1.0 Title Page

Statistical Analysis Plan

Study M16-178

A Randomized, Controlled, Multicenter, Open Label Study with Blinded Assessment of the Efficacy of the Humanized Anti-IL-23p19 Risankizumab Compared to FUMADERM® in Subjects with Moderate to Severe Plaque Psoriasis Who are Naïve to and Candidates for Systemic Therapy

Date: 11 Jan 2018

Version 1.0

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3.0 Introduction

This statistical analysis plan (SAP) describes the statistical analysis to be completed by the AbbVie Clinical Statistics Department for Study Protocol M16-178 dated 28 November 2017, which incorporates Amendments 1, 2 and 3 (original Protocol: 05 January 2017, Amendment 1: 13 March 2017, Amendment 2: 05 July 2017).

This SAP will provide details to further elaborate statistical methods as outlined in the Protocol M16-178 and will describe analysis conventions to guide the statistical programming work. The SAP will be signed off before the study database is locked.

Analyses will be performed using SAS® version 9.4 (SAS Institute, Inc., Cary, NC 27513) or higher using the UNIX operating system.

4.0 Study Objectives, Design and Procedures

4.1 Objectives

The objective of this study is to compare the efficacy and safety of subcutaneous (SC) risankizumab and oral FUMADERM® provided as study medication in subjects with moderate to severe plaque psoriasis who are naïve to and candidates for systemic therapy.

4.2 Design Diagram

This is a randomized, controlled, multicenter, open-label study with blinded assessment of efficacy to demonstrate the efficacy and safety of SC risankizumab in adult subjects with moderate to severe plaque psoriasis who are naïve to and candidates for systemic therapy as compared with oral FUMADERM® provided as study medication. Eligible male and female subjects with moderate to severe plaque psoriasis will be selected to participate in the study according to the selection criteria. Approximately 110 subjects will be enrolled in this study.

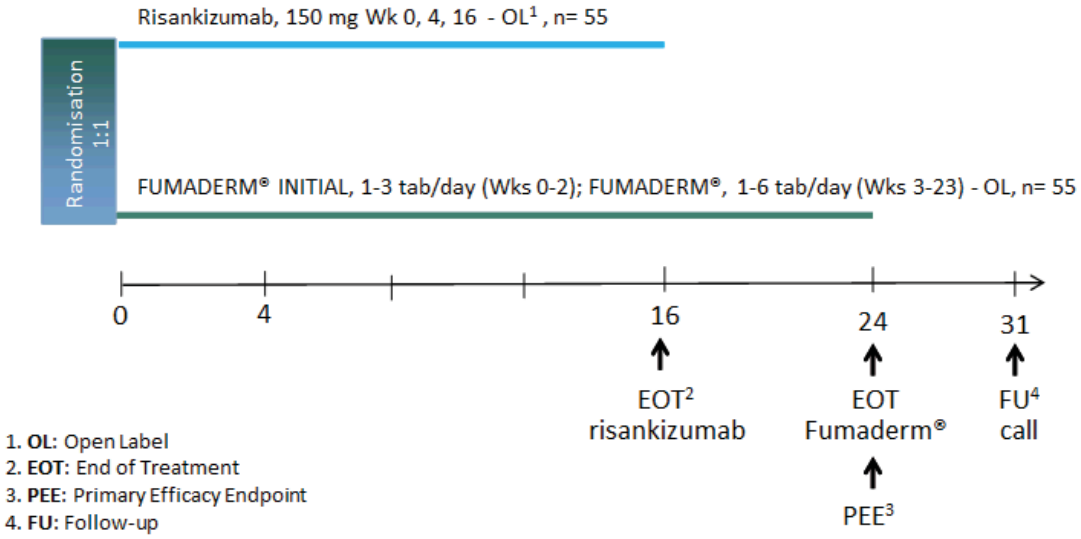
The study will include a 30-day screening period and a 24 week active-controlled treatment period followed by a follow-up phone call at Week 31 for subjects that do not elect to enroll into the extension Study M15-997.

After meeting the selection criteria, enrolled subjects will be randomly assigned in a 1:1 ratio to one of two arms as shown below:

- Risankizumab 150 mg SC at Week 0/Day 1, Week 4 and Week 16 or,
- Oral FUMADERM® INITIAL provided as study medication starting at Week 0/Day 1 until Week 2 and FUMADERM® provided as study medication starting at Week 3 until Week 24 (last intake in the morning on the day of Week 24 visit)

A schematic of the study design is shown below in Figure 1.

Figure 1. Study Design Schematic



4.3 Sample Size

Using a two-sided Chi squared test at level of significance 5%, the sample size of 110 (2 × 55) subjects will provide 94% power assuming response rates of the primary endpoint (PASI 90 at Week 24) of 70% for risankizumab and 35% for FUMADERM®.

These assumptions are in line with what has been observed in recent studies for risankizumab (63/83 (75.9%) at Week 24)[1] and FUMADERM® 61/273 (22.3%) of the subjects achieved PASI 90 at Week 16 in the FUMADERM® arm in the BRIDGE trial.[2]

4.4 Interim Analysis

No interim analysis will be done for this study.

5.0 Analysis Populations and Stratification

5.1 Analysis Populations

Efficacy Population:

Intent-to-Treat (ITT) Population: The ITT Population is defined as all subjects who are randomized. The ITT Population will be used for the efficacy analyses. The ITT Population will be analyzed by treatment group as randomized.

Safety Population:

The Safety Population is defined as all randomized subjects who received at least one dose of study drug. The Safety Population will be used for the safety analyses. The Safety Population will be analyzed based on the actual treatment received.

5.2 Variables Used for Stratification of Randomization

Subjects will be randomized in 1:1 ratio to receive risankizumab or FUMADERM® stratified by prior phototherapy, with a maximum of 20% of subjects with prior phototherapy. Randomization will not be stratified by center due to the limited number of subjects per center. Randomization will be done using an adequate block size.

6.0 Analysis Conventions

Definition of Baseline

The last non-missing observation collected on or before the date of the first dose of study drug will be used as Baseline for summary of demographics and disease characteristics, safety and efficacy analyses.

Definition of Final Observation (Applicable to Safety Analyses)

Final observation is defined as the last non-missing observation collected within 15 weeks (105 days) following the last dose of risankizumab or 1 week (7 days) after the last dose of FUMADERM® provided as study medication. In a sensitivity analysis, adverse events with an onset date until 7 weeks (49 days) after the last dose of FUMADERM® provided as study medication or until rollover into the extension study will be included.

Definition of Rx Days (Days Relative to the Date of First Dose of Study Drug)

Rx Days are calculated for each time point relative to the date of first dose of study drug. They are defined as the number of days between the day of the first dose of study drug and the specific time point. Rx Days are negative values when the time point of interest is prior to the first study drug dose day. Rx Days are positive values when the time point of interest is on or after the first study drug dose day. The day of the first dose of study drug is defined as Rx Day 1, while the day prior to the first study drug dose is defined as Rx Day –1 (there is no Rx Day 0).

Definition of Analysis Windows

All time points and corresponding time windows are defined based on Rx Days.

Analysis windows are constructed using the following algorithm:

- Determine the nominal Rx day for each visit (e.g., Week 4 [4 weeks after Baseline visit] equals Rx Day 29).

- In order to include all post baseline data, the first post-baseline interval starts on the first day after the first dose of study drug (Rx Day 2).
- Determine the window around a specific nominal Rx day by adding or subtracting half of the interval between adjacent visits (e.g., days between Week 4 and Week 8 is 28). The threshold between adjacent visits is determined by splitting the interval evenly between the visits. If the resulting split is between Rx days, then the threshold is determined as the midpoint between the adjacent visits. If the resulting split is on an Rx day, then the threshold is determined as being between that Rx day and the Rx day prior to it (e.g., the split between Week 4 and Week 8 would be between Rx Days 43 and 44).
- If more than one assessment is included in a time window the assessment closest to the nominal day will be used. If there are two observations equidistant to the nominal day, the later one will be used in analyses. If more than one assessment is included on the same day, then the worst assessment on that day will be used in analyses, except those specified in Section 11.0.

For subjects who were randomized and not dosed, the date of randomization will be used for determining window definitions.

The following analysis windows have been specified:

Table 1. Visit Windows for Analysis of Vital Signs, PASI, BSA Involvement, sPGA, Urinalysis, Targeted Safety Laboratory Testing (ITT/Safety Populations)

Window Label	Target Day	Interval
Baseline	1	≤ 1
Week 4	29	[2, 43]
Week 8	57	[44, 71]
Week 12	85	[72, 99]
Week 16	113	[100, 127]
Week 20	141	[128, 155]
Week 24	169	[156, 183[a]]

Rx Day calculated relative to first dose date of study drug. For subjects randomized but not dosed, Rx Day calculated relative to Randomization.

Targeted Safety Laboratory Testing includes CBC with differential count (hematology), ALT, AST, gamma-GT, alkaline phosphatase (AP) and serum creatinine.

a. For safety analyses (urinalysis and targeted laboratory testing): The minimum of upper bound and 105 or 7 days after the last dose for risankizumab and FUMADERM®, respectively.

Table 2. Visit Windows for Analysis of DLQI, PPASI, PSSI, NAPPA-CLIN, PSS, SF-36, PBI, HADS, PtGA, EQ-5D-5L (ITT Population)

Window Label	Target Day	Interval
Baseline	1	≤ 1
Week 16	113	[2, 141]
Week 24	169	[142, 197]

Rx Day calculated relative to first dose date of study drug. For subjects randomized but not dosed, Rx Day calculated relative to Randomization.

Table 3. Visit Windows for Analysis of Complete Safety Laboratory Testing (Safety Population)

Window Label	Target Day	Interval
Baseline	1	≤ 1
Week 8	57	[2, 85]
Week 16	113	[86, 141]
Week 24	169	[142, 197[a]]

Rx Day calculated relative to first dose date of study drug. For subjects randomized but not dosed, Rx Day calculated relative to Randomization.

Complete Safety Laboratory Testing includes all laboratory parameters (see Table 8) excluding CBC with differential count (hematology), ALT, AST, gamma-GT, alkaline phosphatase (AP) and serum creatinine.

a. For safety analyses: The minimum of upper bound and 105 or 7 days after the last dose for risankizumab and FUMADERM®, respectively.

Table 4. Visit Windows for Analysis of ECG (Safety Population)

Window Label	Target Day	Interval
Baseline	1	≤ 1
Week 24	169	[2, 337[a]]

Rx Day calculated relative to first dose date of study drug. For subjects randomized but not dosed, Rx Day calculated relative to Randomization.

a. The minimum of upper bound and 105 or 7 days after the last dose for risankizumab and FUMADERM®, respectively.

Table 5. Visit Windows for Summary of Study Drug Injection of Risankizumab

Window Label	Target Day	Interval
Baseline	1	≤ 1
Week 4	29	[2, 43]
Week 16	113	[44, 155]

Rx Day calculated relative to the first dose date of study drug.

No global imputation is taking place at the database level. Efficacy related imputations are outlined in Section 10.1.2. There is no imputation for missing values in the safety analyses.

Rounding of Numeric Results

Rounding will be performed for presentation of results. No rounding will be performed before or during analyses. The ROUND function of SAS will be used to round results.

When dichotomizing continuous variables from single observations, associated continuous variables will be rounded to 9 decimal points before applying the cutoff point to determine the response status (for example, percent change from baseline in PASI score will be rounded to 9 decimal places before comparing to 90%).

The mean, median and quartiles will be rounded for presentation to 1 decimal more than the data entered into the database. The standard deviation will be rounded to 2 decimal places more than the data entered into the database. The minimum and maximum values will be presented as entered into the database.

Probabilities will be rounded to 3 decimal places before assignment of statistical significance and will be presented in rounded format. Probabilities that round to zero or are reported by SAS as zero will be presented as "< 0.001." Probabilities that round to 1 or are reported by SAS as 1 will be presented as "> 0.999."

7.0 Demographics, Baseline Characteristics, Medical History, and Previous/Concomitant Medications

7.1 Demographic and Baseline Characteristics

Demographic and baseline characteristics will be summarized for each arm and overall for the ITT population. The number of observations, mean, standard deviation, median, first and third quartile, minimum and maximum will be summarized for continuous variables; and treatment groups will be compared using a one-way analysis of variance (ANOVA) model with treatment as the independent factor. Categorical or discrete variables will be summarized via counts and percentages; and treatment groups will be compared using a two-sided Pearson's Chi-Square test (or Fisher's exact test if expected cell count < 5).

The following demographic and baseline parameters will be summarized.

Subject Demographics

- Sex (male, female)
- Age (years), defined as the number of years from date of birth to date of first drug
- Age categories (< 40 years, ≥ 40 – < 65 years, ≥ 65 years)
- Race (White, Black or African American, Asian, American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, Multi Race)
- Asian race (Japanese, Chinese, Korean, Taiwanese, Other)
- Ethnicity (Hispanic or Latino, Not Hispanic or Latino)
- Body weight (kg)
- Body weight category (≤ 100 kg, > 100 kg)
- Height (cm)
- BMI (kg/cm^2)
- BMI category (< 25, ≥ 25 – < 30, ≥ 30)

General Baseline Characteristics

- PASI (Psoriasis Area and Severity Index)
- BSA (Body Surface Area)
- sPGA categories (Static Physician Global Assessment)
- NAPPA-CLIN (Nail Assessment in Psoriasis and Psoriatic Arthritis)
- PSSI (Psoriasis Scalp Severity Index)
- PPASI (Palmoplantar Psoriasis Area Severity Index)
- PSS (Psoriasis Symptom Severity)
- SF-36 (Short Form 36)
- PBI (Patient Benefit Index)
- HADS (Hospital Anxiety & Depression Scale)
- Patient Global Assessment (PtGA)

- EQ-5D-5L (European Quality of Life – 5 Dimensions 5 Level)
- Dermatology Life Quality Index (DLQI)
- CASPAR:
  - Total score
  - Evidence of current personal psoriasis (yes, no)
  - Evidence of history of psoriasis
    - personal history of psoriasis (yes, no)
    - Evidence of family history of psoriasis (yes, no)
  - Psoriatic nail dystrophy (yes, no)
  - Negative test for presence of rheumatoid factor (yes, no)
  - Current or history of dactylitis (yes, no)
  - Radiographic evidence of juxtaarticular bone formation (yes, no)

Disease History

- Time since initial diagnosis of Plaque Psoriasis (years)
- Time since initial symptoms of Plaque Psoriasis (years)
- Prior phototherapy (yes, no)
- For subjects with prior phototherapy: Type of prior phototherapy (UVA, UVB Broad Band, UVB Narrow Band, Balneotherapy, Other) including outcome (success, failure)

General Use

- Smoking history (Never-smoked, Former-smoker, Currently smokes)
- Alcohol History (Non-drinker, Former-drinker, Currently drinks)

Physical Exam and Pregnancy Test will be presented in listing format in the full data listings.

TB History/PPD Test/TB Prophylaxis

- Former BCG vaccination (yes, no)

- Induration of Tuberculin PPD skin test (mm)
- PPD test (positive, negative) – *the PPD test is considered positive for an induration of 5 mm or greater*
- QuantiFERON-TB Gold or equivalent test (positive, negative, indeterminate)
- TB test (positive, negative, indeterminate) – *in the event that both a PPD test and QuantiFERON-TB gold or equivalent test are performed, the result of the QuantiFERON-TB gold or equivalent test will supersede the result of the PPD test*
- Active TB (yes, no)
- Latent TB (yes, no)

7.2 Medical History

Medical history will be summarized using body systems and condition/diagnosis as captured on the eCRF. The body systems will be presented in alphabetical order and the conditions/diagnoses will be presented in alphabetical order within each body system. The number and percentage of subjects with a particular condition/diagnosis will be summarized for each treatment arm. Subjects reporting more than one condition/diagnosis within a body system will be counted only once for that body system.

7.3 Previous Treatment and Concomitant Medications

Prior and concomitant medications will be summarized by generic name, separately for Psoriasis Therapy and other medications, per the category documented on the eCRF. A prior medication is defined as any medication taken prior to the first dose of study drug. A concomitant medication is defined as any medication that started prior to the first dose of study drug and continued to be taken after the first dose of study drug or any medication that started after the first dose of study drug, but not after the last dose of study drug. The number and percentage of subjects who had taken medications will be summarized by generic drug name assigned by the World Health Organization (WHO) for both prior and concomitant medications.

7.4 Protocol Deviations

Number and percentage of subjects who reported at least one of the following protocol deviation categories will be provided.

- Subject entered into the study even though she/he did not satisfy entry criteria
- Subject who developed withdrawal criteria during the study and was not withdrawn
- Subject who received wrong treatment or incorrect dose
- Subject who received excluded or prohibited concomitant treatment

8.0 Patient Disposition

The number of subjects for each of the following categories will be summarized, overall and for each treatment group in the ITT population, overall and per study site:

- Number of subjects randomized
- Number of subjects randomized with prior phototherapy
- Number of subjects treated
- Number of subjects who completed the study
- Number of subjects who discontinued the study drug
- Number of subjects who prematurely discontinued study

In addition, the reasons for premature discontinuation (all reasons and primary reasons) will be summarized with frequencies and percentages.

Beyond patient disposition, number of screening failures and reasons for screening failure will also be summarized among all screened subjects in a subject screening status table.

9.0 Study Drug Exposure and Compliance

Summary of study drug treatment duration and compliance will be provided for each treatment arm in the ITT Population.

Study drug treatment duration (days) will be summarized using the sample size, mean, standard deviation, minimum, first quartile, median, third quartile and maximum. Study drug treatment duration will be summarized as follows:

Risankizumab Exposure (in Days)

Risankizumab Exposure (days) = Date of last injection – Date of first injection + 84 days.

FUMADERM® Exposure (in Days) *[this includes FUMADERM® Initial]*

FUMADERM® Exposure (days) = Date of last dose of oral study drug – date of first dose of oral study drug + 7 days.

For subjects in the FUMADERM® group, there will also be the following analyses

- Interruption of FUMADERM® dosing of more than 7 consecutive days between first and last dose (yes, no)
- For subjects with an interruption of more than 7 consecutive days, total number of days without FUMADERM® dosing between first and last dose

In addition, the total dose of FUMADERM® (mg) and the average daily dose of FUMADERM® (mg) calculated as total dose divided by number of days with doses taken, will be presented. The presentation of average daily dose will be done overall as well as for each week separately.

Compliance

For subjects in the Risankizumab group, there will be a summary of the number of subjects receiving study drug and dose at each study drug administration visit. This will be repeated on the cumulative number of doses.

For subjects in the Risankizumab group, when computing compliance at each study drug administration visit, the denominator will include all subjects in each analysis population who have not prematurely discontinued the study drug prior to the scheduled study drug

injection. Subjects who have prematurely discontinued the study drug but have not prematurely discontinued the study are not used in the denominator.

For subjects in the FUMADERM® group, for each visit (Week 4, 8, 12, 16, 20, 24), the number of subjects deviating from the pre-specified dosing schedule including reasons will be provided, including non-compliance.

10.0 Efficacy Analysis

10.1 General Considerations

The treatment effect will be evaluated based on a two-sided significance level of 0.05 (when rounded to three decimal places).

The ITT population will be used for the analyses of efficacy endpoints.

Subjects' prior phototherapy exposure will be used as the stratum in the stratified analyses.

10.1.1 Analyses of Categorical Variables

For categorical variables, frequencies and percentages will be summarized. Treatment comparison will be conducted using a Cochran-Mantel-Haenszel (CMH) test with the above stratification factor as stratum for the analysis. The CMH test will use weights proposed by Greenland & Robins,[3] which is calculated as follows:

$\hat{\delta}_{MH} = \frac{\sum_{i=1}^{u} w_i \cdot \hat{\delta}_i}{\sum_{i=1}^{u} w_i}$, where

$\hat{\delta}_i = \frac{x_i}{n_i} - \frac{y_i}{m_i}$ denotes the risk difference in stratum $i, i = 1, \cdots, u$

$w_i = \frac{n_i \cdot m_i}{n_i + m_i}$ denotes the weight of stratum $i, i = 1, \cdots, u$

x_i denotes the number of subjects with event in treatment_1 in stratum i, $i = 1, \cdots, u$

y_i denotes the number of subjects with event in treatment_2 in stratum i, $i = 1, \cdots, u$

n_i denotes the number of subjects on treatment_1 in stratum i, $i = 1, \cdots, u$

m_i denotes the number of subjects on treatment_2 in stratum i, $i = 1, \cdots, u$

The estimated variance of $\hat{\delta}_{MH}$ is calculated as:

$$\widehat{var}(\hat{\delta}_{MH}) = \frac{\sum_{i=1}^{u} L_i}{(\sum_{i=1}^{u} w_i)^2}$$

where $L_i = \dfrac{x_i(n_i - x_i)\, m_i^3 + y_i(m_i - y_i)\, n_i^3}{n_i \cdot m_i \cdot (n_i + m_i)^2}$, $i = 1, \cdots, u$

Assuming a normal distribution of $\hat{\delta}_{MH}$, an approximate 95% CI is given as follows, where $z_{0.975}$ is the 97.5% quantile of the standard normal distribution:

$$CI = \left[\hat{\delta}_{MH} \pm z_{0.975} \cdot \sqrt{\widehat{var}(\hat{\delta}_{MH})}\right]$$

Also, the approximate p-value can be calculated using the following:

$$\text{pvalue} = 2 \cdot \Pr\left[Z > \left|\frac{\hat{\delta}_{MH}}{\sqrt{\widehat{var}(\hat{\delta}_{MH})}}\right|\right], \text{where } Z \sim N(0,1)$$

If there is a stratum for a treatment group that has 0 subjects in any cell in the contingency table, all cells from the stratum will be added by 0.1 in order to prevent dividing by 0 in the above equations, as suggested in Greenland & Robins.

10.1.2 Analyses of Continuous Variables

Change from baseline in PSS will be analyzed by stratified van Elteren test. For other continuous variables, the model based mean and standard error will be presented. The Baseline and visit means will also be presented for each treatment group for subjects who have both Baseline and post Baseline visit values. The treatment groups will be compared using ANCOVA with treatment group, Baseline value, and stratification factor in the model.

10.1.3 Missing Data Imputations

Missing data will be imputed using the following methods for the efficacy analyses:

- Non-Responder Imputation (NRI): the NRI analysis will categorize any subject who has a missing value at a specific visit as a non-responder for that visit. The only exception is when the subject is a responder both before and after a specific visit window, and then the subject will be categorized as a responder for the visit. The NRI will be the primary approach in the analyses of categorical variables.
- Last Observation Carried Forward (LOCF): The LOCF analyses will use the completed evaluation from the previous visit for efficacy measures assessed to impute missing data at later visits. Baseline values will not be carried forward. LOCF will be the primary approach in the analyses of continuous variables, and the secondary approach in the analyses of categorical variables.
- As-Observed Cases (OC): The as-observed analysis will not impute values for missing evaluations, and thus a subject who does not have an evaluation on a scheduled visit will be excluded from the as-observed analysis for that visit. As-observed analysis will be the secondary approach in the analysis of continuous variables.
- Multiple Imputation (MI): The MI will be used as sensitivity approach to impute missing data in the primary endpoint. The variables to be included in the imputation model are listed below. If MI is not applicable due to the nature of our data (e.g., MCMC algorithm does not converge), this analysis will not be performed.

The Multiple Imputation analysis will be carried out in three steps.

- Imputation of missing data. The imputation will be generated for the primary endpoint measurement. The variables to be included in the imputation model are: Baseline disease severity (PASI), Baseline weight, treatment group, prior phototherapy exposure, and PASI measurements at each visit from randomization up to the end of the study. For each endpoint, 20 'complete' datasets will be generated using SAS PROC MI. The imputed

post-baseline measurements will be rounded to the same precision as the observed data before the determination of responder status (PASI 90).

- Analysis of imputed data sets. A CMH test, stratified by stratification factor, will be used to analyze categorical endpoints in each imputed dataset. Synthesis of imputation and analysis results. SAS PROC MIANALYZE will be used to generate the final inferences of the risk difference between treatment groups.

Of note, subjects who discontinued due to AE of "worsening of disease under study" will be counted as non-responders in all subsequent visits in the NRI and MI analyses, and will have their last observation prior to discontinuation carried forward in the LOCF analyses.

10.2 Primary Efficacy Analysis

The primary efficacy endpoint is the proportion of subjects with a ≥ 90% reduction from baseline in Psoriasis Area and Severity Index (PASI 90) at Week 24.

The primary null hypothesis is that risankizumab is not different from FUMADERM® in achieving ≥ 90% reduction from baseline in the Psoriasis Area and Severity Index score (PASI 90) at Week 24.

The primary endpoint will be analyzed in the ITT Population. The difference in proportion of subjects achieving PASI 90 between treatment arms will be estimated and tested using the two-sided Cochran-Mantel-Haenszel risk difference estimate stratified by prior phototherapy exposure at level of significance 5%.

Non-responder imputation will be used as the primary approach for missing values. LOCF and MI will be performed as sensitivity analyses.

10.3 Secondary Efficacy Analyses

The secondary endpoints will be analyzed in the ITT Population. The following null hypotheses will be tested using two-sided tests with a type I error of 0.05.

The secondary endpoints are as follows:

- Proportion of subjects with a PASI 50/75/90/100 response at Week 4, 8, 12, 16, 20 and 24.
- Change from baseline in PASI at Week 4, 8, 12, 16, 20 and 24.
- Change from baseline in BSA affected by psoriasis at Week 4, 8, 12, 16, 20 and 24.
- Proportion of subjects with a sPGA of 0 or 1 at Week 4, 8, 12, 16, 20 and 24.
- Proportion of subjects with sPGA of 0 at Week 4, 8, 12, 16, 20 and 24.
- Change from Baseline in PPASI Total Score at Week 16 and 24.
- Change from Baseline in PSSI Total Score at Week 16 and 24.
- Change from Baseline on the NAPPA-CLIN Total Score at Week 16 and 24 (for all subjects and for subjects with NAPPA-CLIN > 0 at baseline).
- Change from Baseline on the NAPSI at Week 16 and 24 (for all subjects and for subjects with NAPSI > 0 at baseline).
- Change from Baseline in Psoriasis Symptom Scale (PSS) total score at Week 16 and 24.
- Proportion of subjects achieving PSS (0) at Week 16 and 24.
- Change from Baseline in DLQI total score at Week 16 and 24.
- Proportion of subject achieving DLQI (0, 1) at Week 16 and 24.
- Change from Baseline in SF-36 PCS and MCS Scores at Week 16 and 24.
- Change from Baseline in PBI at Week 16 and 24
- Change from Baseline on HADS at Week 16 and 24.
- Change from Baseline on PtGA at Week 16 and 24.
- Change from Baseline in EQ-5D-5L Index, EQ-5D Utility Index and VAS at Week 16 and 24.

The order of the secondary endpoints does not reflect a ranking.

10.4 Handling of Multiplicity

The order of the secondary endpoints does not reflect a ranking and secondary endpoints will not be used for confirmatory interpretation, thus no adjustment for multiplicity will be done.

10.5 Efficacy Subgroup Analysis

To evaluate the consistency of the efficacy over demographic and other baseline characteristics, summaries and analyses will be performed for the following subgroups for the primary efficacy endpoint.

- Age (< 40 years, ≥ 40 – < 65 years, ≥ 65 years)
- Sex (male, female)
- Race (white, non-white)
- Smoking (current, former or never)
- BMI (normal: < 25, over weight: ≥ 25 – < 30, obese: ≥ 30)
- Baseline PASI score (by median)
- Baseline sPGA (≤ 2, 3, 4)
- Prior Phototherapy (yes/no)

11.0 Safety Analysis

11.1 General Considerations

Safety evaluations include AE monitoring, physical examinations, vital sign measurements, and clinical laboratory testing (hematology, chemistry, and urinalysis) as a measure of safety and tolerability for the entire study duration. Safety summaries will be provided using the safety population as defined in Section 5.1. Pairwise comparisons of risankizumab vs FUMADERM® will be performed in the Safety Population. AEs will be analyzed using Fisher's exact test, only P values ≤ 0.100, when rounded to three digits, will be presented.

Missing safety evaluations will not be imputed.

11.2 Analysis of Adverse Events

11.2.1 Treatment-Emergent Adverse Events

Treatment-emergent adverse events (TEAE) are defined as events with an onset date on or after the first dose of study drug until 15 weeks (105 days) following the last dose of risankizumab or 1 week (7 days) after the last dose of FUMADERM® or until rollover into the extension study. In a sensitivity analysis, adverse events with an onset date until 7 weeks (49 days) after the last dose of FUMADERM® or until rollover into the extension study will be included. In this sensitivity analysis, the observation period for TEAEs will be identical for both treatment arms, i.e., up to the 31 week safety follow-up call.

SAEs and protocol-related non-serious AEs with onset after informed consent but before the first study drug administration will be considered as pretreatment events and reported separately. Posttreatment events for FUMADERM® are included in the above sensitivity analysis.

If an incomplete onset date is collected for an adverse event, the event will be assumed to be treatment-emergent unless there is other evidence that confirms that the event is not treatment-emergent (e.g., the event end date is prior to the study drug start date).

Summary tables will be presented as follows:

1. **Adverse Event Overview**

   The number and percentage of subjects experiencing treatment-emergent adverse events will be summarized for the following adverse event categories.

   - Any AE
   - Any AE that was assessed as related to study drug by the investigator
   - Any severe AE
   - Any serious AE (SAE)
   - Any SAE that was assessed as related to study drug by the investigator

- Any AE leading to discontinuation of study drug.
- Any AE leading to death.
- Any deaths
- Areas of Safety Interest

2. Adverse Events by System Organ Class and Preferred Term

TEAEs will be summarized and presented using primary Medical Dictionary for Regulatory Activities (MedDRA) system organ classes (SOCs) and preferred terms (PTs). The SOCs will be presented in alphabetical order, and the PTs will be presented in alphabetical order within each SOC.

Subjects reporting more than one adverse event for a given MedDRA preferred term will be counted only once for that term (most severe incident for the severity tables and most related incident for the relationship tables). Subjects reporting more than one type of adverse event within a SOC will be counted only once for that SOC. Subjects reporting more than one type of adverse event will be counted only once in the overall total.

TEAEs will also be summarized presenting PTs in descending order of frequency in the risankizumab arm.

In addition, the number and percentage of adverse events with causal relationship as assessed by the investigator, between the events and the study drug will be summarized using the same conventions described above.

3. Adverse Events by Maximum Severity

The investigator will use the following definitions to rate the severity of each adverse event:

- Mild – The adverse event is transient and easily tolerated by the subject.
- Moderate – The adverse event causes the subject discomfort and interrupts the subject's usual activities.
- Severe – The adverse event causes considerable interference with the subject's usual activities and may be incapacitating or life-threatening.

Adverse events will be summarized by maximum severity. If a subject has an adverse event with unknown severity, then the subject will be counted in the severity category of "unknown," even if the subject has another occurrence of the same event with a severity present. The only exception is if the subject has another occurrence of the same adverse event with the most extreme severity. In this case, the subject will be counted under the "Severe" category.

4. Adverse Events by Maximum Relationship

Adverse events will be summarized by maximum relationship to study drug, as assessed by the investigator. Relationship of an AE to study drug is assessed by the investigator and collected in the CRF as 'Reasonable possibility' or 'No reasonable possibility.' If a subject has an adverse event with unknown relationship, the subject will be counted in the relationship category of "unknown," even if the subject has another occurrence of the same event with a relationship of "No reasonable possibility." If the subject has another occurrence of the same adverse event with a relationship assessment of "Reasonable possibility," the subject will be counted under the "Reasonable possibility" category.

A listing of all pretreatment (i.e., events start prior to the first study drug injection) serious adverse events will be provided.

The following tables are planned.

Treatment-emergent adverse events will be summarized as follows:

- Grouped by SOC and PT
- Grouped by SOC, PT and maximum relationship to study drug
- Grouped by SOC, PT and maximum severity
- By PT in descending order of frequency in the risankizumab arm.

Treatment-emergent SAEs will be summarized as follows:

- Grouped by SOC and PT

- By PT in descending order of frequency in the risankizumab arm.
- A by-subject listing will be provided

Pre-treatment SAEs will be summarized as follows:

- A by-subject listing will be provided

Treatment-emergent adverse events leading to death or premature discontinuation of study drug will be summarized as follows:

- Grouped by SOC and PT
- Separate listings by subject for deaths and premature terminations of study drug due to adverse events will be provided.

Treatment-emergent areas of safety interest will be summarized as follows:

- Grouped by SOC and PT
- A listing by subject will be provided.

Areas of Safety Interest

Areas of Safety Interest groupings are listed in Table 6. These events are of interest due to a higher rate in the moderate to severe psoriasis population, or of interest for all immunoglobulin products or products in general.

Table 6. Areas of Safety Interest

ASI Grouping	Categories (ASI)	Search Criteria	Terms to Display	Include in AE Overview (Y/N)
Adjudicated CV Events	MACE	Adjudicated events	Display underlined terms defined by the following adjudicated terms: • CV Death which includes CETERM values: Fatal CV, Fatal PE, Fatal Non-Cardiac/Non-Neuro Arterial Thrombosis/Thromboembolism, Undetermined Death, Not assessable death (cardiac/neuro/thrombotic), Fatal Stroke • Myocardial infarction • Stroke	Y
	Extended MACE	Adjudicated events	Display underlined terms from MACE and underlined terms below: • Hospitalization for Unstable Angina Coronary Revascularization Procedures	N
Serious infections, TB, fungal and opportunistic infections (including herpes zoster)	Serious infections	SOC Infections and Infestations, serious events only	PTs	Y
	TB	Tuberculosis (including Investigations) CMQ (code 80000033)	PTs	Y
	Opportunistic infections	Opportunistic infections CMQ (code 80000073)	PTs	N

Table 6. Areas of Safety Interest (Continued)

ASI Grouping	Categories (ASI)	Search Criteria	Terms to Display	Include in AE Overview (Y/N)
Serious infections, TB, fungal and opportunistic infections (including herpes zoster) (Continued)	Fungal infections	Fungal infections CMQ (code 80000063)	PTs	N
	Herpes Zoster	Herpes zoster CMQ (code 80000175)	PTs	N
Malignancies	All possible malignancies	Narrow – Malignancies (SMQ 20000090)	PTs	N
	Malignant Tumours	Narrow – Malignant tumours (SMQ 20000194)	PTs	Y
	Non-melanoma skin cancer (NMSC)	Broad – Skin malignant tumours (SMQ 20000204) excluding terms identified by the Melanoma CMQ (code 80000119)	PTs	N
	Malignant Tumours excluding NMSC	'Malignant Tumours excluding NMSC' is identified by the 'Malignant Tumours' search excluding terms identified by the 'Non-melanoma skin cancer (NMSC) search.	PTs	Y

Table 6. Areas of Safety Interest (Continued)

ASI Grouping	Categories (ASI)	Search Criteria	Terms to Display	Include in AE Overview (Y/N)
Hypersensitivity Reaction	Hypersensitivity	Narrow – Hypersensitivity (SMQ 20000214)	PTs	Y – serious events only
	Anaphylactic Reaction	Narrow – Anaphylactic reaction (SMQ 20000021)	PTs	N
Hepatic Events	Hepatic Events	Broad – Hepatic failure, fibrosis and cirrhosis and other liver damage-related conditions (SMQ 20000013) Broad – Hepatitis, non-infectious (SMQ 20000010) Broad – Cholestasis and jaundice of hepatic origin (SMQ 20000009) Broad – Liver related investigations, signs and symptoms (SMQ 20000008) Narrow – Liver-related coagulation and bleeding disturbances (SMQ 20000015)	PTs	N

Adverse Event per 100 Patient-Years of Exposure

AEs occurring during the entire study will be presented by event rate per 100 patient-years. These will be presented for any TEAEs, serious adverse events, Areas of Safety Interest.

AEs per 100 patient-years of exposure is defined as the number of AEs divided by the total exposure in 100 patient-years. Note that one event per preferred term per day per subject will be counted in the calculation of the number of AEs (i.e., a preferred term will not be counted twice on the same day for the same subject). See the calculation method below.

$$100 \times \frac{\text{Number of TEAEs}}{\text{Total Patient Years}}$$

where total patient years is defined as the sum of the study drug exposure (defined as date of last dose – date of first dose + 105 days or + 7 / 49 (sensitivity analysis) days for risankizumab or FUMADERM®, respectively) of all subjects normalized by 365.25, and rounded to one decimal place.

11.2.2 SAEs (Including Deaths) and Adverse Events Leading to Study Drug Discontinuation

Deaths and all SAEs will be presented in listing format. In addition, SAEs will be summarized by System Organ Class and MedDRA Preferred Term.

11.2.3 Safety Subgroup Analysis

The AE overview and AE by SOC and preferred term will also be analyzed by stratification factor prior phototherapy (yes, no) as well as gender (male, female), age (< 65 years; 65 – 74 years; ≥ 75 years) and weight (≤ 100 kg, > 100 kg).

11.3 Analysis of Laboratory Data

For the assessments of laboratory data, values observed more than 105 days after the last dose of risankizumab and 7 days after the last dose of FUMADERM will be excluded (see Section 6.0, Definition of final observation).

Listing and descriptive statistics of laboratory values over time, change from baseline, and extreme abnormal value on treatment will be provided. Extreme abnormal value is the value which is most significantly away from the reference range. Frequency of subjects with transitions relative to reference range and listing of subjects with significant abnormal laboratory values will be presented as well.

11.3.1 Variables and Criteria Defining Abnormality

Clinical laboratory tests performed by central laboratory service provider are listed below.

Table 7. Clinical Laboratory Tests

Category	Test Name
Hematology	Hematocrit (Hct) Hemoglobin (Hb) White Blood Cells/Leukocytes Platelet Count/Thrombocytes
Diff. Automatic	Neutrophils (absolute count) Lymphocytes (absolute count)
Enzymes	AST (GOT) ALT (GPT) Alkaline Phosphatase (ALP) Creatine Kinase (CPK) Gamma-glutamyl gransferase (GGT/γ-GT)
Electrolytes	Calcium Sodium Potassium
Substrates	Glucose Creatinine Bilirubin Total (TBL) Bilirubin Direct (if total is elevated) Albumin C-Reactive Protein (CRP) (high sensitivity) Cholesterol, total[a] Triglycerides[a] LDL-Cholesterol[a] HDL-Cholesterol[a]
Urine	UACR

a. To be done at screening only.

11.3.2 Statistical Methods

Analysis of Continuous Laboratory Parameters

Analyses of laboratory data will presented based on the National Cancer Institute Common Toxicity Criteria for Adverse Event (NCI CTCAE) scale. Change from Baseline to each scheduled visit and to the final value in continuous laboratory parameters will be summarized with the mean, standard deviation and median. The Baseline and visit/final value means will also be presented for subjects who have both the Baseline and

visit/final values (see Section 6.0 for the definition of Baseline and final values). If there are multiple post-baseline measurements on the same day, the average value will be used.

Shift Tables

Shift tables for changes from Baseline according to the normal range will be provided for each hematology and clinical chemistry parameter. Shifts from Baseline to the following endpoints will be considered: minimum value, maximum value and final value. Categories of "low or normal" and "high or normal" will be included at Baseline in addition to the categories of "low," "normal," "high" and "missing." If there are multiple measurements on the same day, the last value will be used.

Potentially Clinically Important Laboratory Values

Frequencies and percentages of subjects with post Baseline lab values meeting the following criteria will be summarized.

Table 8. Criteria for Potentially Clinically Important Chemistry Values

		Definition of Potentially Clinically Important Current (Version 4) NCI CTCAE Grade 3 or Greater	
Chemistry Variables	**Units**	**Very Low**	**Very High**
TBL	mcmol/L		> 3.0 × ULN
SGOT/AST	U/L		> 5.0 × ULN
SGPT/ALT	U/L		> 5.0 × ULN
Albumin	g/L	< 20	
Glucose	mmol/L	< 2.2	> 13.9
Triglycerides	mmol/L		> 5.7
Creatinine	mcmol/L		> 3.0 × ULN
Sodium	mmol/L	< 130	> 155
Potassium	mmol/L	< 3.0	> 6.0
Calcium	mmol/L	< 1.75	> 3.1
CPK	U/L		> 5.0 × ULN
Total Cholesterol	mmol/L		> 10.34
GGT			> 5.0 × ULN
ALP			> 5.0 × ULN

Table 9. Criteria for Potentially Clinically Important Hematology Values

		Definition of Potentially Clinically Important Current (Version 4) Grade 3 or Greater
Hematology Variables	**Units**	**Very Low**
Hemoglobin	g/dL	< 8.0
Platelets count	10^9/L	< 50.0
WBC count	10^9/L	< 2.0
Neutrophils	10^9/L	< 1.0
Lymphocytes	10^9/L	< 0.5

A separate listing will be provided that presents all of the subjects and values that are NCI CTCAE toxicity grade 3 or above. For each of these subjects, the whole course of the respective parameter will be listed. The NCI CTCAE grading is shown in Table 10 below:

Table 10. NCI CTCAE Grading

Test	Grade 1	Grade 2	Grade 3	Grade 4
SGPT/ALT increased	> ULN – 3.0 × ULN	> 3.0 – 5.0 × ULN	> 5.0 – 20.0 × ULN	> 20.0 × ULN
SGOT/AST increased	> ULN – 3.0 × ULN	> 3.0 – 5.0 × ULN	> 5.0 – 20.0 × ULN	> 20.0 × ULN
GGT increased	> ULN – 2.5 × ULN	> 2.5 – 5.0 × ULN	> 5.0 – 20.0 × ULN	> 20.0 × ULN
ALP increased	> ULN – 3.0 × ULN	> 3.0 – 5.0 × ULN	> 5.0 – 20.0 × ULN	> 20.0 × ULN
TBL increased	> ULN – 1.5 × ULN	> 1.5 – 3.0 × ULN	> 3.0 – 10.0 × ULN	> 10.0 × ULN
Creatinine increased	> ULN – 1.5 × ULN	> 1.5 – 3.0 × ULN	> 3.0 – 6.0 × ULN	> 6.0 × ULN
CPK increased	> ULN – 2.5 × ULN	> 2.5 – 5.0 × ULN	> 5.0 – 10.0 × ULN	> 10.0 × ULN
Hemoglobin decreased	< LLN – 100.0 g/L	< 100.0 – 80.0 g/L	< 80.0 – 65.0 g/L	N/A
Neutrophil count decreased	< LLN – 1.5 × 10^9/L	< 1.5 – 1.0 × 10^9/L	< 1.0 – 0.5 × 10^9/L	< 0.5 × 10^9/L
WBC decreased	< LLN – 3.0 × 10^9/L	< 3.0 – 2.0 × 10^9/L	< 2.0 – 1.0 × 10^9/L	< 1.0 × 10^9/L
Lymphocyte count decreased	< LLN – 0.8 × 10^9/L	< 0.8 – 0.5 × 10^9/L	< 0.5 – 0.2 × 10^9/L	< 0.2 × 10^9/L

If there are multiple post-baseline measurements on the same day, the worst value will be used.

Liver Function Tests

Additional summaries will be presented for liver function tests including ALT or serum glutamic-pyruvic transaminase (SGPT), AST or serum glutamic-oxaloacetic transaminase (SGOT), alkaline phosphatase, and total bilirubin. Each laboratory value will be categorized as follows:

- < 1.5 × ULN
- ≥ 1.5 × ULN – < 3.0 × ULN
- ≥ 3.0 × ULN – < 5.0 × ULN
- ≥ 5.0 × ULN – < 10.0 × ULN
- ≥ 10.0 × ULN – < 20.0 × ULN

- ≥ 20.0 × ULN

Shift tables of Baseline to the maximum (relative to the normal range, i.e., the largest multiple relative to the upper limit of normal) values, and from Baseline to final value will be presented using these categories. A listing of potentially clinically important liver function laboratory values will be provided. The listing will include all subjects who met any of the following four criteria:

- ALT ≥ 3 × ULN, or
- AST ≥ 3 × ULN, or
- Alkaline phosphatase ≥ 1.5 × ULN, or
- Total bilirubin ≥ 2 × ULN.

A listing of possible Hy's Law cases, defined as those who meet all of the following conditions will be provided:

- ALT > 3 × ULN or AST > 3 × ULN
- Associated with an increase in bilirubin ≥ 2 × ULN
- Alkaline phosphatase < 2 × ULN.

In addition, a graphical summary highlighting potential cases of Hy's Law within each treatment group will be presented. The maximum on-treatment values of total bilirubin and ALT will be plotted each on a scale as multiples of the upper limit of normal. The figure will show areas that meet the criteria of cholestasis (total bilirubin > 2 × ULN), Temple's corollary (ALT > 3 × ULN) and Hy's Law as the combination of these two factors.

All analyses will be conducted in the Safety Population.

11.4 Analysis of Vital Signs and Weight

11.4.1 Variables and Criteria Defining Abnormality

The following vital sign parameters will be assessed: Systolic blood pressure [mmHg], Diastolic blood pressure [mmHg], Pulse [beats per minute], Respiratory rate [breaths per minute], Temperature [°C], Weight [kg]. The following table presents the Criteria for Potentially Clinically Important Vital Sign Findings.

Table 11. Criteria for Potentially Clinically Important Vital Sign Findings

Vital Sign	Category	Criteria for Potential Clinically Important Vital Signs
Systolic Blood Pressure	Low Value	≤ 90 mmHg and decrease ≥ 20 mmHg from Baseline
	High Value	≥ 160 mmHg and increase ≥ 20 mmHg from Baseline
Diastolic Blood Pressure	Low Value	≤ 50 mmHg or decrease ≥ 15 mmHg from Baseline
	High Value	≥ 105 mmHg or increase ≥ 15 mmHg from Baseline
Pulse	Low Value	≤ 50 bpm or decrease ≥ 15 bpm from Baseline
	High Value	≥ 120 bpm or increase ≥ 15 bpm from Baseline
Respiratory rate	High Value	> 3/min increase from Baseline

11.4.2 Statistical Methods

Changes from Baseline to each visit and to the final value in vital sign parameters will be summarized with the mean, standard deviation and median. The Baseline and final value means will also be presented for subjects who have both the Baseline and final values (see Section 6.0 for the definition of Baseline and final values).

For baseline, if there are multiple measurements on the same day, the last measurement prior to the first dose of study drug will be used as the Baseline vital sign value. If there are multiple post-baseline measurements on the same day, average value will be used.

For systolic blood pressure, diastolic blood pressure and pulse, a listing of all subjects with any vital sign value meeting criteria for potentially clinically important values will be provided. For each of these subjects, the whole course of the respective parameter will be

listed. The number and percentage of subjects who have at least one value meeting criteria for potentially clinically important values will be provided for each selected vital sign parameter.

All analyses will be conducted in the Safety Population.

11.5 Analysis of ECG Parameters

No analyses of ECG will be done.

12.0 Pharmacokinetic Analysis

Pharmacokinetic analysis is not covered in this SAP.

13.0 Biomarkers Analysis

Biomarkers Analysis is not covered in this SAP.

14.0 Summary of Changes

14.1 Summary of Changes Between the Latest Version of Protocol and the Current SAP

In Section 10.1.2 of this SAP, the strategy for analysis of continuous endpoints was further refined. The protocol had specified ANOVA with treatment group and stratification factor in the model. The SAP now clarifies that for change from baseline in PSS a stratified van Elteren test will be used. For other continuous variables, treatment groups will be compared using ANCOVA with treatment group, Baseline value, and stratification factor in the model. This modification was done to align the study with the other studies in the Risankizumab Psoriasis development program.

In Section 10.3, NAPSI was added as a secondary endpoint to make optimal use of the data collected for NAPPA-CLIN assessments.

15.0 Appendix

Appendix A. PASI Calculation

The PASI score is calculated according to the following formula:

$$PASI = 0.1(E_h+I_h+D_h)A_h + 0.3(E_t+I_t+D_t)A_t + 0.2(E_u+I_u+D_u)A_u + 0.4(E_l+I_l+D_l)A_l$$

where E, I, D, and A denote erythema, induration, desquamation, and area, respectively, and h, u, t, and l denote head, upper extremities, trunk, and lower extremities, respectively. PASI scores range from 0.0 to 72.0 with the highest score representing complete erythroderma of the severest degree.

Appendix B. sPGA Calculation

The sPGA is a 5 point score ranging from 0 to 4, based on the physician's assessment of the average thickness, erythema, and scaling of all psoriatic lesions.

Erythema, induration and scaling of all psoriatic lesions are scored from 0 – 4. The composite score is the arithmetic mean of erythema, induration and scaling. The final sPGA is determined from this score as follows:

- Clear 0 = 0 for all three
- Almost clear 1 = mean > 0, < 1.5
- Mild 2 = mean ≥ 1.5, < 2.5
- Moderate 3 = mean ≥ 2.5, < 3.5
- Severe 4 = mean ≥ 3.5

Appendix C. PPASI Calculation

The PPASI is a composite score and will be computed for each palm and sole, left and right and is derived from the sum of the scores for erythema (E), induration (I) and desquamation (D) multiplied by the score recorded for the extent of palm and sole area involved. PPASI is calculated as follows: (sum of scored for E + I + D)*Area *0.2

(location: right palm) + (sum of scored for E + I + D)*Area *0.2 (location: left palm) + (sum of scored for E+I+D)*Area *0.3(location: right sole) + (sum of scores for E+I+D)*Area *0.3 (location: left sole). The range is 0 to 72.

Appendix D. PSSI Calculation

The PSSI is a composite score derived from the sum of the scores for erythema, induration and desquamation multiplied by the score recorded for the extent of scalp area involved. The range is 0 to 72.

Appendix E. NAPPA-CLIN Calculation

The NAPPA-CLIN is calculated by summing the number of quadrants of the nail affected by a nail matrix psoriasis and number of quadrants of the nail affected by a nail bed psoriasis for the least and the worst affected nail for both hands and/or both feet.

Appendix F. NAPSI Calculation

The NAPSI score is calculated by summing the scores of all the nails which for each nail are the sum of the nail matrix score and nail bed score. Each of these is scored as 0 = none, 1 = present in 1/4 nail, 2 = present in 2/4 nail, 3 = present in 3/4 nail, 4 = present in 4/4 nail. The NAPSI score is calculated only if all questions in the CRF are completed.

Appendix G. PSS Calculation

The total PSS score is calculated by summing the score of each question. Each question of the PSS is scored as 0 = none to 4 = very severe. If one or more of the items are missing, the total score will be set to missing.

Appendix H. DLQI Calculation

The DLQI score is calculated by summing the score of each question. Each question of the DLQI is scored as 0 = not at all, 1 = a little, 2 = a lot, 3 = very much, 0 = not relevant. For question no. 7, yes is scored as 3. If one or more of the items are missing, the total score will be set to missing.

Appendix I. SF-36 Calculation

The SF-36 (version 2.0) PCS and MCS scores will be calculated as described in 'SF-36 health survey update. Spine, 2000,' and rounded to 0.1. If one or more of the items are missing, the total score will be set to missing.

Appendix J. PBI Calculation

PBI is the arithmetic mean of all rated benefits (PBQ items) weighted by the relative importance of each corresponding need item (PNQ). Each question of PBQ and PNQ is scored as 0 = not at all, 1 = somewhat, 2 = moderately, 3 = quite, 4 = very.

$$\text{PBI} = \sum_{i=1}^{k} \frac{PNQ_i}{\sum_{j=1}^{k} PNQ_j} \; PBQ_i$$

If one or more of the items are missing, the total score will be set to missing.

Appendix K. HADS Calculation

The HADS considers anxiety and depression. Each question of HADS anxiety and depression is scored as 0 = best to 3 = worst. The scores are summed up to a total score separately for anxiety and depression. If one or more of the four items are missing, the total score will be set to missing. These total scores are categorized as normal (0 – 7), borderline abnormal (8 – 10) and abnormal (11 – 21) for anxiety and depression. If one or more of the items are missing, the total score will be set to missing.

Appendix L. EQ-5D-5L Calculation

For calculation of a single index value the German EQ-5D-5L Crosswalk Value Set[4] is used. If one or more of the items are missing, the total score will be set to missing.

Appendix M. CASPAR Calculation

The score is only calculated as total score based on the sum of 6 questions, if the number of non-missing questions ≥ 3. Allocate 2 points if there is an evidence of current personal psoriasis and allocate 1 point for the other questions if the response is "Yes."

If there is an evidence of current personal history the total score is calculated as sum of all questions other than question 3 (history of Ps). Otherwise the total score is calculated based on the sum of all questions.

16.0 References

1. AbbVie. Risankizumab Investigator's Brochure Edition 1. 22 December 2016.
2. Mrowietz U, Christophers E, Altmeyer P, et al. Treatment of psoriasis with fumaric acid esters: results of a prospective multicenter study. Br J Dermatol. 1998;138(3):456-60.
3. Greenland S, Robins JM. Estimation of a common effect parameter from sparse follow-up data. Biometrics. 1985;41(1):55-68.
4. Van Reenen M, Janssen M. EQ-5D-5L user guide: basic information on how to use the EQ-5D-5L instrument. April 2015. Version 2.1.

17.0 List of Tables, Figures, and Data Listings to Be Programmed

To be provided in a separate document.

Document Approval

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[redacted]	12-Jan-2018 08:35:48 AM	Author
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