab in eligible adult subjects with moderate to severe chronic plaque PSO who complete 1 of the Phase 3 feeder studies. Subjects enrolling in PS0014 after completion of the Phase 3 feeder studies (PS0008, PS0009, PS0013) will be included in Cohort A.

An additional open-label cohort (Cohort B) was added in Japan to allow enrollment of subjects with PSO including moderate to severe chronic plaque PSO, GPP, and EP.

In addition, subjects could consent to participate in the PS0014 sub-studies, DV0002 and DV0006, designed to evaluate the safe and effective use of self-injecting device presentations (ie, prefilled safety syringe and auto-injector presentations) for sc self-injections of bimekizumab by subjects in selected sites in Europe, Japan, Canada, and the US. Details of the analyses and statistical methodology of the PS0014 sub-studies are described in separate SAPs.

2.3.2 Study Periods

For Cohort A PS0014 will include a Treatment Period of 144 weeks (from Baseline/Feeder Study Final Visit to Week 144 Visit) followed by a Safety Follow-Up Period (SFU) of 20 weeks after the last dose of IMP in the Treatment Period.

Eligible subjects from US and Canada sites who have completed the Treatment period (at Week 144), including subjects ongoing in the SFU Period and who have completed the SFU Period, will have the option to enroll in the 48-week OLE2 treatment period , followed by a SFU Period (SFU2, 20 weeks after the last dose of IMP during the OLE2 treatment period).

For Cohort B the study will consist of 3 periods; a screening Period (2 to 5 weeks), a Treatment Period (144 weeks) and a SFU Period (20 weeks after the final dose of IMP).

Subjects withdrawing early from the study will undergo the premature end of treatment (PEOT) Visit assessments and will enter the SFU Period.

Following completion or early withdrawal from the OLE2 treatment period , subjects will undergo the SFU of the OLE2 treatment period (SFU2) and will return for the SFU2 Visit 20 weeks after the last dose of IMP administration in the OLE2 treatment period.

2.3.2.1 Treatment Period

2.3.2.1.1 Cohort A

During the Treatment Period eligible subjects will receive the following IMP regimens as determined by the subject's treatment regimen and PASI response at the end of the feeder study. Subjects receiving:

- Bimekizumab 320mg Q4W who do not achieve PASI90 in the feeder study will receive bimekizumab 320mg Q4W.
- Bimekizumab 320mg Q4W who achieve PASI90 in the feeder study will be randomized 4:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.
- Bimekizumab 320mg Q8W who do not achieve PASI90 in the feeder study will receive bimekizumab 320mg Q4W.
- Bimekizumab 320mg Q8W who achieve PASI90 in the feeder study will receive bimekizumab 320mg Q8W.
- Ustekinumab who do not achieve PASI90 in the feeder study will receive bimekizumab 320mg Q4W.
- Ustekinumab who achieve PASI90 in the feeder study will be randomized 1:1 to receive bimekizumab 320mg Q4W or bimekizumab 320mg Q8W.
- Placebo (after a Week 16 response [≥PASI90] on bimekizumab 320mg Q4W during the Initial Treatment Period of the feeder study) who complete the Randomized Withdrawal Period of the feeder study will receive bimekizumab 320mg Q4W.

During Year 1 of the Treatment Period (Weeks 0 to 44), all subjects will attend study visits at the study site Q4W for study assessments.

At Week 24, for subjects receiving bimekizumab 320mg Q4W, if PASI90 is achieved, the Investigator may change the subject's dosing interval from 320mg Q4W to 320mg Q8W (optional).

For subjects remaining on bimekizumab 320mg Q4W the dosing interval will change to bimekizumab 320mg Q8W at Week 48 or at the next scheduled clinic visit (ie, Week 60, Week 72, Week 84, Week 96, Week 108, Week 120, or Week 132) after implementation of Protocol Amendment #3 or Protocol Amendment #3.2 in Japan, if the subject has already completed the Week 48 visit.

During Years 2 and 3 of the Treatment Period (Weeks 48 to 144), subjects will attend study visits at the study site Q12W for study assessments.

Subjects will have the option to self-inject IMP at home at the time points specified in the protocol. Subjects who do not self-inject IMP at home will attend unscheduled study visits at the study site to receive their injections, either Q4W or Q8W. At study site visits, IMP can either be administered by the site staff or the subject can self-inject.

2.3.2.1.2 Cohort B

During Year 1 of the Treatment Period (Weeks 0 to 44), all subjects will attend study visits at the study site Q4W for study assessments.

Subjects with chronic plaque PSO in Cohort B will receive bimekizumab 320mg Q4W until Week 16 and 320mg Q8W thereafter through Week 40.

At Week 48, Cohort B subjects with chronic plaque PSO will continue bimekizumab 320mg Q8W through to the end of the study (Week 144). If the subject's dosing interval had changed to bimekizumab 320mg Q4W at Week 48 under Protocol Amendment #1.2, the subject's dosing interval will change to bimekizumab 320mg Q8W at the next scheduled clinic visit after implementation of Protocol Amendment #3.2.

Subjects with GPP and EP in Cohort B will receive bimekizumab 320mg Q4W until Week 16. Thereafter, Cohort B subjects with GPP and EP who achieve an IGA response of 0 or 1 at Week 16 will receive bimekizumab 320mg Q8W through Week 40. Cohort B subjects with GPP and EP who do not achieve an IGA response of 0 or 1 at Week 16 will continue bimekizumab 320mg Q4W through to the end of the study.

At Week 48, for Cohort B subjects with GPP and EP receiving bimekizumab 320mg Q8W, if IGA response of 0 or 1 is not achieved, the subject's dosing interval will change from 320mg Q8W to 320mg Q4W through to the end of the study (Week 144). Cohort B subjects with GPP and EP receiving bimekizumab 320mg Q8W who do achieve IGA response of 0 or 1 at Week 48 will continue receiving bimekizumab 320mg Q8W through to the end of the study (Week 144).

2.3.2.2 OLE2 Period (Cohort A only)

After the implementation of Protocol Amendment #3.3 and 3.4 (with the addition of a 48-week Open-Label treatment period, i.e., OLE2 treatment period), subjects from sites in US and Canada will be invited to continue or reinitiate their treatment as per the following OLE2 Groups:

- OLE2 Group A: Subjects in the Treatment Period at the time of Protocol Amendment #3.3/3.4 implementation will attend the Week 144 Visit and may directly roll over to the OLE2

treatment period. These subjects will continue receiving bimekizumab 320mg Q8W for 40 additional weeks, starting from the first treatment visit of the OLE2 treatment period (i.e., Week 144/OLE2 Baseline Visit; the Week 144 Visit will coincide with the Week 144/OLE2 Baseline Visit and data collected at this visit will be used as baseline data for the OLE2 treatment period).

• OLE2 Group B: Eligible subjects who have completed the Treatment Week 144 Visit and who are ongoing in the SFU or have completed the SFU at the time of Protocol Amendment #3.3/3.4 implementation may reinitiate bimekizumab treatment in the OLE2 treatment period after having undergone Screening assessments during a 4-week OLE2 Screening Period.

  – The first dose of the IMP will be administered at the OLE2 Baseline Visit and data collected at this visit will be used as baseline data for the OLE2 Period

  – Subjects in OLE2 Group B with an IGA score ≥3 at the OLE2 Baseline Visit will receive bimekizumab Q4W for the first 16 weeks, and then will switch to bimekizumab 320mg Q8W

  – Subjects in OLE2 Group B with an IGA score <3 at the OLE2 Baseline Visit will receive bimekizumab Q8W from the OLE2 Baseline Visit.

Following completion or early withdrawal from the OLE2 treatment period , subjects will enter the SFU2 and will return for the SFU2 Visit 20 weeks after the last dose of IMP administration.

2.3.2.3 Safety Follow-Up

All subjects, including those withdrawn from IMP, will have a SFU Visit 20 weeks after their final dose of IMP.

Two SFU Periods are considered following the implementation of Protocol Amendments #3.3 and #3.4:

- SFU following the 144 Week Treatment period (Cohort A and B)
- SFU2 following the OLE2 treatment period (Eligible subjects in Cohort A)

2.3.2.4 Premature End of Treatment

Subjects withdrawing early from the study will undergo the premature end of treatment (PEOT) Visit assessments and will enter the SFU Period.

2.3.3 Study duration per subject

For each subject in Cohort A not entering OLE2 treatment period the study will last a maximum of 156 weeks as follows:

- Treatment Period (144 weeks)
- SFU Period (20 weeks).

For each subject in Cohort B, the study will last a maximum of 165 weeks as follows:

- Screening Period (2 to 5 weeks)
- Treatment Period (144 weeks)

- SFU Period (20 weeks).

Cohort A subjects eligible for the OLE2 treatment period will enter the OLE2 treatment period after completing Week 144 of the Treatment Period. The OLE2 treatment period includes a 48-week open-label treatment period with a final visit at OLE2 Week 48, and an SFU Period (SFU2) of 20 weeks after the final dose of IMP administered in the OLE2 treatment period.

For subjects participating in the OLE2 treatment period, the maximum study duration will depend on the time between their participation in the Treatment Period until Week 144 and the start of the OLE2 treatment period:

- 204 weeks for subjects still being treated in the Treatment Period and who will directly roll over to the OLE2 treatment period at Week 144.
- 224 weeks for subjects who have attended Week 144 and who will have completed the SFU; these subjects will have a 4-week Screening Period before reinitiating treatment in the OLE2 treatment period. Note: for these subjects, the study duration will not be continuous.
- Between 204 and 220 weeks for subjects who will have attended Week 144 and are participating the in the SFU. For these subjects, the maximum study duration will depend upon when they will stop the 20-week SFU period to enter the 4-week Screening Period of the OLE2 treatment period.

The end of the study is defined as the date of the last visit of the last subject in the study.

2.3.4 Planned number of subjects

Approximately 1120 subjects (including approximately 60 subjects from the Japanese-specific local amendment) will be enrolled in the study. The anticipated enrollment in the feeder studies is 1250 (450 subjects from PS0008, 560 subjects from PS0009, and 400 subjects from PS0013) and approximately 85% are expected to roll into PS0014.

2.3.5 Anticipated regions and countries

The regions planned for the study conduct are North America, Western Europe, Central/Eastern Europe and Asia/Australia, with possible extension to other regions and countries.

An additional OLE2 treatment period will be conducted in US and Canada only.

2.3.6 Determination of sample size

As the primary objective of this study is to assess the long-term safety and tolerability of bimekizumab, the number of subjects anticipated is based on the number of subjects recruited into and completing the feeder studies and meeting the eligibility requirements for PS0014.

Based on the number of Japanese subjects enrolled in the feeder studies and the estimated rate of dropout, it is expected that 40 to 50 subjects will comprise Cohort A.

As the Japan-specific objective of this study is to assess the long-term safety and tolerability of bimekizumab in adult Japanese subjects with PSO including plaque PSO, GPP, and EP, who may have an additional diagnosis of PsA. The expected number of subjects in Cohort B will be as follows:

- Generalized pustular/erythrodermic PSO (n≥10)
- Plaque PSO (n=45 to 50)

The number of subjects with plaque PSO in Cohort B was selected to ensure at least 100 Japanese subjects were included overall (Cohort A and Cohort B combined).

3 DATA ANALYSIS CONSIDERATIONS

3.1 General presentation of summaries and analyses

Statistical analysis and generation of tables, figures, subject data listings, and statistical output will be performed using SAS Version 9.3 or higher. All tables and listings will use Courier New font size 9.

Descriptive statistics will be displayed to provide an overview of the study results. For continuous variables, descriptive statistics will include number of subjects with available measurements (n), mean, standard deviation (SD), median, minimum, and maximum.

For categorical variables, the number and percentage of subjects in each category will be presented. Unless otherwise noted, the denominator for percentages should be based on the number of subjects included in the respective analysis set. Subjects with missing data can generally be accounted for using either of the following approaches:

- For summaries of demographics and Baseline characteristics: summarize percentages based on all subjects in the analysis set and include a "Missing" category (corresponding to subjects with missing data for the variable being summarized) as the last row in the list of categories being summarized.
- For summaries of efficacy and safety variables, unless otherwise specified: summarize percentages based only on those subjects with observed data for the variable being summarized. As the denominator may be different from the number of subjects in the analysis set being considered, the denominator should be displayed in the table. The general format for displaying this will be "n/Nsub (%)."

Percentages will be presented to 1 decimal place. If the percentage is 100%, do not present a decimal. If the percentage is 0, do not present the percentage. Typically, the % sign should be presented in the column header, but not with each individual value.

For bimekizumab PK concentrations, summary statistics will include geometric mean, geometric coefficient of variation (CV), 95% confidence intervals (CIs) for geometric mean, arithmetic mean, SD, median, minimum, and maximum. All summaries of PK variables will be based on the observed values. No imputation will be used. For the handling of plasma concentration measurements are below the level of quantification (BLQ), please refer to Section 9.1.

Decimal places for descriptive statistics will always apply the following rules:

- "n" will be an integer
- Mean, SD, and median will use one additional decimal place compared to the original data
- CV [%] will be presented with one decimal place

- Minimum and maximum will have the same number of decimal places as the original value.

Derived variables in general will display the mean, SD and median to 1 more decimal place than the variables used in the derivation. If the number of decimal places reported in the raw data is varied, then use either the maximum raw number of reported decimal places or 3, whichever is the lowest, as a guide for the descriptive statistics.

A complete set of data listings containing all documented data as well as calculated data (e.g. change from Baseline) will be generated. Separate data listings will be generated for the OLE2 treatment period.

Per protocol, visit windows of ±7 days from the first dose to Week 144 are permissible for subjects in Cohort A. For subjects in Cohort B, visit windows of ±3 days from the first dose to Week 24 and ±7 days from Week 28 to Week 144 are permissible. For the SFU Visit, visit window is 140 ± 7 days from final dose. All by-visit summaries will contain nominal (i.e. scheduled) visits only. Unscheduled visits will not be mapped to scheduled visits except for some assessments as detailed below.

Per protocol, visit windows of ±14 days from the first OLE2 dose at all OLE2 visits except SFU2 are permissible, the SFU2 visit window is 20 weeks ±7 days from final dose in OLE2 treatment period.

For Cohort A, for missing PASI and IGA assessments at Week 24, Week 48 and Week 144, available data from unscheduled (or scheduled but without a planned assessment) visits will be used:

- Data within +/7 days of Week 24 visit will be used as the Week 24 assessment
- Data within +/7 days of Week 48 visit will be used as the Week 48 assessment
- Data within +/7 days of Week 144 visit will be used as the Week 144 assessment

For Cohort B unscheduled visits will be mapped for all visits through to Week 144, for all efficacy endpoints as follows:

- Data within +/3 days of Week 2 to Week 24 visit will be used as the relevant assessment
- Data within +/7 days of Week 28 to Week 144 visit will be used as the relevant assessment

For all efficacy and safety parameters. in case multiple records are collected for a same analysis visit, the following rules will be applied to determine the record analyzed in visit-based outputs:

- If records have different dates, the one closest to the target day from first injection will be used.
- If records have different dates but the distance to target day is the same, the latest one will be used.
- If records have same dates, the latest one recorded in the Study Data Tabulation Model (SDTM) will be used.

- If multiple records are collected on a visit where the subject switches dose, records after the day of the injection of the new dose will not be used.

3.2 General study level definitions

3.2.1 Analysis time points

3.2.1.1 Relative day

The relative day will be included in different listings and will be calculated as follows:

- If the start (stop) date occurred on or after the first dose in PS0014, but prior to the drug stop date, relative day is calculated as start (stop) date minus first dose date +1
- If the start (stop) date occurred after the last dose of bimekizumab, the relative day to the most recent dose is calculated as start (stop) date minus most recent dose date. The relative day in this situation should be preceded by a '+'
- If the start (stop) date occurred before the first dose in PS0014, the relative day is calculated as start (stop) date minus first dose date. The relative day in this situation should be preceded by a '–'.

For adverse events (AEs), relative days for start and stop dates will be calculated as the number of days since the first injection of the medication in PS0014. Relative day will only be computed for fully completed dates and will be missing for partial dates.

Two relative days will be used as follows:

- Compared to the first dose of study drug in the Treatment Period for all subjects
- Compared to the first dose of study drug in the Open-Label Extension 2 (OLE2) Period for subjects in CA-OL2S only.

3.2.1.2 Mapping of data from early withdrawal visits

If the early withdrawal visit occurs at a scheduled visit as outlined in the schedule of assessments, then no mapping is necessary, and any early withdrawal assessments should correspond to that scheduled visit. Premature study withdrawal visit assessments that occur on a date after a scheduled visit will be assigned to the next scheduled site visit per the protocol following the last visit where assessments were available. This approach means that there is a chance that data will be mapped to a visit where a given assessment was not actually collected per the protocol schedule of assessments. Such data would not be summarized in by-visit tables (though it would be available in the listings).

The only exception to the above rule is for ADAb assessments, in which all early withdrawal visit assessments will be assigned to the next scheduled visit at which anti-bimekizumab antibodies are assessed. All by-visit summaries will contain nominal visits only. Unscheduled visits will not be mapped to scheduled visits. Note that based on the early withdrawal mapping conventions described above, a mapped early withdrawal visit is considered as observed at that visit and should be summarized as such in the tables.

3.3 Definition of Baseline values

3.3.1 Cohort A

There are two definitions of Baseline for subjects who enrolled from a feeder study.

PS0014 Baseline: Baseline value will be defined as the last assessment at the Feeder study final visit.

If a scheduled Baseline assessment is taken on the same day as the first administration of study medication for PS0014 and no time is collected, then the assessment would be assumed to have been taken prior to study medication.

If a PS0014 Baseline measurement is missing or not collected, then the latest assessment from the feeder study on or prior to the date of first injection in PS0014 will be utilized as Baseline instead.

Medical history and prior medication use will only be considered based upon the PS0014 Baseline, any reported "medical history" after the PS0014 Baseline will be considered as an AE.

Feeder Study Baseline: The baseline measurements used in the feeder studies will be considered the Feeder Study Baseline.

All efficacy variables will be summarized based on the Feeder Study Baseline. PS0014 Baseline will be used to assess safety during PS0014.

For subjects enrolled in OLE2 treatment period, the OLE2 treatment period first dose will be administered at the Week 144/OLE2 Baseline Visit and data collected at this visit will be used as baseline data for safety data in the OLE2 treatment period. Efficacy data will continue to use the Feeder Study Baseline as Baseline.

3.3.2 Cohort B

Direct enrollers into the study have one PS0014 baseline, defined as the latest measurement for that subject up to and including the day of administration of first study medication in PS0014, unless otherwise stated.

If a Baseline assessment is taken on the same day as first administration of study medication, it is eligible to be used as the Baseline value, even in the case that the time of the assessment is recorded as taking place after the time of first study medication administration. This is considered acceptable as this measurement is still the best representation of the Baseline value of the given assessment since it is highly unlikely that the study medication could have an impact on any measurement in such a short period of time. However, such cases should be rare as study center personnel are instructed to do all assessments at the Baseline visit prior to administering study medication. One exception to this rule is plasma concentration. If Baseline plasma concentration is measured at a time after the first administration of study medication, then it should not be eligible to be considered as a Baseline plasma concentration. Such cases should be discussed with the quantitative clinical pharmacologist.

If a Baseline measurement is missing or not collected, and a Screening value is available, the Screening value will be utilized as Baseline instead.

Baseline values for component scores should be computed using components from the same visit where the relevant measurements were recorded prior to dosing. For example, if the Screening

visit has all of the components, but the Baseline visit is missing one or more components, the Baseline value for the component score should be calculated using the Screening visit values.

When the time of first dose is derived, it should be based on the first injection of study treatment.

3.4 Protocol deviations

Important protocol deviations are deviations from the protocol which potentially could have a meaningful impact on study conduct or on the key safety, key efficacy, or PK outcomes for an individual subject. The criteria for identifying important protocol deviations will be defined within the appropriate protocol-specific document at study start. Important protocol deviations will be reviewed as part of the ongoing data cleaning process. Important protocol deviations including those that lead to exclusion from the analysis sets will be identified and documented prior to database lock.

The impact on study conduct of the Coronavirus Disease 2019 (COVID-19) global pandemic will be assessed and captured as: confirmed COVID-19 infection, suspected COVID-19 infection, general circumstances around COVID-19 without infection or any other deviation from the protocol due to COVID-19. This information will be reviewed as per the standard data cleaning process.

3.5 Analysis sets

For all analysis sets, each unique subject is only counted once, even if the same subject has more than one unique subject identification.

3.5.1 Cohort A

3.5.1.1 Cohort A Enrolled Set (CA-ES)

The CA-ES will consist of all Cohort A subjects who have given informed consent for PS0014.

3.5.1.2 Cohort A Safety Set (CA-SS)

The CA-SS will consist of all Cohort A subjects who receive at least 1 dose of the IMP in PS0014.

3.5.1.3 Cohort A Full Analysis Set (CA-FAS)

The CA-FAS will consist of all Cohort A enrolled subjects who receive at least 1 dose of the IMP and have a valid efficacy measurement for PASI at Baseline of the Feeder Study and at Baseline of PS0014.

3.5.1.4 Cohort A Pharmacokinetics Per-Protocol Set (CAPK-PPS)

The CAPK-PPS will consist of all Cohort A enrolled subjects who receive at least 1 dose of the IMP and provide at least 1 quantifiable plasma concentration post dose without important protocol deviations that would affect the concentration in PS0014.

3.5.1.5 Cohort A OLE2 Period Set (CA-OL2S)

The Cohort A OLE2 Period Set (CA-OL2S) will consist of all subjects that received at least 1 dose of bimekizumab in OLE2 treatment period (at Week 144/OLE baseline visit or later).

3.5.2 Cohort B

3.5.2.1 Cohort B Enrolled Set (CB-ES)

The CB-ES will consist of all Cohort B subjects who have given informed consent in PS0014.

3.5.2.2 Cohort B Safety Set (CB-SS)

The CB-SS will consist of all Cohort B subjects in the CB-ES who received at least 1 dose of the IMP in PS0014.

3.5.2.3 Cohort B PSO Safety Set (CBPSO-SS)

The CBPSO-SS will consist of all subjects in the CB-SS with a diagnosis of PSO disease at Baseline.

3.5.2.4 Cohort B GPP Safety Set (CBGPP-SS)

The CBGPP-SS will consist of all subjects in the CB-SS with a diagnosis of GPP disease at Baseline.

3.5.2.5 Cohort B EP Safety Set (CBEP-SS)

The CBEP-SS will consist of all subjects in the CB-SS with a diagnosis of EP disease at Baseline.

3.5.2.6 Cohort B Full Analysis Set (CB-FAS)

The CB-FAS will consist of all subjects in the CB-ES who received at least 1 dose of IMP and have a valid efficacy measurement for PASI at Baseline of PS0014.

3.5.2.7 Cohort B PSO Full Analysis Set (CBPSO-FAS)

The CBPSO-FAS will consist of subjects in the CB-FAS with chronic plaque PSO at Baseline.

3.5.2.8 Cohort B GPP Full Analysis Set (CBGPP-FAS)

The CBGPP-FAS will consist of subjects in the CB-FAS with GPP at Baseline.

3.5.2.9 Cohort B EP Full Analysis Set (CBEP-FAS)

The CBEP-FAS will consist of subjects in the CB-FAS with EP at Baseline.

3.5.2.10 Cohort B Pharmacokinetics Per-Protocol Set (CBPK-PPS)

The CBPK-PPS will consist of all Cohort B subjects who received at least 1 dose of IMP and provided at least 1 quantifiable plasma concentration post-dose without important protocol deviations that would affect the concentration in PS0014.

3.6 Treatment assignment and treatment groups

This is an open-label study and as such all subjects will be summarized according to the treatment or treatment combinations that were provided.

3.6.1 Cohort A

For Cohort A, with the inclusion of OLE2, the treatment period is split into the 144 -week treatment period, and the OLE2 treatment period.

PS0014 treatment sequence groups:

This refers to the combination of treatments received during PS0014 study treatment period:

- Bimekizumab 320mg Q8W
- Bimekizumab 320mg Q4W/Q8W
- Bimekizumab 320mg Q4W
- Bimekizumab Total

Note: the bimekizumb 320mg Q8W group will consist of all subjects who received only Q8W during PS0014 study period and did not switch dosing regimen at any timepoint.

Note: the bimekizumb 320mg Q4W/Q8W group will consist of all subjects who switched from Q4W to Q8W dosing at any of the scheduled switching timepoints during the study i.e. at Week 24, if PASI90 is achieved, the Investigator may change the subject's dosing interval from 320mg Q4W to 320mg Q8W optionally, or at Week 48 or at the next scheduled clinic visit (i.e., Week 60, Week 72, Week 84, Week 96, Week 108, Week 120, or Week 132) after implementation of Protocol Amendment #3 or Protocol Amendment #3.2 in Japan, if the subject has already completed the Week 48 visit.

Note: the bimekizumb 320mg Q4W group will consist of subjects who discontinued prior to the planned change of dosing interval from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W.

A separate summary of the number and percentage of subjects switching dose regimen (changing from Q4W to Q8W) by timepoint will be provided for the CA-SS for the bimekizumab 320mg Q4W/Q8W group.

The PS0014 treatment sequence groups will be used for all summaries except for certain safety-related incidence and treatment exposure tables.

All listings with treatment sequence will also specify the timepoint of week when a subject switched dosing regimen.

All tables displayed by treatment sequence will use the actual treatment sequence.

PS0014 treatment group for safety analysis:

This refers to the most recent study treatment regimen received at the time of a safety-related event e.g. an AE or markedly abnormal safety value.

This treatment group assignment will only apply to certain safety incidence analysis and treatment exposure related analysis.

The PS0014 treatment groups are as follows:

- Bimekizumab 320mg Q8W
- Bimekizumab 320mg Q4W
- Bimekizumab total

More detail on assigning events to treatments is provided in Section 10.2.1

Feeder Study/PS0014 treatment groups:

The following feeder study/PS0014 treatment groups will only be used to summarize the following selected key efficacy variables: PASI90, IGA 0/1, IGA 0, PASI100 and DLQI total score of 0/1 response, and TSQM-9 scores up to Week 48.

This refers to the combination of the last treatment received in the Feeder Study and the treatment assigned at the beginning of PS0014. The Feeder Study/PS0014 treatment groups are as follows:

- Placebo/bimekizumab 320mg Q4W
- Bimekizumab 320mg Q8W/Q8W
- Bimekizumab 320mg Q8W/Q4W
- Bimekizumab 320mg Q4W/Q8W
- Bimekizumab 320mg Q4W/Q4W
- Escape bimekizumab 320mg Q4W/bimekizumab 320mg Q8W
- Escape bimekizumab 320mg Q4W/bimekizumab 320mg Q4W
- Ustekinumab/bimekizumab 320mg Q8W
- Ustekinumab/bimekizumab 320mg Q4W

The treatment groups bimekizumab 320mg Q4W/Q4W and bimekizumab 320mg Q4W/Q8W will exclude escapers from the PS0013 Feeder Study, which will only be captured in the Escape bimekizumab 320mg Q4W treatment groups.

Key safety summaries including only those subjects who switched from Ustekinumab to Bimekizumab (Q4W or Q8W) will be provided (see Section 10.2.2.1).

PS0014 PK and Immunogenicity treatment sequence groups :

- Bimekizumab 320mg Q8W (expected n~380)
- Bimekizumab 320mg Q4W/Q8W, switch occurring at Week 24, (expected n~130)
- Bimekizumab 320mg Q4W/Q8W, switch occurring at Week 48 or 60, (expected n~390)
- Bimekizumab 320mg Q4W/Q8W, switch occurring at Week 72 or 84, (expected n~240)
- Bimekizumab 320mg Q4W/Q8W, switch occurring at Week 96 or later, (expected n~65)
- Bimekizumab Total (only for immunogenicity analyses)

Note that subjects who received Bimekizumab 320mg Q4W only (expected n~70), i.e. those who discontinued before switching to Q8W, will be allocated to the corresponding Q4W/Q8W treatment sequence group depending on when the subject discontinued. For example, if a subject discontinued at week 20, they will be allocated to group Bimekizumab 320mg Q4W/Q8W, switch occurring at Week 24 for PK summary table and figure purpose.

For the PK and Immunogenicity listings the full Feeder Study/PS0014 treatment sequence (including BKZ 320 Q4W only group) will be used.

PS0014 OLE2 treatment groups:

Safety and efficacy assessments for the OLE2 period will only include subjects who entered the OLE2 period and will be summarized based on CA-OL2S, by the assigned treatment as follows:

- Subjects who enroll directly from the OLE2 treatment period: Group A
  - Bimekizumab 320mg Q8W Group A
- Subjects in Group B who reinitiate bimekizumab after having completed treatment in the OLE and have an IGA <3 upon entry to the OLE2: Group B
  - Bimekizumab 320mg Q8W Group B
- Subjects in Group B who reinitiate bimekizumab after having completed treatment in the OLE and have an IGA ≥3 upon entry to the OLE2: Group B
  - Bimekizumab 320mg Q4W/Q8W Group B
- For safety summaries only
  - BKZ Total.

3.6.2 Cohort B

PS0014 treatment sequence groups:

These will be used for all summaries except for certain safety-related incidence and treatment exposure tables.

All listing with treatment sequence for cohort B will also specify the timepoint of week by following the same practice of cohort A.

Data will be summarized separately for each psoriasis type using the following treatment sequence groups:

PSO subjects:

- Bimekizumab 320mg Q4W/Q8W (described as "PSO BKZ Total" in data summaries). All PSO subjects should switch from Q4W to Q8W dosing at Week 16 according to the protocol. A subject's dosing could change back to Q4W at Week 48 under protocol amendment #1.2 but subsequently should change to Q8W at the next scheduled clinic visit under protocol amendment #3.2.

All subjects, regardless of any switching occurring at Week 48 or later, will be included in the Q4W/Q8W group. This group will also include subjects who did not reach Week 16 and therefore only received Q4W dosing.

A separate summary of the number and percentage of subjects switching dose regimen (changing from Q4W to Q8W or Q8W to Q4W) by timepoint will be provided for the CBPSO-SS.

For listings using the PSO group, the following full treatment sequences will be listed.

- Bimekizumab 320mg Q4W
- Bimekizumab 320mg Q4W/Q8W
- Bimekizumab 320mg Q4W/Q8W/Q4W
- Bimekizumab 320mg Q4W/Q8W/Q4W/Q8W

EP subjects:

- Bimekizumab 320mg Q4W/Q8W
    - Subjects who received bimekizumab Q4W from baseline to week 16 and then received bimekizumab Q8W from week 16 to week 144 (or early termination)
- Bimekizumab 320mg Q4W/Q8W/Q4W
    - Subjects who received bimekizumab Q4W from week 0 to week 16, bimekizumab Q8W from week 16 to week 48 and then bimekizumab Q4W from week 48 to week 144 (or early termination)
- Bimekizumab 320mg Q4W
    - Subjects who received bimekizumab Q4W through Week 144 (or early termination).
- EP bimekizumab total

GPP subjects

- Bimekizumab 320mg Q4W/Q8W
    - Subjects who received bimekizumab Q4W from baseline to week 16 and then received bimekizumab Q8W from week 16 to week 144 (or early termination)
- Bimekizumab 320mg Q4W/Q8W/Q4W
    - Subjects who received bimekizumab Q4W from week 0 to week 16, bimekizumab Q8W from week 16 to week 48 and then bimekizumab Q4W from week 48 to week 144 (or early termination)
- Bimekizumab 320mg Q4W
    - Subjects who received bimekizumab Q4W through Week 144 (or early termination).
    - from week 48 to week 144
- GPP bimekizumab total

Any treatment sequence groups for EP or GPP which contain no subjects will not be included in summaries.

PS0014 treatment group (for PSO, GPP and EP groups separately) for safety and exposure analysis:

This refers to the most recent study treatment regimen received at the time of a safety-related event e.g. an AE or markedly abnormal safety value.

This treatment assignment will only apply to certain safety incidence analysis and treatment exposure related analysis. The PS0014 treatment groups are as follows:

- Bimekizumab 320mg Q8W

- Bimekizumab 320mg Q4W
- Bimekizumab total

More detail on assigning events to treatments is provided in Section 10.2.1

PS0014 treatment sequence groups for PK and Immunogenicity summaries:

Below treatment group are all disease combined group only (PSO, GPP and EP combined together).

- Bimekizumab 320mg Q4W (expected n=15)
- Bimekizumab 320mg Q4W to Week 16/Q8W Week 16 –Week 144 (expected n=42)
- Bimekizumab 320mg Q4W to Week 16/Q8W Week 16 –Week 48/Q4W Week 48 –Week 144 (expected n=9)
    - This group includes approximately 7 subjects who switch from Q4W to Q8W after Week 48. The PK data collected after the post Week 48 switch for these subjects will not be included in the PK summaries. All data will be included for immunogenicity summaries.
- Bimekizumab Total (only for immunogenicity analyses)

3.7 Center pooling strategy

No pooling of centers is planned for this study.

3.8 Coding dictionaries

All medications other than the study drug will be classified by World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) classification, presenting Anatomical Main Group (ATC Level 1), Pharmacological Subgroup (ATC Level 3), and preferred term (PT), using version SEP/2015 or later of the World Health Organization Drug Dictionary (WHO-DD), according to UCB standard operating procedures (SOP).

All AEs will be classified by primary system organ class (SOC), high level term (HLT) and PT using version 19.0 or later of Medical Dictionary for Regulatory Activities (MedDRA®) according to UCB SOPs.

Previous and ongoing medical history will be classified by version 19.0 or later of MedDRA® SOC and PT.

3.9 Changes to protocol-defined analyses

- Japanese subjects enrolled in Cohort A and Cohort B will not be pooled.
- Shift from baseline in IGA score was removed as an efficacy outcome for both Cohorts.
- It was clarified that IGA, scalp IGA and pp-IGA response (Clear or Almost Clear with at least 2 category improvement relative to Baseline) will be presented only for PSO subjects in Cohort B. For GPP and EP subjects the incidence rate will be presented.
- Summaries of PASE and PGADA will be produced only for PSO subjects in Cohort B. For GPP and EP subjects, the data will be listed only.
- Addition of sensitivity analyses for scalp IGA, pp-IGA, mNAPSI and PGADA, for Cohort A, due to ERT issues leading to incomplete data collection.

- The summaries for TEAEs and SAEs for feeder study and PS0014 study combined (Cohort A) will not be produced for this final analysis.
- The "Time at risk" derivation is adjusted as appropriate for the Week 144 final analysis.
- Baseline for efficacy summaries in Cohort A will be the feeder study baseline only. PS0014 baseline will not be used.
- Change from Baseline in urinalysis parameters will not be presented.
- Immunogenicity analyses will include evaluation of neutralizing anti-bimekizumab antibody (NAb) data, e.g. overall NAb status and status by type of assay (IL-17AA and IL-17FF).
- For immunogenicity summaries, treatment groups will reflect PS0014 treatment only, not feeder study treatment.
- Addition of COVID-19 impact analyses to evaluate the impact of the pandemic on the study data (see details in section below).
- Addition of sensitivity analyses for efficacy and safety to evaluate the impact of potential incorrect initial treatment assignment due to IWRS data entry errors at study start (see Section Section 8.1.1 and Section 10.2.2.1).
- Cohort B Pharmacokinetics Per Protocol Set by disease type to be removed from analysis.

3.9.1 Changes related to COVID-19

The following changes have been introduced due to the COVID-19 pandemic:

- Impact of COVID-19 is defined in Section 3.4 and the presentation of COVID-19 impact is described in Section 5.3.
- Missing data methods for assessing the impact of COVID-19 are described in Section 4.2.4.
- Data considerations for assessing the impact of COVID-19 on TEAEs are described in Section 10.2.1.1 and the associated analysis is described in Section 10.2.1.2.
- COVID-19 vaccinations and the impact of COVID-19 vaccinations on TEAEs are described in Section 6.4 and Section 10.2.1.2 respectively.

4 STATISTICAL/ANALYTICAL ISSUES

4.1 Adjustments for covariates

Not applicable.

4.2 Handling of dropouts or missing data

4.2.1 Handling of missing data for efficacy variables

If a subject discontinued early from the study, all efficacy data that are collected later than 35 days after the last administration of study treatment will be treated as missing and subject to imputation as applicable.

4.2.2 Missing Data Overview and Summary

In summary, the approaches listed below will be used in this study for handling missing data for efficacy variables as appropriate:

- Non-responder imputation (NRI): Subjects who have missing data at the time point of interest are treated as though they did not respond to the treatment.
- Modified non-responder imputation (mNRI): Subjects with missing data at a given week which are preceded by an intercurrent event (discontinuation of study treatment due to lack of efficacy) are counted as non-responders. Otherwise, missing scores at a given week which are not preceded by an intercurrent event are first imputed using MI before deriving the response. MI is based on Markov Chain Monte Carlo (MCMC) for intermittent missing data, followed by monotone regression (for monotone missing data). Note: for all analyses and summaries using MI, subjects with no baseline value will be excluded.
- Multiple Imputation (MI) – Markov Chain Monte Carlo (MCMC): Using multiple imputation methodology, intermittent missing data are imputed based on the MCMC method, and monotone missing data are imputed using monotone regression. Note: for all analyses and summaries using MI, subjects with no baseline value will be excluded.
- Last Observation Carried Forward: Post-Baseline missing data are imputed by carrying forward the last available observation (including Baseline).
- Observed case (OC): Missing data are not imputed. Only subjects with available data who have not discontinued study treatment at the given time point are considered.
- Additional methods for handling of missing data will be used for the secondary efficacy variables PASI90 and IGA (Clear or Almost Clear) responders through to Week 144 to assess the impact of the COVID-19 global pandemic on planned statistical analysis; these are detailed in Section 4.2.4.

4.2.2.1 Cohort A

The following table depicts which missing data handling approaches will be used for each endpoint.

Table 4.1: Missing data approaches for efficacy endpoints Cohort A

Endpoint	NRI	mNRI	MI (MCMC/ Monotone Regression)	LOCF	Observed Case
PASI response (75/90/100)*	X	X			X
PASI scores (and changes from Baseline)			X	B	
PASI score categories	X				X
IGA response (Clear)	X	X			X

Table 4.1: Missing data approaches for efficacy endpoints Cohort A

Endpoint	NRI	mNRI	MI (MCMC/ Monotone Regression)	LOCF	Observed Case
IGA response (Clear or Almost Clear)*	X	X			X
Scalp IGA response	X	X			X
Palmoplantar IGA response	X	X			X
BSA (and changes from Baseline)			X	B	
BSA score categories	X				X
Product of IGA x BSA (and changes from Baseline)			X	B	
DLQI total score (and changes from Baseline)			X	B	
DLQI MCID	X				X
DLQI total score 0/1	X	X			X
mNAPSI scores (and changes from Baseline)			X	B	
mNAPSI response (75/90/100)	X	X			X
PGADA (and changes from BL)			X	B	
PGA of PSO					X
Shift in PGA of PSO					X
PASE (and changes from Baseline)					X
Shift in PASE					X
SF-36 scores (and changes from Baseline)			X	B	
EQ-5D-3L VAS (and changes from Baseline)			X	B	
EQ-5D-3L responses					X
WPAI-SHP (and changes from Baseline)			X	B	
TSQM-9 scores					X
PHQ-9** total score (and changes from Baseline)			X	B	

Table 4.1: Missing data approaches for efficacy endpoints Cohort A

Endpoint	NRI	mNRI	MI (MCMC/ Monotone Regression)	LOCF	Observed Case

X=Analysis Method to be used, B=Backup method
Note: Backup method is only applicable when the MI method is unable to converge due to challenges with the imputation model.
* Sensitivity analyses to assess the impact of missing/out of window data due to the COVID-19 pandemic will be performed on PASI90 and IGA (Clear or Almost Clear)
**PHQ-9 is a Safety parameter but the MI imputation is done the same way as Efficacy parameters and is using planned treatment.

4.2.2.2 Cohort B

Imputation of missing data will be applied to PSO subjects only.
For responder efficacy variables (PASI75, PASI90, PASI100, percent of subjects with absolute PASI score ≤1, ≤2, ≤3 and ≤5, IGA (Clear), IGA (Clear or Almost Clear), DLQI total score of 0 or 1, DLQI MCID, mNAPSI75, mNAPSI90, mNAPSI100, scalp IGA, pp-IGA and percent of subjects with absolute BSA score 0, ≤1, ≤3 and ≤5), missing data will be handled by non-responder imputation (NRI) meaning that subjects who discontinue early or who have missing data at a given time point are imputed as though they did not achieve the given response. Additionally, missing data for PASI90, PASI100, and IGA Clear or Almost Clear, IGA Clear, Scalp IGA, pp-IGA, mNAPSI 75/90/100 and DLQI 0/1 response will be subject to mNRI.

For continuous efficacy variables based on the change from Baseline (PASI, DLQI total score, PHQ-9 total score, PGADA, EQ-5D-3L, SF-36 PCS, MCS, and domain scores, WPAI-SHP and PASE), missing data will be handled by using multiple imputation via the MCMC method for intermittent data and monotone regression for monotone missing data. Supportive summaries will be based on OC data for key efficacy variables PASI90/100 response, IGA response, and DLQI total score of 0 or 1. The following table Table 4.2 depicts which missing data handling approaches should be used based on variable type (responder, continuous, ordinal).

Table 4.2: Missing data approaches for efficacy endpoint Cohort B

Variable Type	NRI	mNRI	MI (MCMC/ Monotone Regression)	LOCF	OC
Responder	X	X**			X
Continuous			X	B	X*
Ordinal					X

Table 4.2: Missing data approaches for efficacy endpoint Cohort B

Variable Type	NRI	mNRI	MI (MCMC/ Monotone Regression)	LOCF	OC

X= Analysis method to be used, B=Backup method
Note: Backup method is only applicable when the MI method is unable to converge due to challenges with the imputation model.
Note: NRI and MI will be used for PSO subjects only. OC Methods will apply to PSO, GPP and EP subjects.
Note: Sensitivity analyses to assess the impact of missing/out of window data due to the COVID-19 pandemic will be performed on PASI90 and IGA (Clear or Almost Clear) for PSO subjects only
*Applied as a method only for key efficacy variables as PASI and DLQI for PSO subjects. Applied for all continuous parameters for subjects with GPP and EP.
**Applied only for PASI90, PASI100, IGA Clear or Almost Clear Response, IGA Clear response, Scalp IGA, pp-IGA, mNAPSI75/90/100, and DLQI 0/1, for PSO subjects.

4.2.3 Missing data algorithms

4.2.3.1 Multiple imputation procedure for continuous efficacy variables

The multiple imputation (MI) procedure for continuous efficacy variables (based on Markov-Chain Monte Carlo (MCMC)) will be applied as follows.

1. Create a dataset, one for each treatment group (note that a separate imputation procedure must be invoked in SAS for each treatment group as the seed cannot be set for by groups beyond the first when using a by statement), of subjects with observed values and those needing estimation by MI. The intermittent missing values in each dataset will be filled in using the MCMC method with a total of 100 sets of imputations being performed. The seed used for these imputations will be 852 (note that all other multiple imputation procedures described in this SAP related to MCMC / Monotone Regression analyses will use this same seed as well). For monotone missing data (i.e., where all subject data is missing after a given time point), monotone regression will then be used to impute missing data. This will be based on the 100 sets of imputations already created using the MCMC method such that there will be 100 imputations in total. In both cases, prior biologic exposure, geographic region and variable value at Baseline and at each post-Baseline visit (in chronological order, see notes below for more detail) will be included in that specific order in the imputation model. Cut-off values will be applied to the imputed data, as appropriate, to ensure that imputed values do not exceed the range of plausible values for the variable being imputed. The resulting data sets for each treatment arm will be combined into one complete data set based on each of the 100 imputations.
   In order to achieve model convergence, prior biologic exposure may be dropped from the model. The adjustment by "Geographic region" will be done using 3 indicator variables instead of a unique variable with 4 modalities.

   If values outside of the pre-defined range of values for endpoints are imputed, they will be cut off as appropriate after the multiple imputation procedure. The ranges are defined in Table 4.3 .

Table 4.3: Imputation allowable ranges by variable

Variable	Minimum value	Maximum value	Integer values only
PASI	0	72	No
IGA	0	4	Yes
Scalp IGA	0	4	Yes
mNAPSI	0	130	No
BSA	0	100	Yes
IGAxBSA	0	400	Yes
DLQI total score	0	30	Yes
PGADA	0	100	Yes
SF-36 scores	0	100	No
EQ-5D-3L VAS	0	100	Yes
WPAI dimension scores	0	100	No for variables "Percent work time missed due to problem" and "Percent overall work impairment due to problem". Yes for variables "Percent impairment while working due to problem" and "Percent activity impairment due to problem" These two variables can only take values that are multiples of 10"
PHQ-9 total score	0	27	Yes

2. The relevant change from Baseline (or percent change from Baseline) values will then be derived based on the datasets which include observed and imputed values for the variable being considered.
3. The results from each of the 100 imputed datasets will be combined for the calculation of means and standard errors using Rubin's rules, which account for the uncertainty associated with the imputed values (Rubin, 1987). This will be done using SAS PROC MIANALYZE. For calculation of other descriptive statistics such as median, min and max, Rubin's rules do not apply. MI estimates will be computed by simply averaging the estimates from the m = 1, …, M independent repetitions of the imputation algorithm:

$$\overline{\theta} = \frac{1}{M}\sum_{m=1}^{M}\hat{\theta}_m$$

Where $\hat{\theta}_m$= estimate of θ from the completed dataset m = 1, …, M.

There may be cases where the multiple imputation model fails to converge (eg, sparse subgroups), in such situations, the last observation carried forward (LOCF) approach will instead be used to impute the missing data. If LOCF is used instead of MI for this reason, this will be clearly specified in the corresponding table summary. Should there be no missing data for a study variable then only OC data will be produced.

Note that the MI procedure specified above will only be performed for the PSO subjects for Cohort B.

Some further detail on the imputation methods:

- Cohort A FAS: PROC MI with a separate data set for each of the 3 treatment sequence groups (BKZ 320mg Q4W, BKZ 320mg Q8W, BKZ 320mg Q4W/Q8W). Include Feeder Study Baseline assessment and all assessment visits from PS0014 Baseline to Week 144. NOTE: Do not run the combined BKZ 320mg group through PROC MI. You will get the combined group using the imputed values of the individual treatment sequence groups. Note, the BKZ 320mg Q4W group consists only of subjects who discontinued from the study prior to switching to BKZ 320mg Q8W. Due to lack of data beyond Week 40, multiple imputation will only be performed up to Week 40 for this group.
- Cohort B PSO FAS: PROC MI including all assessment visits from Baseline to Week 144 for the whole analysis set.

4.2.3.2 Multiple imputation procedure for response efficacy variables (mNRI)

The multiple imputation (MI) procedure for continuous efficacy variables (based on Markov-Chain Monte Carlo [MCMC] regression procedures) with consideration for intercurrent events will be used to account for missing data in the analysis of response efficacy variables. An intercurrent event is defined as treatment discontinuation due to lack of efficacy.

For study participants who experience an intercurrent event, the intercurrent event date is defined as:

Last study treatment date + 28 days (smallest dosing interval) + 7 days (largest visit window)

If subjects have missing data that are not preceded by an intercurrent event, then the standard MI-MCMC/Monotone regression approach will be implemented on the raw continuous score (eg, PASI for the PASI90 endpoint) before deriving the binary endpoint based on the imputed score.

If subjects have an intercurrent event, then:

- The values of the continuous scores used to derive the binary endpoint collected up to the intercurrent event date will be used in the MI-MCMC/Monotone regression approach.

- The values of the continuous scores used to derive the binary endpoint collected after the intercurrent event date will be set to missing prior to running the MI-MCMC/Monotone regression approach.
- After the MI-MCMC/Monotone regression approach is run, the endpoint at all subsequent visits (from the day after the intercurrent event date, whether the data were observed or not) will be set to "non-response".

The following text describes the algorithms to be implemented for the MI-MCMC/Monotone Regression procedures for binary response endpoints. These descriptions focus on the MI procedure itself and do not specifically account for dealing with intercurrent events.

The multiple imputation (MI) procedure for response efficacy variables (based on MCMC) will be applied as follows.

1. Create dataset, one for each treatment group (note that a separate imputation procedure must be invoked in SAS for each treatment group as the seed cannot be set for by groups beyond the first when using a by statement), of subjects with observed values and those needing estimation by MI. The intermittent missing values in each dataset will be filled in using the MCMC method with a total of 100 sets of imputations being performed. The seed used for these imputations will be 852 (note that all other multiple imputation procedures described in this SAP related to MCMC / Monotone Regression analyses will use this same seed as well). For monotone missing data (i.e., where all subject data is missing after a given time point), monotone regression will then be used to impute missing data. This will be based on the 100 sets of imputations already created using the MCMC method such that there will be 100 imputations in total. In both cases, prior biologic exposure, geographic region and variable value at Baseline and at each post-Baseline visit (in chronological order) will be included in the imputation model in that specific order. Cut-off values will be applied to the imputed data, as appropriate, to ensure that imputed values do not exceed the range of plausible values for the variable being imputed. The resulting data sets for each treatment arm will be combined into one complete data set based on each of the 100 imputations.
   In order to achieve model convergence, prior biologic exposure may be dropped from the model. The adjustment by "Geographic region" will be done using 3 indicator variables instead of a unique variable with 4 modalities.
2. For each complete imputed data set, the dichotomous responder variable (PASI90/IGA 0 or 1) based on the PASI/IGA scores will be computed. The proportion of responders will be calculated for each complete imputed data set.
   Note: For derivation of PASI90 response, the PASI value at each visit in the imputed data sets will be compared directly to the observed Baseline PASI value to determine whether or not a reduction of at least 90% was achieved. If values outside of the pre-defined range of values for PASI (0-72) are imputed, they will be cut off as appropriate after the multiple imputation procedure but before deriving the responder variable. For example, an imputed PASI value of -0.5 would be changed to 0 before deriving the PASI90 responder variable.
   Note: Standard rounding rules will be applied to the imputed IGA values in order to derive the binary IGA 0/1 responder variable. In addition, if values outside of the pre-defined range of values for IGA (0-4) are imputed, they will be cut off as appropriate after the multiple

imputation procedure but before deriving the responder variable. For example, if a subject has an IGA score imputed as 1.4 (and assuming a Baseline IGA score of 3), this imputed value would be rounded down to 1, and the minimum change from Baseline of 2 would have been met. Therefore, this subject would be considered an IGA 0/1 responder. See Table 4-1 for pre-defined ranges for each parameter.

3. The results of each of the 100 imputed data sets will be combined for overall inference using Rubin's rules, which account for the uncertainty associated with the imputed values (Rubin, 1987). This will be done using SAS PROC MIANALYZE.
   Note: This procedure indicates that the imputation model will be applied for each treatment group separately in PROC MI, which will be the default method. However, in the event there are computational challenges with the imputation model (eg, due to a standard deviation of 0 for responses of a given imputation), it is acceptable to modify the imputation model to include treatment as a variable in the model rather than running a separate model for each treatment group. It should be noted that doing so assumes that treatment does not interact with any of the other variables in the imputation model.

Note that the MI procedure specified above will only be performed for the PSO subjects for Cohort B.

Some further detail on the imputation methods:

- Cohort A FAS: PROC MI with a separate data set for each of the 3 treatment sequence groups (BKZ 320mg Q4W, BKZ 320mg Q8W, BKZ 320mg Q4W/Q8W). Include all assessment visits from PS0014 Baseline to Week 144 (only to Week 40 for BKZ 320mg Q4W group) . NOTE: Do not run the combined BKZ 320mg group through PROC MI. You will get the combined group using the imputed values of the individual treatment sequence groups.
- Cohort B PSO FAS: PROC MI including all assessment visits from Baseline to Week 144 for the whole analysis set.
- For convergence purposes, only visits with at least 15 observations for the specific treatment group will be included in the models. If there are not enough observations the visit will be considered non estimable (NE) and the LOCF method will be used instead.
- Cohort A: imputation for MI Tables on the subgroup of Japanese subjects, will be done on the overall population. Then the Japanese subjects will be selected to proceed to steps 2 and 3 of the imputation methods described above, for the estimation purposes.
- By definition, we only impute data for subjects with not missing Baseline value. Therefore, the values presented at Baseline in the Tables are the observed data. It will be presented as is in the MI Tables.

4.2.4 Missing data methods for assessing impact of COVID-19

In order to assess the impact of the COVID-19 global pandemic on the planned statistical analysis, additional sensitivity analyses will be performed for the secondary efficacy variables PASI90 and IGA (Clear or Almost Clear) responders through to Week 144 for both Cohort A and Cohort B. The sensitivity analysis in Section 8.2.1 and Section 8.2.2 will also still be performed.

As described in Section 4.2.1, if a subject discontinues early from the study, all efficacy data that are collected later than 35 days after the last administration of study treatment will be treated as missing and subject to imputation as applicable. Thus if a subject discontinues from the study due to COVID-19 (general circumstances related to the COVID-19 pandemic or due to confirmed or suspected infection with the novel coronavirus), all PASI and IGA assessments later than 35 days after the last administration of study treatment will be treated as missing for analyses purposes.

Any PASI or IGA assessments through to Week 144 that are conducted by video call or telephone will be treated as missing since the validity and exchangeability of these assessment modalities have not been established. This will be determined according to collection of COVID-19 protocol impact information (see Section 5.3 for further details).

4.2.4.1 Hybrid approach for assessing the impact of COVID-19

A sensitivity analysis method to assess the impact of the COVID-19 pandemic on planned statistical analysis uses a hybrid approach and will be applied to the analysis of PASI90 response and IGA (Clear or Almost Clear) through to Week 144. This will be done for Cohort A (CA-FAS) and Cohort B PSO (CBPSO-FAS) populations.

If study subjects have missing PASI or IGA scores between PS0014 Baseline and Week 144, then the imputation method will be dependent on the reason for missingness as follows:

- If the data is missing due to COVID-19 (general circumstances related to the COVID-19 pandemic or due to confirmed or suspected infection with the novel coronavirus), then MI-MCMC/monotone regression will be implemented following the method described in Step 1 of Section 4.2.3.2 to impute the missing scores.
- If the data is missing due to other reasons, then PASI90 response/ IGA (Clear or Almost Clear) response will be imputed as a non-response.

MI-MCMC/monotone regression will be implemented as described in Step 1 of Section 4.2.3.2 for all subjects in the respective analysis set. However, when data is missing or the subject dropped out due to other reasons than COVID-19, they will be considered as PASI90 or IGA (Clear or Almost Clear) non-responders at any particular week for each imputation regardless of their MI-MCMC/monotone regression imputed value. Then Step 3 of Section 4.2.3.2 can be applied. If the PROC MIANALYZE leads to non-calculable results (i.e. if there are a low amount of data missing or subjects dropped out due to COVID-19), this analysis will not be reported.

This sensitivity analysis will not be performed for Cohort B EP (CBEP-FAS) and GPP (CBGPP-FAS) populations due to their small size (approximately 10 subjects).

4.2.4.2 Approach to assess the impact of out of window assessments due to COVID-19

Another sensitivity analysis method to assess the impact of the COVID-19 pandemic on planned statistical analysis will treat PASI/IGA assessments that are out of window through to Week 144 due to COVID-19 as missing.

To determine that the visit is performed out of window requires that the actual date of the PASI /IGA assessment is more than 28 days prior to or 28 days after the date of planned visit.

This will be calculated as:

Planned visit = Date of first dose + the number of expected days to visit

e.g. Planned Week 4 = Date of first dose + 28 days

A PASI/IGA assessment will therefore be determined as out of window due to COVID-19 if the following criteria are both met:

- There is a corresponding out of window COVID-19 impact assessment (see Section 3.4 and Section 5.3 for further details)
- The visit is more than 28 days out of window

A hybrid approach will then be applied as in Section 4.2.4.1 such that if the data is missing due to COVID-19 then MI-MCMC/monotone regression will be implemented and if data is missing due to other reasons, data will be imputed as a non-response using NRI. If the PROC MIANALYZE leads to non-calculable results, this analysis will not be reported.

This approach will be used for Cohort A (CA-FAS) and Cohort B PSO (CBPSO-FAS) populations.

For Cohort B EP (CBEP-FAS) and GPP (CBGPP-FAS) populations, these assessments will be treated as missing for the observed case summaries of PASI90 response and IGA (Clear or Almost Clear) response.

4.2.5 Handling of missing data for the safety analyses

For analyses of AEs, concomitant medication (including past psoriasis medications), and medical procedure usage, a complete date must be established in order to correctly identify the AE, medication or procedure as occurring during treatment or not. For purposes of imputing missing components of partially reported start and stop dates for AEs and for medication use and start dates for medical procedure use, the algorithms listed below will be followed. Start and stop dates of AEs or concomitant medication and start dates for medical procedure will be displayed as reported in the subject data listings (i.e., no imputed values will be displayed in data listings).

Partial AE and concomitant medication start dates will be imputed as follows:

Imputation of Partial Start Dates

- If only the month and year are specified and the month and year of first dose is not the same as the month and year of the start date, then use the 1st of the month
- If only the month and year are specified and the month and year of first dose is the same as the month and year of the start date, then use the date of first dose
- If only the year is specified, and the year of first dose is not the same as the year of the start date, then use the 1st of January of the year of the start date
- If only the year is specified, and the year of first dose is the same as the year of the start date, then use the date of first dose
- If the start date is completely unknown and the stop date is unknown or prior to the date of first dose and the event was entered into the database during the feeder study, then use the date of first dose in feeder study.

- If the start date is completely unknown and the stop date is unknown or not prior to the date of first dose and the event was entered into the database during PS0014, then use one day after date of first dose (date of first dose +1) for cohort A, and use the date of first dose for cohort B. Otherwise do not impute the start date.

Imputation of Partial Stop Dates

- If only the month and year are specified, then use the last day of the month
- If only the year is specified, then use December 31st of that year
- If the stop date is completely unknown, do not impute the stop date.

If the (imputed) stop date is prior to the imputed start date:

- If only the month and year are specified and the month and year of first dose is the same as the month and year of the start date and the stop date is before the date of first dose, then set the start date to the 1st of that month.
- If only the year is specified, and the year of first dose is the same as the year of the start date, and the stop date is before the date of first dose, then use the 1st of January of the year of the start date.

Partial start dates for medical procedure will be imputed as follows:

- If only the month and year are specified and the month and year of first dose is not the same as the month and year of the start date, then use the 1st of the month
- If only the month and year are specified and the month and year of first dose is the same as the month and year of the start date, then use the date of first dose
- If only the year is specified, and the year of first dose is not the same as the year of the start date, then use the 1st of January of the year of the start date
- If only the year is specified, and the year of first dose is the same as the year of the start date, then use the date of first dose
- If the start date is completely unknown, do not impute the start date.

In the event of ambiguity or incomplete data which makes it impossible to determine whether a medication or procedure was concomitant or an adverse event was treatment emergent, the medication or procedure will be considered as concomitant or the adverse event will be considered treatment emergent.

4.3 Interim analyses and data monitoring

- After the final Week 48 visit in Cohort B, an interim analysis, which included both Cohort A and Cohort B, was performed and a corresponding interim CSR was written. Details of the interim analysis are documented in a separate interim SAP.
- In addition, a Week 144 data cut will occur after Week 144 visit and SFU. A Week 144 analysis will be performed using Week 144 and SFU data cut and a corresponding Week 144 interim CSR will be written.

- A final analysis will be conducted when all data for the Treatment Period (including SFU), and OLE2 (including SFU2) period have been collected and final CSR will be written based on locked study database.

4.4 Multicenter studies

Not applicable.

4.5 Multiple comparisons/multiplicity

Not applicable.

4.6 Use of an efficacy subset of subjects

Other than the planned analyses based on the CA-FAS, no other efficacy subsets are defined for statistical analyses in Cohort A.

General analyses in Cohort B will be performed by psoriasis type (PSO, GPP or EP), and unless specified in the following sections, the CB-FAS will be used.

4.7 Active-control studies intended to show equivalence

Not applicable.

4.8 Examination of subgroups

A subset of outputs for Cohort A will be repeated for the Japanese subpopulation in that cohort. These outputs are identified in the TFL shell document.

5 STUDY POPULATION CHARACTERISTICS

5.1 Subject disposition

5.1.1 Cohort A

All subject disposition tables will use the PS0014 treatment sequence groups, with the exception of summaries for the OLE2 period, which will use the OLE2 treatment groups as specified in Section 3.6.1 .

The disposition of subjects enrolled by geographical region and overall, including the number of subjects in each analysis set (CA-ES, CA-SS, CA-FAS, CAPK-PPS, CA-OL2S) will be summarized. This summary will be based on the CA-ES and will present subjects overall and by site.

The disposition of analysis sets based on the CA-SS and CA-OL2S will present all bimekizumab treated subjects and broken out by PS0014 treatment sequence group/OLE2 treatment groups.

Disposition and discontinuation reasons during the treatment period will be presented. The number and percentage of subjects who entered the study, completed each year of the treatment period through Week 48, Week 96 and Week 144, and discontinued through Week 144 with reasons for discontinuation will be presented. The number of subjects completing the safety follow-up will also be presented. This summary will be based on the CA-SS and will present all bimekizumab treated subjects by PS0014 treatment sequence group. Disposition and

discontinuation reasons during OLE2 will be presented based on the CA-OL2S using OLE2 treatment groups.

A subject is considered to have completed through Week 48 if they have either completed the Week 48 visit or received study medication from Week 48 onwards. Similar for Week 96.

A subject is considered to have completed the treatment period if they have completed the Week 144 visit. A subject is considered to have completed the safety follow-up if they have a safety follow-up visit date.

A summary of the total treatment sequence from feeder studies will be presented based on the CA-SS and by PS0014 treatment sequence group.

Discontinuations due to AEs will be presented over the treatment period (Week 0 to Week 144) by PS0014 treatment sequence group based on the CA-SS, and during OLE2 by OLE2 treatment group based on the CA-OL2S.

A separate summary of the number and percentage of subjects switching dose regimen (changing from Q4W to Q8W) by timepoint will be provided for the CA-SS for the bimekizumab 320mg Q4W/Q8W group.

The following listings for subject disposition will be produced based on the CA-ES and presented by Feeder study/PS0014 treatment sequence groups:

- A listing of subjects who did not meet study eligibility criteria
- A listing of subject disposition
- A listing of subject analysis sets

The following listings will be produced based on the CA-SS and presented by Feeder study/PS0014 treatment sequence groups:

- A listing of study discontinuation
- A listing of visit dates
- A listing of subjects excluded from analysis set

Similar listings will be provided separately for the OLE2 treatment period.

5.1.2 Cohort B

A summary table of reasons for screen failures will be presented based on the CB-ES.

The disposition of subjects enrolled by site and overall, including the number of subjects in each analysis set (CB-ES, CB-SS, CBPSO-SS, CBGPP-SS, CBEP-SS, CB-FAS, CBPSO-FAS, CBGPP-FAS, CBEP-FAS, CBPK-PPS) will be summarized BKZ Total group. This summary will be based on the CB-ES.

The disposition of analysis sets based on the CB-SS will present all bimekizumab treated subjects and broken out by PS0014 treatment sequence group.

Disposition and discontinuation reasons during the treatment period will be presented. The number and percentage of subjects who entered the study, completed each year of the treatment period Week 48, Week 96 and Week 144, and discontinued through Week 144 with reasons for

discontinuation will be presented. The number of subjects who completed the safety follow-up will also be presented. This summary will be based on the CB-SS and will present all subjects by PS0014 treatment sequence group and psoriasis type.

A subject is considered to have completed through Week 48 if they have either completed the Week 48 visit or received study medication from Week 48 onwards. Similar for Week 96.

A subject is considered to have completed the treatment period if they have completed the Week 144 visit. A subject is considered to have completed the safety follow-up if they have a safety follow-up visit date.

Discontinuations due to AEs will also be presented for Weeks 0-144. These summaries will be based on the CB-SS and will present all bimekizumab treated subjects and will be broken out by PS0014 treatment sequence group and psoriasis type.

The following listings for subject disposition will be produced based on the CB-ES and presented by PS0014 treatment sequence group:

- A listing of subjects who did not meet study eligibility criteria
- A listing of subject disposition
- A listing of subject analysis sets.

The following listings for subject disposition will be produced based on the CB-SS and presented by PS0014 treatment sequence group:

- A listing of study discontinuation
- A listing of visit dates
- A listing of subjects excluded from any analysis set.

5.2 Protocol deviations

5.2.1 Cohort A

A summary of number and percentage of subjects with an important protocol deviation (including a summary of subjects excluded from any analysis set due to important protocol deviations) by PS0014 treatment sequence group/OLE2 treatment group will be provided for the CA-SS and CA-OL2S.

Any COVID-19 impact protocol deviations (as described in Section 5.3) that are determined to be important will be included in this summary.

A by-subject listing of important protocol deviations will be provided based on the CA-SS.

A similar listing will be provided separately for the OLE2 treatment period.

Separate listings of subjects with COVID-19 protocol deviations will also be provided for the 144-week and the OLE2 treatment periods.

5.2.2 Cohort B

A summary of number and percentage of subjects with an important protocol deviation (including a summary of subjects excluded from any analysis set due to important protocol

deviations) will be provided for the CB-SS by PS0014 treatment sequence group psoriasis type (PSO, GPP, EP) and overall.

Any COVID-19 impact protocol deviations (as described in Section 5.3) that are determined to be important will be included in this summary.

A by-subject listing of important protocol deviations will be provided based on the CB-SS.

5.3 COVID-19 Impact

For study participants impacted by the COVID-19 global pandemic, data was collected on a separate eCRF. This form was collected for study visits that were affected by COVID-19, and it collected how the visits were impacted by the pandemic (e.g., performed out of window, done by telephone instead of on-site, not done, etc).

Based on how the visit was affected by the global pandemic, all visits will have a variable indicating how the visit was performed:

- Visit not done at all
- Visit done by video call
- Visit done by telephone
- Visit done at different time point than planned / out of window
- Visit done at different location/center

Additionally, for visits that are affected by COVID-19, all assessments that are missing will be flagged as missing due to COVID-19. Further, the specific reason of missing data will be captured as the following flags:

- Confirmed COVID-19 infection
- Suspected COVID-19 infection
- General circumstances around COVID-19 without infection
- Other

Where data has not been collected per protocol due to COVID-19 circumstances, additional sensitivity analyses will be performed to assess the impact. These are described in Section 4.2.4 and Section 10.2.1.2.

5.3.1 Cohort A

A summary of number and percentage of subjects experiencing an impact of COVID-19 on study conduct by PS0014 treatment group and OLE2 treatment group and visit will be provided separately for the CA-SS and CA-OL2S. These summaries will also be repeated by country.

A by-site, subject and visit listing of COVID-19 protocol deviations will be provided.

5.3.2 Cohort B

A summary of number and percentage of subjects experiencing an impact of COVID-19 on study conduct by PS0014 treatment sequence group and visit will be provided for the CB-SS.

A by-site, subject and visit listing of COVID-19 protocol deviations will be provided.

6 DEMOGRAPHICS AND OTHER BASELINE CHARACTERISTICS

All summaries detailed in this section will be performed on the CA-SS by PS0014 treatment sequence group for the Cohort A, with the exception of summaries on the CA-OL2S which will use OLE2 treatment groups. For subjects enrolling from the Feeder studies, Baseline is taken from the feeder study Baseline unless specified otherwise. For Cohort B, all summaries detailed in this section will be performed on the CB-SS by psoriasis type (PSO, GPP, EP) and overall.

6.1 Demographics

6.1.1 Cohort A

Demographic variables will be summarized by PS0014 treatment sequence group and all bimekizumab treated subjects and will be repeated for feeder study/PS0014 treatment groups. A separate feeder study demographic summary will be provided for CA-OL2S.

The following continuous variables will be summarized using descriptive statistics (number of subjects, mean, SD, minimum, median and maximum).

- Age at the time of feeder study entry (years)
- Height (cm)
- Weight (kg)
- BMI (kg/m^2)

BMI (kg/m^2) will be calculated as:

$$BMI = \frac{\text{Weight (kg)}}{(\text{Height (m)})^2}$$

The following categorical variables will be summarized using frequency counts and percentages.

- Age group (18-<65, 65-<85, ≥85 years)
- Age group (≤18, 19-<65, ≥65 years)
- Age group (<40, 40-<65, ≥65 years)
- Body Weight (≤100kg, >100kg)
- Body Weight (≤120kg, >120kg)
- BMI (<25 kg/m2, 25 to <30 kg/m2, ≥30 kg/m2)
- Gender
- Race
- Ethnicity
- Region (North America [Canada, USA], Western Europe [Belgium, France, Germany, Italy, Netherlands, Norway, Spain, Sweden, Switzerland, United Kingdom],

Central/Eastern Europe [Czech Republic, Hungary, Poland, Russian Federation], Asia/Australia [Australia, Japan, Republic of Korea, Taiwan, Turkey]

- Country

By-subject listings of demographics will be provided.

6.1.2 Cohort B

Demographic variables will be summarized separately by using PS0014 treatment sequence group and each psoriasis type (PSO, GPP, EP) and overall.

The following continuous variables will be summarized using descriptive statistics (number of subjects, mean, SD, minimum, median and maximum).

- Age at the time of feeder study entry (years)
- Height (cm)
- Weight (kg)
- BMI (kg/m^2)

BMI (kg/m^2) will be calculated as:

$$BMI = \frac{\text{Weight (kg)}}{(\text{Height (m)})^2}$$

The following categorical variables will be summarized using frequency counts and percentages.

- Age group (18-<65, 65-<85, ≥85 years)
- Age group (≤18, 19-<65, ≥65 years)
- Age group (<40, 40-<65, ≥65 years)
- Body Weight (≤100kg, >100kg)
- Body Weight (≤120kg, >120kg)
- BMI (<25 kg/m2, 25 to <30 kg/m2, ≥30 kg/m2)
- Gender
- Race
- Ethnicity

By-subject listings of demographics will be provided by psoriasis type.

6.2 Other Baseline characteristics

6.2.1 Cohort A

Baseline characteristics (including Baseline clinical measures) will be summarized by PS0014 treatment sequence group and all bimekizumab treated subjects and will be repeated for feeder study / PS0014 treatment groups. A separate feeder study baseline characteristics summary will be provided for OLE2 treatment period using CA-OL2S.

Generally, the following continuous variables will be summarized using descriptive statistics (number of subjects, mean, SD, minimum, median and maximum). Psoriasis BSA (BSA; %)

- PASI score
- mNAPSI total score
- mNAPSI total score for subjects with nail involvement (i.e. mNAPSI>0)
- PGADA for VAS score
- DLQI total score
- PHQ-9 total score
- Duration of disease (years)

Duration of disease (years) will be calculated as:

$$Disease\ Duration = \frac{(Date\ of\ randomization^{1} - Date\ of\ onset\ of\ Plaque\ Psoriasis^{2})}{365.25}$$

[1]Use Date of randomization for subjects enrolled from a Feeder Study. If the date of randomization is missing, then the duration of disease will be derived using the date of screening for the directly enrolled subjects.

[2]If the date of onset of plaque psoriasis is partial, it should be imputed to the most recent feasible date (ie, last day of the month if only day is missing, or the last day of the year if day and month are missing).

The following categorical variables will be summarized using frequency counts and percentages.

- PGADA (=0, >0)
- DLQI total score (=0, =1)
- Duration of disease (<median, ≥median)
- IGA score
- Baseline disease severity (PASI<20, PASI≥20)
- Nail involvement (yes, no)
- Scalp involvement (yes, no)
- Palmoplantar involvement (yes, no)
- PsA (yes, no)
- Prior biologic exposure (yes, no)
- Prior anti-TNF therapy (yes, no)
- Prior primary failure to biologic (yes/no)
- Prior phototherapy or chemotherapy (yes, no)

- Any prior systemic therapy (yes, no)

The categorization of whether or not subjects had prior exposure to biologic therapy will be based on the Psoriasis Treatment History electronic Case Report Form (eCRF) module of the Feeder Study Baseline.

By-subject listings of Baseline characteristics will be provided.

6.2.2 Cohort B

Baseline characteristics (including Baseline clinical measures) will be summarized by using PS0014 treatment sequence groups and psoriasis type (PSO, GPP, EP) and overall.

The categorization of whether or not subjects had prior exposure to biologic therapy will be based on the Psoriasis Treatment History eCRF module at Screening.

Generally, the following continuous variables will be summarized using descriptive statistics (number of subjects, mean, SD, minimum, median and maximum).

- Psoriasis BSA (BSA; %)
- PASI score
- mNAPSI total score
- mNAPSI total score for subjects with nail involvement (i.e. mNAPSI>0)
- PGADA for VAS score
- DLQI total score
- PHQ-9 total score
- Duration of disease (years)

Duration of disease (years) will be calculated as:

$$Disease\ Duration = \frac{(Date\ of\ enrollment - Date\ of\ onset\ of\ Plaque\ Psoriasis)}{365.25}$$

If the date of enrollment is missing, then the duration of disease will be derived using the date of screening.

If the date of onset of plaque psoriasis is partial, it should be imputed to the most recent feasible date (i.e., last day of the month if only day is missing, or the last day of the year if day and month are missing).

The following categorical variables will be summarized using frequency counts and percentages.

- PGADA (=0, >0)
- DLQI total score (=0, =1)
- Duration of disease (<median, ≥median)
- IGA score
- Baseline disease severity (PASI<20, PASI≥20)
- Nail involvement (mNAPSI>0 at Baseline) (yes, no)

- Scalp involvement (Scalp IGA>0 at Baseline) (yes, no)
- Palmoplantar involvement (pp-IGA>0 at Baseline) (yes, no)
- PsA (yes, no)
- Prior biologic therapy (yes, no)
- Prior anti-TNF therapy (yes, no)
- Prior phototherapy or chemotherapy (yes, no)
- Prior primary failure to biologic (yes/no)
- Any prior systemic therapy (yes, no)
- JDA score for subjects with GPP only

By-subject listings of Baseline characteristics will be provided by psoriasis type.

6.3 Medical history and concomitant diseases

6.3.1 Cohort A

Previous and ongoing medical history (including medical history recorded at the start of the feeder studies and updated medical history recorded at the end of the feeder studies) will be summarized by PS0014 treatment sequence groups, system organ class (SOC) and preferred term (PT) using MedDRA®. Medical procedures are not coded.

The following listings for medical history and concomitant diseases will be provided: psoriasis history, previous and ongoing medical history glossary, previous and ongoing medical history conditions, inflammatory bowel disease and chest X-Ray. For subjects with DILI events in PS0014, history of hepatic events and relevant data (potentially hepato-toxio medication, symptoms of hepatitis and symptoms of hypersensitivity) will be listed.

For subjects entered in OLE2 Group B, any additional medical history collected during OLE2 screening will be flagged in the medical history listing.

6.3.2 Cohort B

Previous and ongoing medical history will be summarized by using PS0014 treatment sequence groups by SOC, and PT using MedDRA®. Medical procedures are not coded.

The following listings for medical history and concomitant diseases will be provided: psoriasis history, previous and ongoing medical history glossary, previous and ongoing medical history conditions, and inflammatory bowel disease and chest X-Ray. For subjects with DILI events in PS0014, history of hepatic events and relevant data (potentially hepato-toxio medication, symptoms of hepatitis and symptoms of hypersensitivity) will be listed.

6.4 Prior and concomitant medications

For Cohort A and Cohort B, concomitant medications which started before Week 144 and were ongoing at the end of the study will be included with the status remaining as ongoing.

Prior medications include any medications that started prior to the start date of study medication in PS0014. Concomitant medications are medications taken at least one day in common with the study medication dosing period.

For subjects who discontinue early, the dosing period ends at the last study medication date + 28 days (Note: This assumes a 4 weekly dosing interval. If the dosing interval is longer [i.e. 8 weekly], then the number added here should be adjusted accordingly). For subjects who complete the study as planned, the dosing period ends at the later of the following two dates:

- Last study medication date + 28 days (Note: This assumes a 4 weekly dosing interval. If the dosing interval is longer [i.e. 8 weekly], then the number added here should be adjusted accordingly)
- The last scheduled visit date

6.4.1 Cohort A

Medication start and stop dates will be compared to the date of the first dose of PS0014 treatment to allow medications to be classified as either prior or concomitant.

Prior medications include any medications that started prior to the start date of study medication in PS0014. Concomitant medications are medications taken at least one day in common with the study medication dosing period. Medications that start prior to the date of the first dose of study medication and are ongoing after the start date will be considered both prior and concomitant.

Prior medication which is completed medication from feeder study will be included as prior medication compared to the first dose of PS0014 study medication.

Details of imputation methods for missing or partial dates are described in Section 4.2.5.

The number and percentage of subjects taking prior and concomitant medications (excluding past psoriasis medications) will be summarized separately by PS0014 treatment sequence group and by ATC class, presenting Anatomical Main Group (ATC Level 1), Pharmacological Subgroup (ATC Level 3), and preferred term.

By-subject listing of all prior and concomitant medications will be provided.

By-subject listings of all Prior and Concomitant medications (including COVID-19 concomitant medications), prior and concomitant medications glossary, and psoriasis treatment history will be provided separately for the 144-week Treatment Period and OLE2 Period. Ongoing concomitant medications from the Treatment Period to OLE2 period will be flagged.

The number and percentage of study participants with concomitant vaccines for COVID-19 will be summarized by treatment sequence group, overall and by World Health Organization Drug Dictionary Standardised Drug Grouping (SDG), presenting SDG subgroup, and preferred term. The SDG subgroup Vaccines for COVID-19 will be used to identify vaccines for COVID-19 using the narrow scope; this subgroup is divided further into separate subgroups which is the level that will be presented. The number of individual occurrences of the vaccine for COVID-19 will also be summarized.

A by-study participant listing of all Concomitant vaccines for COVID-19 will be provided.

An additional listing of concomitant vaccines for COVID-19 will be provided separately for OLE2 treatment period.

6.4.2 Cohort B

Past psoriasis medications will be summarized by using PS0014 treatment sequence groups and psoriasis type (PSO, GPP, EP). These medications are not subject to dictionary coding. Past psoriasis medication as classified in non-biologic systemic agent, biologic agent (e.g. IL12, IL12/IL23, IL17, Anti-TNF, …) via manual review by the study physician. Prior anti-TNFs include etanercept, adalimumab, infliximab, certolizumab pegol, and golimumab. Although the JAK inhibitor tofacitimib was categorized as a biologic agent on the Psoriasis Treatment History eCRF page, JAK inhibitors will be categorized and summarized as a non-biologic systemic agent. In addition, subjects who failed past psoriasis biologic treatment will be summarized by reason of failure as captured on the Psoriasis Treatment History eCRF module.

A by-subject listing of all past psoriasis medication will be provided.

Medication start and stop dates will be compared to the date of the first dose of treatment to allow medications to be classified as either prior or concomitant.

Prior medications include any medications that started prior to the start date of study medication. Concomitant medications are medications taken at least one day in common with the study medication dosing period. Medications that start prior to the date of the first dose of study medication and are ongoing after the start date will be considered both prior and concomitant.

Details of imputation methods for missing or partial dates are described in Section 4.2.5.

The number and percentage of subjects taking prior medications (excluding past psoriasis medications) will be summarized by psoriasis type (PSO, GPP, EP), overall and by ATC class, presenting Anatomical Main Group (ATC Level 1), Pharmacological Subgroup (ATC Level 3), and preferred term.

The number and percentage of subjects taking concomitant medications will be summarized similarly.

A by-subject listing of all prior and concomitant medications will be provided.

The number and percentage of study participants with concomitant vaccines for COVID-19 will be summarized by psoriasis type (PSO, GPP, EP), overall and by World Health Organization Drug Dictionary Standardised Drug Grouping (SDG), presenting SDG subgroup, and preferred term. The SDG subgroup Vaccines for COVID-19 will be used to identify vaccines for COVID-19 using the narrow scope; this subgroup is divided further into separate subgroups which is the level that will be presented. The number of individual occurrences of the vaccine for COVID-19 will also be summarized.

A by-study participant listing of all Concomitant vaccines for COVID-19 will be provided.

6.5 Medical Procedures

Past medical procedures include any procedures that started prior to the start date of study medication in PS0014. Concomitant procedures are procedures with at least one day in common with the study medication dosing period.

For subjects who discontinue early or who completed the study as planned, the dosing period ends at the last study medication date + 28 or +56 days for a 4 weekly (Q4W) or 8 weekly (Q8W) dosing interval, accordingly.

Details of imputation methods for missing or partial dates are described in Section 4.2.5.

6.5.1 Cohort A

A by-subject listing of all concomitant medical procedures will be provided.

6.5.2 Cohort B

A by-subject listing of all concomitant medical procedures and all past medical procedures will be provided.

6.6 Lifestyle

6.6.1 Cohort A

A by-subject listing of the lifestyle data from feeder study baseline will be provided for all Cohort A Safety Set.

6.6.2 Cohort B

A by-subject listing of the lifestyle data will be provided for all Cohort B Safety Set.

7 MEASUREMENTS OF TREATMENT COMPLIANCE

Due to the method of administration of the treatments, compliance will be examined in terms of completed injections in the 144-week period. The sum of the difference in number of injections between the actual used and expected injection will be summarized. In addition, treatment compliance will be further computed based on the number of actual and expected injection. The treatment compliance will be summarized as a continuous variable and categorically (<75% and >=75%).

Treatment compliance will be calculated as:

$$\frac{total\ number\ of\ completed\ injections}{total\ number\ of\ expected\ injections} \times 100$$

where the total number of expected injections is derived relative to when the subject finishes treatment.

7.1 Cohort A

Treatment compliance for the period of Year 1 (prior to Week 48), Year 2 (the period from Week 48 and prior to Week 96) and Year 3 (from Week 96 to the end of the treatment period) and overall (starting from Week 0 through Week 144) Period will be performed on the CA-SS and will be provided by PS0014 treatment sequence group. Separate summary of treatment compliance will be provided for the OLE2 treatment period.

The number of injections expected to be provided would vary dependent upon the dosing regimen as detailed below.

For subjects who did not switch from Q4W to Q8W dosing at Week 24, the dosing interval was changed from Q4W to Q8W at Week 48 or at the next scheduled clinic visit (i.e., Week 60, Week 72, Week 84, Week 96, Week 108, Week 120, or Week 132) after implementation of

Protocol Amendment #3 or Protocol Amendment #3.2 in Japan, if the subject had already completed the Week 48 visit.

The number of expected injections for subjects completing the 144-week treatment period are as follows:

- Bimekizumab Q8W only: 36 injections (2x18 Q8W visit)
- Bimekizumab Q4W/Q8W (Switching at Week 24): 42 injections (2x7 Q4W visit+2x 14 Q8W visit)
- Bimekizumab Q4W/Q8W (Switching at Week 48): 48 injections (2x12 Q4W visit+2x 12 Q8W visit)
- Bimekizumab Q4W/Q8W (Switching at Week 60): 50 injections (2x15 Q4W visit+2x 10 Q8W visit)
- Bimekizumab Q4W/Q8W (Switching at Week 72): 54 injections (2x19 Q4W visit+2x 8 Q8W visit)
- Bimekizumab Q4W/Q8W (Switching at Week 84): 56 injections (2x21 Q4W visit+2x 7 Q8W visit)
- Bimekizumab Q4W/Q8W (Switching at Week 96): 60 injections (2x25 Q4W visit+2x 5 Q8W visit)
- Bimekizumab Q4W/Q8W (Switching at Week 108): 62 injections (2x27 Q4W visit+2x 4 Q8W visit)
- Bimekizumab Q4W/Q8W (Switching at Week 120): 66 injections (2x31 Q4W visit+2x 2 Q8W visit)
- Bimekizumab Q4W/Q8W (Switching at Week 132): 68 injections (2x33 Q4W visit+2x 1 Q8W visit)

If a subject discontinues early, then the number of expected injections is based on the time of early discontinuation relative to the dosing visits.

The number of expected injections for subjects completing the OLE2 treatment period are as follows:

Group A

- Bimekizumab Q8W : 12 injections (2x6 Q8W visit)

Group B

- Q4W IMP administration only applies to those subjects who have entered the OLE2 Period as part of Group B and had an IGA ≥3 upon entry of OLE2 Period. These subjects will receive Q4W dosing for 16 weeks, then will change from Q4W to Q8W dosing.
    - Bimekizumab Q4W/Q8W : 16 injections(2x5 Q4W visit +2x3 Q8W visit)

- Subjects who have entered the OLE2 Period as part of Group B with an IGA <3 upon entry of OLE2 Period will receive Q8W dosing from the OLE2 Screening Visit onwards.
    - Bimekizumab Q8W : 12 injections (2x6 Q8W visit)

A by-subject listing of treatment compliance will be provided. A separate listing of treatment compliance will be provided for the OLE2 treatment period.

7.2 Cohort B

Treatment compliance for Year 1 (prior to Week 48), Year 2 (the period from Week 48 and prior to Week 96) and Year 3 (from Week 96 to the end of the treatment period) and overall (starting from Week 0 through Week 144) will be performed on the CB-SS and will be provided by treatment sequence group and will be presented separately by psoriasis type (PSO, GPP, EP).

Subjects with chronic plaque PSO in Cohort B will receive bimekizumab 320mg Q4W until Week 16 and 320mg Q8W thereafter through Week 40.

At Week 48, Cohort B subjects with chronic plaque PSO will continue bimekizumab 320mg Q8W through to the end of the study (Week 144). If the subject's dosing interval had changed to bimekizumab 320mg Q4W at Week 48 under Protocol Amendment #1.2, the subject's dosing interval will change to bimekizumab 320mg Q8W at the next scheduled clinic visit after implementation of Protocol Amendment #3.2.

Subjects with GPP and EP in Cohort B will receive bimekizumab 320mg Q4W until Week 16. Thereafter, Cohort B subjects with GPP and EP who achieve an IGA response of 0 or 1 at Week 16 will receive bimekizumab 320mg Q8W through Week 40. Cohort B subjects with GPP and EP who do not achieve an IGA response of 0 or 1 at Week 16 will continue bimekizumab 320mg Q4W through to the end of the study.

At Week 48, for Cohort B subjects with GPP and EP receiving bimekizumab 320mg Q8W, if IGA response of 0 or 1 is not achieved, the subject's dosing interval will change from 320mg Q8W to 320mg Q4W through to the end of the study (Week 144). Cohort B subjects with GPP and EP receiving bimekizumab 320mg Q8W who do achieve IGA response of 0 or 1 at Week 48 will continue receiving bimekizumab 320mg Q8W through to the end of the study (Week 144).

The number of expected injections for subjects with plaque PSO completing the treatment period are as follows:

- Bimekizumab Q4W/Q8W (Switching at Week 16): 40 injections (2x5 Q4W visit+2x 15 Q8W visit)
- Bimekizumab Q4W (Switching at Week 16)/Q8W/Q4W (Switching at Week 48)/Q8W (Switching at Week 60): 42 injections (2x5 Q4W visit +2x4 Q8W visit+2x2 Q4W visit+2x 10 Q8W visit)
- Bimekizumab Q4W (Switching at Week 16)/Q8W/Q4W (Switching at Week 48)/Q8W (Switching at Week 72): 46 injections (2x5 Q4W visit +2x4 Q8W visit+2x6 Q4W visit+2x 8 Q8W visit)

- Bimekizumab Q4W (Switching at Week 16)/Q8W/Q4W (Switching at Week 48)/Q8W (Switching at Week 84): 48 injections (2x5 Q4W visit +2x4 Q8W visit+2x8 Q4W visit+2x 7 Q8W visit)
- Bimekizumab Q4W (Switching at Week 16)/Q8W/Q4W (Switching at Week 48)/Q8W (Switching at Week 96): 52 injections (2x5 Q4W visit +2x4 Q8W visit+2x12 Q4W visit+2x 5 Q8W visit)
- Bimekizumab Q4W (Switching at Week 16)/Q8W/Q4W (Switching at Week 48)/Q8W (Switching at Week 108): 54 injections (2x5 Q4W visit +2x4 Q8W visit+2x14 Q4W visit+2x 4 Q8W visit)
- Bimekizumab Q4W (Switching at Week 16)/Q8W/Q4W (Switching at Week 48)/Q8W (Switching at Week 120): 58 injections (2x5 Q4W visit +2x4 Q8W visit+2x18 Q4W visit+2x 2 Q8W visit)
- Bimekizumab Q4W (Switching at Week 16)/Q8W/Q4W (Switching at Week 48)/Q8W (Switching at Week 132): 60 injections (2x5 Q4W visit +2x4 Q8W visit+2x20 Q4W visit+2x 1 Q8W visit)

The number of expected injections for subjects with GPP completing the treatment period are as follows:

- Bimekizumab Q4W only: 72 injections (2x36 Q4W visit)
- Bimekizumab Q4W/Q8W (Switching at Week 16): 40 injections (2x5 Q4W visit+2x 15 Q8W visit)
- Bimekizumab Q4W (Switching at Week 16)/Q8W/Q4W (Switching at Week 48): 64 injections (2x5 Q4W visit +2x4 Q8W visit+2x23 Q4W visit)

The number of expected injections for subjects with EP completing the treatment period are as follows:

- Bimekizumab Q4W only: 72 injections (2x36 Q4W visit)
- Bimekizumab Q4W/Q8W (Switching at Week 16): 40 injections (2x5 Q4W visit+2x 15 Q8W visit)
- Bimekizumab Q4W (Switching at Week 16)/Q8W/Q4W (Switching at Week 48): 64 injections (2x5 Q4W visit +2x4 Q8W visit+2x23 Q4W visit)

If a subject discontinues early, then the number of expected injections is based on the time of early discontinuation relative to the dosing visits.

A by-subject listing of treatment compliance will be provided.

8 EFFICACY ANALYSES

8.1 General statistical considerations

All observed data at scheduled protocol visits up to Week 144 will be analyzed. If a subject discontinues early from the study, all efficacy data that are collected later than 35 days after the last administration of study treatment will be treated as missing.
All missing data at scheduled protocol visits are subject to imputation following rules established in Section 4.2.2.

8.1.1 Cohort A

All efficacy analyses will be performed on the CA-FAS unless otherwise specified.

All efficacy summary tables will be displayed by PS0014 treatment sequence group up to Week 144. For key efficacy variables PASI90, PASI100, IGA 0/1, IGA 0 and DLQI 0/1 the summary will be repeated using Feeder Study/ PS0014 treatment group up to Week 48 only. Changes from Baseline will be calculated using the Feeder Study Baseline. In general, efficacy summaries will include only PS0014 visits. The Feeder Study Baseline will be added for select summaries as specified.

Due to an inconsistency in the ERT data collection system for some Cohort A subjects and some parameters, data were not collected as planned for a period of time until the issue was corrected. The parameters involved were mNAPSI, Scalp-IGA, pp-IGA, PASE and PGADA. Details of the analysis of these parameters to examine the impact of this are described in the relevant sections below.

At the time of entry into PS0014 from the feeder studies, it was required to enter a subject's current PASI response into IWRS in order for the initial PS0014 treatment (Q4W or Q8W) to be assigned according to the randomization rules/ratios stated in the protocol. It was subsequently found that 140 subjects did not have their correct PASI response entered into IWRS and therefore these subjects were potentially incorrectly assigned to their PS0014 treatment. Due to the use of randomization ratios it is not possible to know precisely each subject that was misallocated to either Q4W or Q8W.

To assess the impact of this on the evaluation of efficacy, PASI90 and IGA 0/1 response were summarized excluding the 140 potentially impacted subjects, as described in the relevant sections below.

For all efficacy analyses involving MI, the bimekizumb 320mg Q4W group will only have data displayed up to week 40. This group consists of subjects who discontinued prior to the change of dosing interval from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W and very few subjects remained on Q4W after Week 40.

The OC and NRI approach will be used to summarize the following efficacy variables in the OLE2 treatment period: PASI90, PASI100, IGA (Clear or Almost Clear), IGA response (Clear), and DLQI 0/1.

8.1.2 Cohort B

Efficacy analyses will be summarized based on the CB-FAS unless stated otherwise. Summaries will be presented by PS0014 treatment sequence groups and psoriasis type.

The following efficacy endpoints were collected in a previous version of the Japan specific protocol but were removed in a protocol amendment: Physician's global assessment of disease activity (PhGADA) for arthritis VAS, Patient's Assessment of Arthritic Pain VAS, Health Assessment Questionnaire-Disability Index, American College of Rheumatology criteria, and Swollen and tender join counts. Any data collected for these assessments before the protocol amendment will be listed only.

All assessments will be summarized up to Week 144 for these final analyses.

8.2 Statistical analysis of the efficacy variables

8.2.1 PASI score and response

8.2.1.1 Derivation of PASI score and response

PASI scoring of psoriatic plaques is based on three criteria: redness (R), thickness (T), and scaliness (S). Severity is rated for each index (R, S, T) on a 0-4 scale (0 for no involvement up to 4 for very marked involvement). The body is divided into four areas comprising the head (h), upper extremities (u), trunk (t), and lower extremities (l). In each of these areas, the fraction of total surface area affected is graded on a 0-6 scale (0 for no involvement; up to 6 for 90% - 100% involvement). The various body regions are weighted to reflect their respective proportion of BSA. The composite PASI score is then calculated by multiplying the sum of the individual-severity scores for each area by the weighted area-of-involvement score for that respective area, and then summing the four resulting quantities as follows (note for R, T, and S scores are as follows: 0 = none, 1 = slight, 2 = moderate, 3 = marked, and 4 = very marked):

$$\begin{aligned}\text{PASI} = {} & (0.1 \times (\text{R}_\text{h} + \text{T}_\text{h} + \text{S}_\text{h}) \times \text{A}_\text{h}) + (0.2 \times (\text{R}_\text{u} + \text{T}_\text{u} + \text{S}_\text{u}) \times \text{A}_\text{u}) \\ & + (0.3 \times (\text{R}_\text{t} + \text{T}_\text{t} + \text{S}_\text{t}) \times \text{A}_\text{t}) + (0.4 \times (\text{R}_\text{l} + \text{T}_\text{l} + \text{S}_\text{l}) \times \text{A}_\text{l})\end{aligned}$$

where

Rh, Ru, Rt, Rl = redness score of plaques on the head, upper extremities, trunk, and lower extremities, scored 0-4 respectively;

Th, Tu, Tt, Tl = thickness score of plaques on the head, upper extremities, trunk, and lower extremities, scored 0-4 respectively;

Sh, Su, St, Sl = scaliness score of plaques on the head, upper extremities, trunk, and lower extremities, scored 0-4 respectively;

Ah, Au, At, Al = numerical value translation of % area of psoriatic involvement score for the head, upper extremities, trunk, and lower extremities, respectively (where 0 = 0% [clear], 1 = >0% to <10%, 2 = 10% to <30%, 3 = 30% to <50%, 4 = 50% to <70%, 5 = 70% to <90%, and 6 = 90% to 100%).

The highest potential PASI score is 72 for severe disease; the lowest is 0 for no psoriasis lesions. PASI scores are treated as continuous. The percent improvement in PASI scores from Baseline will be computed as:

$$\text{Percent improvement from Baseline } = 100 \times \frac{\text{Baseline PASI} - \text{Post Baseline PASI}}{\text{Baseline PASI}}$$

If a subject has experienced an improvement, this measure will be positive. If a subject has experienced a worsening in their condition, this measure will be negative.

If a subject is missing 1 or 2 severity measurements for a certain region, the average of the remaining severity measurement(s) within that region will be utilized to substitute for the missing severity measurement(s) in that region. If the area of affected skin and/or all severity measurements for up to 2 regions are missing, then the missing (R+T+S) x A for a region will be substituted by the average of the available (R+T+S) x A. Otherwise, the PASI will be set to missing.

Categorical response variables, PASI75, PASI90 and PASI100 over time are defined to be equal to 1 if the percentage improvement from Baseline to visit timepoint in the PASI scores is 75%, 90% and 100% respectively or greater and 0 if the percentage improvement from Baseline to visit timepoint is less than 75%, 90% and 100% respectively. This definition is introduced for the purpose of identifying subjects who respond to the treatment (1 = responder, 0 = non-responder).

8.2.1.2 Analysis of PASI score and response

8.2.1.2.1 Cohort A

Frequency tables will be produced to show the number and percentage of PASI75, PASI90, and PASI100 responders for each PS0014 visit, by PS0014 treatment sequence group and for all subjects combined. The PASI responder variables will be derived relative to Feeder Study Baseline. This summary will be performed using NRI and observed case data.

The summary for PASI90 and PASI100 will be repeated for Feeder Study/PS0014 treatment groups up to Week 48. Additional summaries will be presented for the number and percentage of PASI90 and PASI100 responders compared to Feeder Study Baseline using the mNRI method defined in Section 4.2. A line plot of the PASI responder (PASI75, PASI90, and PASI100) rates over time, by PS0014 treatment sequence group will be produced where data are imputed using NRI. The figure will be repeated by Feeder Study /PS0014 treatment groups up to Week 48 for PASI90 and PASI100.

Additional summaries and figures (excluding PASI75) will be produced for the OLE2 period, using the CA-OL2S by OLE2 treatment group. This will be summarized using both the observed case (OC) and non-responder imputation (NRI) approach.

Absolute and percent change from Baseline in PASI score will be summarized by scheduled visit and PS0014 treatment sequence groups based on Feeder Study Baseline. This table will display descriptive statistics for the Feeder Study Baseline, followed by descriptive statistics for the change from Feeder Study Baseline for all PS0014 visits.

Missing data for the continuous change from Baseline and percent change from Baseline variables will be handled by using MI via the MCMC and monotone regression method specified in Section 4.2.

A line plot of the percentage improvement in PASI score over time based on Feeder Study Baseline by PS0014 treatment sequence groups using MCMC and monotone regression method will be produced.

Absolute and percent change from Baseline in PASI score will be summarized by scheduled visit during the OLE2 period by OLE2 treatment groups. This table will display descriptive statistics for the Feeder Study Baseline, followed by descriptive statistics for the change from Feeder Study Baseline for all OLE2 visits. No imputation will be applied (OC method).

The number and percent of subjects who achieve an absolute PASI score ≤1, ≤2, ≤3 and ≤5 will be presented over time by visit and the PS0014 treatment sequence groups. These summaries will be performed using NRI and observed case data. Absolute PASI score categories will not be summarized for the OLE2 treatment period.

A by-subject listing of the PASI questionnaire, PASI total score and PASI response data will be provided by Feeder Study /PS0014 treatment sequence group. This listing will also be provided separately for the OLE2 treatment period.

In addition, for PASI90 response through to Week 144, the sensitivity analyses to assess the impact of the COVID-19 pandemic described in Section 4.2.4 will be performed.

The summary and figure of PASI90 through Week 48 will be repeated excluding the 140 subjects potentially impacted by incorrect treatment assignment at Baseline (described in Section 8.1.1).

8.2.1.2.2 Cohort B

Frequency tables will be produced to show the number and percentage of PASI75, PASI90, and PASI100 responders for each visit based on the CBPSO-FAS. This summary will be performed using NRI. Additional summaries will be presented for the CBPSO-FAS for the number and percentage of PASI90 and PASI100 responders using the mNRI method defined in Section 4.2. Summaries will also be presented by PS0014 treatment sequence group and psoriasis type based on the CB-FAS using observed case.

Line plots of the PASI responder (PASI75, PASI90, and PASI100) rates over time will be produced based on the CBPSO-FAS. Line plots for the PASI responder rates over time by treatment sequence group will be created for subgroups GPP and EP based on CBGPP-FAS and CBEP-FAS. Missing data will be imputed using NRI for CBPSO-FAS. No imputation will be applied for CBGPP-FAS and CBEP-FAS.

Absolute and percent change from Baseline in PASI score will be summarized by scheduled visit and PS0014 treatment sequence group. This table will display descriptive statistics for the change from Baseline and for all PS0014 visits.

For PSO subjects, missing data for the continuous change from Baseline and percent change from Baseline variables will be handled by using MI via the MCMC and monotone regression method specified in Section 4.2. For GPP and EP subjects, observed data will be used.

A line plot of the percentage improvement from Baseline in PASI score over time by PS0014 treatment sequence group and psoriasis type will be produced, using observed case data.

The number and percent of subjects who achieve an absolute PASI score ≤1, ≤2, ≤3 and ≤5 will be presented over time by treatment sequence group and psoriasis type based on the CB-FAS using observed case data. Additional summaries will be presented for the CBPSO-FAS where missing data will be imputed using NRI.

A by-subject listing of the PASI questionnaire, PASI total score and PASI response data will be provided by treatment sequence group.

In addition, for PASI90 response through to Week 144, the sensitivity analyses to assess the impact of the COVID-19 pandemic described in Section 4.2.4 will be performed.

8.2.2 IGA Response

8.2.2.1 Derivation of IGA response

A static IGA for psoriasis will be used to assess disease severity in all subjects during the study.

The Investigator will assess the overall severity of psoriasis using the following five-point scale as outlined in Table 8.1 below:

Table 8.1: Investigator's Global Assessment

Score	Short Descriptor	Definition
0	Clear	No signs of psoriasis; post-inflammatory hyperpigmentation may be present
1	Almost clear	No thickening; normal to pink coloration; no to minimal focal scaling
2	Mild	Just detectable to mild thickening; pink to light red coloration; predominately fine scaling
3	Moderate	Clearly distinguishable to moderate thickening; dull to bright red, clearly distinguishable to moderate thickening; moderate scaling
4	Severe	Severe thickening with hard edges; bright to deep dark red coloration; severe/coarse scaling covering almost all or all lesions

The IGA response (Clear) is defined as an IGA score of Clear [0] with at least 2 category improvement relative to Baseline.

The IGA response (Clear or Almost Clear with at least 2 category improvement relative to Baseline) is defined as an IGA score of Clear [0] of Almost Clear [1] with at least a two-category improvement from the Baseline.

8.2.2.2 Analysis of IGA response

8.2.2.2.1 Cohort A

For IGA response the following frequency tables will be produced:

- IGA response (Clear) by visit and PS0014 treatment sequence group.
- IGA response (Clear or Almost Clear) by visit and PS0014 treatment sequence group

Both summaries will be repeated for Feeder Study/PS0014 treatment group up to Week 48

All summaries will be produced on the subset of subjects with IGA at Feeder Study Baseline ≥ 2.

These summaries will be performed using NRI and observed case data. Additional summaries will be presented for the number and percentage of IGA (Clear) and IGA (Clear or Almost Clear) responders using the mNRI method defined in Section 4.2. A line plot of the IGA (Clear) and IGA (Clear or Almost Clear) rates over time, by PS0014 treatment sequence group will be produced where data is imputed using NRI. These will be repeated for Feeder Study/PS0014 treatment group up to Week 48.

Additional summaries and figures will be produced for the OLE2 treatment period, using the CA-OL2S by OLE2 treatment group. This will be summarized using both the observed case (OC) and non-responder imputation (NRI) approach.

A by-subject listing of the IGA score and IGA response data will be provided by Feeder Study /PS0014 treatment sequence group.
In addition, for IGA (Clear or Almost Clear) response through to Week 144, the sensitivity analyses to assess the impact of the COVID-19 pandemic described in Section 4.2.4 will be performed.

The summary and figure of IGA (Clear or Almost Clear) response through Week 48 will be repeated excluding the 140 subjects potentially impacted by incorrect treatment assignment at Baseline (described in Section 8.1.1).

8.2.2.2.2 Cohort B

For PSO:

For IGA response the following frequency tables will be produced by visit for subjects in the CBPSO-FAS with IGA at PS0014 Baseline ≥ 2:

- IGA response (Clear)
- IGA response (Clear or Almost Clear)

These summaries will be performed using NRI. Observed case data will also be presented.

Additional summaries will be presented for the CBPSO-FAS for the number and percentage of IGA (Clear or Almost Clear) and IGA (Clear) responders using the mNRI method defined in Section 4.2.

Line plots of IGA (Clear) and IGA (Clear or Almost Clear) rates over time for all subjects combined will be produced based on the CBPSO-FAS where missing data is imputed using NRI.

For GPP and EP:

IGA response will not be described for these two disease types. The following incidence rates will be described for GPP and EP:

- IGA (Clear) is defined as an IGA score of Clear [0]
- IGA (Clear or Almost Clear) is defined as an IGA score of Clear [0] of Almost Clear [1]

The observed case table will be presented for CBEP-FAS and CBGPP-FAS.

A by-subject listing of the IGA score and IGA response data will be provided by treatment group for all disease types.

In addition, for IGA (Clear or Almost Clear) response through to Week 144, the sensitivity analyses to assess the impact of the COVID-19 pandemic described in Section 4.2.4 will be performed.

8.2.3 Scalp IGA response

8.2.3.1 Derivation of scalp IGA response

A static IGA for scalp PSO will be used to assess disease severity on the scalp.

Only subjects with scalp involvement at Baseline will complete the scalp IGA at the other visits specified in the protocol.

In Cohort A, subjects with scalp involvement at Baseline are defined as those with a scalp IGA score >0 at Baseline of the feeder study.

In Cohort B, subjects with scalp involvement at Baseline in this study are defined as those with a scalp IGA score >0 at PS0014 Baseline.

Scalp lesions will be assessed in terms of clinical signs of redness, thickness, and scaliness using a 5-point scale as outlined in Table 8.2 below.

Table 8.2: Scalp IGA

Score	Short Descriptor	Detailed Descriptor
0	Clear	Scalp has no signs of PSO; post-inflammatory hyperpigmentation may be present
1	Almost clear	Scalp has no thickening; normal to pink coloration; no to minimal focal scaling
2	Mild	Scalp has just detectable to mild thickening; pink to light red coloration; predominately fine scaling
3	Moderate	Scalp has clearly distinguishable to moderate thickening; dull to bright red, moderate scaling
4	Severe	Scalp has severe thickening with hard edges; bright to deep dark red coloration; severe/coarse scaling covering almost all or all lesions

Scalp IGA response (Clear or Almost Clear) is defined as clear [0] or almost clear [1] with at least a two-category improvement from Baseline.

For analysis purposes, the evaluation of scalp IGA response (for Cohort A and Cohort B PSO subjects only) will be limited to subjects with a Baseline scalp IGA of at least 2. Therefore, if a subject has a score of 2 at Baseline, they can only be considered a responder if their scalp IGA is 0 (thereby meeting the criterion for a two-category improvement from Baseline). Only subjects with a Baseline scalp IGA >=2 will be included in the response analysis. Subjects with a

Baseline scalp IGA of 1 will be assessed per the protocol and included in listings but will not be part of the scalp IGA response analysis.

8.2.3.2 Analysis of scalp IGA response

8.2.3.2.1 Cohort A

Frequency tables for Scalp-specific IGA response (Clear or Almost Clear) will be produced by visit and PS0014 treatment sequence group for subjects in the CA-FAS with a Feeder Baseline scalp IGA >=2. These summaries will be performed using NRI and OC data.
An additional summary will be presented for the number and percentage of Scalp IGA Clear or Almost Clear responders using the mNRI method defined in Section 4.2.

An additional summary will be produced using NRI which excludes subjects who experienced an ERT data collection inconsistency for scalp IGA assessments.

A line plot of the Scalp-specific IGA response (Clear or Almost Clear) rates over time, by PS0014 treatment sequence group will be produced where data is imputed using NRI.

A by-subject listing of the scalp IGA score and scalp IGA response data will be provided by PS0014 treatment sequence group.

8.2.3.2.2 Cohort B

For PSO:

Frequency tables for scalp-specific IGA response (Clear or Almost Clear) will be produced by visit for subjects in the CBPSO-FAS with a Baseline scalp IGA >=2. These summaries will be performed using NRI and OC data.

An additional summary will be presented for the number and percentage of Scalp IGA responders using the mNRI method defined in Section 4.2.

A line plot of Scalp IGA (Clear or Almost Clear) rates over time for all subjects combined will be produced based on the CBPSO-FAS where missing data is imputed using NRI.

For GPP and EP:

Frequency tables of subjects with scalp IGA (Clear or Almost Clear), will be produced by visit, treatment group for subjects in the CBGPP-FAS and CBEP-FAS. These summaries will be performed using OC data.

A by-subject listing of the scalp IGA score (for all disease types) and scalp IGA response data (for PSO subjects) will be provided.

8.2.4 Palmoplantar IGA response

8.2.4.1 Derivation of palmoplantar IGA response

A static IGA for palmoplantar PSO will be used to assess palmoplantar disease severity.

Only subjects with palmoplantar involvement at Baseline will complete the pp-IGA at the other visits specified in the protocol.

In Cohort A, subjects with palmoplantar involvement at Baseline are defined as those with a pp-IGA score >0 at Baseline of the feeder study.

In Cohort B, subjects with palmoplantar involvement at Baseline in this study are defined as those with a pp-IGA score >0 at PS0014 Baseline.

Palmoplantar disease will be assessed in terms of clinical signs of redness, thickness, and scaliness using a 5-point scale as outlined in Table 8.3 below.

Table 8.3: Palmoplantar IGA

Score	Short Descriptor	Detailed Descriptor
0	Clear	Palmoplantar has no signs of PSO; post-inflammatory hyperpigmentation may be present
1	Almost clear	Palmoplantar has no thickening; normal to pink coloration; no to minimal focal scaling
2	Mild	Palmoplantar has just detectable to mild thickening; pink to light red coloration; predominately fine scaling
3	Moderate	Palmoplantar has clearly distinguishable to moderate thickening; dull to bright red and clearly distinguishable coloration; moderate scaling
4	Severe	Palmoplantar has severe thickening with hard edges; bright to deep dark red coloration; severe/coarse scaling covering almost all or all lesions; numerous fissures

PSO=psoriasis; pp-IGA=palmoplantar-specific Investigator's Global Assessment

pp-IGA response (Clear or Almost Clear) is defined as clear [0] or almost clear [1] with at least a two-category improvement.

For analysis purposes, the evaluation of pp-IGA response (for Cohort A and Cohort B PSO subjects only) will be limited to subjects with a Baseline pp-IGA of at least 2. Therefore, if a subject has a score of 2 at Baseline, they can only be considered a responder if their pp-IGA is 0 (thereby meeting the criterion for a two-category improvement from Baseline). Only subjects with a Baseline pp-IGA >=2 will be included in the response analysis. Subjects with a Baseline pp-IGA of 1 will be assessed per the protocol and included in listings but will not be part of the pp-IGA response analysis.

8.2.4.2 Analysis of palmoplantar IGA response

8.2.4.2.1 Cohort A

Frequency tables for pp-IGA response (Clear or Almost Clear) will be produced by visit and PS0014 treatment sequence group for subjects in the CA-FAS with a Feeder Baseline pp-IGA >=2. These summaries will be performed using NRI and OC data.
An additional summary will be presented for the number and percentage of pp-IGA responders using the mNRI method defined in Section 4.2.

An additional summary will be produced using NRI which excludes subjects who experienced an ERT data collection inconsistency for pp-IGA assessments.

A line plot of the pp-IGA response (Clear or Almost Clear) rates over time, by PS0014 treatment sequence group will be produced where data is imputed using NRI.

A by-subject listing of the pp-IGA score and pp-IGA response data will be provided by PS0014 treatment sequence group.

8.2.4.2.2 Cohort B

For PSO:

Frequency tables for pp-IGA response (Clear or Almost Clear) will be produced by visit for subjects in the CBPSO-FAS with a Baseline scalp IGA >=2. These summaries will be performed using NRI and OC data.
An additional summary will be presented for the number and percentage of pp-IGA responders using the mNRI method defined in Section 4.2.

A line plot of pp-IGA (Clear or Almost Clear) rates over time for all subjects combined will be produced based on the CBPSO-FAS where missing data is imputed using NRI.

For GPP and EP:

Frequency tables of subjects with pp-IGA (Clear or Almost Clear), will be produced by visit, treatment group for subjects in the CBGPP-FAS and CBEP-FAS. These summaries will be performed using OC data.

A by-subject listing of the pp-IGA score (for all disease types) and pp-IGA response data (for PSO subjects) will be provided.

8.2.5 BSA

8.2.5.1 Derivation of BSA

Absolute change from Baseline in the BSA affected by PSO is defined as visit BSA minus Baseline BSA affected by PSO.

Percent change from Baseline in BSA affected by PSO is defined as

$$\text{Percent change from Baseline } = 100 \times \frac{\text{Post Baseline BSA} - \text{Baseline BSA}}{\text{Baseline BSA}}$$

8.2.5.2 Analysis of BSA

8.2.5.2.1 Cohort A

Change from Baseline in BSA affected by psoriasis will be summarized using descriptive statistics by PS0014 treatment sequence group and visit based on the Feeder Study Baseline. The table will display descriptive statistics for the Feeder Study Baseline, followed by descriptive statistics for the change from Feeder Study Baseline for all PS0014 visits.

Missing data for the continuous change from Feeder Study Baseline and percent change from Feeder Study Baseline variables will be handled by using MI via the MCMC and monotone regression method specified in Section 4.2.

The number and percentage of subjects who achieve BSA =0%, ≤1%, ≤3%, and ≤5% at each visit will be summarized by PS0014 treatment sequence group. This summary will be performed using NRI and OC data. BSA results will be listed but will not be summarized for the OLE2 treatment period.

A by-subject listing of BSA and change from PS0014 Baseline data will be provided by PS0014 treatment sequence group.

8.2.5.2.2 Cohort B

Change from Baseline and percent change from Baseline in BSA affected by psoriasis will be summarized using descriptive statistics by visit based on the CBPSO-FAS where missing data will be handled by using MI via the MCMC and monotone regression method specified in Section 4.2.

For GPP and EP subjects, change from Baseline and percent change from Baseline in BSA affected by psoriasis will be summarized using descriptive statistics by visit based on the CBGPP-FAS and CBEP-FAS respectively using OC data.

The number and percentage of subjects who achieve BSA =0%, ≤1%, ≤3%, and ≤5% at each visit will be summarized by treatment sequence group and psoriasis type based on the CB-FAS using observed case data. Additional summaries will be presented for the CBPSO-FAS where missing data will be imputed using NRI.

A by-subject listing of BSA and change from Baseline will be provided.

8.2.6 Product of IGA and BSA (IGAxBSA)

8.2.6.1 Derivation of IGA and BSA (IGAxBSA)

- Absolute change from Baseline in the product IGAxBSA is defined as Post Baseline IGAxBSA minus product of Baseline IGAxBSA.
- Percent change from Baseline in the product of IGAxBSA is defined as
  - Percent change from Baseline $= 100 \times \frac{\text{Post Baseline IGAxBSA} - \text{Baseline IGAxBSA}}{\text{Baseline IGAxBSA}}$

8.2.6.2 Analysis of IGA and BSA (IGAxBSA)

8.2.6.2.1 Cohort A

Change from Baseline in product of IGA and BSA affected by psoriasis will be summarized using descriptive statistics by visit and PS0014 treatment sequence group. The table will display descriptive statistics for the Feeder Study Baseline, followed by descriptive statistics for the change from Feeder Study Baseline for all PS0014 visits. The product of IGA and BSA will not be summarized for the OLE2 treatment period.

Missing data for the continuous change from Feeder Study Baseline and percent change from Feeder Study Baseline variables will be handled by using MI via the MCMC and monotone regression method specified in Section 4.2.

A by-subject listing of product of IGA and BSA and change from PS0014 Baseline data will be provided by PS0014 treatment sequence group.

8.2.6.2.2 Cohort B

Change from Baseline and percent change in Baseline in product of IGA and BSA affected by psoriasis will be summarized using descriptive statistics by visit based on the CBPSO-FAS

where missing data will be handled by using MI via the MCMC and monotone regression method specified in Section 4.2.

For GPP and EP subjects, change from Baseline and percent change from Baseline in product of IGA and BSA affected by psoriasis will be summarized using descriptive statistics by visit based on the CBGPP-FAS and CBEP-FAS respectively using OC data.

A by-subject listing of product of IGA and BSA and change from Baseline will be provided.

8.2.7 DLQI

8.2.7.1 Derivation of DLQI total score

The DLQI questionnaire has been used for subjects with psoriasis and consists of 10-questions. This is reliable and well-defined, quality-of-life questionnaire that covers 6 domains including symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment, as assessed over the past week.

The scoring of each answer for the DLQI is as follows:

Table 8.4: Dermatology Life Quality Index

DLQI Scoring	
Response	**Score**
Very much	3
A lot	2
A little	1
Not at all	0
Not relevant	0
Question unanswered	0
Q7: 'prevented work or studying' = yes	3

Meaning of DLQI total scores

0-1 = no effect at all on patient's life

2-5 = small effect on patient's life

6-10 = moderate effect on patient's life

11-20 = very large effect on patient's life

21-30 = extremely large effect on patient's life

This categorization will not be utilized in the analysis.

Because Q7 has a sub-question (referred to as Q7a here) after the leading yes/no question, some clarifying rules for scoring are provided:

- If Q7 is marked as "yes", a score of 3 is given regardless of the responses to Q7a.

- If Q7 is marked as “no”, “not relevant”, or is missing and Q7a is “A lot”, a score of 2 is given.
- If Q7 is marked as “no”, “not relevant”, or is missing and Q7a is “A little”, a score of 1 is given.
- If Q7 is marked as “no”, “not relevant”, or is missing and Q7a is “Not at all”, a score of 0 is given.
- If Q7 is marked as “no” or “not relevant” and Q7a is missing, a score of 0 is given.
- If Q7 is missing and Q7a is missing, Q7 is considered unanswered (see below for details on how this impacts the overall DLQI score).

If 1 question is left unanswered, this is scored 0 and the scores are summed and expressed as usual out of a maximum of 30. If 2 or more questions are left unanswered, the questionnaire is not scored.

A subject is considered to have achieved the minimally clinical important difference (MCID) if their individual improvement from Baseline in total score is ≥4. A 4-point improvement in the DLQI total score (DLQI response) has been reported to be meaningful for the subject (within-subject MCID). The summary of MCID will be restricted to subjects with a DLQI total score of at least 4 at Baseline to ensure that it is possible for the subject to achieve the MCID.

The DLQI total score related efficacy variables are defined as follows:

- Change from Baseline in DLQI total score is defined as Post-Baseline DLQI total score minus Baseline DLQI total score.
- Percent of subjects achieving a DLQI total score of 0 or 1 is defined as the number of subjects with DLQI absolute score of 0 or 1 divided by the number of subjects in each treatment group in the appropriate analysis set.
- Percent of subjects achieving a MCID in DLQI total score is defined as the number of subjects with improvement from Baseline score of 4 or more divided by the number of subjects with a Baseline score ≥4.

8.2.7.2 Analysis of DLQI

8.2.7.2.1 Cohort A

Change from Baseline in DLQI total score will be summarized using descriptive statistics by PS0014 treatment sequence group and visit based on the Feeder Study Baseline. The table will display descriptive statistics for the Feeder Study Baseline, followed by descriptive statistics for the change from Feeder Study Baseline for all PS0014 visits.

Missing data for the continuous change from Feeder Study Baseline and percent change from Feeder Study Baseline variables will be handled by using MI via the MCMC and monotone regression method specified in Section 4.2 .

Frequency tables will be produced based on the Feeder Study Baseline to show the number and percentage of DLQI responders for MICD for each PS0014 visit and PS0014 treatment sequence group. Missing data will be imputed via NRI.

The number and percentage of subjects achieving a DLQI total score of 0 or 1 at each visit will be summarized descriptively using counts and percentages by PS0014 treatment sequence group and visit. This summary will be performed using NRI and observed case data. The summary for DLQI total score 0/1 will be repeated up to Week 48 by Feeder Study/PS0014 treatment group. An additional summary will be presented for the number and percentage of subjects achieving a DLQI total score of 0 or 1 using the mNRI method defined in Section 4.2.

An additional summary will be produced for the OLE2 treatment period, using the CA-OL2S by OLE2 treatment group. This will be summarized using both the observed case (OC) and non-responder imputation (NRI) approach.

A by-subject listing of the DLQI questionnaire, responses to individual questions of the DLQI Questionnaire, DLQI total score, change from Feeder Study Baseline and DLQI response for MICD and 0 or 1 data will be provided by Feeder Study /PS0014 treatment sequence group.

8.2.7.2.2 Cohort B

Change from Baseline in DLQI total score will be summarized using descriptive statistics by visit.

For PSO subjects, missing data for the continuous change from Baseline and percent change from Baseline variables will be handled by using MI via the MCMC and monotone regression method specified in Section 4.2. These summaries will be based on the CBPSO-FAS.

Additional summaries will be presented using OC data by treatment group for GPP and EP subjects based on the CBGPP-FAS and CBEP-FAS respectively.

Frequency tables will be produced to show the number and percentage of DLQI responders for MCID for each visit by treatment sequence group and psoriasis type based on the CB-FAS. DLQI responders for MCID will be summarized using observed case data. For PSO subjects, frequency tables will also be produced for each visit based on the CBPSO-FAS where missing data are imputed using NRI.

The number and percentage of subjects achieving a DLQI total score of 0 or 1 at each visit will be summarized descriptively using counts and percentages by treatment sequence group and psoriasis type for the CB-FAS. This summary will be performed using OC data. For PSO subjects, summaries will also be produced for each visit based on the CBPSO-FAS where missing data are imputed using NRI.
An additional summary will be presented for the number and percentage of of subjects achieving a DLQI total score of 0 or 1 in the CBPSO-FAS using the mNRI method defined in Section 4.2.

A by-subject listing of DLQI questionnaire, DLQI total score, and DLQI response for MCID and 0 or 1 data will be provided.

8.2.8 mNAPSI score

8.2.8.1 Derivation of mNAPSI

Psoriatic nail disease will be evaluated at the Baseline visit using the mNAPSI. All affected nails will be scored (0 to 3) for onycholysis/oil drop dyschromia, nail plate crumbling, and pitting and will be scored (0 for “no” or 1 for “yes”) for leukonychia, nail bed hyperkeratosis, splinter

haemorrhages and red spots in the lunula. The score for an individual nail ranges from 0 to 13 with higher scores indicative of more severe nail disease. The total mNAPSI score is the sum of the scores for each individual nail. If a nail is unaffected, it will be recorded as such and will not contribute to the total mNAPSI score.

- In Cohort A, subjects with nail disease at Baseline are defined as those with an mNAPSI score >0 at Baseline of the feeder study.
- In Cohort B, subjects with nail disease at Baseline in this study are defined as those with an mNAPSI score >0 at PS0014 Baseline.

If any of the 7 response items that contribute to mNAPSI is present, while other items are missing (i.e., partial mNAPSI data), then the missing items are assumed to be 0 for the mNAPSI calculation. In some cases, the data may be captured in such a way that only non-zero component scores are present in the database. Again, those components that are not present are simply assumed to be 0 for the mNAPSI calculation.

This analysis will only be presented for the subgroup of subjects with psoriatic nail disease at Baseline, defined as a mNAPSI score >0 at Baseline. Change from Baseline in mNAPSI score for subjects with nail PSO at Baseline is defined as Post-Baseline mNAPSI score minus Baseline mNAPSI. An mNAPSI75, mNAPSI90 or mNAPSI100 responder is defined as a subject who achieved at least a 75%, 90% or 100% improvement from baseline in the mNAPSI score.

8.2.8.2 Analysis of mNAPSI

8.2.8.2.1 Cohort A

Only subjects with mNAPSI > 0 at Feeder Baseline will be included in the tables.

The change from Baseline in mNAPSI will be compared using PS0014 treatment sequence groups. The table will display descriptive statistics for the Feeder Study Baseline, followed by descriptive statistics for the change from Feeder Study Baseline for all PS0014 visits.

Missing data for the continuous change from Feeder Study Baseline will be handled by using MI via the MCMC and monotone regression method specified in Section 4.2.

The proportion of mNAPSI75, mNAPSI90 and mNAPSI100 responders over time will be summarized for PS0014 treatment sequence groups and visit. The mNAPSI75, mNAPSI90 and mNAPSI100 response variables will be derived relative to Feeder Study Baseline. These summaries will be performed using NRI and observed case data.
Additional summaries will be presented for the number and percentage of mNAPSI75, 90 and 100 responders using the mNRI method defined in Section 4.2.

Additional summaries for mNAPSI score (using MI) and mNAPSI response (using NRI) will be produced which exclude subjects who experienced an ERT data collection inconsistency for mNAPSI assessments.

A line plot of the mNAPSI90 and mNAPSI100 rates over time, by PS0014 treatment sequence group will be produced where data is imputed using NRI.

A by-subject listing of the mNAPSI questionnaire, mNAPSI total score and mNAPSI Response data will be provided by PS0014 treatment sequence group.

8.2.8.2.2 Cohort B

Only subjects with mNAPSI > 0 at Baseline will be included in the tables.

A change from Baseline in mNAPSI table will display descriptive statistics for plaque PSO subjects with nail disease at Baseline based on the CBPSO-FAS where missing data is handled by using MI via the MCMC and monotone regression method specified in Section 4.2.

For GPP and EP subjects, change from Baseline in mNAPSI will be summarized using descriptive statistics by visit based on the CBGPP-FAS and CBEP-FAS respectively using OC data.

The proportion of mNAPSI75, mNAPSI90 and mNAPSI100 responders over time will be summarized by visit and treatment sequence group, and psoriasis type based on the CB-FAS. These summaries will be performed using observed case data. Summaries with also be produced by visit for the CBPSO-FAS where data are imputed using NRI.
Additional summaries will be presented for the number and percentage of mNAPSI75, 90 and 100 responders in the CBPSO-FAS using the mNRI method defined in Section 4.2.

A line plot of the mNAPSI 90 and mNAPSI100 rates over time, by PS0014 treatment sequence group will be produced where data is imputed using NRI based on the CBPSO-FAS.

A by-subject listing of the mNAPSI questionnaire, mNAPSI total score and mNAPSI Response data will be provided.

8.2.9 PGADA for arthritis VAS

8.2.9.1 Derivation of PGADA for arthritis VAS

The PGADA for arthritis VAS will be used to provide an overall evaluation of arthritis disease symptoms. Subjects will respond to the question, “Considering all the ways your arthritis affects you, please mark a vertical line on the scale below to show how you are feeling today,” using a VAS where 0 is “very good, no symptoms” and 100 is “very poor, severe symptoms.

All subjects will complete the PGADA at Baseline. Subjects with PsA at Baseline (defined as a past medical history of PsA or PASE ≥47) will complete the PGADA at the visits specified in the protocol. Change from Baseline in PGADA is defined as Post-Baseline PGADA minus Baseline PGADA.

8.2.9.2 Analysis of PGADA score for arthritis VAS

8.2.9.2.1 Cohort A

Only subjects with PsA at Feeder Baseline will be included in the tables.

The change from Baseline in PGADA score will be compared to the Feeder Study Baseline using PS0014 treatment sequence groups. The table will display descriptive statistics for the Feeder Study Baseline, followed by descriptive statistics for the change from Feeder Study Baseline for all PS0014 visits.

Missing data for the continuous change from Feeder Study Baseline will be handled by using MI via the MCMC and monotone regression method specified in Section 4.2.

An additional summary of PGADA score and change from Feeder Study Baseline (using MI) will be produced which exclude subjects who experienced an ERT data collection inconsistency for PGADA assessments.

A by-subject listing of PGADA score and change from PS0014 Baseline data will be provided by PS0014 treatment sequence group.

8.2.9.2.2 Cohort B

Only subjects with PsA at Baseline will be included in the tables.

For PSO subjects, a table of the change from Baseline in PGADA will display descriptive statistics for all visits based on the CBPSO-FAS. Missing data will be handled by using MI via the MCMC and monotone regression method specified in Section 4.2.

- A by-subject listing of PGADA and change from Baseline data will be provided for CB-FAS.

8.2.10 PGA of PSO

8.2.10.1 Derivation of PGA score of PSO

The PGA score of PSO is a PSO-specific item in which the subject responds to the multiple-choice question, "How severe are your psoriasis-related symptoms right now?" Possible responses to the question are "no symptoms," "mild symptoms," "moderate symptoms," "severe symptoms," or "very severe symptoms."

Shift from Baseline in PGA score of PSO score is defined to each Post-Baseline visit timepoint relative to Baseline.

8.2.10.2 Analysis of PGA of PSO

8.2.10.2.1 Cohort A

The PGA score of psoriasis will be summarized based on OC. No imputation is applied.

A shift table of PGA score of PSO compared to the Feeder Study Baseline will be summarized by visit and PS0014 treatment sequence group.

A by-subject listing of PGA score of PSO score will be provided by PS0014 treatment sequence group.

8.2.10.2.2 Cohort B

The PGA score of psoriasis will be summarized based on OC. No imputation is applied.

A shift table of PGA score of PSO compared to Baseline will be summarized by visit, treatment sequence group, and psoriasis type based on the CB-FAS.

A by-subject listing of PGA score of PSO score will be provided.

8.2.11 PASE

8.2.11.1 Derivation of PASE

The PASE questionnaire is a self-administered tool to screen for active PsA in subjects with PSO (Husni et al, 2014). The questionnaire consists of 15 items that are divided into a 7-item symptoms subscale and an 8-item functions subscale. Standardized responses are based on 5 categories relating to agreement (strongly agree [5], agree [4], no idea [3], disagree [2], and

strongly disagree [1]). The total maximum score is 75 points (symptom score: 35 points and function score: 40 points). Psoriatic Arthritis Screening and Evaluation questionnaire scores ≥47 points are indicative of active PsA.

- Change from Baseline in the PASE questionnaire scores (function score, symptom score, and total score) is defined as Post-Baseline PASE questionnaire score (function, symptom, and total) minus Baseline PASE questionnaire score (function, symptom, and total).

8.2.11.2 Analysis of PASE

8.2.11.2.1 Cohort A

PASE will be collected at Feeder Study Baseline, PS0014 Baseline, Week 48, Week 96 and Week 144 visit. PASE will be summarized based on OC only. No imputation is applied.

Change from Baseline in PASE will be summarized using descriptive statistics by PS0014 treatment sequence group and visit based on the Feeder Study Baseline. The table will display descriptive statistics for the Feeder Study Baseline, followed by descriptive statistics for the change from Feeder Study Baseline for all PS0014 visits.

In addition, a shift table in PASE score suggestive of PsA (<47 versus ≥47) compared to Feeder Study Baseline will be summarized by visit (PS0014 Baseline, Week 48, Week 96 and Week 144) and PS0014 treatment sequence groups based on observed data. No imputation is applied.

As data are presented using observed cases only, no additional summaries of PASE will be produced to account for the subjects who experienced an ERT data collection inconsistency for PGADA assessments.

A by-subject listing of PASE and change from PS0014 Baseline data will be provided by PS0014 treatment sequence group.

8.2.11.2.2 Cohort B

PASE will be summarized based on OC only on the CBPSO-FAS population. No imputation is applied.

Change from Baseline to Week 48, Week 96 and Week 144 in PASE will be summarized using descriptive statistics by PS0014 treatment sequence group and psoriasis type on the CBPSO-FAS population. Change from Baseline will be derived based on PS0014 Baseline.

In addition, a shift table in PASE score suggestive of PsA (<47 versus ≥47) compared to Baseline will be summarized for Week 48, Week 96 and Week 144 and PS0014 treatment sequence groups based on observed data on the CBPSO-FAS population. No imputation is applied.

- A by-subject listing of PASE and change from Baseline data will be provided by PS0014 treatment sequence group on the CB-FAS population.

8.2.12 SF-36

8.2.12.1 Derivation of SF-36

The SF-36v2, standard recall, measures the following 8 health domains as rated by the subjects over the past four weeks: Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional, and Mental Health (Maruish, 2011).

The SF-36 Physical and Mental Component Summary scores (PCS and MCS, respectively) are used to measure the two broad components, or aspects, of health-physical and mental. PCS and MCS are based on the aggregate of 8 health concepts described above and all of the 8 health domain scales are used to score both components summary measures.

One additional item asks respondents about health change over the past year.

The SF-36 will be used using QualityMetric's Health Outcomes™ Scoring Software Version 5.1 or later. The software uses updates 2009 U.S. population norms and applies a Full Missing Score Estimation (Full MSE) method as follows:

- A health domain score (except the physical functioning (PF) domain) will be estimated provided that at least one non-missing response is available within that domain
- For the PF domain item response theory will be used to develop a model for estimates of the missing score (Thomas and Cyr, 2002)
- Regression methods are then applied to estimate the PCS and the MCS on the basis of the available domains.

Change from Baseline in Short Form 36-item Health Survey PCS score, and MCS score, and domain scores are defined as respective score at Post-Baseline timepoint minus the Baseline score.

8.2.12.2 Analysis of SF-36

8.2.12.2.1 Cohort A

Summary statistics of the actual values and change from Feeder Study Baseline values will be used to summarize each SF-36 domain scores and the PCS and MCS scores for each visit by PS0014 treatment sequence group. The table will display descriptive statistics for the Feeder Study Baseline, followed by descriptive statistics for the change from Feeder Study Baseline for all PS0014 visits.

Missing data for the continuous change from Feeder Study Baseline will be handled by using MI via the MCMC and monotone regression method specified in Section 4.2.

A by-subject listing of the SF-36 questionnaire, SF-36 domains and components will be provided by PS0014 treatment sequence group.

8.2.12.2.2 Cohort B

Summary statistics of the actual values and change from Baseline values will be used to summarize each SF-36 domain scores and the PCS and MCS scores for each visit based on the CBPSO-FAS. The table will display descriptive statistics for Baseline, followed by descriptive statistics for the change from Baseline for all visits.

Missing data for the continuous change from Baseline will be handled by using MI via the MCMC and monotone regression method specified in Section 4.2.

For GPP and EP subjects, change from Baseline values will be summarized using descriptive statistics by visit based on the CBGPP-FAS and CBEP-FAS respectively using OC data.

A by-subject listing of the SF-36 questionnaire, SF-36 domains and components will be provided.

8.2.13 EQ-5D-3L

8.2.13.1 Derivation of EQ-5D-3L

The EQ-5D-3L health questionnaire provides a descriptive profile and a single index value for health status. The instrument is comprised of a 5-item health status measure and a visual analog scale (VAS).

Responses to EQ-5D-3L are scored as 1 for "no problem", 2 for "some or moderate problems", and 3 for "extreme problems".

Absolute EQ-5D-3L VAS score records the respondent's self-rated health status on a vertical 20cm scale, 0 to 100 graduated (0=worst imaginable health status, 100=best imaginable health status).

A categorical summary of the EQ-5D-3L score will be provided for all visits.

Change from Baseline in EQ-5D-3L VAS scores is defined as Post-Baseline EQ-5D-3L VAS score minus Baseline EQ-5D-3L VAS score.

8.2.13.2 Analysis of EQ-5D-3L

8.2.13.2.1 Cohort A

Summary statistics of the actual values and change from Feeder Study Baseline values will be used to summarize EQ-5D-3L VAS scores for each visit by PS0014 treatment sequence group. The table will display descriptive statistics for the Feeder Study Baseline, followed by descriptive statistics for the change from Feeder Study Baseline for all PS0014 visits.

Missing data for the continuous change from Feeder Study Baseline in VAS scores will be handled by using MI via the MCMC and monotone regression method specified in Section 4.2.

Frequency tables will be produced to summarize answers provided to each of the 5 items of the EQ-5D-3L for each visit by PS0014 treatment sequence groups. Responses to EQ-5D-3L will be summarized based on OC. No imputation is applied to responses to EQ-5D-3L.

A by-subject listing of EQ-5D-3L will be provided by PS0014 treatment sequence group.

8.2.13.2.2 Cohort B

Summary statistics of the actual values and change from Baseline values will be used to summarize EQ-5D-3L VAS scores for each visit for PSO subjects using the CBPSO-FAS. The table will display descriptive statistics for the Baseline, followed by descriptive statistics for the change from Baseline for all visits.

Missing data for the continuous change from Baseline in VAS scores will be handled by using MI via the MCMC and monotone regression method specified in Section 4.2.

For GPP and EP subjects, change from Baseline in EQ-5D-3L VAS will be summarized using descriptive statistics by visit based on the CBGPP-FAS and CBEP-FAS respectively using OC data.

Frequency tables will be produced to summarize answers provided to each of the 5 items of the EQ-5D-3L for each visit by treatment sequence group and psoriasis type using the CB-FAS. Responses to EQ-5D-3L will be summarized based on OC. No imputation is applied to responses to EQ-5D-3L.

A by-subject listing of EQ-5D-3L will be provided.

8.2.14 WPAI-SHP

8.2.14.1 Derivation of WPAI-SHP

The WPAI-SHP is a subject-reported questionnaire that assesses subject's employment status, work absenteeism, work impairment while working, overall work, and daily activity impairment attributable to a specific health problem. Five out of 6 items of the WPAI-SHP are regrouped into the 4 dimensions, with scores expressed as percentage, where higher numbers indicate greater impairment and less productivity, i.e., worse outcomes, as described in the WPAI-SHP scoring rules.

The scoring rules for the WPAI-SHP are as follows:

Questions:

1 = currently employed

2 = hours missed due to specified problem

3 = hours missed other reasons

4 = hours actually worked

5 = degree problem affected productivity while working

6 = degree problem affected regular activities

Scores:

- Percent work time missed due to problem: [Q2 hours/(Q2 hours +Q4 hours)] *100
- Percent impairment while working due to problem: [Q5 score/10] *100
- Percent overall work impairment due to problem:
- [Q2 hours/(Q2 hours +Q4 hours)+[(1-(Q2 hours/(Q2 hours +Q4 hours)))x(Q5 score/10)]] *100
- Percent activity impairment due to problem: [Q6 score/10] *100

Change from Baseline score is derived as post Baseline score minus Baseline score. A negative change score indicates a reduction in the score/improvement for the subject.

8.2.14.2 Analysis of WPAI-SHP

8.2.14.2.1 Cohort A

Tables will not include subjects from the PS0013 Feeder Study. The WPAI-SHP was removed from the PS0013 protocol and there will be no Baseline results for these subjects as a result. Their post-Baseline data will be included in the listings.

Summary statistics of the actual values and change from Feeder Study Baseline values will be used to summarize WPAI-SHP for each visit by PS0014 treatment sequence group. The table will display descriptive statistics for the Feeder Study Baseline, followed by descriptive statistics for the change from Feeder Study Baseline for all PS0014 visits.

Missing data for the continuous change from Feeder Study Baseline will be handled by using MI via the MCMC and monotone regression method specified in Section 4.2.

A by-subject listing of the WPAI-SHP questionnaire, WPAI-SHP domains and change from PS0014 Baseline will be provided by PS0014 treatment sequence group.

8.2.14.2.2 Cohort B

Summary statistics of the actual values and change from Baseline values will be used to summarize WPAI-SHP for each visit for PSO subjects using the CBPSO-FAS. The table will display descriptive statistics for the Baseline, followed by descriptive statistics for the change from Baseline for all visits.

Missing data for the continuous change from Baseline will be handled by using MI via the MCMC and monotone regression method specified in Section 4.2.

For GPP and EP subjects, change from Baseline in WPAI-SHP will be summarized using descriptive statistics by visit based on the CBGPP-FAS and CBEP-FAS respectively using OC data.

A by-subject listing of the WPAI-SHP questionnaire, WPAI-SHP domains and change from Baseline will be provided.

8.2.15 Clinical Global Impressions – Improvement (CGI-I)

8.2.15.1 Derivation of CGI-I

The CGI-I is evaluated by the Investigators on a 4-point scale (remission, improved, no change, worsened) based on changes from the Baseline findings of GPP or EP. The CGI-I will be completed at the visits specified in the protocol.

8.2.15.2 Analysis of CGI-I

8.2.15.2.1 Cohort B

The number and percentage of subjects with each response at each visit will be summarized descriptively using counts and percentages by treatment sequence group for GPP and EP subjects based on the CBGPP-FAS and CBEP-FAS. This summary will be performed using OC data.

8.2.16 Japanese Dermatological Association (JDA) Severity index score for GPP

8.2.16.1 Derivation of JDA Severity index score for GPP

The JDA severity index score for GPP consists of total erythematous area, erythematous area with pustules, edematous area, fever, white blood cell (WBC), C-reactive protein (CRP), and serum albumin.

The total score of JDA severity index for GPP is assigned a score of 0 to 17 (0=best, 17=worst), as presented in Table 8.5

Table 8.5: JDA severity

Severity classification	**Mild**	**Moderate**	**Severe** **Col**
A + B (combined scores)	0 to 6	7 to 10	11 to 17
• Skin symptoms (total scores: 0 to 9)			
Scores	**3**	**2**	**1**	**0**
Erythematous area (BSA %)	≥75	≥25, <75	<25	0
Erythematous area with pustule (BSA %)	≥50	≥10, <50	<10	0
Edematous area (BSA %)	≥50	≥10, <50	<10	0
• Systemic symptoms and laboratory findings (total scores: 0 to 8)			
Scores	**2**	**1**	**0**
Fever (°C)	≥38.5	≥37.0, <38.5	<37.0
WBC count (/μL)	≥15,000	≥10,000, <15,000	<10,000
CRP (mg/dL)	≥7.0	≥0.3, <7.0	<0.3
Serum albumin (g/dL)	<3.0	≥3.0, <3.8	≥3.8

BSA=body surface area; CRP=C-reactive protein; GPP=generalized pustular psoriasis; JDA=Japanese Dermatological Association; PSO=psoriasis; WBC=white blood cell

8.2.16.2 Analysis of JDA Severity index score for GPP

8.2.16.2.1 Cohort B

A table of the change from Baseline in JDA severity index score will display descriptive statistics for all visits by treatment sequence group based on the CBGPP-FAS. This summary will be based on OC data.

A by-subject listing of JDA severity index score and change from Baseline data will be provided.

8.2.17 Global Improvement Score

8.2.17.1 Derivation of Global Improvement Score

The Global Improvement Score is evaluated for subjects with GPP by the Investigator as "very much improved," "much improved," "minimally improved," "no change," or "worsened" based on change from the Baseline JDA severity index scores and components, as presented in Table 8.6 .

Table 8.6: Global Improvement Score

	Change in JDA Severity Classification Score		Other criteria
Very much improved	Reduction by ≥3 points	or	Clear or almost clear of signs of GPP
Much improved	Reduction of 1 or 2 points	or	At least 1 of the following: **1.** Erythema area with pustules (%) reduced by ≥30% compared to Baseline [a] **2.** Clinically meaningful improvement in at least 2 other components of the JDA severity index for GPP (erythema area, edema area, WBC, pyrexia, CRP, albumin)
Minimally improved	0 points (no change)	and	At least 1 of the following: **1.** Erythema area with pustules (%) reduced by ≥20% compared to Baseline [a] **2.** Clinically meaningful improvement in at least 1 other component of the JDA severity index for GPP (erythema area, edema area, pyrexia, WBC, CRP, albumin)
No change	0 points (no change)	and	Not meeting the other criteria of minimally improved
Worsened	≥+1 point	-	Not applicable
Very much improved	Reduction by ≥3 points	or	Clear or almost clear of signs of GPP

CRP=C-reactive protein; GPP=generalized pustular psoriasis; JDA=Japanese Dermatological Association; PSO=psoriasis; WBC=white blood cell

[a] Prior to first study drug administration at Baseline

8.2.17.2 Analysis of Global Improvement Score

8.2.17.2.1 Cohort B

The number and percentage of subjects with each response at each visit will be summarized descriptively using counts and percentages by treatment sequence group for GPP subjects based on the CBGPP-FAS. This summary will be performed using OC data.

8.2.18 TSQM-9

8.2.18.1 Derivation of TSQM-9

The TSQM-9 is a 9-item measure developed to provide a suitable measure of treatment satisfaction with medication. It has 5 to 7 Likert response options per item and consists of 3 subscales: effectiveness (3 items), convenience (3 items), and a global satisfaction scale (3 items). The TSQM-9 was developed from the TSQM 1.4 (Atkinson et al, 2004) which has an additional subscale which measures side effects (3 items). Scores range from 0 (worst) to 100 (best). The scores for each measure are as follows:

- Global Satisfaction:
  - If no items are missing: ([Sum(Item 7 to Item 9) – 3]/14)*100
  - If either Item 7 or 8 is missing: ([Sum(the two completed items)) – 2]/10)*100
  - If Item 9 is missing: ([Sum(Item 7 and Item 8))-2]/8)*100
- Effectiveness
  - If no items are missing: ([Item 1 + Item 2 + Item 3) – 3]/18)*100
  - If one item is missing: ([(Sum(the two completed items) – 2]/12)*100
- Convenience
  - If no items are missing: ([Sum(Item 4 to Item 6) – 3]/18)*100
  - If one item is missing: ([Sum(the two completed items) – 2]/12*100

The TSQM-9 scores will be described at Week 48, or early discontinuation prior to Week 48.

8.2.18.2 Analysis of TSQM-9

8.2.18.2.1 Cohort A

Summary statistics of the actual values will be used to summarize the component scores for each domain at Week 48 by Feeder Study/PS0014 treatment group. This summary will be presented using OC data.

Frequency tables will be produced to summarize answers provided to each of the 9 items of the TSQM-9 at Week 48 by Feeder Study /PS0014 treatment groups. Component scores of responses to TSQM-9 will be summarized based on OC. No imputation is applied.

A by-subject listing of TSQM-9 will be provided by Feeder Study /PS0014 treatment group.

8.2.18.2.2 Cohort B

Summary statistics of the actual values will be used to summarize the component scores for each domain at Week 48 by treatment group and psoriasis type using the CB-FAS. This summary will be presented using OC data.

Frequency tables will be produced to summarize answers provided to each of the 9 items of the TSQM-9 at Week 48. Component scores of responses to TSQM-9 will be summarized based on OC. No imputation is applied.

A by-subject listing of TSQM-9 will be provided by PS0014 treatment group defined in interim analysis 48.

9 PHARMACOKINETICS AND PHARMACODYNAMICS

9.1 Pharmacokinetics

9.1.1 Cohort A

Pharmacokinetic variables will be analyzed for all subjects in the CAPK-PPS. Bimekizumab plasma concentrations will be summarized for each PS0014 PK treatment sequence group detailed in Section 3.6.1 at each scheduled visit for Week 0 - Week 144. No PK or ADAb samples will be collected in the OLE2 treatment period.

PK summaries will be based on observed values. No imputation will be used. However, if plasma concentration measurements are below the level of quantification (BLQ), then for calculation of the derived statistics the result will be set to ½ of the lower level of quantification (LLOQ). Descriptive statistics including geometric mean, geometric coefficient of variation, and geometric mean 95% CI if applicable will be calculated if at least 2/3 of the values of interest are above the LLOQ. If this is not the case, only median, minimum, and maximum will be presented. In cases where n<3 only the minimum and maximum will be presented.

In addition, geometric mean plasma concentration with geometric mean 95% CI will be plotted by PS0014 PK treatment sequence group.

For PK presentations by ADAb status (positive, negative or missing), ADAb status is considered in a cumulative manner at each time point. A subject will be counted positive from the first visit at which the subject achieved a positive ADAb sample result to Week 144, regardless of any missing/inconclusive or negative ADAb sample result. If a subject has only negative ADAb samples or at least 2/3 of protocol scheduled assessments are evaluable as ADAb negative at the time point of assessment or only 1 missing protocol scheduled assessment (at baseline or post baseline), the subject will be classified as negative. Otherwise, ADAb status in this subject will be classified as missing.

The table summaries and figures will be repeated by cumulative anti-BKZ antibody status (positive, negative or missing) and overall neutralizing antibody assay status (IL-17AA, IL17-FF, IL17-AA and IL17-FF, Overall). In both cases, the status will include assessments at SFU, however PK concentrations at SFU will not be included in summary tables/figures:

- Plasma concentration will be summarized by PS0014 PK treatment sequence group, and by cumulative antibody status (positive or negative, missing antibody status) at each scheduled visit.
- Geometric mean plasma concentration with geometric mean 95% CI will be plotted by PS0014 PK treatment sequence group, and by cumulative antibody status on linear and semilogarithmic scale. Missing cumulative antibody status will not be plotted.
- Plasma concentration will be summarized by PS0014 PK treatment sequence group, and by overall neutralizing antibody assay status (IL-17AA, IL17-FF, IL17-AA and IL17-FF, Overall).

- Geometric mean plasma concentration with geometric mean 95% CI will be plotted by PS0014 PK treatment sequence group, and by overall neutralizing antibody assay status (IL-17AA, IL17-FF, IL17-AA and IL17-FF, Overall) on linear and semilogarithmic scale.

If the dosing for a visit is +/- 21 days out of window, then the plasma concentration from that visit will be excluded from the PK summaries and figures. If the PK sample for a visit is collected >1 day after dosing at that visit, the concentration at that visit will be excluded from the PK summary tables and figures.

PK samples will be excluded from summaries if they are scheduled 4 or 8 weeks (depending on the subject's dosing schedule at the time, Q4W/Q8W) after a subject misses an administration of study medication (or receives less or more than the intended dose).

Regardless of exclusions from summaries, all PK concentrations will be listed.

9.1.2 Cohort B

Pharmacokinetic variables will be analyzed for the CBPK-PPS. Bimekizumab plasma concentrations will be summarized by each PS0014 PK treatment sequence group detailed in Section 3.6.2 for Week 0 - Week 144 at each scheduled visit.

PK summaries will be based on observed values. No imputation will be used. However, if plasma concentration measurements are below the level of quantification (BLQ), then for calculation of the derived statistics the result will be set to ½ of the lower level of quantification (LLOQ). Descriptive statistics including geometric mean, geometric coefficient of variation, and geometric mean 95% CI if applicable will be calculated if at least 2/3 of the values of interest are above the LLOQ. If this is not the case, only median, minimum, and maximum will be presented. In cases where n<3 only the minimum and maximum will be presented.

In addition, geometric mean plasma concentration with geometric mean 95% CI will be plotted by PS0014 PK treatment sequence group.

For PK presentations by ADAb status (positive, negative or missing), ADAb status is considered in a cumulative manner at each time point. A subject will be counted positive from the first visit at which the subject achieved a positive ADAb sample result to Week 144, regardless of any missing/inconclusive or negative ADAb sample result. If a subject has only negative ADAb samples or at least 2/3 of protocol scheduled assessments are evaluable as ADAb negative at the time point of assessment or only 1 post baseline missing protocol scheduled assessment, the subject will be classified as negative. Otherwise, ADAb status in this subject will be classified as missing.

The table summaries and figures will be repeated by cumulative anti-BKZ antibody status (positive, negative or missing) and overall neutralizing antibody assay status (IL-17AA, IL17-FF, IL17-AA and IL17-FF, Overall). In both cases, the status will include assessments at SFU, however PK concentrations at SFU will not be included in summary tables/figures:

- Plasma concentration will be summarized by PS0014 PK treatment sequence group, and by cumulative antibody status (positive, or negative, missing antibody status) at each scheduled visit up to Week 144.

- Geometric mean plasma concentration will be plotted by each PS0014 PK treatment sequence group, and by cumulative antibody status for week 0 - week 144 on linear and semi-logarithmic scale. Missing cumulative antibody status will not be plotted.
- Plasma concentration will be summarized by PS0014 PK treatment sequence group, and by overall neutralizing antibody assay status (IL-17AA, IL17-FF, IL17-AA and IL17-FF, Overall).
- Geometric mean plasma concentration with geometric mean 95% CI will be plotted by PS0014 PK treatment sequence group, and by overall neutralizing antibody assay status (IL-17AA, IL17-FF, IL17-AA and IL17-FF, Overall) on linear and semilogarithmic scale.

If the dosing for Week 2 is +/- 7 days out of window or for any other visit is +/- 21 days out of window, then the plasma concentration from that visit will be excluded from the PK summaries and figures. If the PK sample for a visit is collected >1 day after dosing at that visit, the concentration at that visit will be excluded from the PK summary tables and figures.

PK samples will be excluded from summaries if they are scheduled 4 or 8 weeks (depending on the subject's dosing schedule at the time, Q4W/Q8W) after a subject misses an administration of study medication (or receives less or more than the intended dose).

Regardless of exclusions from summaries, all PK concentrations will be listed.

9.2 Pharmacodynamics

Not applicable.

9.3 Immunogenicity

9.3.1 Anti-bimekizumab antibodies

The analysis of anti-bimekizumab antibodies (ADAb) will be based on the 144-week treatment period plus SFU, as detailed below. No immunogenicity samples are collected during the OLE2 treatment period.

9.3.1.1 Cohort A

The analysis of immunogenicity will be based on CA-SS and summarized by each PS0014 immunogenicity treatment sequence group detailed in Section 3.6.1.

Note: at the time of the Week 48 interim analysis, PS0009 subjects who were randomized to Ustekinumab did not have PS0014 baseline values available as the samples taken at the end of PS0009 had not been analyzed. For the Week 48 interim, the PS0009 baseline values were used as PS0014 baseline for these subjects. At the time of the Week 144 analysis all samples for this group of subjects will have been analyzed and therefore the actual PS0014 baseline samples (taken at the end of PS0009) will be used in the data summaries.

Anti-bimekizumab antibodies (ADAb) will be measured using a three-tiered approach: screening assay, confirmatory assay and titration assay. Samples will be taken at PS0014 Baseline, Week 16, Week 24, Week 40, Week 48, Week 72, Week 96, Week 120, Week 144 and at SFU (20 weeks after the last dose of bimekizumab). Some subjects may receive bimekizumab as a concomitant medication during the SFU period which means the immunogenicity sample at the SFU visit is collected <20 weeks after the last dose. Such samples will be included in the

immunogenicity assessments with no adjustment. In addition, due to the planned entry of some subjects to the OLE2 treatment period, not all subjects will have an SFU period immediately following Week 144 with PK and immunogenicity samples.

Screening, confirmatory and titer cut points of the respective assays will be determined by the bioanalytical laboratory based either on using commercially available drug-naive samples or on the pre-dose samples of a given study itself.

The following definitions will be applied regarding ADAb status of each test sample:

- An ADAb status will be confirmed as positive for any sample with an ADAb level that is positive screen and positive immunodepletion.
- An ADAb status of negative will be concluded for any sample with an ADAb level that is either negative screen or positive screen and negative immunodepletion.
- An ADAb status will be concluded as missing (one or more), e.g., if there was insufficient sample left for ADAb testing (NSP), or inconclusive results due to missing negative screen or immunodepletion results .

If the titer for an ADAb level that is positive screen and positive immunodepletion is missing, then a conservative approach will be used and ADAb status will be consider as positive. No imputation rules apply for the missing titer. If the ADAb level is positive screen but no confirmatory result could be determined, then a conservative approach will be used and ADAb status will be considered as positive.

Anomalous values will not be included in summaries/analysis and will be reviewed and flagged by pharmacokinetic expert. All values will be included in the data listings.

For each subject an overall ADAb status in the treatment period (PS0014 Baseline to Week 144, excluding SFU) will be derived as follows:

- Overall Positive is defined as having at least one value that is confirmed positive at PS0014 Baseline or during the treatment period (regardless of missing/inconclusive data).
- Overall Negative is defined as having no values that are confirmed positive at any time up to Week 144 (including PS0014 baseline) and at least 2/3 of the protocol scheduled assessments up to Week 144 (including PS0014 baseline) are evaluable (i.e. neither missing as per schedule nor inconclusive)
- Overall Missing is defined as having no values that are confirmed positive at any visit in the treatment period or at PS0014 baseline, but the subject has more than 1/3 of protocol scheduled assessments missing (or inconclusive) up to Week 144 (including PS0014 baseline).

This differs from the interim analysis where all subjects were defined as either overall positive or overall negative only (a missing category was not considered). As the time on treatment is protracted in this open label extension study (up to 144 Weeks), missing data or subject discontinuation may be more prevalent and is considered for the final analysis.

Additionally, for each subject an overall ADAb status over the 144 Week Treatment Period plus SFU (PS0014 Baseline to SFU) will be derived as follows:

- Overall Positive is defined as having at least one value that is confirmed positive at PS0014 Baseline or during the treatment period and SFU (regardless of missing/inconclusive data).
- Overall Negative is defined as having no values that are confirmed positive at any time up to SFU (including PS0014 baseline) and at least 2/3 of the protocol scheduled assessments up to SFU (including PS0014 baseline) are evaluable (i.e. neither missing as per schedule nor inconclusive)
- Overall Missing is defined as having no values that are confirmed positive at any visit in from PS0014 baseline to SFU, but the subject has more than 1/3 of protocol scheduled assessments missing (or inconclusive) up to SFU (including PS0014 baseline).

  Note: For subjects who entered the OLE2 treatment period and do not have an SFU sample collected as part of the 144 Week Treatment Period, ADAb status over the 144 Week Treatment Period (including the SFU) will be equivalent to the ADAb status to Week 144.

Furthermore, the following sub-categories for each subject will be derived considering sampling points post treatment including SFU (note, OLE2 subjects with no prior SFU visit will only be assessed to Week 144):

1. **Pre ADAb negative – treatment emergent ADAb negative**: Includes subjects who are negative at PS0014 Baseline and antibody negative for at least 2/3 of the scheduled sampling points post-baseline (including SFU)
2. **Pre ADAb negative – treatment emergent ADAb positive**: Includes subjects who are negative at PS0014 Baseline and antibody positive at any sampling point post-baseline (including SFU).
3. **Pre ADAb positive – treatment emergent reduced ADAb**: Includes subjects who are positive at PS0014 Baseline, and antibody negative for at least 2/3 of the scheduled sampling points post-baseline (including SFU).
4. **Pre ADAb positive – treatment emergent unaffected ADAb positive**: Includes subjects who are positive at PS0014 Baseline and are positive at any sampling point post-baseline (including SFU) with titer values of the same magnitude as PS0014 Baseline (ie, less than or equal to a 2.07 fold difference from the PS0014 Baseline value).
5. **Pre ADAb positive – treatment emergent ADAb boosted positive**: Includes subjects who are positive at PS0014 Baseline and are positive at any sampling point post-baseline (including SFU) with increased titer values compared to PS0014 baseline (greater than 2.07 fold difference increase from PS0014 Baseline value which will be defined within the validation of the assay).
6. **Inconclusive**: Includes subjects who have a positive PS0014 Baseline sample and more than 1/3 of post-baseline samples (including SFU) are missing, while other post-baseline samples are ADAb negative.

7. **Total treatment-emergent ADAb positivity** (**Category 7** [Categories 2 and 5 combined]): Includes study participants who are pre ADAb negative – treatment-emergent ADAb positive (Category 2) and pre ADAb positive – treatment boosted ADAb positive (Category 5).
8. **Total prevalence of pre- ADAb positivity (Category 8** [Categories 3, 4 and 5 combined]): Study participants that are tested ADAb positive at PS0014 Baseline.
9. **Missing:** Includes subjects who are antibody negative at PS0014 Baseline, are not positive at any post-baseline visit and have more than 1/3 of post-baseline scheduled assessments missing (including SFU). It includes also subjects who only have non-missing, negative antibody status at PS0014 Baseline but with no post-baseline status available.
10. **Pre ADAb missing**: Includes subjects with missing ADAb status at PS0014 Baseline, who could be overall (including SFU) ADAb positive, negative or missing.

Analysis

In the case that a sample is collected one or more days following the scheduled visit date in which the drug was administered, the ADAb results for that sample will be associated with the scheduled visit and summarized accordingly. Such samples will also be considered when ADAb results are summarized over a given study period.

Immunogenicity will be assessed through summary tables, figures, and listing of individual results by subject. The analysis of immunogenicity will be summarized by immunogenicity treatment sequence as described in Section 3.6.1 and visit. All analyses will be run on the CA-SS, unless specified otherwise.

- Summary of anti-bimekizumab antibody status overall (including and excluding SFU) and by each visit separated by immunogenicity treatment sequence
- The number and percentage of subjects in each of the 10 anti-bimekizumab antibody sub-categories over the treatment period (including SFU) by immunogenicity treatment sequence
- The prevalence of immunogenicity, separated by immunogenicity treatment sequence, and by two defined sub-categories: pre-ADAb negative - treatment emergent ADAb positive and total treatment emergent, will be reported by visit, defined as (cumulative) proportion of subjects having positive anti-bimekizumab status at any visit up to and including that visit. Missing samples will not be included in the denominator
- A summary of PASI75, PASI90 and PASI100 responders, separated by treatment sequence and defined sub-category, at weeks 24, 48 and 144 as a function of ADAb titer will be presented graphically.
- A table summarizing the incidence of TEAEs per 100 Subject-Years by Time of Onset Relative to Overall ADAb (and NAb) Status is described in Section 10.2.2.1.
- Spaghetti plots of ADAb titer (y-axis) by visit (x-axis), separated by immunogenicity treatment sequence (as specified above) for all anti-bimekizumab antibody positive subjects, including PS0014 Baseline positive subjects
- All individual subject-level anti-bimekizumab antibody results will be listed.

9.3.1.2 Cohort B

The analysis of immunogenicity will be performed for the safety set (CB-SS) and summarized for each PS0014 immunogenicity treatment sequence group detailed in Section 3.6.2 .

ADAb will be measured using a three-tiered approach: screening assay, confirmatory assay and titration assay. Samples will be taken at Baseline, Week 4, Week 8, Week 12, Week 16, Week 28, Week 40, Week 48, Week 72, Week 96, Week 120, Week 144 and SFU (20 weeks after the last dose of bimekizumab). Some subjects may receive bimekizumab as a concomitant medication during the SFU period which means the immunogenicity sample at the SFU visit is collected <20 weeks after the last dose. Such samples will be included in the immunogenicity assessments with no adjustment.

Screening, confirmatory and titer cut points of the respective assays will be determined by the bioanalytical laboratory based either on using commercially available drug-naive samples or on the pre-dose samples of a given study itself. In case the cut point is being set on commercially available samples, the representative for the study population is being checked.

The following definitions will be applied regarding ADAb status of each test sample:

- An ADAb status will be confirmed as positive for any sample with an ADAb level that is positive screen and positive immunodepletion.
- An ADAb status of negative will be concluded for any sample with an ADAb level that is either negative screen or positive screen and negative immunodepletion.
- An ADAb status will be concluded as missing (one or more), e.g., if there was insufficient sample left for ADAb testing (NSP), or inconclusive results due to missing negative screen or immunodepletion results.

If the titer for an ADAb level that is positive screen and positive immunodepletion is missing, then a conservative approach will be used and ADAb status will be considered as positive. No imputation rules apply for the missing titer. If the ADAb level is positive screen but no confirmatory result could be determined, then a conservative approach will be used and ADAb status will be considered as positive.

Anomalous values will be not included in summaries/analysis and will be reviewed and flagged by pharmacokinetic expert. All values will be included in the data listings.

For each subject an overall ADAb status during the treatment period (excluding Baseline and SFU) will be derived:

- Overall Positive is defined as having at least one value that is confirmed positive during the treatment period (regardless of missing/inconclusive data).
- Overall Negative is defined as having no values that are confirmed positive at any time during the treatment period up to Week 144 and at least 2/3 of the protocol scheduled post-baseline assessments up to Week 144 are evaluable (i.e. neither missing as per schedule nor inconclusive)

- Overall Missing is defined as having no values that are confirmed positive at any visit in the treatment period, but the subject has more than 1/3 of protocol scheduled post-baseline assessments missing (or inconclusive) up to Week 144.

This differs from the interim analysis where all subjects were defined as either overall positive or overall negative only (a missing category was not considered). As the time on treatment is protracted in this open label extension study (up to 144 Weeks), missing data or subject discontinuation may be more prevalent and is there for considered for the final analysis.

Additionally, for each subject an overall ADAb status over the entire study (excluding Baseline but including SFU) will be derived as follows:

- Overall Positive is defined as having at least one post-baseline value that is confirmed positive during the treatment period, including SFU (regardless of missing/inconclusive data).
- Overall Negative is defined as having no values that are confirmed positive at any time during the treatment period up to SFU and at least 2/3 of the protocol scheduled post-baseline assessments up to SFU are evaluable (i.e. neither missing as per schedule nor inconclusive)
- Overall Missing is defined as having no values that are confirmed positive at any visit in the treatment period/SFU, but the subject has more than 1/3 of protocol scheduled post-baseline assessments missing (or inconclusive) up to SFU.

The same anti-BKZ antibody (ADAb) sub-classification 1 to 10 as for Cohort A will be derived.

Analysis

In the case that a sample is collected one or more days following the scheduled visit date in which the drug was administered, the ADAb results for that sample will be associated with the scheduled visit and summarized accordingly. Such samples will also be considered when ADAb results are summarized over a given study period.

Immunogenicity will be assessed through summary tables, figures, and listing of individual results by subject. The analysis of immunogenicity will be summarized by immunogenicity treatment sequence as described in Section 3.6.2 and visit. All analyses will be run on the CB-SS, unless specified otherwise.

- Summary of anti-bimekizumab antibody status overall (including and excluding SFU) and by each visit separated by immunogenicity treatment sequence
- Summary of the time-point of the first occurrence of anti-bimekizumab antibody positivity by immunogenicity treatment sequence.
- The number and percentage of subjects in each of the 10 anti-bimekizumab antibody sub-categories over the treatment period (including SFU) by immunogenicity treatment sequence
- The prevalence of immunogenicity, separated by immunogenicity treatment sequence, and by two defined sub-categories: pre-ADAb negative - treatment emergent ADAb positive and total treatment emergent, will be reported by visit, defined as (cumulative) proportion of

subjects having confirmed positive anti-bimekizumab antibody samples at any visit up to and including that visit. Missing samples will not be included in the denominator

- A summary of PASI75, PASI90, and PASI100 responders, separated by treatment sequence and defined sub-category, at weeks 16, 48 and 144 as a function of ADAb titer will be presented graphically.
- A table summarizing the incidence of TEAEs per 100 Subject-Years by Time of Onset Relative to Overall ADAb (and NAb) Status is described in Section 10.2.2.1.
- Spaghetti plots of ADAb titer (y-axis) by visit (x-axis), separated by immunogenicity treatment sequence (as specified above) for all anti-bimekizumab antibody positive subjects, including Baseline positive subjects
- All individual subject-level anti-bimekizumab antibody results will be listed.

9.3.2 Neutralizing anti-bimekizumab antibodies

The analysis of neutralizing anti-BKZ antibody (NAb) will be based on the 144-week treatment period plus SFU. No immunogenicity samples were collected during the OLE2 treatment period.

9.3.2.1 Cohort A

The analysis of immunogenicity will be based on CA-SS and summarized by PS0014 immunogenicity treatment sequence group.

Samples confirmed ADAb positive within the confirmatory assay will be evaluated in a neutralizing assay to evaluate the potential of the ADAb to neutralize the activity of bimekizumab (IL17A or IL17F, or both) in-vitro. Samples will be taken at PS0014 Baseline, Week 16, Week 24, Week 40, Week 48, Week 72, Week 96, Week 120, Week 144 and SFU (20 weeks after the last dose of bimekizumab, if not entering OLE2 treatment period).

Screening, confirmatory and titer cut points of the respective assays will be determined by the bioanalytical laboratory based either on using commercially available drug-naive samples or on the pre-dose samples of a given study itself. In case the cut point is being set on commercially available samples, the representative for the study population is being checked.

Subjects will receive an overall neutralizing anti-BKZ antibody (NAb) classification for each neutralizing antibody assay separately (IL-17AA and IL-17FF), inclusive of PS0014 Baseline and post-Baseline results, on the neutralizing antibody assay results. The classifications are as follows:

- **Negative**: No NAb positive samples at PS0014 Baseline or post-Baseline (including SFU, if collected)
- **Positive**: One or more NAb positive samples at PS0014 Baseline or post-Baseline (including SFU, if collected)
- **Missing**: Relevant NAb samples are missing (one or more), e.g., if subject had samples selected for NAb testing based on their ADAb levels, but there was insufficient sample left for NAb testing

- Overall NAb status will be derived as follows:
  - **Negative**: Subject is IL-17AA Negative and IL-17FF Negative
  - **Positive**: Subject is IL-17AA Positive or IL-17FF Positive
  - **Missing**: All other cases (i.e. IL-17AA and IL-17FF both Missing, or 1 Negative and 1 Missing)

Subjects who are determined to be NAb positive will be further classified as follows:
- Positive for IL-17AA only
- Positive for IL-17FF only
- Positive for both IL-17AA and IL-17FF

Analysis

In the case that a sample is collected one or more days following the scheduled visit date in which the drug was administered, the NAb results for that sample will be associated with the scheduled visit and summarized accordingly. Such samples will also be considered when NAb results are summarized over a given study period.

Immunogenicity will be assessed through summary tables, figures and listing of individual results by subject.

- All individual subject-level NAb results will be listed.
- Summary of NAb status by neutralizing antibody assay (IL-17AA only, IL17-FF only, both) and Overall NAb status by immunogenicity treatment sequence.
- Summaries and figures of PK presentations by NAb status are presented in Section 9.1.1.
- A table summarizing the incidence of TEAEs per 100 Subject-Years by Time of Onset Relative to Overall NAb Status is described in Section 10.2.2.1 .

9.3.2.2 Cohort B

The analysis of immunogenicity will be performed for the safety set (CB-SS) and will be summarized for each PS0014 immunogenicity treatment sequence group.

ADAb samples confirmed positive within the confirmatory assay will be evaluated in a neutralizing assay to evaluate the potential of the ADAb to neutralize the activity of bimekizumab (IL17A or IL17F, or both) in-vitro. Samples will be taken at Baseline, Week 4, Week 8, Week 12, Week 16, Week 28, Week 40, Week 48, Week 72, Week 96, Week 120, Week 144 and SFU (20 weeks after the last dose of bimekizumab).

Screening, confirmatory and titer cut points of the respective assays will be determined by the bioanalytical laboratory based either on using commercially available drug-naive samples or on the pre-dose samples of a given study itself. In case the cut point is being set on commercially available samples, the representative for the study population is being checked.

Subjects will receive an overall neutralizing anti-BKZ antibody (NAb) classification for each neutralizing antibody assay separately (IL-17AA and IL-17FF), inclusive of Baseline and post-Baseline results, on the neutralizing antibody assay results. The classifications are as follows:

- **Negative**: No NAb positive samples at Baseline or post-Baseline (including SFU)
- **Positive**: One or more NAb positive samples at Baseline or post-Baseline (including SFU)
- **Missing**: Relevant NAb samples are missing (one or more), e.g., if subject had samples selected for NAb testing based on their ADAb levels, but there was insufficient sample left for NAb testing.

Overall NAb status will be derived as follows:

- **Negative**: IL-17AA Negative and IL-17FF Negative
- **Positive**: IL-17AA Positive or IL-17FF Positive
- **Missing**: IL-17AA and IL-17FF both Missing, or 1 Negative and 1 Missing.

Subjects who are determined to be NAb positive will be further classified as follows:

- Positive for IL-17AA only
- Positive for IL-17FF only
- Positive for both IL-17AA and IL-17FF

Analysis

In the case that a sample is collected one or more days following the scheduled visit date in which the drug was administered, the NAb results for that sample will be associated with the scheduled visit and summarized accordingly. Such samples will also be considered when NAb results are summarized over a given study period.

Immunogenicity will be assesed through summary tables and figures, and listing of individual results by subject.

- All individual subject-level NAb results will be listed
- Summary of NAb status overall by neutralizing antibody assay (IL-17AA only, IL17-FF only, both) and Overall NAb status by immunogenicity treatment sequence.
- Summaries and figures of PK presentations NAb status are presented in Section 9.1.2 .
- A table summarizing the incidence of TEAEs per 100 Subject-Years by Time of Onset Relative to Overall NAb Status is described in Section 10.2.2.2 .

10 SAFETY ANALYSES

For Cohort A, unless otherwise specified, safety variables will be analyzed using the CA-SS up to Week 144 treatment period. Separate selected analyses on CA-OL2S will be performed for OLE2 treatment period.

For Cohort B, safety variables will be analyzed in general for all subjects by psoriasis type using the CBPSO-SS, CBGPP-SS, and CPEP-SS. A few AE summaries will also be produced for the Cohort B total subjects (CB-SS).

For both cohorts, only the safety data occurring during the time at risk, as described in Section 10.1, will be considered for analysis.

Unless otherwise specified, safety analyses will be presented by safety treatment group as defined in Section 3.6.1 and 3.6.2.

10.1 Extent of Exposure

Throughout this section, date of last clinical contact for each subject is defined as the maximum of [last visit date including SFU or SFU2 visit, last AE start date (including imputed AE start dates), date of study termination or completion, last date of study drug administration].

Definitions for study medication duration and time at risk are provided in this section. Although time at risk is ultimately summarized in years, the definitions in this section will be provided in days.

10.1.1 Cohort A

Summaries for exposure through the 144-week treatment period will be provided by using PS0014 treatment group. This consists of a descriptive summary of total study medication duration in days and total time at risk in years through Week 144.

The cumulative study medication duration will be summarized for subjects exposed for given durations of time, these will be based upon cumulative duration in PS0014. For the cumulative duration through Week 144 the following categories for the PS0014 only administrations will be used:

- ≥0 weeks
- ≥8 weeks
- ≥16 weeks
- ≥24 weeks
- ≥48 weeks.
- ≥64 weeks.
- ≥80 weeks.
- ≥96 weeks.
- ≥112 weeks.
- ≥128weeks.
- ≥144 weeks.

In addition, the OLE2 treatment period exposure will be displayed separately as follows:

- >0 weeks
- >=16 weeks

- >=24 weeks
- >=48 weeks.

10.1.1.1 Exposure during Weeks 0-144

The study medication duration (days) will be calculated depending on the treatment.

For subjects who received bimekizumab 320mg Q4W only (who discontinued before switching to Q8W):

- Study medication duration (days):

  Date of last dose – date of first dose + 28 days

- Note: If the date of last dose + 28 days extends to a date beyond the final visit date in the 144 -week treatment period (including PEOT, but not including SFU), then this calculation reverts to:
  - Final visit date in the 144-week treatment period (including PEOT, but not including SFU) – date of first dose in PS0014 + 1.
- Note: For subjects who die, if date of last bimekizumab dose + 28 days extends to a date beyond the date of death, then this calculation reverts to:
  - Date of death – date of first dose in PS0014 + 1 day.

Time at Risk (Days):For all subjects, use the minimum of the following:

- Date of last dose in the 144-week Treatment Period – date of first dose in PS0014 + 140 days,
- Date of first dose in OLE2 treatment period - date of first dose in PS0014 + 1 day
- Date of last clinical contact in 144-week Treatment Period and SFU – date of first dose in PS0014 + 1.
- Date of death – date of first dose in PS0014+ 1 day.

For subjects who received bimekizumab 320mg Q8W only:

Study medication duration (days) use the minimum of:

- Date of last dose in 144-week Treatment Period – date of first dose in PS0014 + 56 days
- Date of first dose in OLE2 treatment period – date of first dose in PS0014 + 1 day
- Note: If the date of last dose + 56 days extends to a date beyond the final visit date in the 144-week treatment period (including PEOT, but not including SFU), then this calculation reverts to:

- Final visit date in the 144-week treatment period (including PEOT, but not including SFU) – date of first dose in PS0014 + 1.

- Note: For subjects who die, if date of last bimekizumab dose + 56 days extends to a date beyond the date of death, then this calculation reverts to:
  - Date of death – date of first dose in PS0014 + 1.

Time at Risk (Days):
For all subjects, use the minimum of the following:

- Date of last dose in the 144 -week Treatment Period – date of first dose in PS0014 + 140 days
- Date of first dose in in OLE2 treatment period - date of first dose in PS0014 + 1 day
- Date of last clinical contact in 144-week Treatment Period and SFU – date of first dose in PS0014 + 1.
- Date of death – date of first dose in PS0014+ 1 day.

For subjects who switch from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W:

Note, the date of the treatment switch will be determined using the information on dosing regimen entered in IXRS. All doses prior to the regimen switch will be assigned to the Q4W treatment period, all doses on or after the switch will be assigned to the Q8W treatment period.

Q4W Period

Study medication duration (days):

- Date of last dose of bimekizumab in the Q4W period – date of first dose in the Q4W period + 28 days

Note: If date of last dose of bimekizumab in the Q4W period + 28 days extends to a date beyond the date of the first dose in the Q8W period, then this calculation reverts to:

- Date of first dose in the Q8W period – date of first dose in the Q4W period + 1.

Time at risk (days):

- Date of first dose in Q8W period – Date of first dose Q4W period + 1

Q8W Period

Study medication duration (days) use the minimum of:

- Date of last dose of bimekizumab in the Q8W period – date of first dose in the Q8W period + 56 days.
- Date of first dose in OLE2 treatment period – date of first dose in the Q8W period + 1 day.

Note: If date of last dose of bimekizumab in the Q8W period + 56 days extends to a date beyond the final visit date (including PEOT, but not including SFU), then this calculation reverts to:

- Final visit date in the Q8W period (including PEOT, but not including SFU) – date of first dose in the Q8W period + 1.

Note: For subjects who die, if date of last dose of bimekizumab in the Q8W period + 56 days extends to a date beyond the date of death, then this calculation reverts to:

- Date of death – date of first dose in the Q8W period + 1.

Time at risk (days):

- For all subjects, use the minimum of the following:
  - Date of last BKZ 320mg Q8W dose – date of first BKZ 320mg Q8W dose + 140 days.
  - Date of first dose in OLE2 treatment period - date of first BKZ 320mg Q8W dose + 1 day.
  - Date of last clinical contact – date of first BKZ 320mg Q8W dose + 1 day.
  - Date of death – date of first BKZ 320mg Q8W dose + 1 day.

<u>Q4W and Q8W period combined (attributed to BKZ Total)</u>

- Sum of study medication duration attributed to BKZ 320mg Q4W and study medication duration attributed to BKZ 320mg Q8W-1.

<u>Time at risk (days):</u>

- For all subjects, use the minimum of the following:
  - Date of last dose in the 144-week Treatment Period – date of first dose in PS0014 + 140 days
  - Date of first dose in OLE2 treatment period - date of first dose in PS0014 + 1 day
  - Date of last clinical contact in 144-week Treatment Period and SFU – date of first dose in PS0014 + 1.
  - Date of death – date of first dose in PS0014+ 1 day.

A by-subject listing of exposure to study medication data will be provided. This listing will be presented and will include: date and time of first dose, date and time of last dose for week 0 to week 144 and time at risk and study medication duration for BKZ 320 mg Q4W, BKZ 320mg Q8W and BKZ total.

10.1.1.2 Time at risk for AE summaries through Week 48

Time at risk for the first 48 weeks of PS0014 (used for summaries described in Section 10.2.2.1) will be derived as the minimum of:

- Date of Week 48 visit – Date of first dose +1
- Total time at risk in PS0014 (as derived in Section 10.1.1.1)

For subjects who switch from Q4W to Q8W dosing at Week 24, the time at risk for each regimen will be derived as follows:

- Time at risk on Q4W = date of Week 24 dose – date of first dose +1
- Time at risk on Q8W = Total time at risk through Week 48 – time at risk on Q4W

10.1.1.3 Exposure during the OLE2 Treatment Period

Eligible subjects from sites in the US or Canada who have completed the Week 144 Visit or are in the SFU or have completed the SFU can roll over to an additional OLE2 treatment period.

Definitions for study medication duration (days) and time at risk (days) during the OLE2 treatment period will be provided for the following subjects:

- Group A: Subjects who roll over directly from treatment period to OLE2 treatment period
- Group B: Subjects who reinitiate bimekizumab and who were in the SFU or had completed the SFU of the treatment period.

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10.1.1.3.1 Group A: Subjects who roll over directly from the treatment period to OLE2 Treatment Period

Study medication duration (days)

- Date of last bimekizumab dose in the OLE2 treatment period – date of first dose in the OLE2 treatment period + 56 days

  Note: If date of last bimekizumab dose in the OLE2 treatment period + 56 days extends to a date beyond the final visit date (including PEOT, but not including SFU2), then this calculation reverts to:

  – Final visit date (including PEOT, but not including SFU2) – date of first dose in the OLE2 treatment period + 1.

Note: For subjects who die, if date of last bimekizumab dose in the OLE2 treatment period + 56 days extends to a date beyond the date of death, then this calculation reverts to:

- Date of death – date of first dose in the OLE2 treatment period + 1.

Time at risk (days)

- Use the minimum of the following:
  - Date of last dose in the OLE2 Period – date of first dose in the OLE2 treatment period + 140 days.
  - Date of last clinical contact – date of first dose in OLE2 treatment period + 1.
  - Date of death – date of first dose in the OLE2 treatment period +1.

10.1.1.3.2 Group B: Subjects who reinitiate bimekizumab

1) Subjects reinitiated to receive BKZ Q8W at OLE2 period treatment start

- Study medication duration (days)
  - Date of last bimekizumab dose in the OLE2 treatment period – date of first bimekizumab dose in the OLE2 treatment period + 56 days

  Note: If date of last bimekizumab dose in the OLE2 treatment period + 56 days extends to a date beyond the final visit date (including PEOT, but not including SFU2), then this calculation reverts to:
  - Final visit date (including PEOT, but not including SFU2) – date of first dose in the OLE2 treatment period + 1.

  Note: For subjects who die, if date of last bimekizumab 320mg Q8W dose + 56 days extends to a date beyond the date of death, then this calculation reverts to:
  - Date of death – date of first dose in OLE2 treatment period + 1.
- Time at risk (days)
  - Use the minimum of the following:
    - Date of last dose in OLE2 treatment period – date of first dose in Open-Label Extension 2 Period+ 140 days.
    - Date of last clinical contact – date of first dose in Open-Label Extension 2 Period+ 1.
    - Date of death – date of first dose in Open-Label Extension 2 Period + 1.

2) Subjects reinitiated to receive BKZ Q4W/Q8W at OLE2 treatment period start

Study medication duration (days)

- Attributed to BKZ Q4W/Q8W
  - Date of last BKZ 320mg Q8W dose in the OLE2 treatment period – date of first BKZ 320mg Q4W dose in the OLE2 treatment period + 56 days.

Note: If date of last bimekizumab dose in the OLE2 treatment period + 56 days extends to a date beyond the final visit date (including PEOT, but not including SFU2), then this calculation reverts to:

- Final visit date (including PEOT, but not including SFU2) – date of first BKZ 320mg Q4W dose in the OLE2 treatment period + 1.

Note: For subjects who die, if date of last bimekizumab dose in the OLE2 treatment period + 56 days extends to a date beyond the date of death, then this calculation reverts to:

- Date of death – date of first dose in the OLE2 treatment period + 1.

- If the subject discontinued prior to the switch to Q8W then:
  - Date of last BKZ 320mg Q4W dose in the OLE2 treatment period – date of first BKZ 320mg Q4W dose in the OLE2 treatment period + 28 days.

If date of last bimekizumab dose in the OLE2 treatment period + 28 days extends to a date beyond the final visit date (including PEOT, but not including SFU2), then this calculation reverts to:

- Final visit date (including PEOT, but not including SFU2) – date of first BKZ 320mg Q4W dose in the OLE2 treatment period + 1.

Note: For subjects who die prior to switch to Q8W, if date of last bimekizumab dose in the OLE2 treatment period + 28 days extends to a date beyond the date of death, then this calculation reverts to:

- Date of death – date of first dose in the OLE2 treatment period + 1.

Time at risk (days)

- Attributed to BKZ Q4W/Q8W:
  - Use the minimum of the following:
    - Date of last dose in Open-Label Extension 2 Period – date of first dose in OLE2 treatment period + 140 days.
    - Date of last clinical contact – date of first dose in Open-Label Extension 2 Period + 1.
    - Date of death – date of first dose in Open-Label Extension 2 Period + 1.

10.1.2 Cohort B

Summaries for overall exposure (week 0-144 period) will be provided by using Safety treatment groups. This consists of a descriptive summary of study medication duration in days. In addition, total study medication duration and time at risk will be summarized in years by Safety treatment groups and psoriasis type (PSO, GPP or EP).

The cumulative study medication duration will be summarized for subjects exposed for given durations of time. These will be based upon cumulative duration through Week 144 by Safety

treatment groups and psoriasis type (PSO, GPP or EP). For the cumulative duration the following categories will be used:

- ≥0 weeks
- ≥8 weeks
- ≥16 weeks
- ≥24 weeks
- ≥48 weeks.
- ≥64 weeks.
- ≥80 weeks.
- ≥96 weeks.
- ≥112 weeks.
- ≥128 weeks.
- ≥144 weeks.

10.1.2.1 Exposure during Weeks 0-144

The study medication duration (days) will be calculated depending on the treatment.

For subjects who received bimekizumab 320mg Q4W only:

- Study medication duration (days):
  Date of last dose – date of first dose + 28 days
- Note: If the date of last dose + 28 days extends to a date beyond the final visit date (including PEOT, but not including SFU), then this calculation reverts to:
  - Final visit date (including PEOT, but not including SFU) – date of first dose + 1.
- For subjects who die:
  - Date of death – date of first dose + 1.

Time at Risk (Days):

For all subjects, time at risk will be the minimum of the following:

- Date of last dose– date of first dose + 140 days.
- Date of last clinical contact – date of first dose + 1 day.
- Date of death - Date of first dose + 1 day

For subjects who switch from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W:

Note, the date of the treatment switch will be determined using the information on dosing regimen entered in IXRS. All doses prior to the regimen switch will be assigned to the Q4W

treatment period, all doses on or after the regimen switch will be assigned to the Q8W treatment period.

Q4W Period

Study medication duration (days):

- Date of last dose of bimekizumab in the Q4W period – date of first dose in the Q4W period + 28 days

Note: If date of last dose of bimekizumab in the Q4W period + 28 days extends to a date beyond the date of the first dose in the Q8W period, then this calculation reverts to:

- Date of first dose in the Q8W period – date of first dose in the Q4W period + 1.

Time at risk (days):

- Date of first dose in Q8W period – Date of first dose Q4W period + 1

Q8W Period

Study medication duration (days):

- Date of last dose of bimekizumab in the Q8W period – date of first dose in the Q8W period + 56 days.

Note: If date of last dose of bimekizumab in the Q8W period + 56 days extends to a date beyond the final visit date (including PEOT, but not including SFU), then this calculation reverts to:

- Final visit date in the Q8W period (including PEOT, but not including SFU) – date of first dose in the Q8W period + 1.

Note: For subjects who die, if date of last dose of bimekizumab in the Q8W period + 56 days extends to a date beyond the date of death, then this calculation reverts to:

- Date of death – date of first dose in the Q8W period + 1.

Time at risk (days):

For all subjects, use the minimum of the following:

- Date of last dose in the Q8W period – date of first dose in the Q8W period + 140 days.
- Date of last clinical contact– date of first dose in the Q8W period + 1
- Date of death – date of first dose in the Q8W period + 1.

Q4W and Q8W period combined (attributed to BKZ Total)

- Sum of study medication duration attributed to BKZ 320mg Q4W and study medication duration attributed to BKZ 320mg Q8W-1.

Time at risk (days):

For all subjects, use the minimum of the following:

- Date of last dose – date of first dose + 140 days.
- Date of last clinical contact – date of first dose + 1.
- Date of death – date of first dose + 1 day.

For subjects who switch from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at week 16, and then switch from bimekizumab 320mg Q8W to bimekizumab 320mg Q4W at week 48:

Note, the date of treatment switches will be determined using the information on dosing regimen entered in IXRS. All doses prior to a regimen switch are attributed to the previous period, all doses on or after a regimen switch (and prior to any subsequent switch) are attributed to the current period.

1st Q4W Period

Study medication duration (days):

- Date of last dose of bimekizumab in the 1st Q4W period – date of first dose in the 1st Q4W period + 28 days

Note: If date of last dose of bimekizumab in the 1st Q4W period + 28 days extends to a date beyond the date of the first dose in the Q8W period, then this calculation reverts to:

- Date of first dose in the Q8W period – date of first dose in the 1st Q4W period + 1.

Time at risk (days):

- Date of first dose in Q8W period – Date of first dose 1st Q4W period + 1

Q8W Period

Study medication duration (days):

- Date of last dose of bimekizumab in the Q8W period – date of first dose in the Q8W period + 56 days

Note: If date of last dose of bimekizumab in the Q8W period + 56 days extends to a date beyond the date of the first dose in the second Q4W period, then this calculation reverts to:

- Date of first dose in the 2nd Q4W period – date of first dose in the Q8W period + 1.

Time at risk (days):

- Date of first dose in 2nd Q4W period – Date of first dose Q8W period + 1

2nd Q4W Period

Study medication duration (days):

- Date of last dose of bimekizumab in the 2nd Q4W period – date of first dose in the 2nd Q4W period + 28 days.

Note: If date of last dose of bimekizumab in the 2nd Q4W period + 28 days extends to a date beyond the final visit date (including PEOT, but not including SFU), then this calculation reverts to:

- Final visit date in the 2nd Q4W period (including PEOT, but not including SFU) – date of first dose in the 2nd Q4W period + 1.

Note: For subjects who die, if date of last dose of bimekizumab in the 2nd Q4W period + 28 days extends to a date beyond the date of death, then this calculation reverts to:

- Date of death – date of first dose in the 2nd Q4W period + 1.

Time at risk (days):
For all subjects, use the minimum of the following:

- Date of last dose in the 2nd Q4W period – date of first dose in the 2nd Q4W period + 140 days.
- Date of last clinical contact– date of first dose in the 2nd Q4W period + 1.
- Date of death – date of first dose in the 2nd Q4W period + 1 day.

<u>1st Q4W, Q8W and 2nd Q4W period combined (attributed to BKZ Total)</u>

- Total study medication duration, attributed to BKZ Total, will be obtained by summing the study medication durations in each individual study period -2.
  Total study medication duration for Q4W will be obtained by summing the two individual Q4W durations -1.

<u>Time at risk (days):</u>

<u>Total time at risk for Q4W will be obtained by summing the time at risk in the two individual Q4W periods -1.</u>

<u>Total time at risk for BKZ (including Q4W and Q8W), attributed to BKZ Total, will be derived as follows:</u>

For all subjects, use the minimum of the following:

- Date of last dose – date of first dose + 140 days.
- Date of last clinical contact – date of first dose + 1.
- Date of death – date of first dose +1 day.

For subjects who switch from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at week 16, and then switch from bimekizumab 320mg Q8W to bimekizumab 320mg Q4W at week 48 and then switch from bimekizumab 320mg Q4W to bimekizumab 320mg Q8W at any visit after week 48:

Note, the date of treatment switches will be determined using the information on dosing regimen entered in IXRS. All doses prior to a regimen switch are attributed to the previous period, all doses on or after a regimen switch (and prior to any subsequent switch) are attributed to the current period.

1st Q4W Period

Study medication duration (days):

- Date of last dose of bimekizumab in the 1st Q4W period – date of first dose in the 1st Q4W period + 28 days

Note: If date of last dose of bimekizumab in the 1st Q4W period + 28 days extends to a date beyond the date of the first dose in the first Q8W period, then this calculation reverts to:

- Date of first dose in the 1st Q8W period – date of first dose in the 1st Q4W period + 1.

Time at risk (days):

- Date of first dose in 1st Q8W period – Date of first dose 1st Q4W period + 1

1st Q8W Period

Study medication duration (days):

- Date of last dose of bimekizumab in the 1st Q8W period – date of first dose in the 1st Q8W period + 56 days

Note: If date of last dose of bimekizumab in the 1st Q8W period + 56 days extends to a date beyond the date of the first dose in the 2nd Q4W period, then this calculation reverts to:

- Date of first dose in the 2nd Q4W period – date of first dose in the 1st Q8W period + 1.

Time at risk (days):

- Date of first dose in 2nd Q4W period – Date of first dose 1st Q8W period + 1

2nd Q4W Period

Study medication duration (days):

- Date of last dose of bimekizumab in the 2nd Q4W period – date of first dose in the 2nd Q4W period + 28 days

Note: If date of last dose of bimekizumab in the 2nd Q4W period + 28 days extends to a date beyond the date of the first dose in the second Q8W period, then this calculation reverts to:

- Date of first dose in the 2nd Q8W period – date of first dose in the 2nd Q4W period + 1.

Time at risk (days):

- Date of first dose in 2nd Q8W period – Date of first dose 2nd Q4W period + 1

2nd Q8W Period

Study medication duration (days):

- Date of last dose of bimekizumab in the 2nd Q8W period – date of first dose in the 2nd Q8W period + 56 days.

Note: If date of last dose of bimekizumab in the 2nd Q8W period + 56 days extends to a date beyond the final visit date (including PEOT, but not including SFU), then this calculation reverts to:

- Final visit date in the 2nd Q8W period (including PEOT, but not including SFU) – date of first dose in the 2nd Q8W period + 1.

Note: For subjects who die, if date of last dose of bimekizumab in the 2nd Q8W period + 56 days extends to a date beyond the date of death, then this calculation reverts to:

- Date of death – date of first dose in the 2nd Q8W period + 1.

Time at risk (days):

For all subjects, use the minimum of the following:

- Date of last dose in the 2nd Q8W period – date of first dose in the 2nd Q8W period + 140 days.
- Date of last clinical contact– date of first dose in the 2nd Q8W period + 1.
- Date of death – date of first dose in the 2nd Q8W period + 1 day.

1st Q4W, 1st Q8W, 2nd Q4W and 2nd Q8W period combined (attributed to BKZ Total)

- Total study mediation duration, attributed to BKZ Total, will be obtained by summing the study medication durations in each individual study period - 3.
  Total study medication duration for each dosing regimen will be obtained by summing the individual durations for a regimen -1.

Time at risk (days):

Total time at risk for Q4W will be obtained by summing the time at risk in the individual Q4W periods -1.

Total time at risk for Q8W will be obtained by summing the time at risk in the individual Q8W periods -1.

Total time at risk, attributed to BKZ Total, will be derived as follows:

For all subjects, use the minimum of the following:

- Date of last dose – date of first dose + 140 days.
- Date of last clinical contact – date of first dose + 1.
- Date of death – date of first dose + 1 day.

A by-subject listing of exposure to study medication data will be provided. This listing will be presented by treatment group and will include: date and time of first dose, date and time of last dose for week 0 to week 144 and time at risk and study medication duration for BKZ 320 mg Q4W, BKZ 320mg Q8W and BKZ total.

10.2 Adverse events

An AE is any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether related to the medicinal (investigational) product or not.

10.2.1 Data considerations

Definition of treatment-emergent AEs:

Cohort A:

Treatment-emergent AEs (TEAEs) are defined as those AEs that have a start date following the first dose of PS0014 study treatment and during the time at risk, as defined in Section 10.1.1. If it is not possible (due to partial dates) to determine whether or not an AE is treatment-emergent then it will be assumed to be a TEAE.

If an adverse event occurs on the first dose of the study treatment, the event is considered non-emergent. The only exception to this is if the AE fulfills any of the criteria specified below:

- Events that fulfill the anaphylaxis criteria for acute events (refer to Appendix A in Section 12.1)
- Events with a SMQ “Hypersensitivity (SMQ)”
- Events with an HLT of “Administration site reactions NEC”
- Events with an HLT of “Injection site reactions”

Cohort B:

Treatment-emergent AEs (TEAEs) are defined as those AEs that have a start date on or following the first dose of study treatment and during the time at risk, as defined in Section 10.1.2 . If it is not possible (due to partial dates) to determine whether or not an AE is treatment-emergent then it will be assumed to be a TEAE.

For both cohorts, if an adverse event occurs on the date of a treatment switch, the event is attributed to the original treatment. The only exception to this is if the AE fulfills any of the criteria specified below:

- Events that fulfill the anaphylaxis criteria for acute events (refer to Appendix A in Section 12.1)
- Events with a SMQ "Hypersensitivity (SMQ)"
- Events with an HLT of "Administration site reactions NEC"
- Events with an HLT of "Injection site reactions"

The rules for imputing partial start or stop dates are outlined in Section 4.2.

Duration of AEs will not be calculated if there is missing stop date information.

If the intensity of an adverse event is unknown, it is considered as severe. If the relationship to study drug is missing, it is considered as related.

AEs will be presented as "number of subjects (percentage of subjects) [number of events]". In this style of output, "[number of events]" will include all cases of an AE including repeat occurrences in individual subjects, while "number of subjects" will count each subject only once.

Subject time at risk represents the time a subject is at risk for having an AE. The definitions for subject time at risk (in days) are outlined in Section 10.1. These definitions will be used for exposure-adjusted AE summaries.

Selected AE summaries will include the exposure-adjusted incident rate (EAIR) with associated 95% CI and the exposure adjusted event rate (EAER).

The EAIR is defined as the number of subjects (n) with a specific AE adjusted for the exposure and will be scaled to 100 patient-years:

$$EAIR = 100 \times n / \sum_{i=1}^{N} \left(T_{Exp(i)}\right)$$

Where $T_{Exp(i)}$ is the exposure time and N is the number of subjects at risk.

If a subject has multiple events, the time of exposure is calculated to the first occurrence of the AE being considered. If a subject has no events, the total time at risk is used.

Exact Poisson 95% confidence intervals for incidence rates are calculated using the relationship between the Poisson and the Chi-square distribution (Ulm, 1990; Fay and Feuer, 1997):

$$LCL = \chi^2_{2n,\alpha/2}/2$$

$$UCL = \chi^2_{2(n+1),1-\alpha/2}/2$$

where n is the number of subjects with a specific AE for the incidence rate of interest and is the basis for the number of the degrees of freedom for the chi-square quantile for the upper tail probability χ^2.

The EAER will be the number of AEs including repeat occurrences in individual subjects divided by the total time at risk scaled to 100 patient-years and calculated using:

$$EAER = 100 \times N_{AE} / \sum_{i=1}^{N} (T_{Risk(i)})$$

where N_{AE} is the total number of AEs, T_{Risk} is the time at risk for each subject, and N is the total number of subjects at risk.

No confidence interval will be computed for EAER.

Separate by-subject listings of all TEAEs for the OLE2 treatment period will be provided.

10.2.1.1 COVID-19 related data considerations

In order to assess the impact of the COVID-19 global pandemic on TEAEs, an additional AE summary will be presented. The following data considerations are introduced to support this presentation by the following periods:

- Prior to COVID-19 pandemic
- During COVID-19 pandemic

The COVID-19 pandemic start date is defined as 11 March 2020, the date the World Health Organization declared COVID-19 as a pandemic. Note that the final analysis may be conducted during the pandemic therefore a post COVID-19 pandemic period is not yet defined. A pandemic end date may be defined subsequently for the final analysis to support presentation of a post COVID-19 pandemic period.

Where a subject's time at risk includes 11 March 2020, the subject is included in the denominator for both periods and their time at risk is split as follows:

- Prior to COVID-19 pandemic:
  - Start of time at risk to 10 March 2020
- During COVID-19 pandemic:
  - 11 March to end of time at risk

Where a subject's time at risk does not include 11 March 2020, the subject is only included in the denominator for the Prior to COVID-19 pandemic period and their time at risk would be included entirely in the Prior to COVID-19 pandemic period. Detailed definitions for subject time at risk are outlined in Section 10.1. AEs are assigned to the appropriate period according to start date:

- Prior to COVID-19 pandemic:

- AE start date ≤ 10 March 2020

- During COVID-19 pandemic:
  - AE start date ≥ 11 March 2020.

In addition, the incidence of COVID-19 TEAEs will be summarized for both Cohort A and Cohort B.
The following PTs will be used to classify COVID-19 adverse events:

- Corona virus infection
- Coronavirus test positive

A separate by-subject listing will be produced for COVID-19 TEAEs. By-subject listings of COVID-19 TEAEs will be produced separately for OLE2 treatment period.

10.2.1.2 TEAEs and COVID-19 Vaccine considerations

To assess the impact of COVID-19 mass vaccination on TEAEs, a sensitivity analysis will present all TEAEs excluding TEAEs assessed as exclusively related to COVID-19 vaccine by the investigator. TEAEs recorded as related to both study medication and COVID-19 vaccination should not be excluded. A complementary table and listing of TEAEs related to COVID-19 vaccine will be presented.

Another sensitivity analysis will present all TEAEs excluding TEAEs with start date on or up to 5 days after date of COVID-19 vaccine. Note that study participants may receive more than one administration of COVID-19 vaccine. A complementary table and listing of TEAEs with start date on or up to 5 days after date of COVID-19 vaccine will also be presented. Complementary listings of TEAEs related to COVID-19 vaccine will be presented for the OLE2 treatment period separately.

The following AE summaries related to COVID-19 vaccine will be provided for both Cohort A (CA-SS) and Cohort B (CB-SS only, not split by disease type):

- Incidence of TEAEs Excluding TEAEs Exclusively Related to COVID-19 Vaccine by SOC, HLT, and PT
- Incidence of TEAEs Exclusively Related to COVID-19 Vaccine by SOC, HLT, and PT including only those subjects who received at least one COVID-19 vaccine
- Listing of TEAEs Related to COVID-19 Vaccine
- Incidence of COVID-19 Vaccine Interval Censored TEAEs by SOC, HLT, and PT
- Incidence of COVID-19 Vaccine Interval TEAEs by SOC, HLT, and PT including only those subjects who received at least one COVID-19 vaccine
- Listing of COVID-19 Vaccine Interval TEAEs

The below tables of AE summaries and listings related to COVID-19 vaccine will be provided for the CA-OL2S.

- Incidence of TEAEs Excluding TEAEs Exclusively Related to COVID-19 Vaccine by SOC, HLT, and PT
- Listing of TEAEs Related to COVID-19 Vaccine

10.2.2 AE summaries

10.2.2.1 Cohort A

The following AE summaries will be provided for the CA-SS by PS0014 treatment group at the time of the onset of the event (see Section 3.6.1). In addition, all summaries of TEAEs based on "100 subject years" will include EAIR (with 95% CI) and EAER. For all below AE summaries with above reporting threshold of cut-off of 5%, the cut off will be applied in any treatment group including BKZ 320mg Q8W, BKZ 320mg Q4W and BKZ Total.

- Incidence of TEAEs – Overview
- Incidence of TEAEs – Overview by manufacturing process (Process 4 and Process 5)
    - Only BKZ total group by process will be displayed
- Incidence of TEAEs per 100 subject years by SOC, HLT, and PT
- Incidence of TEAEs per 100 subject years by SOC, HLT, and PT and manufacturing process (Process 4 and Process 5)
    - Only BKZ total group by process will be displayed
- Incidence of Serious TEAEs per 100 subject years by SOC, HLT, and PT
- Incidence of TEAEs Leading to Discontinuation per 100 subject years by SOC, HLT, and PT
- Incidence of TEAEs Leading to Death by SOC, HLT, and PT
- Incidence of TEAEs by Maximum Relationship, SOC, HLT, and PT
- Incidence of Serious TEAEs by Relationship, SOC, HLT, and PT
- Incidence of TEAEs Leading to Death by Relationship by SOC, HLT, and PT - Note: For EudraCT reporting purposes
- Incidence of TEAEs by Maximum Severity, SOC, HLT, and PT
- Incidence of TEAEs by decreasing frequency of PT
- Incidence of TEAEs Above Reporting Threshold of 5% by SOC and PT
- Incidence of Non-Serious TEAEs by SOC, HLT, and PT
- Incidence of Non-Serious TEAEs by Maximum Relationship, SOC, HLT, and PT
- Incidence of Non-Serious TEAEs Above Reporting Threshold of 5% by SOC and PT
- Incidence of Non-Serious TEAEs Above Reporting Threshold of 5% by Relationship, SOC
- Incidence of Related TEAEs by SOC, HLT, and PT
- Incidence of Related Serious TEAEs by SOC, HLT, and PT
- Incidence of Related TEAEs Above Reporting Threshold of 5% by SOC and PT

- Incidence of TEAEs per 100 subject years by SOC, HLT, and PT and by Time of Onset Relative to COVID-19 pandemic (prior to COVID-19 pandemic, during COVID-19 pandemic, as defined in Section 10.2.1.1)
- Incidence of COVID-19 TEAEs by SOC, HLT, and PT

Selected AE summaries for OLE2 treatment period will be provided by PS0014 OLE2 treatment period groups as specified in Section 3.6.1 separately and will be based on CA-OL2S.

The following selected AEs summaries will be provided separately based on the CA-OL2S:

- Incidence of TEAEs Overview
- Incidence of TEAEs per 100 Subject-Years
- Incidence of Serious TEAEs per 100 Subject-Years
- Incidence of TEAEs Leading to Discontinuation per 100 subject-years
- Incidence of TEAEs Leading to Death
- Incidence of TEAEs Leading to Death by Relationship by SOC, HLT, and PT - Note: For EudraCT reporting purposes
- Incidence of Serious TEAEs by Relationship
- Incidence of Non-Serious TEAEs Above Reporting Threshold of 5% by SOC and PT
- Incidence of Non-Serious TEAEs Above Reporting Threshold of 5% by Relationship SOC and PT

The following summaries will be produced for subjects who entered PS0014 from PS0009, having completed PS0009 treated with either Ustekinumab or Bimekizumab throughout (subjects who received placebo in PS0009 are not included):

- Incidence of TEAEs during the first 48 weeks of PS0014 – Overview
- Incidence of TEAEs during the first 48 weeks of PS0014 per 100 subject years by SOC, HLT, and PT

These summaries will include all TEAEs occurring in 144-week treatment period (up to the end of the time at risk as defined in Section 10.1.1.2), by previous PS0009 treatment/PS0014 treatment (i.e. Ustekinumab/Bimekizumab or Bimekizumab/Bimekizumab).

In addition, the two following tables of TEAE by time of onset relative to antibody status will be produced:

- a Table presenting the incidence of TEAEs per 100 Subject-Years by Time of Onset Relative to Overall ADAb Status (including SFU) for CA-SS. The following time of onset will be considered:
    - AEs Starting Before 1st Anti-BKZ Antibody Positive Result

- AEs Starting On or After 1st Anti-BKZ Antibody Positive Result (for subjects who are ADAb positive at PS0014 baseline).
- AEs Starting On or After 1st Anti-BKZ Antibody Positive Result (for subjects who are not ADAb positive at baseline)
- AEs for Subjects who are Overall Anti-BKZ Antibody Negative

- a Table presenting the incidence of TEAEs per 100 Subject-Years by Time of Onset Relative to Overall NAb (including SFU) for CA-SS. The following time of onset will be considered:
  - AEs Starting Before 1st NAb Positive Result
  - AEs Starting On or After 1st NAb Positive Result (for subjects who are NAb positive at PS0014 baseline).
  - AEs Starting On or After 1st NAb Positive Result (for subjects who are not NAb positive at baseline)
  - AEs for Subjects who are Overall NAb Antibody Negative

At the time of entry into PS0014 from the feeder studies, it was required to enter a subject's current PASI response into IWRS in order for the initial PS0014 treatment (Q4W or Q8W) to be assigned according to the randomization rules/ratios stated in the protocol. It was subsequently found that 140 subjects did not have their correct PASI response entered into IWRS and therefore these subjects were potentially incorrectly assigned their PS0014 treatment. Due to the use of randomization ratios it is not possible to know precisely each subject that was misallocated to either Q4W or Q8W.

To assess the impact of this on the evaluation of safety, the following summaries will be produced for all subjects in CA-SS and separately excluding the 140 potentially impacted subjects:

- Incidence of TEAEs – Overview through Week 48
- Incidence of TEAEs by PS0014 Treatment in PS0014- Overview through Week 48 (Excluding 140 subjects with potentially impacted treatment assignment)
- Incidence of TEAEs per 100 subject years by SOC, HLT, and PT through Week 48
- Incidence of TEAEs per 100 Subject-Years by PS0014 Treatment through Week 48 (Excluding 140 subjects with potentially impacted treatment assignment)

These summaries will include all TEAEs occurring in PS0014 (up to the end of the time at risk as defined in Section 10.1.1.2)

The following summaries will also be provided for CA-SS and only for BKZ total group:

- Incidence of TEAEs per 100 subject years by Weight Group (using groups <70 kg, >=70 to <95 kg, >=95 to <120 kg, >=120 kg)
- Incidence of TEAEs per 100 subject years by Gender (Male/Female)
- Incidence of TEAEs per 100 subject years by Race (White/ Other including Black)

The following by-subject listings will be provided:

- All TEAEs
- All Non-TEAEs
- All serious TEAEs
- All TEAEs related to study medication
- All TEAEs leading to discontinuation of study treatment
- All TEAEs leading to subject discontinuation
- All COVID-19 TEAEs
- TEAEs which Code to the "Infections and Infestations" SOC and Emerged within 30 days of when a CTCAE Grade 3 or 4 Neutrophil Value Occurred
    - AEs which emerged within 30 days (either before or after) of when a CTCAE Grade 3 or 4 neutrophil value occurred (per the lab data).

10.2.2.2 Cohort B

All AE summaries described in the initial list in Section 10.2.2.1 will be presented for the CBPSO-SS, CBGPP-SS, and CBEP-SS by PS0014 treatment group at the time of the onset of the event (see Section 3.6.2), unless specified otherwise below.

AE summaries of TEAE above reporting threshold of 5% will not be produced for CBGPP-SS and CBEP-SS.

Incidence of TEAE leading to death, incidence of TEAEs by time of onset relative to COVID-19 pandemic and incidence of COVID-19 TEAEs will be presented for the CB-SS only.

In addition, the two tables including incidence of TEAEs per 100 Subject-Years by Time of Onset Relative to Overall ADAb status and overall NAb status will be produced for CB-SS by following the definition:

- a Table presenting the incidence of TEAEs per 100 Subject-Years by Time of Onset Relative to Overall ADAb Status (including SFU) for CA-SS. The following time of onset will be considered:
    - AEs Starting Before 1st Anti-BKZ Antibody Positive Result
    - AEs Starting On or After 1st Anti-BKZ Antibody Positive Result (for subjects who are not ADAb positive at baseline)
    - AEs for Subjects who are Overall Anti-BKZ Antibody Negative
- a Table presenting the incidence of TEAEs per 100 Subject-Years by Time of Onset Relative to Overall NAb (including SFU) for CB-SS. The following time of onset will be considered:
    - AEs Starting Before 1st NAb Positive Result
    - AEs Starting On or After 1st NAb Positive Result (for subjects who are not NAb positive at baseline)
    - AEs for Subjects who are Overall NAb Antibody Negative

The following by-subject listings will be provided:

- All TEAEs
- All Non-TEAEs
- All serious TEAEs
- All TEAEs related to study medication
- All TEAEs leading to discontinuation of study treatment
- All TEAEs leading to subject discontinuation
- All COVID-19 TEAEs
- TEAEs which Code to the "Infections and Infestations" SOC and Emerged within 30 days of when a CTCAE Grade 3 or 4 Neutrophil Value Occurred
    - AEs which emerged within 30 days (either before or after) of when a CTCAE Grade 3 or 4 neutrophil value occurred (per the lab data).

10.2.3 Other Safety topics of interest

The following sub-sections contain the definitions and approach for summarizing the AEs that have been identified as safety topics of interest. All table summaries for TEAEs identified as safety topics of interest will include EAIRs (with 95% confidence interval) and EAERs. No safety topics of interest AE summaries will be produced for the Open-Label Extension 2 treatment period (OLE2).

10.2.3.1 Cohort A

The AE of safety topics of interest will be summarized overall and PS0014 treatment group for the CA-SS.

A by-subject listing of all AEs of safety topics of interest will be provided. Listings of all treatment emergent adverse events of other safety topics of interest will be provided separately for the OLE2 treatment period for the CA-OL2S.

10.2.3.1.1 Infections (serious, opportunistic, fungal and TB)

- Serious infections will be identified based on MedDRA classification (SOC "Infections and infestations") using the Serious TEAE table. A separate table does not need to be produced to summarize these events.
- Fungal infections will be summarized in a stand-alone table. The table will include all TEAEs (serious and non-serious) which code into the High Level Group Term (HLGT) "Fungal infectious disorders"
- Opportunistic infections (including tuberculosis) will be summarized in a stand-alone table. The table will include all TEAEs identified using UCB-defined search criteria which were adjudicated as opportunistic infections.

10.2.3.1.2 Malignancies

These events will be presented in the following tables:

- One table will be based on the criteria Standardized MedDRA Query (SMQ) = "Malignant or unspecified tumours (SMQ)"
- One table will be based on the criteria SMQ = "Malignant tumours (SMQ)".

SMQ search should include all TEAEs which code to a PT included in the Scope=Narrow group within each SMQ.

Note that the events included in the "Malignant tumours" table will be a subset of the events included in the "Malignant or unspecified tumours" table. While the "Malignant tumours (SMQ)" is most relevant, "Malignant or unspecified tumours (SMQ)" must be reviewed for potential malignancies.

The output table based on the SMQ="Malignant or unspecified tumours (SMQ)" will include 2 different overall incidence rows:

- The first overall incidence row will summarize "Any malignancies (including unspecified)" and this row will summarize the incidence of all TEAEs flagged for inclusion in the table, regardless of the High Level Term (HLT) it codes to.
- The second overall incidence row will summarize "Any malignancy excluding non-melanomic skin cancers HLT" and this row will summarize the incidence of AEs flagged for inclusion in the table (using the appropriate SMQ depending on the table), excluding those which code to an HLT of "Skin neoplasms malignant and unspecified (excl melanoma)".

10.2.3.1.3 Major adverse cardiac event

Potential cardiovascular events are adjudicated by the independent Cardiovascular Event Adjudication Committee (CV-CAC) according to the CV-CAC Charter (version 6.0). Adjudicated events are classified by the CV-CAC to one of the event types as defined in Table 1. The classification of an event as a Major Adverse Cardiac Event (MACE) is also determined by the CV-CAC. Events which are classified by the CV-CAC as any of the events types identified in the third column of Table 10.1 will be considered an extended MACE. Note that extended MACE is determined programmatically and includes a broader scope definition of MACE.

MACE as determined by the CV-CAC will be presented in a table and listing. Extended MACE will be presented separately in a table and listing. Additional listings of all MACE as determined by the CV-CAC will be presented separately for the OLE2 treatment period.

Another table and listing will present the adjudicated cardiovascular events by type. For each cardiovascular event type, the individual PTs which fall within each event type will be summarized. This listing will indicate whether each event was determined to be a MACE and/or an extended MACE. Similar listings of the adjudicated cardiovascular events by type will be presented separately for the OLE2 treatment period.

Additionally, a listing of all events identified for potential review by the CV-CAC will be produced. This listing will indicate whether each event was identified by the CV-CAC Chair for

full committee review. Similar listings of all events identified for potential review by the CV-CAC will be produced separately for the OLE2 treatment period.

Table 10.1: Cardiovascular event classifications

Event Type Code	Event Type	Extended MACE
1	Non-Fatal Myocardial Infarction (MI)	Yes
2	Non-Fatal Stroke: hemorrhagic	Yes
3	Non-Fatal Stroke: ischemic	Yes
4	Non-Fatal Stroke: embolic	Yes
5	Non-Fatal Stroke: undeterminable	Yes
6	Hospitalization or ER for Unstable Angina with urgent revascularization	Yes
7	Hospitalization or ER for Unstable Angina without urgent revascularization	No
8	Hospitalization for Heart Failure	Yes
9	Transient Ischemic Attack (TIA)	No
10	Coronary Revascularization Procedures (e.g. percutaneous coronary intervention, coronary artery bypass grafting)	Yes
11	Urgent Revascularization Procedures (i.e. due to symptoms of brain ischemia or pending infarction)	Yes
12	Arrhythmia (not associated with ischemia)	No
13	Peripheral Arterial Event	No
14	Venous Thromboembolic Event: pulmonary embolism (PE)	No
15	Venous Thromboembolic Event: deep vein thrombosis (DVT)	No
16	Venous Thromboembolic Event: PE and DVT	No
17	Other CV Event	No
18	Death due to Myocardial Infarction (MI)	Yes
19	Death due to Stroke	Yes
20	Sudden Cardiac Death	Yes
21	Other CV Death (e.g. heart failure, pulmonary embolism, cardiovascular procedure-related)	Yes
22	Cardiovascular: Undetermined Cause of Death (i.e. cause of death unknown)	Yes

Table 10.1: Cardiovascular event classifications

Event Type Code	Event Type	Extended MACE
23	Non-Cardiovascular Death	No
24	Non-Cardiovascular Event	No
99	Inadequate information to adjudicate	No

CV=Cardiovascular; DVT=Deep Vein Thrombosis; ER=Emergency Room; MACE= Major Adverse Cardiac Event; MI=Myocardial Infarction; PE=Pulmonary Embolism; TIA=Transient Ischemic Attack.
MACE is determined by the adjudication committee and is not identified programmatically based on event type.

10.2.3.1.4 Neutropenia

A table will be based on the following PTs (regardless of seriousness):

- Autoimmune neutropenia
- Band neutrophil count decreased
- Cyclic neutropenia
- Febrile neutropenia
- Idiopathic neutropenia
- Neutropenia
- Neutropenic infection
- Neutropenic sepsis
- Neutrophil count decreased

10.2.3.1.5 Suicidal Ideation and Behavior

Potential neuropsychiatric events are adjudicated by the independent Neuropsychiatric Adjudication Committee according to the Neuropsychiatric Adjudication Committee (version 8.0). Adjudicated events are classified by the Committee as Suicidal or Non-suicidal. Adjudicated events are also further classified by the Committee to one of the event types as defined in Table 10.2 Suicidal Ideation and Behavior (SIB) is defined as events classified by the Committee as Suicidal.

A table and listing will present SIB events. The listing will also be provided separately for OLE2 treatment period.

Another table and listing will present the adjudicated neuropsychiatric events by type. For each neuropsychiatric event type, the individual PTs which fall within each event type will be summarized. This listing will indicate whether each event was determined to be Suicidal or Non-Suicidal. For event type suicidal ideation, the listing will also indicate if intent was present and if the suicidal ideation was clinically significant.

Additionally, a listing of all events identified for potential review by the Committee will be produced. This listing will indicate whether each event was identified by the Neuropsychiatric Event Adjudication Committee Chair for full committee review. Similar listings will be provided separately for the OLE2 treatment period.

Table 10.2: Neuropsychiatric event classifications

Event Type Code	Event Classification	Event Type
1	Suicidal	Suicidal events/completed suicide
2	Suicidal	Suicide attempt
3	Suicidal	Preparatory acts toward imminent suicidal behavior
4	Suicidal/Non-suicidal[a]	Suicidal ideation
7	Non-suicidal	Nonsuicidal Self-injurious behavior
8	Non-suicidal	Nonsuicidal Other
99	Not applicable	Inadequate information to adjudicate

[a] Suicidal ideation event types can be classified by the Neuropsychiatric Adjudication Committee as Suicidal or Non-suicidal depending on whether intent to die was present.

10.2.3.1.6 Inflammatory bowel disease

Selected gastrointestinal events are adjudicated by the independent Inflammatory Bowel Disease (IBD) Adjudication Committee (IBD-CAC) according to the IBD-CAC Charter (version 3.0). Adjudicated events are classified by the IBD-CAC into one of the diagnostic types as defined in Table 10.3:. The events will further be classified as definite, probable or possible IBD.

An overview of adjudicated IBD events will be stratified by subjects with or without a previous medical history of IBD. Previous medical history of IBD will be determined using the information recorded on the Extra-Articular Assessment at Screening CRF page ("Does subject have a history of IBD?"). This overview table will present events adjudicated by the IBD-CAC as either possible, probable or definite IBD. Definite and probable IBD will also be aggregated and summarized in this table. In addition, this table will summarize each IBD event classification (possible, probable or definite) separately.

Another table and listing will present the adjudicated IBD events by type. For each IBD event type, the individual PTs which fall within each event type will be summarized. Similar listings of the adjudicated IBD events by type will be presented separately for the OLE2 treatment period.

Additionally, a listing of all events identified for potential review by the IBD-CAC will be produced. This listing will indicate whether each event was identified by the IBD-CAC Chair for full committee review. Similar listings of all events identified for potential review by the IBD-CAC Chair for full committee review will be produced separately for the OLE2 treatment period.

A further supportive listing will present the individual diagnostic criteria met for each adjudicated IBD event. This listing will also be presented separately for the OLE2 treatment periods combined.

Table 10.3: IBD event classifications

Event Type Code	Event Type (Classification and diagnosis)	Classification
1	Possible Inflammatory Bowel Disease – Crohn's Disease	Possible
2	Probable Inflammatory Bowel Disease – Crohn's Disease	Probable
3	Definite Inflammatory Bowel Disease – Crohn's Disease	Definite
4	Possible Inflammatory Bowel Disease – Ulcerative Colitis	Possible
5	Probable Inflammatory Bowel Disease – Ulcerative Colitis	Probable
6	Definite Inflammatory Bowel Disease – Ulcerative Colitis	Definite
7	Possible Inflammatory Bowel Disease – type unclassified	Possible
8	Probable Inflammatory Bowel Disease – type unclassified	Probable
9	Definite Inflammatory Bowel Disease – type unclassified	Definite
10	Symptoms not consistent with Inflammatory Bowel Disease	Not applicable
11	Possible Inflammatory Bowel Disease – Microscopic Colitis	Possible
12	Probable Inflammatory Bowel Disease – Microscopic Colitis	Probable
13	Definite Inflammatory Bowel Disease – Microscopic Colitis	Definite
14	Possible Inflammatory Bowel Disease – no further differentiation possible	Possible
15	Probable Inflammatory Bowel Disease – no further differentiation possible	Probable
16	Definite Inflammatory Bowel Disease – no further differentiation possible	Definite
99	Not enough information to adjudicate	Not applicable

IBD=inflammatory bowel disease.
Note: IBD diagnoses of "microscopic colitis" and "no further differentiation possible" were added in an adjudication charter amendment, accounting for the event type numbering.

10.2.3.1.7 Hypersensitivity (including anaphylaxis)

A table will be prepared based on the MedDRA anaphylaxis algorithm (see Section 12.1) for acute anaphylactic events (reported on the same day as when an injection was administered or one day after). An AE glossary listing will also be produced to summarize the MedDRA coding for these events. The glossary listing will include the following fields: reported term, PT, LLT, HLT, and SOC.

A separate table will be prepared to summarize hypersensitivity events, identified using the SMQ "Hypersensitivity (SMQ)". All TEAEs which code to a PT included in the Scope=Narrow search will be included in this table. In addition, a separate table will be prepared to summarize serious hypersensitivity events, identified using the SMQ "Hypersensitivity (SMQ)". All serious TEAEs which code to a PT included in the Scope=Narrow search will be included in this table. An AE glossary table will also be produced to summarize the MedDRA coding for these events. The glossary table will include the following fields: reported term, PT, LLT, HLT, and SOC.

Furthermore a separate table will be prepared to summarize injection site reactions, identified

using the HLTs: “Administration site reactions NEC” and “Injection site reactions”.

A glossary and listing of injection site reactions occurring during the DV0002 and DV0006 device sub-studies (1mL and 2mL) will be produced.

10.2.3.1.8 Hepatic events

A table for hepatic events will be created based on the SMQ of “Drug related hepatic disorders - comprehensive search (SMQ)”. However, these 2 sub-SMQs are to be excluded: “Liver neoplasms, benign (incl cysts and polyps) (SMQ)” and “Liver neoplasms, malignant and unspecified (SMQ)”. For each of the above SMQs, all TEAEs which code to a PT in the Scope=Broad and/or Scope=Narrow will be included.

Cases of potential Hy’s Law will be reported separately in a liver function test table.

In addition, potential Drug Induced Liver Injury (pDILI) events are adjudicated by the independent Hepatology Adjudication Committee (HAC) based on liver function test (LFT) elevations according to the HAC Charter (version 3.0). Adjudicated events will receive a causality assessment score as defined in Table 10.4 indicating the likelihood of the LFT elevations being a drug-induced liver injury related to the blinded investigational medicinal product.

A table will summarize the maximum final causality score and likelihood category for study participants with adjudicated events. Additionally, a listing of all study participants with events identified for potential review by the HAC will be produced. This listing will indicate the final causality assessment score. If a study participant has more than one causality assessment score, the worst score will be presented.

Table 10.4:: Causality assessment scoring by HAC for drug-induced liver injury

Causality Score	Numeric Causality Score	Likelihood (%)
Definite	1	>95
Highly likely	2	75-95
Probable	3	50-74
Possible	4	25-49
Unlikely	5	<25
Insufficient Data	99	NA

10.2.3.2 Cohort B

AEs of other safety topics of interest specified in Section 10.2.3.1 will be summarized by psoriasis type for the CBPSO-SS, CBGPP-SS, and CBEP-SS.

A by-subject listing of all AEs of safety topics of interest by type of safety topic of interest will be provided.

10.3 Clinical laboratory evaluations

10.3.1 Cohort A

Descriptive statistics for observed values and change from Baseline will be presented for each scheduled visit for the following parameters by PS0014 treatment sequence group:

- Hematology: basophils, eosinophils, lymphocytes, monocytes, neutrophils, hematocrit, hemoglobin, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, mean corpuscular volume, platelets, red blood cells and white blood cells
- Chemistry: calcium, chloride, magnesium, sodium, potassium, total calcium, glucose, creatinine, blood urea nitrogen
- Liver Functions: alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyltransferase (GGT), total bilirubin

- The values from urinalysis will be only listed for the following parameters:
  - Urinalysis dipstick: pH, Albumin (protein), Glucose, Blood, Leukocyte esterase, Nitrite

Markedly abnormal values are defined as those with a severity of Grade 3 and above based on the CTCAE criteria Version 4.03. Definitions of CTCAE grades are summarized in Section 12.2. Definitions of markedly abnormal values using the Grade 3 cut points are given in the tables below for age ranges of ≥17 years (Table 10.5 for markedly abnormal biochemistry values and Table 10.6 for markedly abnormal hematology values).

Table 10.5: Definitions of Markedly Abnormal Biochemistry Values

Parameter name	Conventional		Standard		Abnormal Designation
	Unit	Criteria	Unit	Criteria	
Creatinine	mg/dL	>3.0 x ULN	mmol/L	>3.0 x ULN	AH
Glucose	mg/dL mg/dL	<40 >250	mmol/L	<1.7 >13.9	AL AH
Calcium	mg/dL	>12.5 <7.0	mmol/L	>3.1 <1.75	AH AL
Magnesium	mg/dL	>3.0 <0.9	mmol/L	>1.23 <0.4	AH AL
Potassium	mmol/L	>6.0 <3.0	mmol/L	>6.0 <3.0	AH AL
Sodium	mmol/L	>155 <130	mmol/L	>155 <130	AH AL

AH=abnormal high; AL=abnormal low; dL=deciliter; L=liter; mg=milligram; mmol=millimoles; ULN=upper limit of normal.

Table 10.6: Definitions of Markedly Abnormal Hematology Values

Parameter name	Conventional		Standard		Abnormal Designation
	Unit	Criteria	Unit	Criteria	
Hemoglobin	g/dL	<8.0 >4.0 above ULN	g/L	<80 >40 above ULN	AL AH
Lymphocytes Absolute	10^9/L	<0.5 >20.0	10^9/L	<0.5 >20.0	AL AH
Neutrophils Absolute	10^9/L	<1.0	10^9/L	<1.0	AL
Platelets	10^9/L	<50	10^9/L	<50	AL
WBC/ Leukocytes	10^9/L	<2.0 >100	10^9/L	<2.0 >100	AL AH

AH=abnormal high; AL=abnormal low; dL=deciliter; L=liter; g=gram; ULN=upper limit of normal.

The following variables will have summaries produced for shifts from Baseline to the minimum (for value decreases)/maximum (for value increases) post-Baseline CTCAE value: Hemoglobin (decreased and increased), Platelets (decreased), WBC (decreased and increased), Lymphocytes (decreased and increased), Neutrophils (decreased), Creatinine (increased), Sodium (decreased and increased), Potassium (decreased and increased), Glucose (decreased), Calcium (decreased and increased). Subjects who meet the decreased potassium criteria of 3.0-<LLN, which is specified as the criteria for both CTCAE grade 1 and grade 2, will be counted as CTCAE grade 2. Shifts from Baseline to the minimum/maximum post-Baseline CTCAE value during the study period will be presented categorically for each parameter for which a CTCAE grading is defined (ie, those shown above).

Laboratory values (including markedly abnormal laboratory values) will be presented descriptively by PS0014 treatment group for the CA-SS. For tables where data are summarized by visit, unscheduled and repeat visits will not be summarized, but these data will be included in listings. For tables where multiple measurements over a period of time are considered (as in shift tables), unscheduled and repeat visits will be considered as long as they were collected in the period being summarized. All summaries will be presented in SI units and will be based on observed case values. In the case where laboratory values are below the lower limit of quantification, then these will be set to the midpoint between 0 and the lower limit of quantification for the purpose of summarizing the data. The following summaries will be produced:

- A summary of the absolute and change from Baseline values in each laboratory variable by PS0014 treatment sequence group (Hematology, Chemistry and Liver Functions)

- A summary of the number and percentage of subjects experiencing markedly abnormal values at any time during the time at risk, by laboratory variable and by PS0014 treatment group at the time of abnormality (Hematology, Chemistry and Elevated Liver Functions)
- A summary of the number and percentage of subjects with a given CTCAE grade (0, 1, 2, 3, or 4) based on minimum/maximum post-Baseline value by laboratory variable and PS0014 treatment group at the time of minimum/maximum. For subjects who switch treatment regimen, a minimum/maximum for both regimens will be presented.
- A shift table of the number and percentage of subjects experiencing CTCAE grade 0,1,2,3, or 4 values (as applicable) at Baseline to maximum post-Baseline CTCAE grade, by laboratory variable and treatment sequence group at the time of maximum. For subjects who switch treatment regimen, a minimum/maximum for both regimens will be presented.
- A figure presenting neutrophil CTCAE grade over time for subjects with at least one markedly abnormal neutrophil value (Grade 3 or above).

- Spaghetti plots presenting ALT values over time for subjects with at least one markedly abnormal ALT value (Grade 3 or above).
- Spaghetti plots presenting AST values over time for subjects with at least one markedly abnormal AST value (Grade 3 or above).

A by-subject listing of all laboratory data will be provided. Separate by-subject listings for the OLE2 treatment period will be provided. This listing will be presented by treatment group and will include: center, subject identifier, age, sex, race, weight, visit, laboratory variable, result (with abnormal values flagged as "L" or "H" accordingly if values outside of the reference range) and unit.

The urinalysis data will be listed.

Hepatitis B virus deoxyribonucleic acid (DNA) is performed only for subjects who were either hepatitis B surface antibody-positive or hepatitis B core antibody-positive (and negative for HBsAg and HBV-DNA) at Screening in the feeder study. These data will be listed only.

The table for elevated liver function tests (LFTs) will contain data beyond the CTCAE Grade 3 thresholds in order to allow for a more thorough review of elevated LFTs. There will be one table which will list the count and percentage of study participants meeting the below criteria at any time during the study:

- AST: >3xULN, >5xULN, >8xULN, >10xULN, >20xULN
- ALT: >3xULN, >5xULN, >8xULN, >10xULN, >20xULN
- AST or ALT: >3xULN, >5xULN, >8xULN, >10xULN, >20xULN
- Bilirubin: >1.5xULN, >2xULN
- ALP: >1.5xULN

The definition of potential drug induced liver injuries (pDILI) for following table will be used:

- [AST ⩾3xULN or ALT ⩾3xULN] and Total Bilirubin ⩾1.5xULN
- [AST ≥3xULN or ALT ≥3xULN] and Total Bilirubin ≥2xULN
- [AST ≥3xULN or ALT ⩾3xULN] and Total Bilirubin ⩾2xULN in the absence of ALP ⩾2xULN (Hy's law)

A table for potential drug induced liver injuries (pDILI) will be presented by PS0014 treatment group for subjects with at least one post-Baseline liver laboratory assessment. Number and percentage of subjects meeting laboratory criteria for pDILI for at least 1 visit and reporting at least 1 symptom potentially associated with hepatitis or hypersensitivity according to the Investigator on the pDILI CRF will be presented. Subjects who potentially meet Hy's law criteria at least 1 time during exposure. To be counted as potential Hy's Law, all criteria must be met at the same visit.

Two figures of evaluation of drug-induced serious hepatotoxicity (eDISH) will be created.

- eDISH for maximum Total Bilirubin (y-axis) versus maximum alanine/aspartate aminotransferase (ALT/AST). Maximum bilirubin and maximum ALT/AST are values of each ULN on a log 10 scale, the two values can occur at different timepoints.
- eDISH for maximum concurrent Total Bilirubin versus maximum alanine/aspartate aminotransferase (ALT/AST). In this figure, each participant is plotted based on their maximum concurrent total bilirubin (y-axis) and transaminase (ALT or AST, whichever is higher), where concurrent is defined as total bilirubin elevation occurring on or within 30 days after the maximum ALT or AST elevation. The transaminase elevation has to occur first. Maximum bilirubin and maximum ALT/AST are values of each ULN on a log 10 scale.

For Cohort A the data will be plotted using BKZ Total only, not split by Q4W/Q8W and each subject is only plotted once in each figure.

10.3.2 Cohort B

Testing for hepatitis B surface antigen and antibodies to hepatitis C and HIV will be performed at Screening. These data will be listed only.

Laboratory values will be summarized by psoriasis type in the same way as described in Section 10.3.1 for the CBPSO-SS, CBGPP-SS, and CBEP-SS. In addition of the parameters presented for Cohort A, Albumin and C-Reactive Protein will be also be summarized.

A by-subject listing of all laboratory data will be provided. This listing will be presented by treatment group and will include: center, subject identifier, age, sex, race, weight, visit, laboratory variable, result (with abnormal values flagged as "L" or "H" accordingly if values outside of the reference range) and unit.

The figures of evaluation of drug-induced serious hepatotoxicity (eDISH) for maximum Total Bilirubin versus maximum alanine aminotransferase (ALT) will be created as the same way as described in Section 10.3.1 for the CB-SS.

For Cohort B the data will be plotted by BKZ Total (not by Q4W/Q8W) but different symbols will be used for the three disease types. Similarly to Cohort A eDISH figures, each subject will be only plotted once in each figure.

10.4 Vital signs, physical findings, and other observations related to safety

Generally, vital signs, physical findings, and other observations related to safety will not be summarized for the OLE2 treatment period unless specified otherwise.

10.4.1 Vital Signs

10.4.1.1 Cohort A

The following vital signs variables will be summarized: systolic blood pressure (mmHg), diastolic blood pressure (mmHg), body temperature (°C) and heart rate (beats/min). Vital signs will not be summarized for the OLE2 treatment period. The following summary will be provided for the CA-SS:

- A summary of the absolute and change from PS0014 Baseline value for each vital sign variable by PS0014 treatment sequence group
- A summary of the number and percentage of subjects experiencing at least one markedly abnormal value for a vital sign variable as defined in Table 10.7, by PS0014 treatment group at the time of abnormality

Table 10.7: Definitions of Markedly Abnormal Blood Pressure Values

Parameter (unit)	Markedly Abnormal Low	Markedly Abnormal High
Systolic blood pressure (mmHg)	<90 and a decrease from Baseline of ≥20	>180 and an increase from Baseline of ≥20
Diastolic blood pressure (mmHg)	<50 and a decrease from Baseline of ≥15	>105 and an increase from Baseline of ≥15

A by-subject listing of all vital signs data will be provided. This listing will be presented by treatment group and will include: center, subject identifier, age, sex, race, weight, visit, vital sign variable and result (with abnormal values flagged as "L" or "H" accordingly). This listing will also be provided separately for the OLE2 treatment periods.

Blood pressure values will also be categorized into the six groups defined below:

1. Hypotension: systolic blood pressure <90 mmHg *or* diastolic blood pressure <60
2. Normal: systolic blood pressure ≥90 and <120 mmHg *and* diastolic blood pressure ≥60 and <80 mmHg
3. Elevated: systolic blood pressure between 120-129 mmHg *and* diastolic blood pressure <80
4. Stage 1: systolic blood pressure between 130-139 mmHg *or* diastolic blood pressure between 80-89
5. Stage 2: systolic blood pressure ≥140 and ≤180 mmHg *or* diastolic blood pressure ≥90 and ≤120 mmHg

6. Hypertensive crisis: systolic blood pressure >180 mmHg *and/or* diastolic blood pressure >120 mmHg

Shifts from Baseline to the maximum blood pressure category and to the minimum blood pressure category will be summarized for the CA-SS using PS0014 sequence treatment group.

10.4.1.2 Cohort B

Vital sign values will be summarized by psoriasis type in the same way as described in Section 10.4.1.1 for the CBPSO-SS, CBGPP-SS, and CBEP-SS.

10.4.2 Physical examination

10.4.2.1 Cohort A

Abnormal results of the physical examination together with details of abnormalities: abnormality clinically significant or not, will be listed by subject and visit based on CA-SS. This listing will also be provided separately for the OLE2 treatment period on CA-OL2S.

10.4.2.2 Cohort B

Abnormal results of the physical examination together with details of abnormalities: abnormality clinically significant or not, will be listed by subject and visit based on CB-SS.

10.4.3 Electrocardiograms

10.4.3.1 Cohort A

Electrocardiogram data will be analyzed by PS0014 treatment sequence group and visit for the CA-SS.

A summary of the number and percentage of subjects with normal and abnormal ECG results at all applicable visits will be provided.

The change from Baseline tables will be presented using descriptive statistics by PS0014 treatment sequence group. The table presentations will display descriptive statistics for PS0014 Baseline followed by descriptive statistics for the observed and change from PS0014 Baseline results by scheduled visit.

The following ECG variables will be summarized (absolute values and change from PS0014 Baseline) by visit: QTcF, RR, PR, QRS and QT.

QTc outliers are defined as QTcF values following dosing that are greater than 450 ms or are increases from Baseline greater than 30 ms. QTcF outliers will be highlighted in the data listings and summarized using the following categories:

- Values >450 ms, >480 ms, >500 ms
- Increase from PS0014 Baseline of >30 ms, increase from PS0014 Baseline of >60 ms, increase from Baseline of >90 ms
- Values >450 ms and increases of >30 ms from PS0014 Baseline. Values >500 ms and increases of >60 ms from PS0014 Baseline

The number and percentage of subjects who meet the ECG outlier criteria at any assessment post-date first dose will be summarized by PS0014 treatment sequence group.

Two separate by-subject listings of all 12-lead ECG data will be provided based on interpretation from central reader and from site.

10.4.3.2 Cohort B

Electrocardiogram data will be summarized overall and by psoriasis type in the same way as described in Section 10.4.3.1 for the CBPSO-SS, CBGPP-SS, and CBEP-SS by PS0014 treatment sequence group.

10.4.4 Other safety variables

Generally, other safety will be only listed for the OLE2 treatment period unless specified otherwise.

10.4.4.1 TB test

10.4.4.1.1 Cohort A

IGRA Tuberculosis test will be summarized at PS0014 Baseline, Week 48, Week 96 and Week 144 by PS0014 treatment sequence group for the CA-SS.

A by-subject listing of the TB test data will be provided. This listing will also be provided separately for the OLE2 treatment period.

10.4.4.1.2 Cohort B

IGRA Tuberculosis test will be summarized at Screening, Week 48, Week 96 and Week 144 for each psoriasis type for the CBPSO-SS, CBGPP-SS, and CBEP-SS by PS0014 treatment sequence group.

A by-subject listing of the TB test data will be provided.

10.4.4.2 Electronic Columbia Suicide Severity Rating Scale (eC-SSRS)

10.4.4.2.1 Cohort A

eC-SSRS questionnaire will be self-administered by the subject and assessed by trained study personnel. This scale will be used to assess suicidal ideation and behavior that may occur during the study. Results of the eC-SSRS will be summarized using the number of subject and percentage with (i) events in suicide behavior, (ii) suicidal ideation, (iii) suicidal behavior and ideation, and (iv) self-injurious behavior without suicidal intent.

Suicidal ideation is defined as an event in any of the following 5 categories:

- Wish to be dead
- Non-specific active suicidal thoughts
- Active suicidal ideation with any methods (not plan), without intent to act
- Active suicidal ideation with some intent to act, without specific plan
- Active suicidal ideation with specific plan and intent

Suicidal behavior is defined as an event in any of the following 4 categories:

- Actual attempt
- Interrupted attempt
- Aborted attempt
- Preparatory acts or behavior

Suicidal behavior or ideation is defined as an event in any of the above 9 categories.

Self-injurious behavior without suicidal intent is defined as an event in the category non-suicidal self-injurious injuries.

The incidence of subjects with suicidal ideation, suicidal behavior, suicidal ideation or behavior, and self-injurious behavior will be summarized by PS0014 treatment sequence group. Data for subjects who completed the wrong questionnaire at a visit (for example, the 'lifetime' assessment was completed at the PS0014 Baseline visit) will not be summarized in the table but will be included in a separate listing.

A by-subject listing of the eC-SSRS questionnaire data will be provided. This listing will be repeated for subjects with positive responses. This listing will also be provided separately for the OLE2 treatment period.

10.4.4.2.2 Cohort B

eC-SSRS data will be summarized by psoriasis type in the same way as described in Section 10.4.4.2.1 for the CBPSO-SS, CBGPP-SS, and CBEP-SS by PS0014 treatment sequence group.

10.4.4.3 Pregnancy testing

10.4.4.3.1 Cohort A

A by-subject listing of the pregnancy test data will be provided.

10.4.4.3.2 Cohort B

Serum pregnancy testing will be performed at Screening. The pregnancy test will be urine at all other visits.

A by-subject listing of the pregnancy test data will be provided.

10.4.5 PHQ-9

The PHQ-9 is a multipurpose instrument for screening, diagnosing, monitoring, and measuring the severity of depression. The PHQ-9 scores for depression range from 0 to 27 with higher scores indicating worse state. A score of 5-9 is considered to be minimal symptoms of depression. A score of 10 to 14 is considered minor depression, dysthymia, or mild major depression. A score of 15 to 19 is considered to indicate moderately severe major depression, and a score ≥20 is considered to be severe major depression. If any of the 9 questions are missing, then the score is treated as missing.

Change from Baseline in PHQ-9 is derived as post-Baseline score minus PS0014 Baseline score.

PHQ-9 is a Safety parameter described on the Safety Population. Nevertheless, identification of observable data and implementation of MI methodology is done the same way as Efficacy

parameters. Therefore, if a subject discontinued early from the study, all PHQ-9 data after last treatment date + 35 days will be treated as missing and subject to imputation as applicable.

10.4.5.1 Cohort A

A change from PS0014 Baseline in PHQ-9 table will display descriptive statistics for all visits by PS0014 treatment sequence group.

Missing data for the continuous change from PS0014 Baseline will be handled using MI via the MCMC and monotone regression method specified in Section 4.2.

A Table presenting the number of subjects with PHQ-9 total score ≥15 and ≥20 by scheduled visit during 144-week treatment period (including Baseline) through SFU and overall will be provided by PS0014 treatment group using OC data.

A by-subject listing of PHQ-9 data will be provided separately for the treatment period and the OLE2 treatment period. This listing will include site, subject number, visit, total score observed result, and total score change from PS0014 Baseline value.

10.4.5.2 Cohort B

A change from Baseline in PHQ-9 table will display descriptive statistics for all visits by treatment sequence group and disease type using the CBPSO-SS, CBGPP-SS, and CBEP-SS.

For PSO subjects, missing data for the continuous change from Baseline will be handled by using MI via the MCMC and monotone regression method specified in Section 4.2.

For GPP and EP subjects, change from Baseline will be summarized using descriptive statistics by visit using OC data.

A Table presenting the number of subjects with PHQ-9 score ≥15 and ≥20 by scheduled visit during PS0014 (including Screening, Baseline) through SFU, and overall will be provided by disease type using PS0014 treatment groups.

A by-subject listing of PHQ-9 total score and change from Baseline data will be provided.

10.5 Assessment of Process 5

10.5.1 Cohort A

Bimekizumab will be manufactured using 2 manufacturing processes: Process 4 (Phase 3 clinical supply manufacturing process) and Process 5 (planned commercial manufacturing process). Process 5 will be utilized in Germany, Hungary and Poland for the entire duration of PS0014. Process 4 will be utilized for rest of countries. This assessment of Process 5 does not apply to Cohort B.

This refers to the study treatment assigned to the subject by different process of manufacturing. The PS0014 treatment groups of process are as follows:

- Bimekizumab Total (Process 4)
- Bimekizumab Total (Process 5)

The Incidence of TEAEs of Overview summaries will be provided for the CA-SS by PS0014 treatment group of process. In addition, incidence of TEAEs based on “100 subject years” by PS0014 treatment group of process will also be provided with EAIR (with 95% CI) and EAER.

A by-subject listings of all TEAE with process 5 or process 4 will be provided with additional column.

11 REFERENCES

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12 APPENDICES

12.1 MedDRA algorithmic approach to anaphylaxis

The SMQ *Anaphylactic reaction* consists of three parts:

- A **narrow search** containing PTs that represent core anaphylactic reaction terms
  Cat A

- SMQ Anaphylactic reaction (SMQ)
  - PT Anaphylactic reaction
  - PT Anaphylactic shock
  - PT Anaphylactic transfusion reaction
  - PT Anaphylactoid reaction
  - PT Anaphylactoid shock
  - PT Circulatory collapse
  - PT Dialysis membrane reaction
  - PT Kounis syndrome
  - PT Shock
  - PT Shock symptom
  - PT Type I hypersensitivity

- A **broad search** that contains additional terms that are added to those included in the narrow search. These additional terms are signs and symptoms possibly indicative of anaphylactic reaction and categorized in B, C or D
  - Cat B

- PT B Acute respiratory failure
- PT B Asthma
- PT B Bronchial oedema
- PT B Bronchospasm
- PT B Cardio-respiratory distress
- PT B Chest discomfort
- PT B Choking
- PT B Choking sensation
- PT B Circumoral oedema
- PT B Cough
- PT B Cyanosis
- PT B Dyspnoea
- PT B Hyperventilation
- PT B Irregular breathing
- PT B Laryngeal dyspnoea
- PT B Laryngeal oedema
- PT B Laryngospasm
- PT B Laryngotracheal oedema
- PT B Mouth swelling
- PT B Nasal obstruction
- PT B Oedema mouth
- PT B Oropharyngeal spasm
- PT B Oropharyngeal swelling
- PT B Respiratory arrest
- PT B Respiratory distress
- PT E Respiratory dyskinesia
- PT B Respiratory failure
- PT B Reversible airways obstruction
- PT B Sensation of foreign body
- PT B Sneezing
- PT B Stridor
- PT B Swollen tongue
- PT B Tachypnoea
- PT B Throat tightness
- PT B Tongue oedema
- PT B Tracheal obstruction
- PT B Tracheal oedema
- PT B Upper airway obstruction
- PT B Wheezing

- Cat C

- Allergic oedema
- Angioedema
- Erythema
- Eye oedema
- Eye pruritus
- Eye swelling
- Eyelid oedema
- Face oedema
- Flushing
- Generalised erythema
- Injection site urticaria
- Lip oedema
- Lip swelling
- Nodular rash
- Ocular hyperaemia
- Oedema
- Periorbital oedema
- Pruritus
- Pruritus allergic
- Pruritus generalised
- Rash
- Rash erythematous
- Rash generalised
- Rash pruritic
- Skin swelling
- Swelling
- Swelling face
- Urticaria
- Urticaria papular

- Cat D

- Blood pressure decreased
- Blood pressure diastolic decreased
- Blood pressure systolic decreased
- Cardiac arrest
- Cardio-respiratory arrest
- Cardiovascular insufficiency
- Diastolic hypotension
- Hypotension

- An **algorithmic approach** which combines a number of anaphylactic reaction symptoms in order to increase specificity. A case must include one of the following where both occur on either the same day as when an injection was administered or one day after, and for scenarios where two events must have been reported, both events must have occurred within one day of each other (as anaphylaxis is an acute event, imputed dates should not be used in the algorithmic approach)**:**
  - A narrow term or a term from Category A;
  - A term from Category B - (Upper Airway/Respiratory) AND a term from Category C - (Angioedema/Urticaria/Pruritus/Flush);
  - A term from Category D - (Cardiovascular/Hypotension) AND [a term from Category B - (Upper Airway/Respiratory) OR a term from Category C - (Angioedema/Urticaria/ Pruritus/Flush)]

12.2 Definitions of CTCAE grades

Definitions of CTCAE grades that will be summarized are listed in Table 12.1 for biochemistry parameters and Table 12.2 for hematology parameters.

Table 12.1: Definitions of CTCAE grades by biochemistry parameter

Parameter (unit)	Definition	Unit	Grade 1	Grade 2	Grade 3	Grade 4
Creatinine	High	mmol/L	>ULN-1.5 x ULN	(>1.5 – 3.0) x ULN	(>3.0 – 6.0) x ULN	>6.0 x ULN
Sodium	Low	mmol/L	130-<LLN	N/A	120-<130	<120
Sodium	High	mmol/L	>ULN-150	>150-155	>155-160	>160
Potassium	Low	mmol/L	3.0-<LLN	3.0-<LLN	2.5-<3.0	<2.5
Potassium	High	mmol/L	>ULN-5.5	>5.5-6.0	>6.0-7.0	>7.0
Calcium	Low	mmol/L	2.0-<LLN	1.75-<2.0	1.5-<1.75	<1.5
Calcium	High	mmol/L	>ULN-2.9	>2.9-3.1	>3.1-3.4	>3.4
Magnesium	Low	mmol/L	0.5-<LLN	0.4-<0.5	0.3-<0.4	<0.3
Magnesium	High	mmol/L	>ULN-1.23	N/A	>1.23-3.30	>3.30

Abbreviations: LLN=lower limit of normal, mmol=millimoles.
Subjects who meet the grade 1 and 2 low potassium criteria will be classified as grade 2.

Table 12.2: Definitions of CTCAE grades by hematology parameter

Parameter (unit)	Definition	Unit	Grade 1	Grade 2	Grade 3	Grade 4
Hemoglobin	Low	g/L	100-<LLN	80-<100	<80	N/A
Hemoglobin	High	g/L	>0-20 above ULN	>20-40 above ULN	>40 above ULN	N/A
Platelets	Low	10^9/L	75-<LLN	50-<75	25-<50	<25
WBC	Low	10^9/L	3-<LLN	2-<3	1-<2	<1
WBC	High	10^9/L	N/A	N/A	>100	N/A
Lymphocytes	Low	10^9/L	0.8-<LLN	0.5-<0.8	0.2-<0.5	<0.2
Lymphocytes	High	10^9/L	N/A	>4-20	>20	N/A
Neutrophils	Low	10^9/L	1.5-<LLN	1.0-<1.5	0.5-<1.0	<0.5
Parameter (unit)	Definition	Unit	Grade 1	Grade 2	Grade 3	Grade 4

Abbreviations: g=gram; L=liter; LLN=lower limit of normal.

12.3 Efficacy analyses by data cut visit

Table 12–3: Efficacy analyses reporting

Parameter	Week 48	Week 144	OLE2
PASI100	X	X	X
PAS90	X	X	X
PASI75	X	X	
Absolute change and percent change from Baseline in PASI score	X	X	
Absolute PASI scores of ≤1, ≤2, ≤3, ≤5,	X	X	
IGA Clear	X	X	X
IGA Clear or Almost Clear	X	X	X
IGA Change from Baseline	X		
Scalp IGA Clear or Almost Clear	X	X	
Palmoplantar IGA Clear or Almost Clear	X	X	
Change from Baseline in DLQI Total Score	X	X	
DLQI Total Score of 0 or 1	X	X	X
MCID ≥4 more in DLQI	X	X	
mNAPSI100	X	X	
mNAPSI90	X	X	
mNAPSI75	X	X	
Change from Baseline in mNAPSI score	X	X	
Change from Baseline in Psoriasis BSA	X	X	
Patient Global Assessment of PSO	X		
Absolute and percent change from Baseline in BSA affected by PSO	X	X	
Psoriasis BSA values of 0%, ≤1%, ≤3%, ≤5%,	X	X	
Absolute and percent change from Baseline in the product of IGA and BSA	X	X	
PGADA for arthritis VAS	X	X	
PASE	X	X	
PASE (<47 versus ≥47)	X		
SF-36			
EQ-5D-3L	X	X	

Parameter	Week 48	Week 144	OLE2
WPAI-SHP	X	X	
TSQM-9	X	X	

12.4 STATISTICAL ANALYSIS PLAN SIGNATURE PAGE

This document has been reviewed and approved per the Review and Approval of Clinical Documents Standard Operating Procedures. Signatures indicate that the final version of the Statistical Analysis Plan (SAP) or amended SAP is released for execution.

Approval Signatures

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