1.0 Title Page

Statistical Analysis Plan

Study M15-997

A multicenter, open Label study to assess the safety and efficacy of rIsankizuMab for MaInTenance in moderate to severe pLaquE type pSoriaSis

(LIMMITLESS)

Date: 14 January 2022

Version 2.0

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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 M15-997 Amendment 8 dated 18 October 2021.

This SAP will provide details to further elaborate statistical methods as outlined in the Protocol M15-997 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 Primary Study Objective

The primary objective of Study M15-997 is to investigate long-term safety and tolerability of risankizumab in subjects with psoriasis who have completed one of the preceding Phase 2/3 studies.

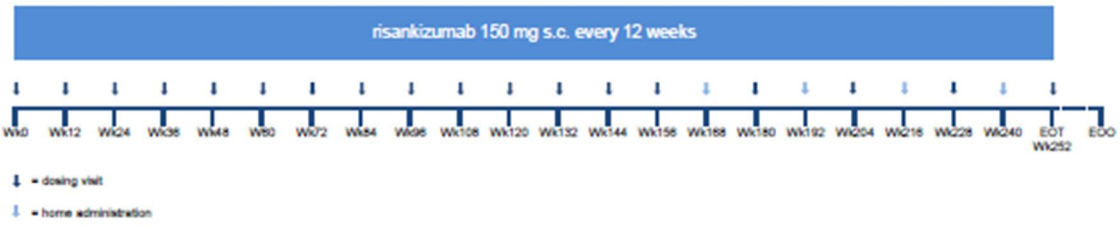
The secondary objective of Study M15-997 is to investigate the long-term efficacy of risankizumab in the treatment of psoriasis.

4.2 Design Diagram

This is a Phase 3, single-arm, multicenter, OLE study designed to investigate the long term safety and efficacy of risankizumab 150 mg E12W in the treatment of moderate to severe chronic plaque psoriasis. Approximately 2200 subjects who meet the entry criteria are planned to be enrolled in this study, rolling over from the preceding Studies 1311.3, 1311.4, 1311.13, 1311.28, 1311.30, 1311.38, and M16-178 (Phase 2/3, randomized clinical studies in subjects with moderate to severe chronic plaque psoriasis, conducted by Boehringer Ingelheim or AbbVie).

All subjects need to complete one of the preceding Phase 2/3 psoriasis studies. The subject preferably has the Baseline visit of Study M15-997 on the same day of the completion visit of the preceding study; however, the Baseline visit can be delayed up to 8 weeks if needed. All subjects will be administered 150 mg risankizumab s.c. at the Baseline visit, and from the Baseline visit onwards, risankizumab will be administered subcutaneously E12W during the study. Study visits for dosing, efficacy and safety assessments will be performed E12W starting from Baseline until the Week 156 visit. After this visit until the End of Treatment (EOT) visit at Week 252, study visits will be performed E24W. The schematic of the study is shown in Figure 1.

Figure 1. Study Schematic



There is a ± 7 days visit window for study visits. Every effort will be made to bring subjects back to their original scheduled visit (calculated from Baseline) if they are out of the visit window. Subjects who discontinue study drug treatment early will need to attend an early EOT visit ideally within 2 weeks after the decision and preferably prior to the administration of any new therapies.

All subjects, including those that prematurely discontinued study drug treatment, will return to the clinic for an End of Observation Visit (EOO) 20 weeks after their last administered dose of risankizumab. Study completion is defined as a subject having completed the EOO visit.

4.3 Sample Size

The sample size is determined by the completion of preceding studies and the consenting for the extension.

Multiple clinical studies will be rolling into this OLE study. Eligible subjects from Studies 1311.3, 1311.4, 1311.13 (extension study of 1311.2), 1311.28, 1311.30, 1311.38, and M16-178 will be offered participation in this OLE study at their respective or referring sites. The check for subject eligibility will be based upon a successful completion of the preceding study, signing the informed consent for this study, and the other inclusion and exclusion criteria.

A 10% to 15% dropout rate from preceding studies is expected, leaving approximately 2200 subjects to be entered in this study.

4.4 Interim Analysis

The first interim analysis was performed in 2017, after the last patient in Study 1311.4 either had completed Week 52 visit or discontinues from the study, and at the time approximate to the database lock of all other preceding studies, whichever occurs later, to generate sufficient evidence for long-term safety and efficacy of risankizumab in subjects with psoriasis.

To support regulatory activities in Switzerland, a second interim analysis will be conducted to include all available patient data up to the data cut-off date of November 01, 2021.

Additional interim analyses may be performed based on regulatory or other requirements.

5.0 Analysis Populations

Subjects are required to have at least one dose of risankizumab in Study M15-997 to be included in any of the analysis populations.

5.1 Definition for Analysis Populations

RZB Population:

The RZB population consists of subjects who were randomized to risankizumab 150 mg in Studies 1311.3, 1311.30, 1311.28, 1311.38, and M16-178. This population will be used to evaluate the long-term safety and efficacy of risankizumab 150 mg with loading dose. For subjects from Japan, data after the first dose of risankizumab 150 mg from the preceding studies, and prior to the start of 75 mg dose will be used for the analyses.

RZB_NL Population:

The RZB_NL population consists of subjects who were randomized to placebo in the initial study and switched to risankizumab 150 mg (without loading dose) in Studies 1311.3, 1311.4, 1311.28, and 1311.38. This population will be used to evaluate the long-term safety and efficacy of risankizumab 150 mg without initial loading dose. For subjects from Japan, data after the first dose of risankizumab 150 mg from the preceding studies, and prior to the start of 75 mg dose will be used for the analyses.

Retreatment Population:

The Retreatment population consists of subjects who were re-randomized to placebo in Part B of Study 1311.4 and received retreatment of risankizumab 150 mg. This population will be used to evaluate the safety and efficacy of re-treatment after temporary withdrawal. For subjects from Japan, data after the re-treatment and prior to the start of 75 mg dose will be used for the analyses.

UST_RZB Population:

The UST_RZB population consists of subjects who were randomized to ustekinumab in Studies 1311.3 and 1311.28. This population will be used to assess the safety and efficacy of risankizumab 150 mg when subjects switch from ustekinumab to risankizumab

150 mg. For subjects from Japan, data prior to the start of 75 mg dose will be used for the analyses.

ADA_RZB Population:

The ADA_RZB population consists of subjects who were randomized to adalimumab in Study 1311.30 and switched to risankizumab. This population will be used to assess the safety and efficacy of risankizumab when subjects from adalimumab to risankizumab.

FUM_RZB Population:

The FUM_RZB Population consists of subjects who were randomized to Fumaderm® (fumaric acid esters) in Study M16-178. This population will be used to assess the safety and efficacy of risankizumab when subjects switch from Fumaderm® to risankizumab.

RZB_Japan Population:

The RZB Japan Population consists of subjects from Japan during the visits in the OLE period, regardless of dose. This population will be used to assess safety and efficacy during the OLE period, regardless of dose. The RZB Japan Population will only be analyzed in the final analysis, upon study completion.

All Risankizumab Treated (ALL_RZB) Population:

The All Risankizumab Treated Population consists of subjects who received at least one dose of risankizumab in this Study M15-997. This population will be used to provide a comprehensive summary of safety, and will be summarized by risankizumab 150 mg, and by any dose of risankizumab.

5.2 Variables Used for Stratification of Randomization

For this open-label study, no randomization of subjects into different treatment groups or stratification of randomization is required.

6.0 Analysis Conventions

Since this is an open-label continuation study, no statistical test will be conducted. Summary statistics will be provided. Data from preceding studies will be integrated with data from this study in the summaries.

Definition of Baseline

For this study, the following two types of baseline values are defined.

1. Preceding Study Baseline Value (BL): These values represent the baseline values of preceding studies, that is, the last non-missing values on or before the date of the first dose of study drug in the preceding study. For vital sign assessments, only assessments prior to first dose time will be considered, since vital signs are to be assessed both pre- and post-dose in some visits. The efficacy analysis based on RZB, RZB_NL, Retreatment, UST_RZB, ADA_RZB, FUM_RZB, and RZB_Japan populations will use these baseline values. These baseline values will be referred to as "BL" in this document. Unless otherwise specified, this will be the "baseline" for analysis.
2. RZB baseline value (BL_RZB): These values are the last non-missing values on or before the date of the first dose of risankizumab in the preceding study or Study M15-997. For vital sign assessments, only assessments prior to first dose time will be considered, since vital signs are to be assessed both pre- and post-dose in some visits. These values will be referred to as BL_RZB in this document. BL_RZB will be used for safety analyses in all populations.

Definition of Final Observation (Applicable to Safety Analyses)

Final observation in the entire study is defined as the last non-missing observation collected within 140 days after the last dose of risankizumab.

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 risankizumab in the corresponding study period. They are defined as the number of days between the day of the first dose of risankizumab and the specific time point. Rx days are negative values when the time point of interest is prior to the first risankizumab dose day. Rx days are positive values when the time point of interest is on or after the first risankizumab dose day. The day of the first dose of risankizumab is defined as Rx Day 1, while the day prior to the first risankizumab 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.

For efficacy analyses, local tolerability, laboratory parameters, and vital sign variables, 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 risankizumab (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 2 and Week 4 is 14). 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 2 and Week 4 would be between Rx Days 22 and 23).
- 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 one after the nominal day will be used in analyses. If more than one post baseline 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.

The protocol specified visits and corresponding time windows used in the efficacy analyses, local tolerability, laboratory parameters, and vital sign variables, are presented in the following tables.

Table 1. Visit Windows for Analysis of PASI, sPGA, Local Tolerability Assessment, Clinical Laboratory Tests, and Vital Signs (RZB Population)

Window Label	Target Day	Interval
Baseline[a]	1	≤ 1[b]
Week 4	29	[2, 43]
Week 8	57	[44, 71]
Week 12	85	[72, 99]
Week 16	113	[100, 155]
Week 28	197	[156, 239]
Week 40	281	[240, 323]
Week 52	365	[324, 407]
Week 64	449	[408, 491]
Week 76	533	[492, 575]
Week 88	617	[576, 659]
Week 100	701	[660, 743]
Week 112	785	[744, 827]
Week 124	869	[828, 911]
Week 136	953	[912, 995]
Week 148	1037	[996, 1079]
Week 160	1121	[1080, 1163]
Week 172	1205	[1164, 1247]
Week 184	1289	[1248, 1331]
Week 196	1373	[1332, 1415]
Week 208	1457	[1416, 1541]
Week 232	1625	[1542, 1709]
Week 256	1793	[1710, 1877]
Week 280	1961	[1878, 2045]
Week 304	2129	[2046, 2199]

a. There is no baseline for local tolerability measurements.

b. If time is collected in vital signs, restrict to records prior to the first dose of study drug.

Note: Rx Day calculated relative to first dose date of risankizumab.

Table 2. Visit Windows for Analysis of Efficacy Variables (DLQI/NAPSI/PSSI/PPASI) (RZB Population)

Window Label	Target Day	Interval
Baseline	1	≤ 1
Week 16	113	[2, 239]
Week 52	365	[240, 449]
Week 76	533	[450, 617]
Week 100	701	[618, 785]
Week 124	869	[786, 953]
Week 148	1037	[954, 1121]
Week 172	1205	[1122, 1289]
Week 196	1373	[1290, 1415]
Week 208	1457	[1416, 1541]
Week 232	1625	[1542, 1709]
Week 256	1793	[1710, 1877]
Week 280	1961	[1878, 2045]
Week 304	2129	[2046, 2199]

Note: Rx Day calculated relative to first dose date of risankizumab.

Table 3. Visit Windows for Analysis of PASI, sPGA, Local Tolerability Assessment, Clinical Laboratory Tests, and Vital Signs (RZB_NL Population)

Window Label	Target Day	Interval
Switch to RZB	1	≤ 1[a]
Week 12S	85	[2, 127]
Week 24S	169	[128, 211]
Week 36S	253	[212, 295]
Week 48S	337	[296, 379]
Week 60S	421	[380, 463]
Week 72S	505	[464, 547]
Week 84S	589	[548, 631]
Week 96S	673	[632, 715]
Week 108S	757	[716, 799]
Week 120S	841	[800, 883]
Week 132S	925	[884, 967]
Week 144S	1009	[968, 1051]
Week 156S	1093	[1052, 1135]
Week 168S	1177	[1136, 1219]
Week 180S	1261	[1220, 1303]
Week 192S	1345	[1304, 1429]
Week 216S	1513	[1430, 1597]
Week 240S	1681	[1598, 1765]
Week 264S	1849	[1766, 1933]
Week 288S	2017	[1934, 2087]

S = Switch to Risankizumab

a. If time is collected in vital signs, restrict to records prior to the first dose after switch to RZB.

Note: Rx Day calculated relative to first dose date of risakizumab for subjects switched from Placebo.

Table 4. Visit Windows for Analysis of Efficacy Variables (DLQI/NAPSI/PSSI/PPASI) (RZB_NL Population)

Window Label	Target Day	Interval
Switch to Risankizumab	1	≤ 1
Week 36S	253	[2, 337]
Week 60S	421	[338, 505]
Week 84S	589	[506, 673]
Week 108S	757	[674, 841]
Week 132S	925	[842, 1009]
Week 156S	1093	[1010, 1177]
Week 180S	1261	[1178, 1303]
Week 192S	1345	[1304, 1429]
Week 216S	1513	[1430, 1597]
Week 240S	1681	[1598, 1765]
Week 264S	1849	[1766, 1933]
Week 288S	2017	[1934, 2087]

S = Switch to Risankizumab

Note: Rx Day calculated relative to first dose date of risankizumab for subjects switched from Placebo.

Table 5. Visit Windows for PASI and sPGA (Relapsed and Retreatment Subjects in Retreatment Population)

Window Label	Target Day	Interval
Entry of Retreatment	1	≤ 1
Week 8R	57	[2, 85]
Week 16R	113	[86, 155]
Week 28R	197	[156, 239]
Week 40R	281	[240, 323]
Week 52R	365	[324, 407]
Week 64R	449	[408, 491]
Week 76R	533	[492, 575]
Week 88R	617	[576, 659]
Week 100R	701	[660, 743]
Week 112R	785	[744, 827]
Week 124R	869	[828, 911]
Week 136R	953	[912, 995]
Week 148R	1037	[996, 1079]
Week 160R	1121	[1080, 1163]
Week 172R	1205	[1164, 1289]
Week 196R	1373	[1290, 1457]
Week 220R	1541	[1458, 1625]
Week 244R	1709	[1626, 1793]
Week 268R	1877	[1794, 1961]
Week 292R	2045	[1962, 2115]

R = Retreatment of Risankizumab

Note: Rx Day calculated relative to first dose date of retreatment with risankizumab.

Table 6. Visit Windows for PASI and sPGA (OLE Retreated Subjects in Retreatment Population)

Window Label	Target Day	Interval
Entry of OLE	1	≤ 1
Week 12R	85	[2, 127]
Week 24R	169	[128, 211]
Week 36R	253	[212, 295]
Week 48R	337	[296, 379]
Week 60R	421	[380, 463]
Week 72R	505	[464, 547]
Week 84R	589	[548, 631]
Week 96R	673	[632, 715]
Week 108R	757	[716, 799]
Week 120R	841	[800, 883]
Week 132R	925	[884, 967]
Week 144R	1009	[968, 1051]
Week 156R	1093	[1052, 1177]
Week 180R	1261	[1178, 1345]
Week 204R	1429	[1346, 1513]
Week 228R	1597	[1514, 1681]
Week 252R	1765	[1682, 1849]

R = Retreatment of Risankizumab

Note: Rx Day calculated relative to first dose date of retreatment with risankizumab.

Table 7. Visit Windows for DLQI, NAPSI, PSSI, and PPASI (OLE Retreated Subjects in Retreatment Population)

Window Label	Target Day	Interval
Entry of OLE	1	≤ 1
Week 24R	169	[2, 253]
Week 48R	337	[254, 421]
Week 72R	505	[422, 589]
Week 96R	673	[590, 757]
Week 120R	841	[758, 925]
Week 144R	1009	[926, 1093]
Week 156R	1093	[1094, 1177]
Week 180R	1261	[1178, 1345]
Week 204R	1429	[1346, 1513]
Week 228R	1597	[1514, 1681]
Week 252R	1765	[1682, 1849]

R = Retreatment of Risankizumab

Note: Rx Day calculated relative to first dose date of retreatment with risankizumab.

Table 8. Visit Windows for PASI, sPGA, Local Tolerability Assessment, Clinical Laboratory Tests, and Vital Signs (ADA_RZB Population)

Window Label	Target Day	Interval
Switch at Week 16		RxDay_B
Switch to Risankizumab	1	≤ 1[a]
Week 4S	29	[2, 43]
Week 8S	57	[44, 71]
Week 12S	85	[72, 99]
Week 16S	113	[100, 127]
Week 20S	141	[128, 155]
Week 24S	169	[156, 183]
Week 28S	197	[184, 239]
Week 40S	281	[240, 323]
Week 52S	365	[324, 407]
Week 64S	449	[408, 491]
Week 76S	533	[492, 575]
Week 88S	617	[576, 659]
Week 100S	701	[660, 743]
Week 112S	785	[744, 827]
Week 124S	869	[828, 911]
Week 136S	953	[912, 995]
Week 148S	1037	[996, 1079]
Week 160S	1121	[1080, 1163]
Week 172S	1205	[1164, 1247]
Week 184S	1289	[1248, 1373]
Week 208S	1457	[1374, 1541]
Week 232S	1625	[1542, 1709]
Week 256S	1793	[1710, 1877]
Week 280S	1961	[1878, 2031]

Table 8. Visit Windows for PASI, sPGA, Local Tolerability Assessment, Clinical Laboratory Tests, and Vital Signs (ADA_RZB Population) (Continued)

Window Label	Target Day	Interval
Switch at OLE		RxDay_OL
Entry of OLE	1	≤ 1[a]
Week 12S	85	[2, 127]
Week 24S	169	[128, 211]
Week 36S	253	[212, 295]
Week 48S	337	[296, 379]
Week 60S	421	[380, 463]
Week 72S	505	[464, 547]
Week 84S	589	[548, 631]
Week 96S	673	[632, 715]
Week 108S	757	[716, 799]
Week 120S	841	[800, 883]
Week 132S	925	[884, 967]
Week 144S	1009	[968, 1051]
Week 156S	1093	[1052, 1177]
Week 180S	1261	[1178, 1345]
Week 204S	1429	[1346, 1513]
Week 228S	1597	[1514, 1681]
Week 252S	1765	[1682, 1835]

S = Switch to Risankizumab

a. If time is collected in vital signs, restrict to records prior to the first dose after switch to RZB.

Note: RxDay_B calculated relative to the first dose date in Part B.
RxDay_OL calculated relative to the first dose date of OLE.

Table 9. Visit Windows for NAPSI, PPASI, PSSI, and DLQI (ADA_RZB Population)

Window Label	Target Day	Interval
Switch at Week 16		RxDay_B
Switch to Risankizumab	1	≤ 1
Week 28S	197	[2, 281]
Week 52S	365	[282, 449]
Week 76S	533	[450, 617]
Week 100S	701	[618, 785]
Week 124S	869	[786, 953]
Week 148S	1037	[954, 1121]
Week 172S	1205	[1122, 1247]
Week 184S	1289	[1248, 1373]
Week 208S	1457	[1374, 1541]
Week 232S	1625	[1542, 1709]
Week 256S	1793	[1710, 1877]
Week 280S	1961	[1878, 2031]
Switch at OLE		RxDay__OL
Entry of OLE	1	≤ 1
Week 24S	169	[2, 253]
Week 48S	337	[254, 421]
Week 72S	505	[422, 589]
Week 96S	673	[590, 757]
Week 120S	841	[758, 925]
Week 144S	1009	[926, 1051]
Week 156S	1093	[1052, 1177]
Week 180S	1261	[1178, 1345]
Week 204S	1429	[1346, 1513]
Week 228S	1597	[1514, 1681]
Week 252S	1765	[1682, 1835]

S = Switch to Risankizumab

Note: RxDay_B calculated relative to the first dose date in Part B.
RxDay__OL calculated relative to the first dose date of OLE.

Table 10. Visit Windows for Analysis of PASI, sPGA, Local Tolerability Assessment, Clinical Laboratory Tests, and Vital Signs (UST_RZB, FUM_RZB, RZB_Japan Populations)

Window Label	Target Day	Interval
Entry of Study M15-997	1	≤ 1[a]
Week 12	85	[2, 127]
Week 24	169	[128, 211]
Week 36	253	[212, 295]
Week 48	337	[296, 379]
Week 60	421	[380, 463]
Week 72	505	[464, 547]
Week 84	589	[548, 631]
Week 96	673	[632, 715]
Week 108	757	[716,799]
Week 120	841	[800, 883]
Week 132	925	[884, 967]
Week 144	1009	[968, 1051]
Week 156	1093	[1052, 1177]
Week 180	1261	[1178, 1345]
Week 204	1429	[1346, 1513]
Week 228	1597	[1514, 1681]
Week 252	1765	[1682, 1835]

a. If time is collected in vital signs, restrict to records prior to the first dose of RZB in Study M15-997.

Note: Rx Day calculated relative to first dose date of risankizumab.

Table 11. Visit Windows for Analysis of NAPSI, PPASI, PSSI, and DLQI (UST_RZB, FUM_RZB, RZB_Japan Populations)

Window Label	Target Day	Interval
Entry of Study M15-997	1	≤ 1
Week 24	169	[2, 253]
Week 48	337	[254, 421]
Week 72	505	[422, 589]
Week 96	673	[590, 715]
Week 108	757	[716, 799]
Week 120	841	[800, 925]
Week 144	1009	[926, 1051]
Week 156	1093	[1052, 1177]
Week 180	1261	[1178, 1345]
Week 204	1429	[1346, 1513]
Week 228	1597	[1514, 1681]
Week 252	1765	[1682, 1835]

Note: Rx Day calculated relative to first dose date of risankizumab.

Definition of Missing Data Imputation

No global imputation is taking place at the database level. Efficacy related imputations are outlined in Section 10.0. 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, 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 and median 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

Demographics and Baseline characteristics will be summarized for RZB, RZB_NL, Retreatment, UST_RZB, ADA_RZB, FUM_RZB, RZB_Japan populations. Continuous variables will be summarized with the number of non-missing observations by mean, standard deviation, first quartile, median, third quartile, minimum and maximum values. Categorical data will be summarized using frequencies and percentages. No Statistical tests will be performed for this study.

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 (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, Multi Race)
- Ethnicity (Hispanic or Latino, Not Hispanic or Latino)

- Body weight (kg)
- Body weight category (≤ 100 kg, > 100 kg)
- Height (cm)
- BMI (kg/m^2)
- BMI category (< 25, ≥ 25 – < 30, ≥ 30)
- Prior exposure to TNF antagonists (0 versus ≥ 1)

General Baseline Characteristics

- PASI (Psoriasis Area and Severity Index)
- BSA (Body Surface Area)
- sPGA (Static Physician Global Assessment)
- NAPSI (Nail Psoriasis Severity Index)
- PSSI (Psoriasis Scalp Severity Index)
- PPASI (Palmoplantar Psoriasis Area Severity Index)
- Dermatology Life Quality Index (DLQI)

Psoriasis and Cardiovascular History

- Psoriatic arthritis (diagnosed, suspected, no)
- Cardiovascular Diseases (myocardial infarction, angina pectoris, transient ischemic attack, stroke, deep vein thrombosis)
- Cardiovascular Risk Factors (hypertension, hyperlipidemia, diabetes mellitus, obesity)

General Use

- Smoking status (Never-smoked, Ex-smoker, Currently smokes)
- Alcohol status (Non-drinker, drinks – no interference, drinks – possible interference)

Prior Treatment:

- Psoriasis Biologic Treatment History – by Response to Prior Treatment
- Psoriasis Treatment – by Therapy Type (topical therapy, phototherapy, photochemotherapy, non-biologic systemic therapy, TNF antagonist, other biologic)

Also, Physical Exam and Pregnancy Test will be presented in listing format.

7.2 Medical History

Medical history (at the time of enrollment in the preceding study as well as new information and updates collected in this study) will be summarized using body systems and condition/diagnosis as captured on the eCRF for the All Risankizumab Treated Population. 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 for the ALL_RZB Population by generic name. A prior medication is defined as any medication taken at the time of entry into the study and prior to the first dose of risankizumab. A concomitant medication is defined as any medication that started prior to the first dose of risankizumab and continued to be taken after the first dose of risankizumab or any medication that started after the first dose of risankizumab, but not after the last dose of risankizumab + 140 days. 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 Deviation

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

- 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 medication?

8.0 Patient Disposition

For each population, the number of subjects for each of the following categories will be summarized.

- Number of subjects treated in Study M15-997
- Subjects completed or ongoing Study M15-997
- Subjects who discontinued study drug in Study M15-997
- Subjects who discontinued the Study M15-997

A table show the number and percent of subjects by the preceding study and treatment group in the preceding study will be presented.

In addition, the number and percentage of subject who discontinued the study drug will be summarized by reason (primary and all).

9.0 Study Drug Exposure and Compliance

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

Risankizumab Exposure (in Days):

The Risankizumab Exposure (total duration during the preceding study and Study M15-997) will be defined as follows:

The Risankizumab Exposure = Last risankizumab dose date – First risankizumab dose date (either in Study M15-997 or preceding study) + 84 days, except:

- The Risankizumab Exposure in the Retreatment Population is defined as: Last risankizumab dose date – First retreatment of risankizumab date (either in Study M15-997 or preceding study) + 84 days
- The Risankizumab Exposure in the ALL_RZB Population among subjects who were re-randomized to placebo during Study 1311.4 Part B is defined as: Last risankizumab dose date during Study 1311.4 Part A – First risankizumab dose date + 84 days + Last risankizumab dose date – First retreatment of risankizumab date + 84 days

In addition, number of subjects who have at least one dose of self-injected study drug during Study M15-997 will also be summarized.

A data cutoff date (September 01, 2017) was applied during the first interim analysis in 2017.

A data cutoff date (November 01, 2021) will be applied during the second interim analysis. The duration of study drug exposure will be defined up to this cutoff date.

10.0 Efficacy Analysis

10.1 General Considerations

The efficacy analysis will be performed for each population except the ALL_RZB Population. The efficacy analysis will use the data from this study and preceding study after subjects started to take risankizumab. The BL values (baseline values from the

preceding studies) will be used to determine responses and changes in the efficacy variables.

Continuous variables will be summarized by the number of observations, mean, standard deviation, median, minimum, maximum, 25th and 75th percentiles, as well as the 95% confidence intervals (CIs) of the mean values. Categorical variables will be summarized by counts and percentages, as well as the 95% CIs of the percentages. No statistical tests will be performed in this study.

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

- Last Observation Carried Forward (LOCF): The LOCF analyses will use the last observed non-missing evaluation (last completed non-missing evaluation, from composite endpoint) from the previous visit within the particular period for efficacy measures assessed to impute missing data at later visits in the same period. Baseline efficacy evaluations will not be carried forward. Of note, post-baseline observations from Part A1 in Study 1311.4 can be carried forward to ITT_A2 subjects from ARM 1 since treatment is the same.
- 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.

LOCF will be used as the primary imputation method and OC will be used as sensitivity analysis for both categorical variables and continuous variables. Both LOCF and OC will not include values after discontinuation of study drug.

All endpoints will be analyzed up to the last visit with at least one subject has observed measurements of that variable, by the time of the interim data cutoff.

10.2 Key Efficacy Variables

The following key efficacy variables will be summarized at all visits for each population:

- Proportion of subjects achieving ≥ 90% reduction in Psoriasis Area and Severity Index (PASI) score (PASI 90)
- Proportion of subjects achieving the Static Physician Global Assessment (sPGA) score of clear or almost clear
- Proportion of subjects achieving ≥ 75% reduction in PASI score (PASI 75)
- Proportion of subjects achieving 100% reduction in PASI score (PASI 100)
- Proportion of subjects achieving the sPGA score of clear

10.3 Additional Efficacy Analyses

The following additional efficacy variables will be summarized at all visits for each population:

- Proportion of subjects achieving ≥ 50% reduction in PASI score (PASI 50)
- Proportion of subjects achieving absolute PASI of < 3
- Proportion of subjects achieving DLQI score of 0
- Proportion of subjects achieving DLQI score of 0 or 1
- Proportion of subjects achieving a reduction of at least 5 points in DLQI, among subjects with baseline value ≥ 5
- Change and percent change from baseline in PASI
- Change and percent change from baseline in DLQI
- Change and percent change from baseline in NAPSI, among subjects with baseline value > 0
- Change and percent change from baseline in PPASI, among subjects with baseline value > 0
- Change and percent change from baseline in PSSI, among subjects with baseline value > 0

10.4 Efficacy Variables for Interim Analysis

All key efficacy and additional efficacy variables listed in Section 10.2 and Section 10.3 will be performed for the interim analysis for each population except for ALL_RZB

Population. All endpoints will be analyzed up to the last visit with at least one subject has observed measurements of that variable, by the time of the interim data cutoff.

10.5 Efficacy Subgroup Analysis

For RZB, RZB_NL, Retreatment and UST_RZB Populations, key efficacy variables will be summarized in the subgroup including subjects from Japan only. This subgroup analysis will only be performed in the final analysis, upon study completion.

In addition, PASI 90 and sPGA clear or almost clear will be summarized among the RZB Population at Week 208 and Week 256, by anti-drug antibody (ADA) and by neutralizing antibody (nAB) status by Week 208 and Week 256, respectively.

11.0 Safety Analysis

11.1 General Considerations

Safety analyses will include adverse events, laboratory, local tolerability, and vital sign measurements.

For the safety analyses, a baseline value (BL_ RZB) is defined as the last non-missing observation on or prior to the date of the first dose of Risankizumab either in Study M15-997 or the preceding studies whichever is the earlier.

For subjects from Japan among the RZB, RZB_NL, Retreatment and UST_RZB Populations, only data prior to the start of risankizumab 75 mg dose will be used in the safety analyses. This subgroup analysis will only be performed in the final analysis, upon study completion.

When summarizing the safety for risankizumab 150 mg among the ALL_RZB Population, safety data collected (i) from feeder studies not using risankizumab 150 mg dose and/or (ii) from subjects in Japan who have started the risankizumab 75 mg dose will not be included for the safety summary of risankizumab 150 mg dose.

For the RZB Japan Population, safety data will be summarized regardless of dose.

Summaries of treatment-emergent adverse events (TEAEs), potentially clinically important laboratory values and vital sign values, and liver function tests will be provided for all populations. Analysis of change from baseline in laboratory values and vital sign values, shift tables and local tolerability will be provided for RZB, RZB_NL, UST_RZB, ADA_RZB, FUM_RZB, RZB Japan populations.

11.2 Analysis of Adverse Events

11.2.1 Treatment-Emergent Adverse Events

Treatment emergent adverse events (TEAEs) are defined as any event with an onset date that is after the first dose of risankizumab and with an onset date within 140 days after the last dose of study drug in the analysis period except:

- **TEAE of Retreatment:** TEAE are defined as any event with an onset date that is after the first dose of retreatment and no more than 140 days after the last dose of study drug, and prior to the start of risankizumab 75 mg (if any, for subjects in Japan).
- **TEAE of ALL_RZB (any dose):** TEAEs are defined as any event with an onset date after the first dose of risankizumab through 140 days after the last dose of risankizumab, except for AEs with an onset date during protocol-designed treatment gaps (i.e., placebo period in subjects re-randomized to placebo during Study 1311.4 Part B) that was more than 140 days from the last dose of previous risankizumab treatment and before the first dose of retreatment in the ALL_RZB Population.
- **TEAE of RZB, RZB_NL, UST_RZB, ADA_RZB, FUM_RZB and ALL_RZB (150 mg):** TEAEs are defined as any event with an onset date after the first dose of risankizumab 150 mg through 140 days after the last dose of risankizumab 150 mg, and prior to the start of risankizumab 75 mg (if any, for subjects in Japan), except for AEs with an onset date during protocol-designed treatment gaps (i.e., placebo period in subjects re-randomized to placebo during Study 1311.4 Part B) that was more than 140 days from the last dose of

previous risankizumab 150 mg treatment and before the first dose of retreatment in the ALL_RZB Population.

Events where the onset date is the same as the study drug start date are assumed to be treatment emergent, unless the adverse event start time is prior to the study drug start time. 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).

The number and percent of subjects experiencing treatment-emergent TEAEs will be tabulated using the Medical Dictionary for Drug Regulatory Activities (MedDRA®) system organ class and preferred term.

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
   - Any serious AE 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
   - Any COVID-19 Related AE

2. **Adverse Events by System Organ Class and Preferred Term**

   TEAEs will also 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.

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

3. **Adverse Events by Maximum Severity**

   The severity grading of AEs follows Rheumatology Common Toxicity Criteria (RCTC).

   - Grade 1 – mild
   - Grade 2 – moderate
   - Grade 3 – severe
   - Grade 4 – life threatening

   Adverse events will also 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 – ("Life-threatening"). In this case, the subject will be counted under the "Life-threatening" 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 'Yes' or 'No.' 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." If the subject has another occurrence of the same adverse event with a relationship assessment of "Yes," the subject will be counted under the "yes" 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 System Organ Class and Preferred Term
- Grouped by System Organ Class, Preferred Term and Maximum Relationship to Study Drug
- Grouped by System Organ Class, Preferred Term and Maximum Severity

Treatment-emergent serious adverse events will be summarized as follows:

- Grouped by System Organ Class and Preferred Term
- A by-subject listing will be provided

Pre-treatment serious adverse events 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 System Organ Class and Preferred Term
- 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 System Organ Class and Preferred Term
- A listing by subject will be provided.

Areas of Safety Interest:

Areas of Safety Interest (ASIs) will be summarized according to the search criteria provided in Table 12.

The final list will be based on the most updated final version of risankizumab Product Safety Statistical Analysis Plan, which is consistent to the most updated risankizumab Risk Management Plan.

Table 12. Areas of Safety Interest

Area of Safety Interest	Search Criteria	
MACE	Adjudicated terms will be identified as described in PSSAP Table 4a using CECAT and CETERM from the CE SDTM dataset.	
Extended MACE	Adjudicated terms will be identified as described in PSSAP Table 4a (for MACE +) using CECAT and CETERM from the CE SDTM dataset.	
Serious Infections	Serious AEs in the Infections and Infestations SOC	
Active Tuberculosis	Active Tuberculosis CMQ (code 80000188)	
Opportunistic Infections excluding tuberculosis and herpes zoster	Opportunistic infection excluding tuberculosis and herpes zoster CMQ (code 80000189)	
Injection Site Reactions	Narrow	Injection site reaction CMQ (code 80000019)
Malignancies	Narrow	Malignant tumours (SMQ 20000194)
Non-melanoma Skin Cancer (NMSC)	Broad	Skin malignant tumours (SMQ 20000204) excluding terms identified by the Melanoma CMQ (code 80000119)
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.	
Hypersensitivity	Narrow	Hypersensitivity (SMQ 20000214)
Serious hypersensitivity reactions	Narrow	Serious AEs in the Hypersensitivity (SMQ 20000214)
Adjudicated Anaphylactic Reaction*	Adjudicated terms will be identified using SDTM data (e.g., CE and PR domains).	
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)

* Events will be identified for adjudication by Anaphylactic Reaction SMQ Broad search as specified in the RISA AAC Charter.

Adverse Event per 100 Patient-Years of Exposure

Adverse events occurring during the analysis period for each population will be presented by event rate per 100 patient-years. These will be presented for any TEAEs, serious adverse events, Areas of Special 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 + 140 days (5 half-lives)) 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 and AE leading to study drug discontinuation will be summarized by System Organ Class and MedDRA Preferred Term.

11.3 Analysis of Laboratory Data

Listing and descriptive statistics of laboratory values over time, changes from baseline, and extreme abnormal value on treatment will be provided. Baseline is understood as the last available measurement before risankizumab administration (i.e, BL_RZB defined in Section 6.0). Extreme abnormal value on treatment is understood as the on treatment laboratory value which is most significantly away from the reference range. Frequency of subjects with transitions relative to the toxicity grade according to NCI CTCAE

Version 4.03 and listing of subjects with important abnormal laboratory values will be presented as well.

11.3.1 Variables and Criteria Defining Abnormality

Clinical laboratory tests performed are listed in Table 13.

Table 13. Clinical Laboratory Tests

Category	Test Name
Haematology	Hematocrit (Hct) Hemoglobin (Hb) Glycosylated Hbc (HbA1c) White Blood Cells/Leukocytes Platelet Count/Thrombocytes
Diff. Automatic	Neutrophils (relative count) Eosinophils (relative count) Lymphocytes (relative count)
Enzymes	AST (GOT) ALT (GPT) Alkaline Phosphatase (AP) Creatine Kinase (CK) Gamma-Glutamyl Transferase (GGT/γ-GT) Lactic Dehydrogenase (LDH) Amylase Lipase
Electrolytes	Calcium Sodium Potassium
Substrates	Glucose BUN (blood urea nitrogen) Uric acid Creatinine eGFR (estimated by CKD-EPI formula) Bilirubin Total Albumin C-Reactive Protein (high sensitive) Cholesterol, total Triglycerides LDL-Cholesterol HDL-Cholesterol
Urinalysis (Stix)	Urine Protein Urine Glucose

11.3.2 Statistical Methods

Analysis of Quantitative Laboratory Parameters (Hematology, Chemistry)

Though the protocol indicates utilizing the Rheumatology Common Toxicity Criteria (RCTC) scale for grading laboratory values, given that the National Cancer Institute Common Toxicity Criteria for Adverse Events (NCI CTCAE) scale includes a more comprehensive list of laboratory values, the sponsor will present the lab analyses based on the NCI CTCAE scale. Changes 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 (BL_RZB) and visit/final value means will also be presented for subjects who have both the Baseline and visit/final values. If there are multiple post-baseline measurements on the same day, average value will be used.

Shift Tables

Laboratory parameters will be tabulated using shift tables from Baseline to worst values, categorized by the toxicity grade according to NCI CTCAE Version 4.03 of the laboratory used for each sample. A similar shift table will also be provided to summarize shifts from Baseline to the final post-baseline value.

Potentially Clinically Important Laboratory Values

Frequencies and percentages of subjects with post Baseline lab values met the following criteria in Table 14 and Table 15 will be summarized. Of note, a post baseline grade must be more extreme than the baseline grade to be considered a potentially clinically important finding.

Table 14. 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 (> 3.0 × BL)
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 15. 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.

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

Liver Function Tests

The frequencies and percentages of subjects with post baseline liver specific function test values in ALT/SGPT, AST/SGOT, alkaline phosphatase, and total bilirubin will be categorized as follows:

- ALT > 3.0 × ULN
- ALT > 5.0 × ULN
- ALT > 10.0 × ULN
- ALT > 20.0 × ULN
- AST > 3.0 × ULN
- AST > 5.0 × ULN
- AST > 10.0 × ULN
- AST > 20.0 × ULN
- Alkaline phosphatase > 1.5 × ULN
- Total bilirubin > 1.5 × ULN
- Total bilirubin > 2.0 × ULN
- ALT and/or AST > 3× ULN and Total bilirubin > 1.5× ULN
- ALT and/or AST > 3× ULN and Total bilirubin > 2× ULN
- ALT > 3× ULN and Total bilirubin > 1.5× ULN
- ALT > 3× ULN and Total bilirubin > 2× ULN

The listing will include all subjects who met any of the following four criteria:

- ALT > 3 × ULN, or
- AST > 3 × ULN, or
- ALP > 1.5 × ULN, or
- Total bilirubin > 1.5 × ULN.

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

- ALT of > 3 × ULN or AST of > 3 × ULN,
- Total bilirubin > 2 × ULN

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 16 presents the Criteria for Potentially Clinically Important Vital Sign Findings. Of note, a post baseline value must be more extreme than the baseline value to be considered a potentially clinically important finding.

Table 16. 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 and decrease ≥ 10 mmHg from Baseline
	High Value	≥ 100 mmHg and increase ≥ 10 mmHg 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.

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 and diastolic blood pressure, 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.

11.5 Local Tolerability

Local tolerability of the subcutaneous injection will be assessed by the investigator according to 6 items: swelling, induration, heat, redness, pain, and other findings. Number and proportion of subjects reporting each condition will be summarized.

11.6 Safety Subgroup Analysis

For RZB, RZB_NL, Retreatment and UST_RZB Populations, AE overview tables will be provided in the subgroup including subjects from Japan only. This subgroup analysis will only be performed in the final analysis, upon study completion.

In addition, the number and percentage, as well as exposure adjusted event rate of hypersensitivity events and injection site reactions will also be summarized among the ALL_RZB Population (150 mg), by the anti-drug antibody (ADA) status during the analysis period.

12.0 Pharmacokinetic Analysis

Pharmacokinetic analysis will not be covered in this SAP.

13.0 Biomarkers Analysis

Biomarker 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

14.2 Summary of Changes Between the Previous Version and the Current Version of the SAP

Version	Date	Summary
1.0	02 Oct 2017	Original version
2.0	14 Jan 2022	Updated the analysis population in Section 5.0 and the analysis window in Section 6.0, to be consistent with the most recent protocol amendment 8. Updated the ASI, lab, and vital sign criteria in Section 12.0, to be consistent with the most updated product safety SAP for risankizumab. Corrected typos in Table 8. Added TEAE definition for ADA_RZB and FUM_RZB in Section 11.2.1.

15.0 Appendix

None.

16.0 References

Not applicable.

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

To be provided in a separate document.

Appendix A. Table Shells for Non-Standard Tables, Listings, and Figures

Table 14.1__1

Psoriasis Medication History - Biologics By Response to Prior Treatment
(ALL_RZB Populations)

Category Generic Name Treatment	N	Lack of Initial Response n (%)	Loss of Response n (%)	Lack of Tolerability n (%)	Other n (%)	Unknown n (%)
TNF Antagonist						
RZB	XXX	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)
XXX						
RZB	XXX	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)

Program Source Code: /barrejd/SDA/ABBV-066/Psoriasis/CSR/M15-997/G/14.1/PCMS_RUN/s1311_31_hs_medhx_rspt.sas

TABLE 14.1__2

Psoriasis Medication History – By Treatment Type
(ALL_RZB Population)

Therapy Type	Placebo (N=XXX) n (%)	UPA 30 mg QD (N=XXX) n (%)	Total (N=XXX) n (%)
Topical Therapy [A]	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)
Phototherapy or Photochemotherapy	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)
Phototherapy	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)
Photochemotherapy	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)
Non-Biologic Systemic Therapy	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)
Any Biologics	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)
TNF Antagonist	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)
Other Biologic (Non-TNF Antagonist)	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)
Naïve to Systemic Therapy	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)
Naïve to All (Other than Topical Therapy	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)

Note: [A]: ONLY THERAPIES USED AT THE TIME OF ENTRY INTO THE STUDY OR USED FOR THE DURATION OF STUDY PARTICIPATION WERE COLLECTED.

Program Source Code: /barrejd/SDA/ABBV-066/Psoriasis/CSR/M15-997/G/14.1/PCMS_RUN/s1311_31_cm_cat.sas

Table 14.1__3

Number of Subjects with At Least One Self-Injected Study Drug
(ALL_RZB Populations)

Variable	RZB (N=) n (%)	RZB_NL (N=) n (%)	Retreatment (N=) n (%)	UST_RZB (N=) n (%)	… (N=) n (%)
At Least One Self-Injected Study Drug					
Yes	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)
No	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)
Missing	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)

Program Source Code: /barrejd/SDA/ABBV-066/Psoriasis/CSR/M15-997/G/14.1/PCMS_RUN/s1311_31_hs_medhx_rspt.sas

Table 14.3__1

Subjects with Treatment-Emergent Adjudicated CV Adverse Events
(RZB Population)

Category Sub-Category	RZB (N=) n (%)
Subjects with:	
MACE	
Myocardial Infarction	XXX (XX.X)
…	XXX (XX.X)
Extended MACE	XXX (XX.X)
Myocardial Infarction	XXX (XX.X)
…	XXX (XX.X)
Other CV Events	XXX (XX.X)

Program Source Code: /barrejd/SDA/ABBV-066/Psoriasis/CSR/M15-997/G/14.3/PCMS_RUN/s1311_31_aesi.sas

Table 14.3__2

Subjects with Treatment-Emergent AESI
(RZB Population)

Category MEDDRA 20.0 Preferred Term	RZB (N=) n (%)
Subjects with:	
Fungal Infections	
…	XXX (XX.X)
…	XXX (XX.X)
Herpes Zoster	XXX (XX.X)
…	XXX (XX.X)

Program Source Code: /barrejd/SDA/ABBV-066/Psoriasis/CSR/M15-997/G/14.3/PCMS_RUN/s1311_31_aesi.sas

Table 14.3__3

Subjects with Treatment-Emergent Hypersensitivity by Subgroup
(RZB Population)

Subgroup Status Category MEDDRA 20.0 Preferred Term	RZB (N=) n (%)
Antidrug Antibody Positive Status (Yes, No)	
Yes	
Hypersensitivity	XXX (XX.X)
xxx	XXX (XX.X)
…	XXX (XX.X)
Anaphylactic Reaction	XXX (XX.X)
…	XXX (XX.X)
No	
Hypersensitivity	XXX (XX.X)
xxx	XXX (XX.X)

Program Source Code: /barrejd/SDA/ABBV-066/Psoriasis/CSR/M15-997/G/14.3/PCMS_RUN/s1311_31_aesi.sas

Table 14.3__4
Subjects with Treatment-Emergent Injection Site Reaction by Subgroup
(RZB Population)

Subgroup	RZB
Status	(N=)
MEDDRA 20.0 Preferred Term	n (%)
Antidrug Antibody Positive Status (Yes, No)	
Yes	XXX (XX.X)
xxx	XXX (XX.X)
No	XXX (XX.X)
xxx	XXX (XX.X)

Program Source Code: /barrejd/SDA/ABBV-066/Psoriasis/CSR/M15-997/G/14.3/PCMS_RUN/s1311_31_aesi.sas

Table 14.3__5

Treatment-Emergent Adjudicated CV Adverse Events
(RZB Population)

Category Sub-Category	RZB (N=) (PYS=) Events (E/100PY)
Subjects with:	
MACE	
Myocardial Infarction	XXX (XX.X)
…	XXX (XX.X)
Extended MACE	XXX (XX.X)
Myocardial Infarction	XXX (XX.X)
…	XXX (XX.X)
Other CV Events	XXX (XX.X)

Program Source Code: /barrejd/SDA/ABBV-066/Psoriasis/CSR/M15-997/G/14.3/PCMS_RUN/s1311_31_aesipy.sas

Table 14.3__6

Treatment-Emergent AESI
(RZB Population)

Category MEDDRA 20.0 Preferred Term	RZB (N=) (PYS=) Events (E/100PY)
Subjects with:	
Fungal Infections	
…	XXX (XX.X)
…	XXX (XX.X)
Herpes Zoster	XXX (XX.X)
…	XXX (XX.X)

Program Source Code: /barrejd/SDA/ABBV-066/Psoriasis/CSR/M15-997/G/14.3/PCMS_RUN/s1311_31_aesipy.sas

Table 14.3__7

Treatment-Emergent Hypersensitivity by Subgroup
(RZB Population)

Subgroup Status Category MEDDRA 20.0 Preferred Term	RZB (N=) (PYS=) Events (E/100PY)
Antidrug Antibody Positive Status (Yes, No)	
Yes	
Hypersensitivity	XXX (XX.X)
Dermatitis	XXX (XX.X)
…	XXX (XX.X)
Anaphylactic Reaction	XXX (XX.X)
…	XXX (XX.X)

Program Source Code: /barrejd/SDA/ABBV-066/Psoriasis/CSR/M15-997/G/14.3/PCMS_RUN/s1311_31_aesipy.sas

Table 14.3__8

Treatment-Emergent Injection Site Reaction by Subgroup
(RZB Population)

Subgroup Status MEDDRA 20.0 Preferred Term	RZB (N=) (PYS=) Events (E/100PY)
Antidrug Antibody Positive Status (Yes, No)	
Yes	XXX (XX.X)
xxx	XXX (XX.X)
No	XXX (XX.X)
xxx	XXX (XX.X)

Program Source Code: /barrejd/SDA/ABBV-066/Psoriasis/CSR/M15-997/G/14.3/PCMS_RUN/s1311_31_aesi.sas

TABLE 14.3__9

Listing of Treatment Emergent Serious Adverse Events
(RZB Population)

Subject Number	Name	Epoch Interval	Day	Rx Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22 Preferred Term L: Lower Level Term (U/L)	E: Rx Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	S: Severity R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: AbbVie Opinion of Causality
INV: Forman, Seth (37884) TRT: RISANKIZUMAB 103007 Age: 63 Sex: Female Race: White Weight: 110.0 KG								
XX	XX	XX to XXX	XX	XX	R: Acute appendicitis S: Infections and infestations P: Appendicitis L: Acute appendicitis	E:XX L: X days I: No	S: severe R: No reasonable possibility A: Drug interrupted	S: yes, hospitalization or prolonged hospitalization O: Idiopathic A: No reasonable possibility

Program Source Code: /barrejd/SDA/ABBV-066/Psoriasis/CSR/M15-997/G/14.3/PCMS_RUN/s1311_31_aelist.sas

Table 14.1__10

Local Tolerability Findings
(RZB Populations)

Visit	Event	Status	RZB (N=) n (%)
Week XX			
	Swelling	Yes	XXX (XX.X)
		No	XXX (XX.X)
		Unknown	XXX (XX.X)
		Missing	XXX (XX.X)
	Induration	Yes	XXX (XX.X)
		No	XXX (XX.X)
		Unknown	XXX (XX.X)
		Missing	XXX (XX.X)
	…		
…			
Overall (At Least One Occurrence)	Swelling	Yes	XXX (XX.X)
	Induration	Yes	XXX (XX.X)
	…		

Program Source Code: /barrejd/SDA/ABBV-066/Psoriasis/CSR/M15-997/G/14.1/PCMS_RUN/s1311_31_hs_medhx_rspt.sas

Table 14.1__10

Disease History (PsA, Cardiovascular Diseases, Cardiovascular Risk Factors)
(All Populations)

Variable	RZB	RZB_NL	…
PsA (Psoriatic Arthritis)			
Diagnosed	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)
Suspected	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)
No	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)
Missing	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)
Cardiovascular Disease			
Myocardial Infarction			
Yes	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)
No	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)
Missing	XXX (XX.X)	XXX (XX.X)	XXX (XX.X)

Program Source Code: /barrejd/SDA/ABBV-066/Psoriasis/CSR/M15-997/G/14.1/PCMS_RUN/s1311_31_mh_cat.sas