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Clinical Study Report (CSR)

Statistical Analysis Plan

A Phase III, Randomised, Double-blind, MultiCentre Clinical Study to Evaluate the Efficacy, Safety, Tolerability, Pharmacokinetics, and Immunogenicity of SB17 (proposed ustekinumab biosimilar) Compared to Stelara in Subjects with Moderate to Severe Plaque Psoriasis

Protocol Number	SB17-3001
Study Phase	Phase III
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LIST OF ABBREVIATIONS

AE	Adverse Event
AESI	Adverse Event of Special Interest
ALP	Alkaline Phosphatase
ALT	Alanine Transaminase
AST	Aspartate Transaminase
ATC	Anatomical Therapeutic Chemical
BSA	Body Surface Area
COVID-19	Corona Virus Disease 19
CRP	C-reactive Protein
ECG	Electrocardiogram
ENR	Enrolled Set
EOS	End of Study
FAS	Full Analysis Set
HBcAb	Hepatitis B Virus Core Antibody
HBsAg	Hepatitis B Virus Surface Antigen
HCV Ab	Hepatitis C Virus Antibody
HCV RNA	Hepatitis C Virus RNA
HIV Ab	HIV 1/2 Antibody
HIV RNA	HIV-1/2 RNA
IP	Investigational Product
LSM	Least Squares Means
MedDRA	Medical Dictionary for Regulatory Activities
PASI	Psoriasis Area and Severity Index
PGA	Physician's Global Assessment
PK	Pharmacokinetic
PPS	Per-protocol Set
PT	Preferred Term
RAN	Randomised Set
SAE	Serious Adverse Event
SAF	Safety Set
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOC	System Organ Class
TEAE	Treatment-Emergent Adverse Event
WHO	World Health Organization

1. INTRODUCTION

This document describes the rules and conventions to be used in the presentation and analysis of efficacy, safety, pharmacokinetics (PK) and immunogenicity data for Protocol SB17-3001.

It describes the data to be summarized and analysed, including specifics of the statistical analyses to be performed. This Statistical Analysis Plan (SAP) is based on the Protocol Amendment 2.0, dated Feb 15, 2021. The following analyses will be performed for this study.

- The main analysis will take place once all subjects complete the procedures at Week 28 and 100 subjects complete Week 52, or its corresponding visit. Available efficacy, safety, PK, and immunogenicity data will be analysed and reported. At the time of this reporting, a limited number of identified individuals of the Sponsor or CRO will be unblinded for reporting purpose. However, subjects, Investigators, and other study personnel will remain blinded throughout the entire study period.
- For final CSR the safety, efficacy, pharmacokinetic and immunogenicity analyses will be performed after the last subject completes the procedures at Week 52 or the corresponding visit. All study data will be analysed and reported for final CSR. The data after the early termination with information provision will be listed.

2. STUDY OBJECTIVES

2.1 Primary Objective

The primary objective is to demonstrate the equivalence of SB17 to Stelara, in terms of the percent change of baseline in Psoriasis Area and Severity Index (PASI) at Week 12 in subjects with moderate to severe plaque psoriasis.

2.1.1 Primary Estimand

Table 1: Primary Estimand

Population	Variable/Endpoint	Intercurrent events (IEs)	Intercurrent event handling strategy	Population-level summary measure
CCI [redacted]	Percent change from baseline in PASI at Week 12	• CCI [redacted]	CCI [redacted]	Mean difference of percent change from baseline in

Population	Variable/Endpoint	Intercurrent events (IEs)	Intercurrent event handling strategy	Population-level summary measure
CCI		CCI	CCI CCI CCI	PASI at Week 12

2.2 Secondary Objectives

The secondary objectives are:

- To evaluate the efficacy of SB17 compared to Stelara
  - Percent change from baseline in PASI other than Week 12
  - Physician's Global Assessment (PGA)
  - PASI50, PASI75, PASI90, and PASI100 response rate
  - Change from baseline in Dermatology Life Quality Index (DLQI)
- To evaluate safety and tolerability of SB17 compared to Stelara
- To evaluate the pharmacokinetics (PK) of SB17 compared to Stelara in subjects participating in PK evaluation
- To evaluate the immunogenicity of SB17 compared to Stelara
- To evaluate safety and immunogenicity in subjects who transitioned to SB17 and who maintained Stelara at Week 28 for the transition period

2.3 Sample Size Calculation

To calculate equivalence margin, the percent change from baseline in PASI at Week 12 were referred from five randomised controlled studies of ustekinumab.

A fixed-effect meta-analysis of the above five studies estimates a risk difference of CCI with a CCI . Although an equivalence limit of CCI is statistically calculated to preserve CCI of the effect of ustekinumab over and above placebo, a clinical equivalence margin [-15%, 15%] was set for the comparison with the 95% CI of the mean difference in the percent change from baseline in PASI at Week 12.

Based on this equivalence margin, a sample size of 192 subjects per treatment group was calculated with the assumptions of common SD of 31.33, 10% loss from the primary analysis and approximately 100 remainders per treatment group after transition at Week 28 at the overall 5% significance level, providing over 90% power. Overall, 464 subjects (232 per treatment group) will be randomised into the study to determine equivalence of percent change from baseline in PASI at Week 12.

The nQuery Advisor option two one-sided equivalence tests (TOST) for two-group design gives the following result to estimate the n per group to show the equivalence: When the sample size in each group is 232 (including expected dropout), a two group design will have 99.86% power to reject both the null hypothesis that the test mean minus the standard mean is below -15 and the null hypothesis that the test mean minus the standard mean is above 15 i.e., that the test and standard are not equivalent, in favor of the alternative hypothesis that the means of the two groups are equivalent, assuming that the expected difference in means is 0, the common standard deviation (SD) is 31.33 and that each test is made at the 2.5% level.

The equivalence margin for the comparison with the 90% CI of the difference in the percent change from baseline in PASI at Week 12 will be [-10%, 10%] by the agency recommendation.

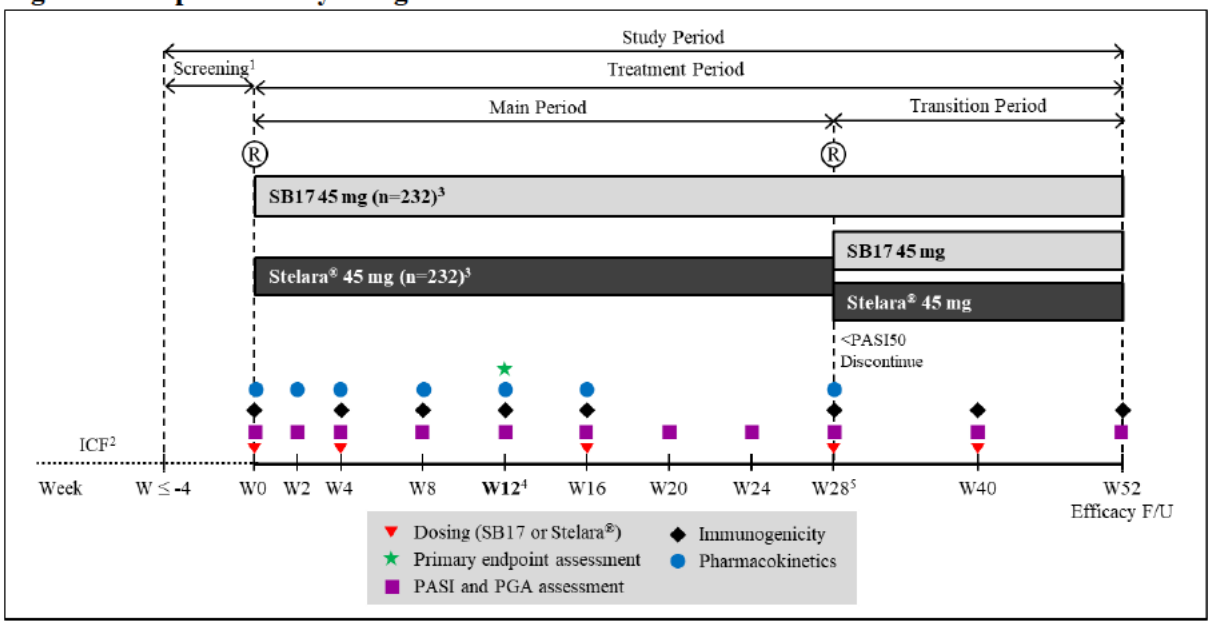
Based on this equivalence margin, a sample size of 169 subjects per treatment group was calculated with the assumption of the common SD of 31.33 at the overall 10% significance level, providing 80% power. Overall 338 subjects (169 per treatment group) will be randomised into the study to determine equivalence of percent change from baseline in PASI at Week 12.

The nQuery Advisor option TOST for two-group design gives the following result to estimate then per group to show the equivalence: When the sample size in each group is 169, a two group design will have 80% power to reject both the null hypothesis that the test mean minus the standard mean is below -10 and the null hypothesis that the test mean minus the standard mean is above 10 i.e., that the test and standard are not equivalent, in favor of the alternative hypothesis that the means of the two groups are equivalent, assuming that the expected difference in means is 0, the common standard deviation is 31.33 and that each test is made at the 5% level.

Therefore, the sample size of 464 allows enough power to detect the equivalence in both situations.

3. GENERAL CONSIDERATION

Figure 1. Graphical Study Design



F/U = Follow-up; ICF = Informed Consent Form; PASI = Psoriasis Area and Severity Index; PGA = Physician's Global Assessment; ® = Randomisation

All summaries by period defined in the SAP refers to the analysis period. The analysis period consists of screening, main period and transition period (Figure 1). Each period is defined as below:

Screening period is defined as study period from informed consent date prior to randomisation at Week 0 (Day 1).

Main period is defined as study period on or after randomisation at Week 0 (Day 1) and before re-randomisation at Week 28, or until last study participation date if patients withdrew/discontinued before Week 28.

Transition period is defined as study period from the re-randomisation at Week 28 until end of study (Week 52) or until last study participation date if patients withdrew/discontinued after Week 28.

Overall period is defined as study period consisting of screening period, main period and transition period.

For the summary of main period, treatment group refers to the following main period treatment groups in general:

- SB17
- Stelara

Treatment effect comparison will be performed between SB17 and Stelara.

For the summary of **transition period**, treatment group refers to the following transition period treatment groups in general:

- SB17+SB17
- Stelara Overall (Stelara+SB17, Stelara+Stelara)
- Stelara+SB17
- Stelara+Stelara

Summary of **overall study period** will be provided by the following overall treatment groups in general:

- SB17 (SB17*, SB17+SB17)
- StelaraOverall (Stelara*, Stelara+Stelara, Stelara+SB17)
- Stelara+SB17
- Stelara+Stelara

SB17* or Stelara* means subjects initially randomised to SB17* or Stelara group and early terminated IP before transition at Week 28.

Treatment groups for the listing will be presented as below:

- SB17
- SB17+SB17
- Stelara
- Stelara+SB17
- Stelara+Stelara

3.2. Analysis Sets

The following sets will be used for the analyses performed:

- Enrolled Set (ENR) consists of all subjects who provide informed consent for this study.
- Randomised Set (RAN) consists of all subjects who receive a randomisation number.
- Full Analysis Set (FAS) consists of all subjects who are randomised. Following the intent-to-treat principle, subjects will be analysed according to the treatment group they are assigned to at Randomisation. However, subjects who do not have any efficacy assessment result after randomisation or do not receive IP during the study period will be excluded from FAS
- Per-Protocol Set (PPS) consists of all FAS subjects who weight ≤ 100 kg and received 45 mg IP at Week 0 and Week 4 and have PASI assessment result at Baseline and Week 12 without any major protocol deviations (PDs) that have impact on primary efficacy assessment. Major PDs that will lead to exclusion from this set will be pre-defined prior to unblinding the treatment group assignment for analyses.
- Safety Set 1 (SAF1) consists of all subjects who receive at least one IP during the study period. Subjects will be analysed according to the IP received.
- Safety Set 2 (SAF2) consists of all subjects in the SAF1 who receive at least one IP after re-randomisation at Week 28. Subjects will be analysed according to the IP received.
- PK Analysis Set (PKS) consists of all subjects in the SAF1 who have at least one serum concentration data.

The number of subjects in the analysis sets will be summarised by treatment group for the RAN. A by-subject listing of subjects excluded from analysis sets will be provided for the RAN by treatment group and will include country, centre, subject identifier, inclusion/exclusion flag for each analysis set, and reason for exclusion from FAS and PPS.

3.3.Protocol Deviations

A by-subject listing of PDs will be provided including subject identifier, PD classification, PD description, Category, and exclusion from specific analysis set (Yes/No) for the RAN.

Protocol deviations (PDs) will be pre-defined prior to subject enrollment and documented separately named as Protocol Deviation definition list which includes classification (e.g., violation of inclusion/exclusion criteria, use of prohibited medication, non-compliance with treatment), deviation description, category (major or minor), time point for each PD. Major PDs are defined as those deviations from the study protocol likely to have an impact on the perceived efficacy and/or safety of study treatments. The PD definition list will be included in blinded data review meeting (BDRM) minute as an attachment.

PDs and analysis sets will be reviewed and confirmed through the BDRM to decide which subjects and/or subject data will be excluded from certain analyses prior to database lock. Decisions regarding the exclusion of subjects and/or subject data from analyses will be made prior to treatment code unblinding and will be documented and approved.

A summary of the number and percentage of subjects with PD by PD category (major and minor), exclusion from per protocol set and PD classification will be presented for the RAN by main period treatment group. Percentages will be based on the number of subjects randomised. The summary of PD will also be provided by Centre and main period treatment group. A summary of protocol deviations related to COVID-19 and protocol deviations related to war in Ukraine will each be presented by main period treatment group.

A by-subject listing of PDs will be provided including subject identifier, timepoint, PD classification, PD description, PD category, relationship with COVID-19, relationship with war in Ukraine, and exclusion from specific analysis sets.

3.4.Disposition and Withdrawals

Subject Disposition

A clear accounting of the disposition of all subjects who enter the study will be provided for the ENR, from enrolment to study completion. The subject disposition summaries include the following:

- A summary of the number of screened subjects, the number and percentage of screen failures and reasons for screen failure (does not meet eligibility criteria, consent withdrawal, lost to follow-up, and other), using the ENR.
- Subjects randomised at Week 0, subjects completed main period at Week 28, subjects discontinued from IP on or before re-randomisation at Week 28, reasons for discontinuation from IP, subjects discontinued from IP on or before Week 28 related to COVID-19, subjects discontinued from IP on or before Week 28 related to war in Ukraine will be summarised by treatment group.

- Subjects re-randomised at Week 28, subjects completed transition period after re-randomisation at Week 28 up to Week 52, subjects discontinued from IP after re-randomisation at Week 28, the reasons for discontinuation from IP, subjects discontinued from IP after re-randomisation at Week 28 related to COVID-19, subjects discontinued from IP after re-randomisation at Week 28 related to war in Ukraine will be summarised by treatment group.

Summary of subject disposition described above will also be provided by Centre and treatment group.

A by-subject listing of subject disposition will be generated using the ENR, including start/end date of treatment period, primary reasons for withdrawal or screening failure.

Visit not performed/window deviation (including relatedness to COVID-19)

Subjects with planned visit not done, visit window deviation, reason for visit not done and visit window deviation including relatedness to COVID-19 will be summarised using the RAN by visit and treatment group.

A by-subject listing of planned visits not performed, visit window deviation will be generated using the RAN, including reasons not performed, reasons for visit window deviation, and relatedness to COVID-19.

3.5.Study Day

Study day will be calculated from the first Investigational Product (IP) dosing date and will be used to show start/stop day of assessments and events. Study day of the first IP dosing date will be Day 1.

- If the date of the event is on or after the first IP dosing date, then:

  Study Day = (date of event – first IP dosing date) + 1

- If the date of the event is prior to the first IP dosing date, then:

  Study Day = (date of event – first IP dosing date)

When the event date is partial or missing, study day will be calculated after proper imputation by described in APPENDIX 1, and the event date will appear as it is along with the calculated study day in the listing.

3.6.Baseline

Baseline value will be defined as the last available measurement value recorded prior to the first IP administration including unscheduled measurements.

3.7.Retests, Unscheduled Visits and Early Termination Data and Visit Mapping

In general, the data recorded at the nominal visit will be presented in the by-treatment and visit summaries.

Early discontinuation data will be mapped to the next scheduled visit of each assessment for by-treatment and visit summaries.

Unscheduled/repeated measurements (except for the baseline value) will not be included in the by-treatment and visit summaries. However, unscheduled/repeated measurements will contribute to the worst-case value for shift tables and incidence of significant abnormality tables and incidence of overall ADA results.
Listings will include scheduled, unscheduled, repeated, and early discontinuation data.

3.8.Windowing Conventions

There will be no windowing conventions considered for the study analysis. There will be only one assessment for each visit, and all other additional assessments, if exists, will be entered as an unscheduled visit in data and that data will be considered for analysis.

3.9.Common Calculations

For the purpose of converting days to years or months, 1 year will be equal to 365.25 days, 1 month will be equal to 30.44 days and 1 week will be equal to 7 days.

For quantitative measurements, change and percent change from baseline at Visit X will be calculated as follows:

- Change from baseline at Visit X = Test Value at Visit X – Baseline Value
- Percent change from baseline at Visit X
  = (Test Value at Visit X - Baseline Value) / Baseline Value X 100

3.10. Software Version

All report outputs will be conducted using SAS version 9.4 or higher.

4. STATISTICAL CONSIDERATIONS

4.2.Multicentre Studies

This study will be conducted by multiple investigators at multiple centres internationally. The participating countries in the study are Czech Republic, Estonia, Hungary, Korea, Lithuania, Latvia, Poland, and Ukraine.

Individual sites mentioned in Table 2 below will be considered as centre.

Table 2: Regions for analysis with Pooled Centres

Region for analysis (Country)	Country code	Centre
PPD		

4.3.Missing Data

Missing safety data will not be imputed. Missing efficacy data will be handled as described in Section 7.1.3. Handling method of partial or missing dates is described in APPENDIX 1.

4.4.Multiple Comparisons/Multiplicity

No multiple comparison adjustment will be performed.

4.5.Active-Control Studies Intended to Show Equivalence

This is an active control study to demonstrate equivalence in terms of percent change from baseline in PASI at Week 12 between SB17 and EU sourced Stelara based on a pre-specified equivalence margin. The null hypothesis tested for the primary efficacy analysis is that either (1) SB17 is inferior to Stelara or (2) SB17 is superior to Stelara.

The equivalence between the two treatment groups will be declared if the two-sided 95% Confidence Interval (CI) of the mean difference of percent change from baseline in PASI at Week 12 is entirely contained within the pre-defined equivalence margin of [−15%, 15%]. Primary efficacy analysis would be performed for PPS. Similar analysis will be performed for the FAS to support the primary analysis.

Additionally, the two-sided 90% CI of the mean difference between the two treatment groups will be estimated for both PPS and FAS with a narrower pre-defined equivalence margin of [-10%, 10%] as a sensitivity analysis.

4.6.Examination of Subgroups

Subgroup analyses of treatment group differences for assessing Percent change in PASI will be presented for the primary endpoint based on non-imputed data for per protocol analysis set (PPS) at Week 12. Analysis will be presented by providing LSMeans estimate and Standard Error (SE) for individual treatments and Mean differences (SB17 - Stelara) between treatment groups involving Means, SE and if the two-sided 95% CI of the mean difference.

The following subgroups will be assessed for endpoints which are specified above:

1. Age group (< 65 years vs. ≥ 65 years)
2. Gender
3. Overall ADA up to Week 52
4. Prior Biologic use
5. History of Psoriatic Arthritis

5. DEMOGRAPHIC AND BASELINE CHARACTERISTICS

Subject demographics and baseline characteristics will be summarised by Country and each treatment group for the RAN and PKS. Continuous variables (e.g., age, height, weight, BMI) will be summarised by treatment group with descriptive statistics (n, mean, standard deviation, median, minimum, and maximum). Qualitative variables (e.g., gender, Child bearing potential for Female subjects, race, ethnicity, and country) will be summarised by treatment group with frequency and

percentages. The summary of subject demographics and baseline characteristics will be also provided by country and treatment group.

By-subject listings of demographic and other baseline characteristics will be provided.

5.1 Demographics Characteristics

- Age (years) – calculated as difference between year of birth and year of informed consent
- Country –Czech Republic, Estonia, Hungary, Korea, Lithuania, Latvia, Poland, Ukraine
- Gender – Male, Female
- Child bearing potential – Yes, No, Not applicable (Male)
- Race – American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, Other
- Ethnicity – Hispanic or Latino, Indian (Indian subcontinent), Chinese, Japanese, Korean, Mixed ethnicity, Other
- Weight (kg) at Baseline and Height (cm) at Screening
- Body Mass Index (BMI) (kg/m^2) – derived as weight (kg)/ [height (m)]^2

5.2 Other Baseline Characteristics

- Duration of psoriasis (years) – calculated as difference between date of informed consent and diagnosed date of plaque psoriasis
- Total psoriasis Body Surface Area (BSA) involvement (%)
- PASI at Baseline
- PGA score of $\geq$ 4 at Baseline
- DLQI at Baseline
- Use of Prior Psoriasis Topical treatment – Yes, No

  Status will be 'Yes' if the subject had at least one prior medication with conditions below:

  - [CM form] Reason for medication taken = 'Plaque Psoriasis' AND

  - [CM form] Medication category = 'Topical'

- Use of prior conventional systemic treatment for psoriasis – Yes, No

  Status will be 'Yes' if the subject had at least one prior medication with conditions below:

  - [CM form] Reason for medication taken = 'Plaque Psoriasis' AND
  - [CM form] Medication category = 'Systemic Non-biologic'

- Use of prior biologic treatment – Yes, No

  Status will be 'Yes' if the subject had at least one prior medication with the condition below:

  - [CM form] Medication category = 'Systemic Biologic'

- History of psoriatic arthritis – Yes, No

  Status will be 'Yes' with the condition below:

  - [MH form] Does the subject have Psoriatic Arthritis? = 'Yes'.

- Smoking Status – Current smoker, Past-smoker, Non-smoker
- Alcohol Status – Current drinker, Past-drinker, Non-drinker

5.3 Statistical Tests for Demographic and Other Baseline Characteristics

Comparison between treatment groups in baseline characteristics will be performed in RAN using the Fisher's exact test/chi-square test or F-test as appropriate. Continuous characteristics will be tested based on F-test and association of variables (discrete cases) would be tested using Fisher's exact test/chi-square test. If frequency of n in one cell is less than 5, then Fisher's exact test would be implemented. The results of these tests will be provided including the p-value only for descriptive purposes and will not be used as a formal basis to determine the factors to be included in primary or secondary efficacy analysis models. If baseline imbalances are detected for any of the factors, additional analyses may be performed to adjust for these baseline differences as ad-hoc analysis after database lock.

6. SURGICAL AND MEDICAL HISTORY

Medical and surgical histories will be coded using Medical Dictionary for Regulatory Activities central coding dictionary (MedDRA version 23.1).

- Medical and surgical histories will be summarised separately by system organ class (SOC) and preferred term (PT) for each treatment group for the RAN
- By-subject listings will be provided for medical or surgical history for the RAN.

7. EFFICACY AND PHARMACOKINETIC ANALYSES

7.1 Primary Efficacy Analysis

7.1.1 Analysis of Primary Efficacy Endpoint

The primary efficacy analysis will aim to demonstrate equivalence in terms of percent change from baseline in PASI at Week 12 between SB17 and Stelara.

The primary efficacy analysis will be performed for the PPS with percent change from baseline in PASI at Week 12 using Analysis of Covariance (ANCOVA) with the baseline value of PASI as a covariate and pooled centres (country) and treatment groups as factors. Individual treatment Least Squares Means (LSMeans) estimates, LSMeans estimates based on differences between treatment groups, Standard error and 95% CI would be provided.

The equivalence between the two treatment groups will be declared if the two-sided 95% confidence interval (CI) of the mean difference of percent change from baseline in PASI at Week 12 is entirely contained within the pre-defined equivalence margin of [−15%, 15%].

The similar analysis will be performed for the FAS to support the primary analysis.

7.1.2 Primary Efficacy Variable

PASI

PASI incorporates the extent of psoriasis at four anatomic sites with the signs of erythema, scale, and elevation. PASI scores range from 0 to 72.

In the PASI system, the body is divided into 4 areas: The head (h), trunk (t), upper extremities (u), and lower extremities (l), which account for 10%, 30%, 20%, and 40% of the total BSA, respectively.

The area of psoriatic involvement of these four areas (Ah, At, Au, and Al) is given a numerical value:

- 0 = No involvement
- 1 = 1% to < 10% involvement
- 2 = 10% to < 30% involvement
- 3 = 30% to < 50% involvement
- 4 = 50% to < 70% involvement
- 5 = 70% to < 90% involvement
- 6 = 90% to 100% involvement

The signs of severity, erythema (E), induration (plaque thickness, I), and scaling (desquamation, S) of these four areas are assessed using a numeric scale 0 to 4:

- 0 = No symptoms
- 1 = Slight
- 2 = Moderate
- 3 = Severe
- 4 = Very severe

The PASI score is calculated according to the following formula:

- PASI = 0.1 × (Eh + Ih + Sh) × Ah + 0.3 × (Et + It + St) × At + 0.2 × (Eu + Iu + Su) × Au + 0.4 × (El + Il+ Sl) × Al

Change from baseline and percent change from baseline of PASI score are calculated as follows:

- Change from baseline of PASI score at Week X = (PASI score at baseline - PASI score at Week X)
- Percent change from baseline of PASI score (%) at Week X = [(PASI score at baseline – PASI score at Week X)/ PASI score at baseline] × 100

7.1.3 Missing Data Imputation Methods of Primary Efficacy Endpoint

The primary efficacy analysis for percent change from baseline in PASI will be performed for PPS. No missing data will be imputed for PPS.

For the sensitive analysis to primary efficacy analysis, missing data for PASI score will be imputed for subjects who drop out for the study prior to the primary analysis time-point. A missing-at-random approach will assume that subjects who withdraw from a study had missing values similar to similar subjects who completed the study in that treatment group. This approach ensures that evidence of lack of equivalence is not diluted when there are missing data.

The missing value will be imputed by multiple imputation method with the assumption of monotone missing pattern and regression method. Multiple imputations would be conducted based on change from baseline values. The sample SAS code for the multiple imputation can be found in *APPENDIX 4*

7.1.4 Sensitive Analysis of Primary Efficacy Endpoint

Two-sided 90% CI of the mean difference between the two treatment groups will be estimated for both PPS and FAS with a narrower pre-defined equivalence margin of [-10%, 10%] as a sensitivity analysis.

To conduct the sensitivity analysis for the FAS, missing data will be imputed using multiple imputation method with the assumption of monotone missing pattern and regression method for subjects who drop out for the study prior to the primary analysis time point. Available case analysis will also be performed for the FAS.

A sensitivity analysis would be conducted using multiple imputation by excluding any subject which is impacted due to Ukraine war at Week 12 to assess the impact of war on Primary analysis. Analysis would be conducted in the FAS using Analysis of Covariance (ANCOVA) with the baseline value of PASI as a covariate and pooled centres (country) and treatment groups as factors. Individual treatment LSMeans estimates, LSMeans estimates based on differences between treatment groups, standard error and 95% CI would be provided.

7.1.5 Supportive Analysis of Primary Efficacy Endpoint

A supportive analysis for primary efficacy analysis will be performed to demonstrate equivalence in terms of percent change from baseline in PASI at Week 12 between SB17 and Stelara.

A supportive analysis to primary efficacy analysis will be performed for both available case (subjects with non-missing primary endpoint) and MI under FAS with percent change from baseline in PASI at Week 12 using Analysis of Covariance (ANCOVA) with the baseline value of PASI as a covariate and pooled centres (Country)and treatment groups as factors. Individual treatment LSMeans estimates based on differences between treatment groups, standard error and p-values would be provided.

The equivalence between the two treatment groups will be declared if the two-sided 95% confidence interval (CI) of the mean difference of percent change from baseline in PASI at Week 12 is entirely contained within the pre-defined equivalence margin of [−15%, 15%].

7.2 Secondary Efficacy Analysis

Secondary efficacy endpoints will be summarised by treatment group and visit for the FAS and PPS.

7.2.1. Secondary Efficacy Variable

The secondary efficacy variables are:

Physician's Global Assessment

The PGA is used to determine the subject's psoriasis lesions overall.

Overall lesions will be graded for induration, erythema, and scaling based on scales as below. The sum of the 3 scales will be divided by 3 to obtain a final PGA score.

Induration (I) (averaged over all lesions)

- 0 = No evidence of plaque elevation
- 1 = Minimal plaque elevation, = 0.25 mm
- 2 = Mild plaque elevation, = 0.5 mm
- 3 = Moderate plaque elevation, = 0.75 mm
- 4 = Marked plaque elevation, = 1 mm
- 5 = Severe plaque elevation, = 1.25 mm or more

Erythema (E) (averaged over all lesions)

- 0 = No evidence of erythema, hyperpigmentation may be present
- 1 = Faint erythema
- 2 = Light red coloration
- 3 = Moderate red coloration
- 4 = Bright red coloration
- 5 = Dusky to deep red coloration

Scaling (S) (averaged over all lesions)

- 0 = No evidence of scaling
- 1 = Minimal; occasional fine scale over less than 5% of the lesion
- 2 = Mild; fine scale dominates
- 3 = Moderate; coarse scale predominates
- 4 = Marked; thick, nontenacious scale dominates
- 5 = Severe; very thick tenacious scale predominates

Total Average = (I + E + S)/3

Physician's Static Global Assessment based upon above Total Average

- 0 = Cleared, except for residual discoloration
- 1 = Minimal - majority of lesions have individual scores for (I + E + S)/3 that averages 1
- 2 = Mild - majority of lesions have individual scores for (I + E + S)/3 that averages 2
- 3 = Moderate- majority of lesions have individual scores for (I +E + S)/3 that averages 3
- 4 = Marked - majority of lesions have individual scores for (I + E + S)/3 that averages 4

- 5 = Severe - majority of lesions have individual scores for (I + E + S)/3 that averages 5

***Note**: Scores should be rounded to the nearest whole number. If total ≤ 1.49, score = 1; if total ≥1.50, score = 2.*

PASI Response

A PASI50, PASI75, PASI90, and PASI100 response is defined as a ≥ 50%, ≥ 75%, ≥ 90%, and 100% improvement of PASI score from baseline.

- PASI50 at Week X:
  - Yes if percent change of PASI score at Week X ≥ 50
  - No if percent change of PASI score at Week X < 50
- PASI75 at Week X:
  - Yes if percent change of PASI score at Week X ≥ 75
  - No if percent change of PASI score at Week X < 75
- PASI90 at Week X:
  - Yes if percent change of PASI score at Week X ≥ 90
  - No if percent change of PASI score at Week X < 90
- PASI100 at Week X:
  - Yes if percent change of PASI score at Week X = 100
  - No if percent change of PASI score at Week X ≠ 100

Dermatology Life Quality Index

The DLQI consists of 10 questions concerning patients' perception of the impact of skin diseases on different aspects of their health-related quality of life over the last week.

The scoring of each question is as follows:

- Very much = 3 points
- A lot = 2 points
- A little = 1 point
- Not at all, Not relevant, or unanswered = 0 point

- For Question 7, if 'prevented work or studying' is Yes = 3 points

The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0.

Change from baseline of DLQI score is calculated as follows:

- Change from baseline of DLQI score at Week X = (DLQI score at baseline - DLQI score at Week X)

7.2.2 Secondary Efficacy Endpoints

Percent change from baseline in PASI

Percent change from baseline in PASI at Week 2, 4, 8, 12, 16, 20, 24, 28, 40, and 52.

PASI50, PASI75, PASI90, and PASI100 response rate

Percentage of patients with a PASI50, PASI75 and PASI90 response at Week 2, 4, 8, 12, 16, 20, 24, 28, 40, and 52.

Physician's Global Assessment

Percentage of patients with a Physician's Global Assessment score of Cleared or Minimal (PGA score of 0 or 1) at Week 2, 4, 8, 12, 16, 20, 24, 28, 40, and 52.

Change from baseline in Dermatology Life Quality Index

Change from baseline in DLQI at Week 4, 12, 16, 28, 40, and 52.

7.2.3 Analysis of Secondary Efficacy Endpoints

The following analyses will be performed for the secondary efficacy endpoints.

Percent change from baseline in PASI

Continuous summary statistics will be provided for PASI Scores by treatment group and visit for all protocol specified visits. Summary statistics of observed value change from baseline, and percent change from baseline will be provided for the overall period for SB17, Stelara Overall, Stelara+SB17, and Stelara+Stelara. The percent change from baseline in PASI will be plotted by treatment group and visits up to Week 28 for the FAS and PPS with mean and standard error based on available case.

PASI50, PASI75, PASI90, PASI100 response rate

PASI50, PASI75, PASI90 will be summarised by treatment group and visit using counts and percentages. Summary statistics will be provided for overall period for SB17, Stelara Overall, Stelara+SB17, and Stelara+Stelara.

Physician's Global Assessment

Discrete summary statistics for PGA scores (Cleared, Minimal, Mild, Moderate, Marked, Severe) will be provided by treatment group and visits using counts and percentages. An additional summary table would be provided to summarize the proportion of subjects with PGA scores of Cleared or Minimal. Summary statistics will be provided for overall period for SB17, Stelara Overall, Stelara+SB17, and Stelara+Stelara.

Change from baseline in Dermatology Life Quality Index

Continuous summary statistics will be provided for DLQI Scores by treatment group and visit for all protocol specified visits. Summary statistics of observed value, baseline value, and change from baseline will be provided for overall period for SB17, Stelara Overall, Stelara+SB17, Stelara+Stelara.

7.2.4 Missing Data Imputation Methods of Secondary Efficacy Analysis

Not Applicable

7.2.5 Sensitive Analysis of Secondary Efficacy Endpoint

Not Applicable

7.2.6 Supportive Analysis of Secondary Efficacy Endpoint

Not Applicable

7.2.7 Exploratory Efficacy Analysis

Not Applicable

7.2.8 Pharmacokinetic Analysis

The pharmacokinetic analysis will be performed for the PKS.

All concentrations will be reported and analysed with the same precision as the source data provided by the bioanalytical laboratory regardless of how many significant figures or decimals the data carry.

A listing of PK blood sample collection times as well as derived sampling time deviations will be provided. Serum concentrations will be summarised for each treatment and each scheduled sampling time using descriptive statistics including number of observations (n), mean, SD, coefficient of

variation (CV%), median, minimum, maximum, geometric mean, geometric SD, and geometric CV%. Concentrations that are below the limit of quantitation (BLQ) will be treated as zero for the computation of descriptive statistics, except for geometric mean, geometric SD, and geometric CV%, for which they will be excluded.

Blood samples for PK not collected at scheduled visit or scheduled pre-dose blood samples collected after IP administration at scheduled visit, will be excluded from summary tables and figures and will only be listed.

A subject listing of all concentration-time data for each treatment will be presented.

Concentration summaries by treatment and overall Anti-drug Antibody (ADA) status up to Week 28 will also be provided.

The following figures of the serum concentration will be provided:

- The arithmetic mean (±SD) serum concentration versus nominal time will be presented for each treatment group on a linear scale. The treatments will be overlaid on the same plot.
- Individual serum concentration versus actual time will be presented by subject on linear scales.

Individual concentrations which are BLQ will be displayed as zero in the graphic presentations on linear scale. Means which fall below the lower limit of quantitation (LLOQ) will be displayed as zero in the graphic presentations on linear scale.

8. SAFETY ANALYSIS

All outputs for safety outcomes will be based on the SAF unless stated otherwise.

Safety analyses will be performed for main period (or screening + main period to include assessments and events occurred at screening period), transition period, and overall study period unless specified otherwise.

- Analyses for screening and main period will be performed in the SAF1 by actual treatment group received at main period (SB17, Stelara).
- Analyses for transition period will be performed in the SAF2 by actual treatment group (SB17+SB17, Stelara+SB17, Stelara+ Stelara, and Stelara overall (Stelara+SB17 and Stelara+ Stelara)),
- Analyses for the overall study period will be performed in the SAF1 by actual treatment group (SB17, Stelara+SB17, Stelara+ Stelara, and Stelara overall (subjects received Stelara treatment at initial randomisation)).

There will be no statistical comparisons for safety data, unless otherwise specified with the relevant section.

8.1 Study Medication Exposure

The duration of exposure to IP in days will be based on Safety set 1 and will be calculated as follows.

- If the last IP administration date was known,

  Exposure duration = last IP administration date – first IP administration date +1

- If the last IP administration date was unknown,

  Exposure duration = last available visit date – first IP administration date + 1

Interruptions and compliance are not taken into account for duration of exposure.

The duration of exposure to IP in days and number of IP administrations will be summarised descriptively including n, mean, median, standard deviation, minimum, and maximum for each treatment group for SAF1. Count and percentage will be provided for summarizing duration of exposure to IP.

A by-subject listing of IP administration and compliance will be provided.

A by-subject listing of randomised allocation to IP treatment consisting of randomisation number, treatment allocation and randomised date will be provided for the RAN.

A by-subject listing of allocated IP information consisting of IWRS dispensed medication ID, treatment and lot number, and actual medication ID, treatment and lot number will be provided for the RAN.

8.2 Prior/Concomitant Medications

Prior/concomitant medications will be coded using World Health Organization Drug Dictionary (WHO DD Global B3 Version September 2020).

A summary of prior and concomitant medication giving the number and percentage of subjects and the number of events will be provided by ATC Drug Class and/or preferred term for each treatment.

- Concomitant medications will contain medications that ended on or after the first injection of IP or medications that were ongoing after the first injection of IP.

- Prior medications will contain medications ended prior to the first dose of IP.

Handling method of partial or missing dates is described in APPENDIX 1. For the medication, which is impossible to define as prior or concomitant, the medication will be considered as concomitant medication (i.e., worst-case).

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

Phototherapy will be divided into two categories, concomitant and prior phototherapy.

- Concomitant phototherapy will contain phototherapies ended on or after the first injection of IP or phototherapies that were ongoing after the first injection of IP.
- Prior phototherapy will contain phototherapies ended prior to the first dose of IP.

Summary of concomitant phototherapy giving the number and percentage of subjects and the number of events will be provided by therapy type (PUVA, UVB, Other) for each treatment group. By-subject listing of prior and concomitant phototherapies will be provided.

Any medication/phototherapy with an onset date on or after the date of the first administration of IP and before IP dose post re-randomization will be included in the main period analysis. Any medication/phototherapy that start in the main period and continue into the transition period will be included in the main period only. Any medication/phototherapy with an onset date on or after the date of IP administration at Week 28 will be included in the transition period.

Refer to APPENDIX 1 for handling of partial dates for medication/phototherapy. In the case where it is not possible to define the medication/phototherapy as prior/concomitant, the medication/phototherapy will be classified as the worst-case: i.e., Concomitant.

8.3 Prohibited Medications

Prohibited medications (excluding phototherapy) will be coded using WHO DD Global B3 Version September 2020.

Prohibited medications will be defined in APPENDIX 5 with ATC code/preferred term and will be confirmed by medical reviewer during PD review. Final confirmed prohibited medications will be reported as protocol deviations.

Summary of prohibited medication giving the number and percentage of subjects and the number of events will be provided by ATC drug class and/or preferred term for each treatment group. By-subject listing of prohibited medications will be provided.

8.4 Laboratory Evaluations

The following clinical laboratory test results from the central laboratory will be reported in SI unit:

- **Haematology**: Haemoglobin, Haematocrit, Platelet count, Total white blood cell count, Neutrophils, Lymphocytes, Monocytes, Eosinophils, Basophils, Neutrophils Absolute, Lymphocytes Absolute, Monocytes Absolute, Eosinophils Absolute, Basophils Absolute.

- **Chemistry**: Sodium, Potassium, Creatinine, Glucose, Calcium, Phosphorus, Total bilirubin, Albumin, Alanine Transaminase (ALT), Aspartate Transaminase (AST), Alkaline phosphatase (ALP), C-reactive protein (CRP).

- **Urinalysis (Dipstick)**: Protein, Blood, Leucocytes, Nitrite, Glucose, Ketone, pH, Specific gravity, Bilirubin, Urobilinogen.

- **Virology**: Hepatitis B Virus Core Antibody (HBcAb), Hepatitis B Virus Surface Antigen (HBsAg), Hepatitis C Virus Antibody (HCV Ab), Hepatitis C Virus RNA (HCV RNA), HIV 1/2 Antibody (HIV Ab), HIV-1/2 RNA (HIV RNA), HIV-1/2 Antibody confirmation (HIV Ab confirmation).

The following summaries will be provided by parameter, treatment group, and visit for laboratory tests:

- Summary of baseline, actual value and change from baseline for Haematology and Chemistry

- Shift from baseline (worst-case change from baseline) for Haematology (Total white blood cell count, Neutrophils Absolute, Haemoglobin, and Platelet count) and Chemistry (ALT, AST, ALP, Bilirubin, Creatinine and CRP parameters with respect to normal range for interval [W0~W28] and [W0~W52 (cumulative)] in SAF1 and for interval [W28~W52 (cumulative)] in SAF2 based on result at Week 28

- Summary of the number and percentage of subjects experiencing significant laboratory abnormality defined in APPENDIX 2 (L2, H2) for Haematology and Chemistry for all protocol specified visits and overall incidence up to Week 28 and Week 52 each

- By-subject listings of Haematology, Chemistry, Urinalysis (dipstick), and Virology will be provided respectively.

- By-subject listings of subjects experiencing significant laboratory abnormality defined in APPENDIX 2 (L2, H2) will be provided for Haematology, Chemistry respectively.

The quantitative lab values with < x will be replaced by x and > y will be replaced by y where x and y are lower limit of quantification and upper limit of quantification respectively. However, for the listing, the original values of '<x' or '>y' will be presented as it is recorded.

Laboratory reference ranges (APPENDIX 2) will also be listed with corresponding low and high range in SI unit.

Due to the war circumstances in Ukraine, some haematology and chemistry samples were not able to be analysed in the central lab (due to sample delivery disruption, etc.) so they were analysed locally.

Results from the local laboratory will not be included in the by-subject listing and summary tables for laboratory tests, but will be presented as an attachment in the CSR appendix

8.5 Vital Signs

- Vital signs (blood pressure, pulse rate and body temperature) will be reported for this study.
- A summary of each vital sign parameter will be provided for baseline, actual value, and change from baseline by treatment group and visit.

By-subject listings of vital sign parameters will be provided.

8.6 Immunogenicity Analysis

Immunogenicity assessment will be performed for subjects falling under safety analysis set.

The number and percentage of subjects with ADA results (i.e., Positive, Negative) and neutralizing antibodies (NAbs) results (i.e., Positive, Negative) will be presented by treatment groups at each protocol specified visit using SAF1.

The incidence of overall ADA results (i.e., Positive, Negative, Inconclusive) up to Week 12, Week 28 and Week 52 will be presented by overall treatment group using SAF1. Subjects with no ADA result after first IP administration at Week 0 or missing baseline result will be excluded from summary statistics but will be presented in listing. Overall ADA result is defined as below:

- "Positive" for a subject with treatment-induced or treatment-boosted ADA, where treatment-induced ADA indicates at least one positive result after first IP administration at Week 0 for subjects with negative ADA at baseline, and treatment-boosted ADA indicates at least one positive result with higher titre level compared to baseline after first IP administration at Week 0 for subjects with positive ADA at baseline.
- "Negative" for a subject with negative ADA at baseline and without positive ADA post-baseline.
- "Inconclusive" for a subject with positive ADA at baseline and without positive result with higher titre level observed post-baseline.

In addition, the incidence of overall ADA results (i.e., Positive, Negative, Inconclusive) for the transition period (from Week 28 to Week 52) will be presented by transition treatment group using the SAF2.

Overall ADA results for the transition period will be summarised for subjects with at least one ADA result after transition up to Week 52. Subjects with no ADA result after IP administration at Week 28 or no overall ADA result up to Week 28 will be excluded from summary statistics but will be presented in listing. Overall ADA result for the transition period is defined as below:

- "Positive" for a subject with treatment-induced or treatment-boosted ADA, where treatment-induced ADA indicates at least one positive result after IP administration at Week 28 for subjects with overall negative ADA up to Week 28, and treatment-boosted ADA indicates at least one positive result with higher titre level after IP administration at Week 28 compared to maximum positive ADA up to Week 28, for subjects with at least one positive ADA results up to Week 28.

- "Negative" for a subject with overall negative ADA up to Week 28 and without positive ADA after IP administration at Week 28 until Week 52.

- "Inconclusive" for a subject with at least one positive ADA up to Week 28 and without positive result with higher titre level observed after IP administration at Week 28 up to Week 52, compared to the maximum positive ADA up to Week 28.

A by-subject listing of immunogenicity assessment will be presented for all available data.

8.7 Other Observations Related to Safety

Following observations will be provided:

- Weight: summary for baseline, actual value, and change from baseline by treatment group and visit; by-subject listing will also be provided.

- 12-lead ECG at Screening (listing only)

- Physical examination (listing only)

- Tuberculosis evaluation (listing only)

- QuantiFERON Gold Plus Test (listing only)

- Chest X-ray (listing only)

- Pregnancy test and FSH test (listing only)

9. ADVERSE EVENTS

Analysis for AE will be performed for main period, transition period, and overall study period. Analyses for main and transition period will be performed in the SAF1 and SAF2 respectively and analyses for the overall study period will be performed in the SAF1.

All reported terms for AEs will be coded using MedDRA version 23.1.

- Pre-treatment AE will be defined as any AE with an onset date before the date of first administration of IP.
- A Treatment Emergent Adverse Event (TEAE) will be defined as any AE with an onset date on or after the date of the initiation of study drug.
- AEs which are already present before the initiation of study drug and increase in severity after the initiation of study drug will be considered as TEAEs. Pre-treatment AEs before the initiation of study drug with no increase in severity after the initiation of study drug will not be considered as TEAEs.
- The following AEs will be classified as Adverse Events of Special Interest (AESI):
    a) Systemic hypersensitivity
    b) Infections
    c) Pulmonary events
    d) Injection site reaction.
- AEs diagnosed/related with COVID-19 will be divided into two categories:
    - TEAEs for COVID-19: includes TEAEs, where the preferred term contains key text "COVID". TEAEs related to COVID-19 vaccine, where the verbatim term contains "sign/symptom/disease related to COVID-19 vaccine" will not be included. The Italic text will be replaced with actual disease, or sign/symptom.
    - TEAEs related to COVID-19: includes TEAEs, where

      Where AETERM contains "COVID-19"AND Where Preferred Term does NOT contain "COVID" (as this will already be 'TEAEs for COVID-19') AND Where Preferred Term is NOT "Vaccination complication"
- TEAEs related with war in Ukraine includes TEAEs, where the verbatim contains key text "Due to War".

In general, AE summaries will provide the number and percentages of subjects reporting at least one AE and the total number of events reported by SOC, PT and treatment group. Subject will be counted once under each PT and each SOC. SOC will be presented alphabetically, and PT will be sorted within each SOC in descending order of subject frequency based on SB17, then alphabetically if tied.

Any TEAE with an onset date on or after the date of the first administration of IP and before IP dose post re-randomisation will be included in the main period analysis. AEs that start in the main period and continue into the transition period will be included in the main period only. Any TEAE with an onset date on or after the date of IP administration at Week 28 will be included in the transition period.

Refer to APPENDIX 1 for handling of partial dates for AEs. In the case where it is not possible to define as AE as treatment-emergent or not, the AE will be classified by the worst-case: i.e., treatment-emergent.

9.1 Summary of All Adverse Events

All AEs will be summarised by number, percentage of subjects and event. The following categories will be presented in the summary of adverse events for different study periods as specified at *Section 9*.

- All AEs
- TEAEs by severity and causality
- TEAEs of special interest by category
- TEAEs leading to discontinuation of IP
- TEAEs leading to death
- Serious Adverse Events (SAE)
- Serious TEAEs by causality
- Serious TEAEs leading to discontinuation of IP
- TEAEs for COVID-19
- TEAEs related to COVID-19
- Serious TEAEs for COVID-19
- Serious TEAEs related to COVID-19
- TEAEs related to war in Ukraine

By-subject listing for AEs will be provided.

In addition, the following category will be presented in the summary of adverse events for main period (including screening period):

- Pre-treatment Adverse Events (Pre-AEs)

9.2 TEAEs

Incidence of all TEAEs by treatment group will be presented by SOC and PT using number and percentage of subjects and number of events.

Incidence of TEAEs with incidence > 5% in either treatment group of subjects by SOC and PT will be presented.

Incidence of other TEAEs (all TEAEs excluding serious TEAEs) with incidence > 5% of subjects in either treatment group by SOC and PT will be presented.

9.3 TEAEs by Severity

Incidence of all TEAEs by treatment group will be presented by SOC, PT, and severity using number and percentage of subjects and number of events.

Severity will be reported as mild, moderate, or severe. TEAEs with a missing severity will be considered as severe TEAE (i.e., worst-case). If a subject reported TEAEs in the same SOC (or PT) more than once with different severity, the subject will be counted once in the worst-case severity.

9.4 TEAEs by Causality (Relationship with IP)

Incidence of all TEAEs by treatment group will be presented by SOC, PT, and causality using number and percentage of subjects and number of events.

Causality will be reported as related or not related. TEAEs with a missing causality will be considered as related TEAE (i.e., worst-case). If a subject reports the same AE more than one within that SOC/PT, the AE with the worst-case relationship to IP will be used in the corresponding relationship summaries.

9.5 TEAEs of Special Interest

Incidence of all TEAEs of special interest by treatment group will be presented by SOC and PT using number and percentage of subjects with number of events.

9.6 TEAEs leading to discontinuation of IP

Incidence of all TEAEs leading to discontinuation of IP by treatment group will be presented by SOC and PT using number and percentage of subjects and number of events.

By-subject listing for TEAEs leading to discontinuation of IP will be provided.

9.7 Serious TEAEs

Incidence of all serious TEAEs by treatment group will be presented by SOC and PT using number and percentage of subjects and number of events.

9.8 Serious Adverse Events

By-subject listing for SAEs will be provided.

9.9 TEAEs leading to death

Incidence of all TEAEs leading to death by treatment group will be presented by SOC and PT using number and percentage of subjects and number of events.

By-subject listing for TEAEs leading to death will be provided.

9.10 TEAEs Diagnosed/Related with COVID-19

Incidence of TEAEs diagnosed/related with COVID-19 by treatment group will be presented by SOC and PT using number and percentage of subjects and number of events.

9.11 TEAEs Related to War in Ukraine

Incidence of TEAEs related to war in Ukraine by treatment group will be presented by SOC and PT using number and percentage of subjects and number of events.

9.12 TEAEs by Subgroup

Incidence of TEAEs by treatment group will be presented by subgroups, SOC and PT using number and percentage of subjects and number of events.

The Following subgroups will be assessed.

1. Age group (< 65 years vs. ≥ 65 years)
2. Gender
3. Overall ADA up to Week 52

10.REFERENCES

1. A Phase III, Randomised, Double-blind, Multicentre Clinical Study to Evaluate the Efficacy, Safety, Tolerability, Pharmacokinetics, and Immunogenicity of SB17 (proposed ustekinumab

biosimilar) Compared to Stelara in Subjects with Moderate to Severe Plaque Psoriasis, Protocol V2.0

2. Subject Case Report Forms Version 2.0, 16 Jun 2021

APPENDIX 1. PARTIAL DATE CONVENTIONS

Imputed dates will NOT be presented in the listings. However, in general, when calculating relative days, partial dates with missing day only will be assumed to be 15th of the month, and partial dates with both missing day and month will be assumed to be June 30. Otherwise, the following rules in the given table will be applied for each case.

For medical history where there may be partial start/end dates, if complete (imputed) end date is available and the imputed start date is greater than the (imputed) end date, then imputed start date will be set to the (imputed) end date. If complete start date is available and the imputed end date is less than the complete start date, then end date will be set to the start date.

Algorithm for Adverse Events and Medications

When the start date is missing,

	Case	Imputed Value
Missing Day	year and month = year and month of first IP taken date	first IP taken date
	year and month <> year and month of first IP taken date	the 1st of the month
Missing Day and Month	year = year of first IP taken date	first IP taken date
	year <> year of first IP taken date	1st of January
Completely Missing	N/A	

If complete (imputed) end date is available and the imputed start date is greater than the (imputed) end date, then imputed start date should be set to the (imputed) end date.

When the end date is missing,

	Case	Imputed Value
Missing Day	year and month < year and month of last visit date	last day of the month
	year and month = year and month of last visit date	last visit date

	Case	Imputed Value
Missing Day and Month	year < year of last visit date	31st of December
	year = year of last visit date	last visit date
Completely Missing	N/A	

Algorithm for Treatment-Emergent

After imputation for partial dates is implemented, whether AE is TEAE will be decided.

When start date is present,

- If known/imputed start date ≥ the date of first dose of IP, then AE is considered as TEAE

When start date is completely missing but end date is present,

- If known/imputed end date ≥ the date of first dose of IP, then AE is considered as TEAE

When both start date and end date are completely missing,

- AE is considered as TEAE

Algorithm for Concomitant

After imputation for partial dates is implemented, whether medication is concomitant will be decided.

When both start date and end date are present,

- If known/imputed end date ≥ the date of first dose of IP and known/imputed start date ≤ the date of EOS visit, then medication is considered as concomitant

When start date is present and end date is completely missing,

- If known/imputed start date ≤ the date of EOS visit, then medication is considered as concomitant

When start date is completely missing but end date is present,

- If known/imputed end date ≥ the date of first dose of IP, then medication is considered as concomitant

When both start date and end date are completely missing,

- Medication is considered as concomitant

APPENDIX 2. LABORATORY TEST PARAMETERS

Ranges_EP4540.xlsx

Ranges_SP5933.xlsx

APPENDIX 3. VISIT NAME

Period	Source Visit Name	Visit Long Name
Screening Period	Screening	Screening
Main Period	Visit 1 Week 0	Week 0
	Visit 2 Week 2	Week 2
	Visit 3 Week 4	Week 4
	Visit 4 Week 8	Week 8
	Visit 5 Week 12	Week 12
	Visit 6 Week 16	Week 16
	Visit 7 Week 20	Week 20
	Visit 8 Week 24	Week 24
Transition Period	Visit 9 Week 28	Week 28
	Visit 10 Week 40	Week 40
	Visit 11 Week 52	Week 52
	Early Termination or End of Study	Early Termination

APPENDIX 4. SAMPLE CODES FOR PRIMARY ANALYSIS

CCI [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

CCI

APPENDIX 5. PROHIBITED MEDICATIONS

PD Definition List.xlsx

STATISTICAL ANALYSIS PLAN SIGNATURE PAGES

SIGNATURE PAGE

Declaration of the authors

Protocol Title Applicable to this Statistical Analysis Plan: A Phase III, Randomised, Double-blind, Multicentre Clinical Study to Evaluate the Efficacy, Safety, Tolerability, Pharmacokinetics, and Immunogenicity of SB17 (proposed ustekinumab biosimilar) Compared to Stelara in Subjects with Moderate to Severe Plaque Psoriasis

Protocol Number: SB17-3001

Protocol Version and Effective Date: Version 2.0 Feb 15, 2021

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(Mmm dd, yyyy)

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Signature: will be provided in e-signature Date:

(Mmm dd, yyyy)

Name: PPD

Institution: Samsung Bioepis

Signature: will be provided in e-signature Date:

(Mmm dd, yyyy)